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VOOR KINDERGENEESKUNDE
SOCIÉTÉ BELGE DE PÉDIATRIE

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BJP SUPPLEMENT OF

BVK/SBP CONGRESS 46TH EDITION

08 & 09.03.18

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Belgische Vereniging voor Kindergeneeskunde
Société Belge de Pédiatrie

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CONGRESS

46TH EDITION

ACCREDITATIONS REQUESTED

BELGISCHE VERENIGING VOOR KINDERGENEESKUNDE
SOCIETE BELGE DE PEDIATRIE

1ST EDITION

PHYSIOTHERAPY SESSION
09.03.18

BVK/SBP CONGRESS

08 & 09.03.18

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The 46th BVK/SBP Congress' Accreditation

Thursday March 8, 2018
- Accreditation: 17029197
  Rubrique: 3 C.P.: 6
- Ethics: 17029200
  Rubrique: 6 C.P.: 1,5

Friday March 9, 2018
- Accreditation: 17029199
  Rubrique: 3 C.P.: 6
- Ethics: 17029201
  Rubrique: 6 C.P.: 2

Access will be possible on the website:

- With the wifi connection at Square Brussels
- By download of the abstracts files from the website on your computer or tablet ahead of time before arriving at the Congress Venue.
- Click on the congress image
- On the congress homepage click on the BJP icon to access the BJP Abstracts Supplement
- The Specialties Index will lead you to the abstracts
- The Search engine will allow you different selections: author's name, title abstracts, words…

If you encounter any trouble, we will be able to help you at the Desk of the Congress on-site.

c/o DME Events SPRL
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Dear Colleagues and Friends,

I am delighted to welcome you in Brussels for the 46th edition of the Annual Congress of the Belgian Society of Paediatrics (BVK-SBP).

During this meeting, entitled The Fundamentals of Paediatrics in a Changing World, we want to bring together paediatricians and future colleagues in order to think about the basic principles of our profession: excellence of care, both preventive and curative, for children and adolescents.
Beside the plenary sessions and the meetings organised by each subspecialty, we have several state of the art sessions covering : Hot topics in vaccination, Lung diseases in Neonates, Dermatology in children and the BPCRN (Belgian Paediatric Clinical Research Network) meeting, including the young investigators session.

The oral presentations have been selected for their high quality as well as general interest to all of us, and will be presented in the Silver Hall on Thursday and Friday. As for the posters, we have chosen the old fashion way, with a traditional walking poster tour.

Two sessions are dedicated to “Ethics and Economy”. The first one will cover the aspects of “connected” health care and the second one will focus on our role in the development and wellbeing of the child, confronted with a changing world.

Furthermore, for those who want to improve their practical skills in neonatology and paediatric intensive care, several workshops will be available in French and in Dutch during the meeting.

For the first time, we are happy to host the Belgian congress of Paediatric Physiotherapy which will be held in parallel on Friday march 9, 2018.

And last but not least, don’t forget to join us on Thursday evening for a musical cocktail organised by our young talented colleagues.

I wish to express my sincere thanks to the scientific committee, the board of the BVK-SBP, the very precious administrative help, our international faculty, the speakers, the musicians, and all of you for attending this 46th annual meeting of our society,

Prof Christiane Vermylen
BVK/SBP Congres President

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BELGISCHE VERENIGING
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SBP - RENOUVELLEMENT ADHÉSION 2018

Cher Collègue,

Vous pourrez renouveler votre cotisation annuelle 2018 à partir du 1er Octobre 2017.
Votre adhésion courra jusqu'au 30 Septembre 2018.

La SBP est avant tout une association de scientifiques sensibilisés aux aspects médicaux et sociaux et auxquels sont confrontés l'enfant, l'adolescent ainsi que leurs parents. Depuis bientôt 100 ans, cette mission reste toujours aussi primordiale.

L'adhésion de tout pédiatre établi et de tout assistant en formation de pédiatrie contribue à optimaliser et moderniser le rayonnement et l'extension de notre association, en tant que porte-parole scientifique reconnu au niveau national non seulement au sein de notre propre discipline, mais tout autant vis-à-vis d'autres professionnels de la santé, des autorités, de nos patients et de leur famille et aussi d'un plus large public.

La procédure pour devenir ou rester membre de notre société est simple, mais uniquement possible en passant par le site web www.bvk-sbp.be.

Les cotisations annuelles restent inchangés:

-120€ pour les **pédiatres**

-60€ pour les **assistants en pédiatrie**

-60€ pour les **pédiatres pensionnés**

Les avantages d'une adhésion à la Société sont nombreux:

À part le tarif réduit d'inscription au congrès annuel, les membres bénéficient, via le site de la SBP, d'un accès à la bibliothèque virtuelle CEBAM (Belgian Center for Evidence Based Medecine). Je vous rappelle que l'accès au volet pédiatrique du site de la CEBAM permet la lecture et le téléchargement d'articles des principaux journaux pédiatriques (entre autres Pediatrics, Journal of Pediatrics, Pediatric Infectious Disease Journal).

Le site donne également accès aux "big five" (New England Journal of Medicine, Lancet, BMJ, JAMA et Annals of Internal Medicine) ainsi qu'à de nombreuses bases de données d'Evidence Based Medecine (Cochrane Library) ainsi qu'à des livres électroniques.

Les membres reçoivent gratuitement le BJP (Belgian Journal of Paediatrics), journal aussi accessible online sur le site web www.bvk-sbp.be. Vous y trouverez à part des contributions scientifiques de chez nous, aussi les comptes rendu de l'Académie belge de Pédiatrie ainsi que des liens bien utiles.

Les membres profitent aussi de l'accès gratuit au Club Privilege What's Up Doc.

Je vous remercie de contribuer à la réalisation de notre avenir, en renouvelant votre cotisation.

Très cordialement.

Prof Dr Anne MALFROOT

Présidente BVK/SBP

BELGISCHE VERENIGING
VOOR KINDERGENEESKUNDE

SOCIETE BELGE DE PEDIATRIE

BVK - HERNIEUWING LIDMAATSCHAP 2018

Beste Collega,

U kan uw volgend jaarlijks lidmaatschap 2018 vanaf 1 oktober 2017 hernieuwen.
Dit lidmaatschap zal lopen tot 30 september 2018.

De procedure om lid te worden
of te blijven is eenvoudig en gebeurt via de website www.bvk-sbp.be.

De BVK is in de eerste plaats een vereniging van zorgverleners en wetenschappers bezorgd om de medische en sociale aspecten waarmee het kind, de adolescent alsook de ouders geconfronteerd worden. Sinds bijna 100 jaar, blijft deze opdracht primordiaal.

Het lidmaatschap van elke kinderarts en iedere kinderarts in opleiding, draagt bij tot het optimaliseren en het moderniseren van de uitstraling van onze vereniging, alsook tot de erkenning als wetenschappelijke woordvoerder op nationaal en internationaal vlak.

Dit geldt niet alleen binnen onze eigen discipline, maar ook tegenover andere professionals in de gezondheidssector, onze patiënten en hun familie en tegenover een nog breder publiek.

De jaarlijkse bijdragen blijven ongewijzigd:

-120€ voor de **kinderartsen**

-60€ voor **kinderartsen in opleiding**

-60€ voor de **kinderartsen op rust**

De voordelen van een BVK lidmaatschap zijn talrijk:

Naast een verlaging van het inschrijvingsgeld van het jaarlijks congres krijgen de leden, via de site van de BVK, toegang tot de numerieke bibliotheek van de CEBAM (Belgian Center for Evidence Based Medicine). De toegang tot het pediatrisch luik van de CEBAM maakt het mogelijk de artikels van de belangrijkste pediatrische tijdschriften te lezen en te downloaden (Pediatrics, Journal of Pediatrics, Pediatric Infectious Disease Journal, etc.).

De site geeft ook toegang tot de “big five” (New England Journal of Medicine, Lancet, BMJ, JAMA en Annals of Internal Medicine) alsook tot talrijke databases van Evidence-Based Medicine zoals de Cochrane Library en andere elektronische boeken.

Verder krijgen de leden ook gratis het tijdschrift BJP (Belgian Journal of Paediatrics) toegestuurd, dat tevens online kan geraadpleegd worden via **www.bvk-sbp.be**, website waarvan het deel artsen enkel toegankelijk is voor leden.

De BJP bevat naast interessante wetenschappelijke bijdragen en guidelines ook de verslagen van de Belgische Academie voor Kindergeneeskunde en nuttige links.

Leden hebben ook gratis toegang tot Privilege Club What’s Up Doc.

Hartelijke dank voor uw lidmaatschap waardoor u uw eigen professionele discipline steunt en een bijdrage levert aan de bevordering van de gezondheid van het kind in België!

Met collegiale groeten,

Prof Dr. Anne MALFROOT

Voorzitter BVK/SBP

DE BVK BEDANKT ZIJN PARTNERS VOOR HUN STEUN

LA SBP REMERCIE SES PARTENAIRES POUR LEUR SOUTIEN

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Congrès BVK/SBP 2018
Index of the Specialities letters

SPA REINE

le premier choix pour la fonction rénale du nourrisson

Une eau très faiblement minéralisée comme SPA REINE, rigoureusement pure, d'une composition constante et strictement contrôlée, est recommandée chez les enfants de moins de 2 ans pour limiter la charge osmolaire des reins immatures.

LE REIN ENCORE EN DÉVELOPPEMENT APRÈS LA NAISSANCE

Après la naissance, le rein du nourrisson continue sa maturation morphologique et fonctionnelle pour aboutir à une fonction rénale normale (adulte) vers l'âge de 2 ans. Cette immaturité entraîne plusieurs conséquences: limitation du volume d'eau éliminé dû au faible débit de filtration du rein, sensibilité à une charge osmotique trop grande, besoins en sel augmentés liés à l'excrétion plus élevée à la naissance couplés à une difficulté d'éliminer la charge sodée.

SENSIBILITÉ À LA CHARGE OSMOTIQUE

Chez le nouveau-né et le nourrisson la capacité de concentration des urines est insuffisante (valeurs de l'adulte atteintes vers l'âge d'un an) et l'osmolalité urinaire n'atteint que 600 mOsm pour 1400 mOsm chez l'adulte. Le nourrisson est donc sensible à une charge osmotique trop grande et a besoin d'un volume d'eau plus important pour excréter une même charge osmotique.

QUEL EAU RECOMMANDER ?

Tout excès d'apports dans l'alimentation (sels minéraux, azotés,...) surcharge le fonctionnement des reins. Ceci peut être évité par la consommation régulière et en quantité suffisante de **SPA REINE**, une eau minérale naturelle très faiblement minéralisée qui permet l'élimination des déchets métaboliques sans apporter d'éléments supplémentaires, voire nuisibles .

LES APPORTS RECOMMANDÉS EN EAU POUR LE NOURRISSON*	
ml/kg/jour	
120-100	> 1 semaine (nourrisson à terme)
150-130	> 0-3 mois
130-120	> 4-8 mois
110-100	> 9-12 mois

* Recommandations nutritionnelles pour la Belgique CSS n°8309 (révision 2009)

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SPA® NATURAL SINCE 1583 A la vie

Cardiology - C

Oral Presentations

C 01 **The effect of weight loss on endothelial function and sleep-disordered breathing in obese children.**
M. Ysebaert (1,2), A. Van Eyck (1,2), L. Bruyndonckx (1,2), B. De Winter (1), A. De Guchtenaere (3), K. Van Hoorenbeeck (1,2), S. Verhulst (1,2) / [1] UAntwerpen, [2] UZ Antwerpen, [3] Zeepreventorium, De Haan

C 02 **Systemic to pulmonary shunts: morbidity, mortality risk factors and pulmonary tract development.**
F. Van Vyve, A. Poncelet, S. Moniotte, J. Rubay, T. Sluysmans / UCL Saint-Luc, Brussels

Posters with short oral presentations

C 03 **Use of a biodegradable airway stent to manage airway compression in a child With ALCAPA.**
O. Polle (1), A. Durward (2), A. Nyman (2), P. James (2) / [1] UCL Saint-Luc, Brussels, [2] Evelina London Childrens Hospital, London, UK

C 04 **Association between major sickle cell anemia and dilated cardiomyopathy: an unusual condition.**
A. Famerie (1), I. Astadicko (2), B. Cools (3), M-F Dresse (1), M-C Seghaye (1) / [1] CHU de Liège CHU N.D. des Bruyères, [2] CHR de la Citadelle, [3] UZ Leuven, UZ Sint-Pieter

C 05 **Cardiac papillary fibroelastoma of a bicuspid aortic valve: a case report and Review of the literature.**
S. Dénes (1), B. Daron (2), M.-C. Seghaye (1) / [1] ULiège, CHU Liège, [2] CHR Verviers

Posters

C 06 **Congenital cardiac malformation in spinal muscle atrophy: clinical case and review of literature.**
K. Kairet, L. Bruyndonck, T. Mulder, F. Marchau, W. Dewals / UZ Antwerpen

C 07 **Non syndromic supravalvular aortic-, supravalvular pulmonary- and peripheral pulmonary artery stenosis in an infant: a rare association.**
I.Sadek, A. Jacquinet, M-C Seghaye / University Hospital, Liège

C 08 **Unusual cause of thoracic pain and raised cardiac markers: a case report.**
K. Kaïret, W. Dewals, L. Bruyndonck, B. Ceulemans, FEJF. Marchau / UZ Antwerpen

C09 **Pheochromocytoma in an 11-year-old girl with acquired long QTc and aortic root Dilation.**
L. D'Angelo, AS. Parent, MC. Seghaye / ULiège, CHU N.D. des Bruyères, Liège.

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Dermatology - D

Posters with short oral presentations

D 01 **Case report of a 5-year-old child presenting an idiopathic linear IgA bullous dermatosis.**
V. Catinus (1), M. Slaedts (1), L. Vega (1), J.-L. Hennecker (2) / [1] UCL Saint-Luc, Brussels, [2] Clinique Notre-Dame de Grâce, Gosselies

D 02 **Acute febrile purpuric rash in young infants: if sometimes we should not fear for the worst?**
M. Rodesch, F. Vermeulen / ULB Erasme, Brussels

D 03 **Infantile Digital Fibromatosis: A Rare Benign Fibroproliferative Tumor in Early Childhood.**
MKF. Docx (1), S. Van Cauwenberghe (1), D. Vervloessem (1), W. Buffet (2) / [1] ZNA Koningin Paola Kinderziekenhuis, Antwerpen, [2] ZNA Middelheim, Antwerpen

D 04 **Recurrent superficial lymphangitis after insect bites.**
Blauen (1), E. Hoornaert (1), J. Moortgat (1), J. Louis (2) / [1] UCL Saint –Luc, Brussels, [2] GHDC, Charleroi

Posters

D 05 **Cutaneous necrosis of the foot secondary to local Ketoprofen application.**
K. Farhat, A. Anthopoulou, M-C Seghaye / ULiège, CHU Liège

SPA REINE

de eerste keuze voor de nierfunctie van de zuigelingen

Zeer licht gemineraliseerd water zoals SPA REINE dat op en top zuiver is, een constante samenstelling heeft en streng gecontroleerd wordt, is aanbevolen voor kinderen jonger dan 2 jaar om de osmolaire belasting van de nog niet volledig ontwikkelde nieren te beperken.

DE NOG NIET VOLLEDIG ONTWIKKELDE NIER NA DE GEBOORTE

Na de geboorte blijven de nieren van de zuigeling zich morfologisch en functioneel ontwikkelen om rond de leeftijd van 2 jaar een normale (volwassen) nierfunctie te bereiken. Het feit dat de nieren nog niet volledig ontwikkeld zijn, heeft meerdere gevolgen: beperking van het volume water dat wordt uitgescheiden als gevolg van het geringe filterdebiet van de nieren, gevoeligheid voor een te grote osmotische belasting, en grotere nood aan zout als gevolg van de grotere uitscheiding bij de geboorte gekoppeld aan de moeilijkheid om de natriumbelasting te elimineren.

GEVOELIGHEID VOOR DE OSMOTISCHE BELASTING

Bij pasgeborenen en zuigelingen is de urineconcentratiecapaciteit onvoldoende (de waarden van volwassenen worden bereikt rond de leeftijd van één jaar) en de urinaire osmolaliteit bedraagt slechts 600 mOsm, ten opzichte van 1400 mOsm bij volwassenen. De zuigeling is dus gevoelig voor een te grote osmotische belasting en heeft een groter volume water nodig om eenzelfde osmotische belasting uit te scheiden.

WELK WATER AANBEVELEN?

Elke overmatige opname via de voeding (minerale zouten, stikstof, ...) overbelast de nierwerking. Dit kan vermeden worden door regelmatig en voldoende **SPA REINE**, te drinken, een zeer licht gemineraliseerd natuurlijk mineraalwater dat de mogelijkheid biedt om metabolische afvalstoffen te elimineren zonder bijkomende en zelfs schadelijke elementen op te nemen.

DE AANBEVOLEN WATEROPNAME VOOR DE ZUIGELING*	
ml/kg/dag	
120-100	> 1 week (voldragen zuigeling)
150-130	> 0-3 maanden
130-120	> 4-8 maanden
110-100	> 9-12 maanden

* Voedingsaanbeveling voor België HGR nr. 8309 (Herziening 2009)

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SPA® NATURAL SINCE 1583 Op het leven

Endocrinology - E

Oral Presentations

E 01 **Birth weight in the offspring of obese mothers: comparison of bariatric surgery pre-pregnancy to lifestyle intervention during pregnancy.**
K. Van De Maele (1,2), I. Gies (1), A. Bogaerts (2,3,4), I. Guelinckx (2), R. Devlieger (2,5,6) / [1] UZBrussel, [2] KU Leuven, [3] CRIC UAntwerp, [4] University College Limburg-Leuven, [5] UZ Leuven, [6] St-Augustinus Hospital Wilrijk

E 02 **New algorithm for modification of insulinotherapy during exercise in MDI and insulin pump-treated children with type 1 diabetes.**
P. Lysy, M. Owen, A. Robert, T. Barrea, S. Moniotte / UCL Saint-Luc, Brussels

Posters with short oral presentations

M 01 **Overweight and insulin resistance in metabolic diseases requiring a high carbohydrate diet.**
G. Jannone (1), A. Maiorana (2), A. Olivieri (2), S. Biondo (2), C. Dionisi-Vici (2) / [1] UCL, Saint-Luc, Brussels, [2] Bambino Gesù Childen's Hospital, Romel

E 03 **A novel mutation of the AMHR2 gene in twin brothers with Persistent Müllerian Duct Syndrome.**
K. Van De Maele, M. de Rademaeker, I. Gies, J. Vanbesien, S. Verheyden, V. DeBoe, J. De Schepper / UZ Brussel

E 04 **Integration Of Routine Parameters Of Glycemic Variability In A Simple Screening Method For Partial Remission In Children With Type 1 Diabetes.**
N. Nielens, O. Polle, A. Robert, PA. Lysy / UCL Saint-Luc, Brussels

E 05 **Rhabdomyolysis following the initiation of methimazole in a 14-year-old girl with Graves'disease.**
V. Malherbe (1), B. Brasseur (2), C. Pavlopoulos (2), M. Michel (2) / [1] UCL Saint-Luc, Brussels, [2] Clinique Saint-Pierre, Ottignies

E 06 **Early Cushing's syndrome: differential diagnosis and etiological exploration.**
J. Léonard, T. Froyland, O. Chivu, M. Lewin, J. Khamis, P. Philippet, S. Lambert / ULiège, CHC Clinique de l'Espérance, Liège

E 07 **Stunted growth and alopecia totalis : A case report.**
F. Boodhoo, C. Barrea, J. Lombet, MC. Seghaye / ULg, CHR Citadelle, Liège

E 08 **Type 2 diabetes in children and adolescents: experience in a single center in Brussels.**
K. Stabenow, K. Van De Maele, I. Gies, J. De Schepper, J. Vanbesien / UZ Brussel

Posters

E 09 **Pituitary hyperplasia in a female adolescent: a challenging diagnosis.**
W. Staels, S. Van Aken, N. Herregods, J. De Schepper / UZ Gent

E 10 **An adolescent girl with sudden weight gain and secondary amenorrhoea.**
M. Ysebaert, A. France, K. Van Hoorenbeeck / UZ Antwerpen

E 11 **Cushing Syndrome and virilization revealing malignant adrenocortical tumor: Case Report.**
A. Revercez (1), C. Navarro Moreno (2), M. Demay (1), N. Delvaux (1), E. Cavatorta (1), V. Beauloye (2), P. Lysy (2), C. Boulanger (2), M.-L. Colaiacovo (2), M. de Ville (2), G. Levy (2), A. Van Damme (2), B. Brichard (2) / [1] Hôpital Marie Curie, Charleroi, [2] UCL Saint-Luc, Brussels

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1. Salazar-Lindo et al - New England Journal of Medicine 2000; 343: 463-7
2. Turck D et al - Alimentary Pharmacology and Therapeutics 1999; 13(Suppl.6) 27-32
3. Cézard JP et al - Gastroenterology 2001; 120: 799-805
4. Alfredo Guarino et al - Journal of Pediatric Gastroenterology and Nutrition 46:S81–S122, 2008

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INDICATIONS THERAPEUTIQUES 10 et 30 mg : Traitement symptomatique adjuvant de la diarrhée aiguë chez les nourrissons (âgés de plus de 3 mois) et les enfants, en association avec une réhydratation orale et les mesures de soutien habituelles, dans le cas où elles ne suffisent pas à elles seules à contrôler l'affection clinique, et si on ne peut pas remédier à la cause de la diarrhée. Le racécadotril peut être administré comme médication complémentaire si le traitement de la cause est possible. 100 mg : Tiorfix est indiqué pour le traitement symptomatique de la diarrhée aiguë chez les adultes dans le cas où elles ne suffisent pas à elles seules à contrôler l'affection clinique, et si on ne peut pas remédier à la cause de la diarrhée. Le racécadotril peut être administré comme médication complémentaire si le traitement de la cause est possible. POSOLOGIE ET MODE D'ADMINISTRATION 10 et 30 mg : Tiorfix Baby et Tiorfix Junior sont administrés par voie orale en association avec une réhydratation orale (voir le RCP). Tiorfix Baby est destiné aux enfants de poids <13 kg. Tiorfix Junior est destiné aux enfants de poids ≥13 kg. La dose recommandée dépend du poids corporel: 1,5 mg/kg par prise, (correspondant à 1 ou 2 sachets), trois fois par jour, à des heures régulières. Chez les enfants de moins de 9 kg : un sachet de 10 mg 3 fois par jour. Chez les enfants de 9 kg à 13 kg : deux sachets de 10 mg 3 fois par jour. Chez les enfants de 13 à 27 kg: un sachet de 30 mg 3 fois par jour. Chez les enfants de plus de 27 kg: deux sachets de 30 mg 3 fois par jour. • La durée du traitement dans les essais cliniques chez les enfants était de 5 jours. Le traitement doit se poursuivre jusqu'à ce que deux selles normales peuvent être observées. Le traitement ne devra pas être poursuivi au-delà de 7 jours. Le traitement au long cours par le racécadotril est déconseillé. Il n'existe pas d'études cliniques chez les nourrissons de moins de 3 mois. • Populations particulières: Il n'existe pas d'études chez les nourrissons et les enfants souffrant d'insuffisance rénale ou hépatique (voir le RCP). La prudence est de mise chez les patients insuffisants hépatiques ou rénaux. Les granulés peuvent être ajoutés à la nourriture, dissous dans un verre d'eau ou dans un biberon. Le tout doit être bien mélangé et immédiatement administré. 100 mg : Seulement pour adultes: Une gélule d'emblée quelque soit le moment de la journée. Ensuite une gélule trois fois par jour de préférence avant les repas principaux. Le traitement doit être poursuivi jusqu'à ce que deux selles normales sont observées. Le traitement ne devrait pas durer plus de 7 jours. Populations particulières: Personnes âgées: la posologie ne doit pas être ajustée pour les personnes âgées. La prudence est de mise chez les patients insuffisants hépatiques ou rénaux. CONTRE-INDICATIONS Hypersensibilité à la substance active ou à l'un des excipients mentionnés dans le RCP. Tiorfix Baby et Tiorfix Junior contiennent du sucrose. Ces médicaments sont contre-indiqués chez les patients présentant une intolérance au fructose, un syndrome de malabsorption du glucose et du galactose ou un déficit en sucrase/isomaltase (maladies héréditaires rares). EFFETS INDESIRABLES 10 et 30 mg : Les données disponibles émanent d'études cliniques incluant 860 enfants atteints de diarrhée aiguë traités par racécadotril et 411 enfants traités par placebo. 100 mg : Les données disponibles émanent d'études cliniques incluant 2193 patients atteints de diarrhée aiguë adultes traités par racécadotril et 282 patients traités par placebo. Les effets indésirables suivants ont été observés plus fréquemment avec racécadotril qu'avec le placebo, ou ont été rapportés après la mise sur le marché. La fréquence des effets indésirables est définie selon la convention suivante: très fréquent (≥1/10), fréquent (≥1/100, <1/10), peu fréquent (≥1/1 000, <1/100), rare (≥1/10 000, <1/1 000), très rare (<1/10 000), fréquence indéterminée (ne peut être estimée sur la base des données disponibles). 10 et 30 mg : Infections et infestations Peu fréquent: amygdalite. Affections de la peau et du tissu sous-cutané (voir le RCP) Peu fréquent: éruption cutanée, érythème. Fréquence indéterminée: érythème polymorphe, œdème de la langue, du visage, des lèvres ou de la paupière, angio-œdème, urticaire, érythème noueux, éruption cutanée papuleuse, prurigo, prurit. 100 mg : Affections du système nerveux Fréquent: mal de tête. Affections de la peau et du tissu sous-cutané (voir le RCP) Peu fréquent: éruption cutanée, érythème. Fréquence indéterminée: érythème polymorphe, œdème de la langue, du visage, des lèvres ou de la paupière, angio-œdème, urticaire, érythème noueux, éruption cutanée papuleuse, prurigo, prurit, nécrolyse épidermique toxique. Déclaration des effets indésirables suspectés : La déclaration des effets indésirables suspectés après autorisation du médicament est importante. Elle permet une surveillance continue du rapport bénéfice/risque du médicament. Les professionnels de santé déclarent tout effet indésirable suspecté via le système national de déclaration : Belgique Agence fédérale des médicaments et des produits de santé Division Vigilance EUROSTATION II Place Victor Horta, 40/ 40 B-1060 Bruxelles - Site internet: www.afmps.be e-mail: adversedrugreactions@fagg-afmps.be Luxembourg Direction de la Santé – Division de la Pharmacie et des Médicaments • Villa Louvigny – Allée Marconi L-2120 Luxembourg Site internet: http://www.ms.public.lu/fr/activites/pharmacie-medicament/index.html TITULAIRE DE L'AUTORISATION DE MISE SUR LE MARCHE Bioprojet Europe Ltd., 101 Furry Park road, Killester, Dublin-5, Irlande NUMERO D'AUTORISATION DE MISE SUR LE MARCHE 10 mg : BE400723 30 mg : BE400732 100 mg : BE400741 MODE DE DELIVRANCE 10 et 30 mg : Médicament soumis à prescription médicale 100 mg: Délivrance libre DATE DE MISE A JOUR DU TEXTE 05/2017

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Gastroenterology - H

Oral Presentations

H 01 **Clinical use of infliximab trough levels during maintenance in pediatric patients with inflammatory bowel disease.**
K. van Hoeve (1), I. Hoffman (1), E. Dreesen (2), M. Ferrante (1), A. Gils (2), S. Vermeire (1) /[1] UZ Leuven, [2] KU Leuven

Posters with short oral presentations

H 02 **Sufficient exposure during induction is essential for a long and better response in paediatric patients with inflammatory bowel disease.**
K. van Hoeve, I. Hoffman, E. Dreesen, M.Ferrante, A.Gils, S.Vermeire / KUL, UZ Leuven

H 03 **An adjusted Bristol Stool Scale for young, non-toilet-trained children: the Brussels Infant and Toddler Stool Scale (BITSS).**
C. De Geyter, K. Huysentruyt, Y. Vandenplas./ VUB, UZ Brussel

H 04 **Current practice of pediatric gastro-intestinal endoscopy in Belgium.**
E. Peeters (1,2), E. De Greef (1,2), Y Vandenplas (2) / [1] ZNA Koningin Paola Kinderziekenhuis, Antwerp, [2] UZ Brussel

H 05 **Triple A syndrome, a challenging race for the diagnosis in a deadly pathology: a case report.**
T. Brose, S. Lambert, J. Khamis, S. Colinet, I. Paquot, O. Bauraind, M. Dirix, P. Philippet, A. Bobarnac / CHC - Clinique de l'Espérance, Liège

H 06 **Role / impact of pediatric clinical studies in the pediatric gastroenterology and hepatology department of Saint-Luc University Clinics.**
S. Bensarsa, J. Versavau, V. Jacobs, E.M. Sokal / UCL Saint-Luc, Brussels

H 07 **vWFpp/Adams 13 ratio is a usefull marker of thrombotic microangiopathy post liver transplant: A pediatric Case report.**
L. Duquenne (1), S. Balbeur (2), E. Everard (1), R.Reding (1), S. Eeckhoudt (1), B. Brichard (1), N. Godefroid (1), E. Derycke (1), I.Scheers(1), F.Smets (1), E.Sokal (1), X. Stéphenne (1) / [1] UCL Saint-Luc, Brussels, [2] Clinique Saint-Pierre, Ottignies

Posters

H 08 **Severe enterocolitis, life-threatening presentation of Hirschsprung disease: case report.**
S. Bierlaire, S. Colinet, O. Bauraind, I. Paquot, A. Bobarnac / CHC Clinique de l' Espérance, Liège

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General Paediatrics - GP

Oral Presentations

GP 01 Clinical outcome of children born to mothers living in social precarity in Brussels.
E. Rotunno, T. Goetghebuer / ULB Saint-Pierre, Brussels

Posters with short oral presentations

GP 02 A five-year-old girl with Henoch Schönlein purpura presenting with a rare cause of abdominal pain and vomiting.
E. Desclée, K. Poschet, A. Kurotova, T. Jonckheer, F. De Meulder / GZA Campus Sint-Vincentius, Antwerpen

GP 03 Medical devices marketed as medicines: safety and regulatory concerns in children.
S. Huijghebaert (1), P. De Bruyne (2), R. De Bruyne (2), S. Vande Velde (2), S. Van Biervliet (2), M. Van Winckel (2), K. Allegaert (3) / [1] Pharmacist, [2] UZ Gent, [3] Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands and KULeuven

GP 04 Medical devices in EU claiming oropharyngeal or gastrointestinal barrier action: barrier products or hidden pharmacological agents?
S. Huijghebaert (1), P. De Bruyne (2), R. De Bruyne (2), S. Vande Velde (2), S. Van Biervliet (2), M. Van Winckel (2), Karel Allegaert (3) / [1] Pharmacist, [2] UZ Gent, [3] Erasmus MC Sophia Children's Hospital, Rotterdam, the Netherlands and KULeuven

GP 05 EU medical device legislation (CE label) opens the door to unstudied products for OTC "medical" treatment of cough, based on "barrier" claim.
S. Huijghebaert (1), Pauline De Bruyne (2), Ruth De Bruyne (2), Saskia Vande Velde (2), Stephanie Van Biervliet (2), Karel Allegaert (3), Myriam Van Winckel (2) / [1] Pharmacist, independent researcher, [2] UZ Gent, [3] Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands & KULeuven

GP 06 Malnutrition in hospitalized children in Mayotte: prevalence and management.
Z. Ouchinsky, C. De Laet / ULB HUDERF, Brussels

Posters

GP 07 Anisocoria: not always alarming – a case report.
K. Kaïret, J. Van den Heurck, S. Verhulst, M. Mattheij / UZ Antwerpen

Genetics – G

Posters with short oral presentations

G 01 **Confirmation of an Association Between CTNNB1 Mutations and Hyperekplexia.**
S. Alkan, P. Leroy, MC. Seghaye, S. Bulk / ULiège, CHU La Citadelle, Liège

G 03 **Whole exome sequencing identifies atypical progeroid syndrome due to a recurrent LMNA mutation.**
T. Beyltjens, G. Mortier / UZ Antwerpen

G 04 **Early onset epileptic encephalopathy caused by a 'de novo' KCNQ2 gene mutation in a boy: from phenotype, genotype and treatment.**
S. Duquesne (1), B. El M'Kaddem (1), S. Paquay (1), D.Lederer (2), Y. Sznajer (1) / [1] UCL Saint-Luc, Brussels, [2] IPG, Gosselies

Posters

G 02 **Isolated hyperferritinemia in a newborn revealing hereditary hyperferritinemia cataract syndrome.**
J. Longton (1,2), E. Jeziorski (2), S. Cunat (2), N. Sirvent (2), P. Martinez (2), M. Lalande (2) / [1] CHU Liège, [2] University Hospital Montpellier, France

G 05 **Variable presenting symptoms of Costello syndrome.**
S. Verelst, A. Smits, C. Vanhole, J. Breckpot, G. Naulaers / UZ Leuven

G 06 **One diagnosis for twins.**
K. Ssoussi Addi, Y. Hennequin, J. Horkos, G. Smits, AB. Johansson / ULB, HUDERF, Brussels.

G 07 **Suspicion of Infantile Cortical Hyperostosis or Caffey disease: A case report.**
H. Warnier (1), T. Froyland (1), C. Genin (1), N. Allington (2), FG. Debray (1) / [1] CHC Clinique de l'Espérance Montegnée, Liège, [2] ULiège, CHR Citadelle, Liège

Hematology / Oncology - O

Oral Presentations

O 01 **The link between neurocognitive functioning and health-related quality of life in pediatric brain tumors.**
L. Van den Wyngaert, T. Vercruysse, K. Vandenabeele, M. Haers, C. Sleurs, A. Uyttebroeck, S. Jacobs, J. Lemiere / UZ Leuven

O 02 **Assessment of pulmonary function in a cohort of children with sickle cell disease.**
S. Tebbache, A. Ferster, L. Hanssens, N. Lefèvre / ULB HUDERF, Brussels

Posters with short oral presentations

O 03 **Prognostic value of molecular alterations in infantile spindle cell Rhabdomyosarcoma.**
E. Pozzo, M. Debiec, R. Sciot, M. Renard, A. Uyttebroeck, H. Segers / KULeuven, UZ Leuven

O 04 **Individual pain management in vaso-occlusive crisis in pediatric sickle cell disease.**
A.Remy (2), A. Bruwier (1,2), V. Goldberg (1), A. Van Damme (2) / [1] GHDC Charleroi, [2] UCL Saint-Luc, Brussels

O 05 **Diagnosis and management of CLOVES syndrome.**
A. Van der Borght, L. Boon / UCL Saint-Luc, Brussels

O 06 **Retrospective study of a series of acute infant leukemia.**
G. Col (1), H. Antoine Poirel (2), A. Ferster (3), B. Brichard (1), A. Van Damme (1) / [1] UCL Saint-Luc, Brussels, [2] Belgian Cancer Registry, Brussels, [3] ULB HUDERF, Brussels

O 07 **Recessively pathogenic MSH2 missense mutation causing biallelic mismatch Repair deficiency syndrome.**
C. Vandebosch (1), N. Janin (1), B. Brichard (1), MC. Nassogne (1), U.Tabori (2), A. Van Damme (1) / [1] UCL Saint-Luc, Brussels, [2] Hospital for Sick Children, Toronto, Canada

O 08 **Clinical response and Pharmacokinetics Profiles of Hydroxyurea in Children with Sickle Cell Disease.**
M. Karimi, A. Rodriguez Cheang, L. Dedeken, P.-Q. Le, L. Rozen, M. Ngalula Mujinga, B. Wenderickx, A. Ferster / ULB HUDERF, Brussels

O 09 **MTHFR polymorphisms and susceptibility to methotrexate toxicity: a literature Review.**
C. Geurten (1), C. Hoyoux (2) / [1] CHC Clinique de l'Espérance, Liège, [2] CHR de la Citadelle, Liège

O 10 **Vascular tumors of infancy: from the good diagnosis to the good treatment. A retrospective monocentric study.**
L. Dethioux (1), V. Segers (2), M. Ghassemi (1), C. Lelubre (3), C. Dangoisse (1), C. Devalck (1) / [1] ULB HUDERF, Brussels, [2] CHU Brugmann Brussels, [3] CHU de Charleroi Hôpital Marie Curie

O 11 **Gardner Fibroma during childhood: a benign disease?**
S. Cahen (1), N. VItali (1), M. Cassart (1), D. Franck (2), C. Devalck (2), P-Q Lê (1-2) / [1] Hôpitaux Iris Sud Site Etterbeek-Ixelles, Brussels, [2] ULB HUDERF, Brussels

O 12 **Hypereosinophilic Syndrome in Children: a case report.**
M. Gerbaux (1), Le Phu-Quoc 1,2, L. Dedeken (2), S. Stormacq (2), G. de Crombrugghe (1), E. Juvene (1), F. Carlier (1), A. Ferster (2) / [1] Hopitaux Iris-sud Site Etterbeek-Ixelles, Brussels, [2] ULB HUDERF, Brussels

O 13 Cerebellar mutism syndrome in posterior fossa tumors: a better understanding for a better counseling. A retrospective analysis of pediatric patients from 1990 to 2015.
L. Mertens, (1), LMH. De Waele, (2, 1), V. Labarque, (1, 2), J. Lemiere, (1), S. Jacobs (1, 2); [1] UZ Leuven, [2] KU Leuven

O 14 **Long-term outcome in survivors of pediatric low-grade glioma: the Leuven Database.**
L. Grossar, AM. Vink, A. Uyttebroeck, Sandra Jacobs / KULeuven, UZ Leuven

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1. Salazar-Lindo et al - New England Journal of Medicine 2000; 343: 463-7
2. Turck D et al - Alimentary Pharmacology and Therapeutics 1999; 13(Suppl.6) 27-32
3. Cézard JP et al - Gastroenterology 2001; 120: 799-805
4. Alfredo Guarino et al - Journal of Pediatric Gastroenterology and Nutrition 46:S81–S122, 2008

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THERAPEUTISCHE INDICATIES 10 en 30 mg: Aanvullende symptomatische behandeling van acute diarree bij zuigelingen (ouder dan 3 maanden) en kinderen samen met orale rehydratatie en de gebruikelijke ondersteunende maatregelen, als die op zichzelf niet volstaan om de klinische aandoening onder controle te krijgen en wanneer een oorzakelijke behandeling niet mogelijk is. Als een oorzakelijke behandeling mogelijk is, kan racecadotril toegediend worden als een aanvullende behandeling. 100 mg: Tiorfix is geïndiceerd voor de symptomatische behandeling van acute diarree bij volwassenen wanneer de oorzakelijke behandeling niet mogelijk is. Als een oorzakelijke behandeling mogelijk is, kan racecadotril toegediend worden als een aanvullende behandeling. DOSERING EN WIJZE VAN TOEDIENING 10 en 30 mg: Tiorfix Baby en Tiorfix Junior worden oraal toegediend samen met orale rehydratatie (zie SKP). Tiorfix Baby is bedoeld voor kinderen < 13 kg. Tiorfix Junior is bedoeld voor kinderen ≥13 kg. De aanbevolen dosis hangt af van het lichaamsgewicht: 1,5 mg/kg per dosis (overeenkomend met 1 tot 2 zakjes), driemaal daags op regelmatige tijdstippen. Bij kinderen minder dan 9 kg: één zakje van 10 mg 3 maal per dag. Bij kinderen van 9 kg tot 13 kg: twee zakjes van 10 mg 3 maal per dag. Bij kinderen van 13 kg tot 27 kg: één zakje van 30 mg 3 maal per dag. Bij kinderen van meer dan 27 kg: twee zakjes van 30 mg 3 maal per dag. In de klinische studies bij kinderen bedroeg de behandelingsduur 5 dagen. De behandeling moet worden voortgezet tot er twee normale stoelgangen worden waargenomen. De behandeling mag niet langer duren dan 7 dagen. Langdurige behandeling met racecadotril is niet aanbevolen. Er werden geen klinische studies uitgevoerd bij zuigelingen jonger dan 3 maanden. Speciale populaties: Er zijn geen studies uitgevoerd bij zuigelingen of kinderen met nierinsufficiëntie of leverinsufficiëntie (zie SKP). Voorzichtigheid is geboden bij patiënten met lever- of nierinsufficiëntie. • Het granulaat kan worden toegevoegd aan voedsel, gedispergeerd in een glas water of in de zuigfles. Het moet goed worden gemengd en onmiddellijk worden toegediend. 100 mg: Enkel voor volwassenen: Aanvankelijk één capsule, ongeacht het uur van de dag. Daarna één capsule driemaal daags bij voorkeur vóór de hoofdmaaltijden. De behandeling moet worden voorgezet tot er twee normale stoelgangen worden waargenomen. De behandeling mag niet langer duren dan 7 dagen. • Speciale populaties: Ouderen: de dosering hoeft niet te worden aangepast bij ouderen. Voorzichtigheid is geboden bij patiënten met lever- of nierinsufficiëntie. CONTRA-INDICATIES Overgevoeligheid voor de werkzame stof of voor een van de in de SKP vermelde hulpstoffen. Tiorfix Baby en Tiorfix Junior bevatten sucrose. Patiënten met zeldzame erfelijke aandoeningen als fructose-intolerantie, glucose-galactose malabsorptie of sucrase-isomaltase insufficiëntie dienen dit geneesmiddel niet te gebruiken. BIJWERKINGEN 10 en 30 mg: Er zijn gegevens van klinische studies beschikbaar over 860 pediatrische patiënten met acute diarree die werden behandeld met racecadotril en over 411 kinderen behandeld met placebo. 100 mg: Er zijn gegevens van klinische studies beschikbaar over 2,193 volwassen patiënten met acute diarree die werden behandeld met racecadotril en 282 die werden behandeld met placebo. De volgende bijwerkingen zijn vaker opgetreden met racecadotril dan met de placebo of werden gerapporteerd tijdens de postmarketingbewaking. De frequentie van bijwerkingen wordt volgens de volgende conventie gedefinieerd: zeer vaak (≥ 1/10), vaak (≥ 1/100 tot < 1/10), soms (≥ 1/1.000 tot < 1/100), zelden (≥ 1/10.000 tot < 1/1.000), zeer zelden (< 1/10.000), niet bekend (kan niet worden geraamd op grond van de beschikbare gegevens). 10 en 30 mg: Infecties en parasitaire aandoeningen Soms: tonsillitis. Huid- en onderhuidaandoeningen (zie SKP) Soms: uitslag, erytheem. Niet bekend: erythema multiforme; oedeem van de tong, het gezicht, de lippen of het ooglid; angio oedeem, urticaria, erythema nodosum, papuleuze uitslag, prurigo, pruritus. • 100 mg: Zenuwstelselaandoeningen Vaak: hoofdpijn. Huid- en onderhuidaandoeningen (zie SKP) Soms: uitslag, erytheem. Niet bekend: erythema multiforme, oedeem van de tong, het gelaat, de lippen of het ooglid; angio oedeem, urticaria, erythema nodosum, papuleuze uitslag, prurigo, pruritus, toxische huideruptie. Melding van vermoedelijke bijwerkingen Het is belangrijk om na toelating van het geneesmiddel vermoedelijke bijwerkingen te melden. Op deze wijze kan de verhouding tussen voordelen en risico's van het geneesmiddel voortdurend worden gevolgd. Beroepsbeoefenaren in de gezondheidszorg wordt verzocht alle vermoedelijke bijwerkingen te melden via het nationale meldsysteem: België Federaal agentschap voor geneesmiddelen en gezondheidsproducten-Afdeling Vigilantie EUROSTATION II Victor Hortaplein, 40/ 40 B-1060 Brussel Website: www.fagg.be e-mail: adversedrugreactions@fagg-afmps.be HOUDER VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN Bioprojet Europe Ltd., 101 Furry Park road, Killester, Dublin-5, Ierland NUMMER VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN 10 mg: BE400723 30 mg: BE400732 100 mg: BE400741 AFLEVERINGSWIJZE 10 en 30 mg: Op medisch voorschrift. 100 mg: Vrije aflevering. DATUM VAN HERZIENING VAN DE TEKST 05/2017

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O 15 **A Sertoli-Leydig tumor in a 3-year-old girl: a case report.**
K. Ssoussi Addi, T. Nsengiyumva, Y. Weinblum, B. Belhadi, P. Lingier, M.-F. Dehou / Edith Cavell Clinic, Brussels

O 16 **Neonatal renal vein thrombosis: about a case.**
A. Remy (1), A. Bachy (1), A. Bruwier (1,2), V. Goldberg (1) / [1] GHDC Charleroi, [2] UCL Saint-Luc, Brussels

O 17 **A big belly like no other.**
L. De Doncker, H. Barake, M. Cassart, E. Kadz, T. Balfroid / Hôpitaux Iris Sud Site Etterbeek-Ixelles, Brussels

O 18 **Jaundice and unexplained cholestasis as the first presenting symptoms in a child with mature B cell non-Hodgkin lymphoma.**
L. Kornreich, L. Dedeken, A. Ferster, S. Diallo, C. Dimitriou, P. Bontemps, C. Devalck / ULB HUDERF, Brussels

O 19 **Desmoid pancreatic tumor in a 12-years-old child.**
F. Dockx, G. Levy, C. Boulanger, B. Brichard, L. Coubeau, A. Pire, R. Reding, A. Van Damme / UCL Saint-Luc, Brussels

O20 **Diarrhea-negative Hemolytic Uremic Syndrome: about a case.**
H. Warnier (1), L. Zambelli (1), E. Defontaine (1), J. Frère (2), N. Cajgfinger (2), T. Carvelli (1), J. Lombet (2), M-F. Dresse (3) / [1] CHR Verviers East Belgium, [2] ULiège, CHR Citadelle, Liège, [3] ULiège, CHU Liège

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NAAM VAN HET GENEESMIDDEL: Synagis 100 mg/ml oplossing voor injectie. **KWALITATIEVE EN KWANTITATIEVE SAMENSTELLING:** 1 ml Synagis-oplossing bevat 100 mg palivizumab*. Elke 0,5 ml injectieflacon bevat 50 mg palivizumab. Elke 1 ml injectieflacon bevat 100 mg palivizumab. * Palivizumab is een recombinant humaan monoklonaal antilichaam geproduceerd door middel van DNA technologie in muis myeloom gastcellen. Voor de volledige lijst van hulpstoffen, zie rubriek 6.1. **FARMACEUTISCHE VORM:** Oplossing voor injectie. De oplossing is helder of licht opaalachtig. **THERAPEUTISCHE INDICATIES:** Synagis is bestemd voor de preventie van ernstige lagere luchtwegaandoeningen, waarbij ziekenhuisopname vereist is, veroorzaakt door respiratoir syncytieel virus (RSV) bij kinderen die risico lopen op RSV-ziekte: kinderen die geboren zijn na een zwangerschapsduur van 35 weken of minder en die bij het begin van het RSV-seizoen jonger waren dan 6 maanden; kinderen jonger dan twee jaar die in de voorafgaande 6 maanden een behandeling voor bronchopulmonale dysplasie nodig hadden; kinderen jonger dan 2 jaar die een congenitale hartaandoening hebben die hemodynamisch significant is. **DOSERING EN WIJZE VAN TOEDIENING:** Dosering: De aanbevolen dosis palivizumab is 15 mg/kg lichaamsgewicht, eens per maand toegediend gedurende te verwachte periodes van RSV-risico in de samenleving. Het volume palivizumab (uitgedrukt in ml) dat maandelijks dient te worden toegediend = [patiëntgewicht in kg] vermenigvuldigd met 0,15. Waar mogelijk moet de eerste dosis worden toegediend voor het begin van het RSV-seizoen. Volgende doses dienen maandelijks gedurende het RSV-seizoen te worden toegediend. De werkzaamheid van palivizumab bij doses anders dan 15 mg per kg of doseringen anders dan maandelijks gedurende het RSV-seizoen is niet vastgesteld. Het grootste deel van de kennis, waaronder de cruciale fase III klinische studies met palivizumab, is opgedaan met 5 injecties per seizoen (zie rubriek 5.1). Gelimiteerde data zijn aanwezig over meer dan 5 doses (zie rubrieken 4.8 en 5.1), daarom is het profijt in de term van protectie voor meer dan 5 doses niet vastgesteld. Om het risico van een nieuwe ziekenhuisopname te verminderen, is het aan te bevelen om bij kinderen die behandeld worden met palivizumab en in het ziekenhuis opgenomen worden met RSV de behandeling voort te zetten met maandelijkse doses palivizumab, voor de duur van het RSV-seizoen. Bij kinderen die een cardiale-bypass ondergaan wordt geadviseerd een injectie van 15 mg/kg lichaamsgewicht van palivizumab toe te dienen zodra ze stabiel zijn na de operatie, om adequate serumconcentraties palivizumab te garanderen. Een maandelijkse dosis dient te worden vervolgd voor de rest van het RSV-seizoen voor kinderen die een hoog risico houden op RSV-ziekte (zie rubriek 5.2). Wijze van toediening: Palivizumab wordt intramusculair toegediend, bij voorkeur anterolateraal in de dij. De musculus gluteus dient niet routinematig als injectieplaats gebruikt te worden vanwege het risico op beschadiging van de nervus sciaticus. Bij het geven van de injectie moet een standaard aseptische techniek gebruikt worden. Injectiehoeveelheden groter dan 1 ml dienen in verdeelde doses te worden gegeven. Synagis-oplossing voor injectie is een gebruiksklaar preparaat. Voor instructies over speciale hanteringseisen, zie rubriek 6.6. **CONTRA-INDICATIES:** Overgevoeligheid voor de werkzame stof of voor (één van) de in rubriek 6.1 vermelde hulpstof(fen), of voor andere gehumaniseerde monoklonale antilichamen. **BIJWERKINGEN:** Samenvatting van het veiligheidsprofiel: De meest ernstige bijwerkingen die optreden bij gebruik van palivizumab zijn anafylaxie en andere acute overgevoeligheidsreacties. Vaak voorkomende bijwerkingen die optreden bij gebruik van palivizumab zijn koorts, uitslag en reactie op de injectieplaats. Getabelleerde lijst van bijwerkingen: Bijwerkingen op zowel klinisch gebied als laboratoriumbevindingen, zijn weergegeven per orgaansysteem en frequentie (zeer vaak ≥ 1/10; vaak ≥ 1/100, < 1/10; soms ≥ 1/1.000, < 1/100; zelden ≥ 1/10.000, < 1/1.000) en zijn afkomstig uit studies uitgevoerd bij prematuren en pediatrische patiënten met bronchopulmonaire dysplasie en bij pediatrische patiënten met congenitale hartaandoeningen. De bijwerkingen geïdentificeerd via postmarketingsurveillance zijn vrijwillig gemeld uit een populatie van onbekende grootte; het is niet altijd mogelijk om een betrouwbare schatting van hun frequentie te maken of om een causaal verband met palivizumabblootstelling aan te tonen. De frequentie van deze bijwerkingen, zoals weergegeven in de onderstaande tabel, werd geschat met de veiligheidsgegevens uit de twee klinische registratiestudies. De incidenties van deze gebeurtenissen in deze studies toonden geen verschil tussen de palivizumab- en de placebogroepen en de gebeurtenissen waren niet medicatiegerelateerd. **Bijwerkingen uit klinische studies* en uit postmarketingsurveillance bij pediatrische patiënten:** - Bloed- en lymfestelselaandoeningen: soms, trombocytopenie# - Immuunsysteemaandoeningen: niet bekend; anafylaxie, anafylactische shock (in enkele gevallen is een fatale afloop gemeld.)# - Zenuwstelselaandoeningen: soms; convulsies# - Ademhalingsstelsel-, borstkas- en mediastinumaandoeningen: vaak; apneu# - Huid- en onderhuidaandoeningen: zeer vaak; uitslag, soms; urticaria# - Algemene aandoeningen en toedieningsplaatsstoornissen: zeer vaak; koorts, vaak; reactie op de injectieplaats. *Voor een volledige beschrijving van de studie, zie rubriek 5.1 Klinische studies #Bijwerkingen bepaald uit postmarketingsurveillance. Beschrijving van geselecteerde bijwerkingen: *Postmarketingervaring:* De postmarketing spontaan gemelde ernstige bijwerkingen van palivizumab behandelingen tussen 1998 en 2002, welke periode 4 RSV-seizoenen beslaat, zijn geëvalueerd. In totaal zijn er 1291 ernstige rapporten ontvangen waarbij palivizumab toegediend was zoals aangegeven en de duur van de therapie binnen één seizoen viel. Het begin van de bijwerkingen vond in slechts 22 van deze rapporten plaats na de zesde of hogere dosis (15 na de zesde dosis, 6 na de zevende dosis en 1 na de achtste dosis). Deze bijwerkingen zijn van aard vergelijkbaar met de bijwerkingen na de eerste 5 doses. Het palivizumab behandelingsschema en de bijwerkingen zijn gemonitord in een groep van bijna 20.000 kinderen die gevolgd zijn door een patiënten compliance register tussen 1998 en 2000. Van deze groep kregen 1250 kinderen 6 injecties, 183 kinderen kregen 7 injecties en 27 kinderen kregen 8 of 9 injecties. Waargenomen bijwerkingen in patiënten na de zesde of hogere dosis waren vergelijkbaar van aard en frequentie met de bijwerkingen na de eerste vijf doses. In een observationele, postmarketing, database-studie werd een kleine toename in de frequentie van astma waargenomen bij premature palivizumab-ontvangers; het causale verband is echter onzeker. Melding van vermoedelijke bijwerkingen: Het is belangrijk om na toelating van het geneesmiddel vermoedelijke bijwerkingen te melden. Op deze wijze kan de verhouding tussen voordelen en risico's van het geneesmiddel voortdurend worden gevolgd. Beroepsbeoefenaren in de gezondheidszorg wordt verzocht alle vermoedelijke bijwerkingen te melden via: **België:** Federaal agentschap voor geneesmiddelen en gezondheidsproducten, Afdeling Vigilantie, EUROSTATION II, Victor Hortaplein, 40/40, B-1060 Brussel. 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Immunology / Rheumatology – L

Oral Presentations

L 01 **Is the Concept of Rheumatogenic Group A Streptococcus a Myth? A Systematic Literature Review from 1944 to 2016 and a Molecular Analysis of the M-Protein.**
G. de Crombrugghe (1, 2), N. Baroux (3), D. Williamson (4), N. Moreland (5), A. Steer (3), P. Smeesters (1, 2, 3,) / [1] HUDERF, Brussels, [2] ULB, Brussels, [3] Murdoch Childrens Research Institute, Melbourne, Victoria, Australia, [4] (MDU) Public Health Laboratory, Melbourne, Victoria Australia, [5] University of Auckland, New Zealand

Posters with short oral presentations

L 02 **Pediatric systemic lupus erythematosus presenting with pancytopenia and retinal vasculitis.**
E. Snoeck (1), J. Dehoorne(1), M. De Laat (2), I. Balikova (1), B. De Moerloose (1) / [1] UZ Gent, [2] OLV Campus Aalst

L 03 **Leopard skin-like colitis.**
E. Costenoble, O. Bauraind, S. Colinet, C. Chantrain, N. Bletard, A. Bobarnac, I. Paquot, P. Philippet / CHC Clinique de l'Espérance, Montegnée

L 04 **Stem cell transplantation in a patient affected by a Purine Nucleoside Phosphorylase deficiency.**
A.Etienne (1), B. Brichard (1), M. de Ville de Goyet (1), G. Levy (1), I. Maystadt (2), A. Van Damme (1), C. Vermylen (1), C. Boulanger (1) / [1] UCL Saint-Luc, Brussels, [2] IPG, Gosselies

L 05 **An unusual manifestation of Behcet's disease.**
G. Conti, N. Van Beirs, A. Machado, D. Brucella, A. Theunis, P-Q Le / Hôpital Iris Sud Etterbeek-Ixelles Hospital, Brussels

L 06 **Absence of B-cells & NK-cell lymphopenia mimicking primary immune deficiency in neonatal period due to anti-lymphocyte maternofetal allo-immunisation.**
J. Nyssen (1), C. Lefebvre (1,2), V. Rigo (1,2), J-M. Minon (2), M-F. Dresse (1), M-C. Seghaye (1), S. Borte (3), B. Florkin (1,2) / [1] CHU Liège, [2] CHR Citadelle, Liège, [3] Karolinska University Hospital Huddinge, Stockholm, Sweden

L 07 **Severe combined immunodeficiency and metaphyseal osteochondrodysplasia: A case report.**
Z. Depuis, J. Frere, B. Florkin, MC. Seghaye / ULiège, CHR de la Citadelle, Liège

L 08 **Cerebral venous sinus trombosis as the presenting symptom for Behçet's disease in a 15-year old boy.**
L. Depoorter L.(1), A. Jansen (1), M. Van den Akker (1) , B. Ogunjimi B.(1, 2, 3 ,4), T. Vanderhasselt (1), J. Van der Werff ten Bosch J.(1), S. Abdelhadi (1), M. Deneyer (1) / [1] UZ Brussel, [2] UZ Gent, [3] UZ Antwerpen, [4] ZNAntwerpen

L 09 **Hereditary angioedema in two sisters due to parental mosaicism.**
A. Van Gasse (1), D. Ebo (1), M. Hagendorens (1), V. Sabato (1), E. Reyniers (1), W. Wuyts (1), H. Poirel (2), G. Mortier (1) / [1] UZ Antwerpen, [2] UCL Saint-Luc, Brussels

Posters

L 10 **The good and bad sides of Intravenous Immunoglobulin Therapy.**
S. Cahen, S. Cadar, P-Q Lê / Hôpitaux Iris Sud Etterbeek-Ixelles Hospital, Brussels

L 11 **Case report of systemic juvenile idiopathic arthritis.**
G. Delens (1), J.-L. Hennecker(1), O. Gilliaux (2) / [1] Clinique Notre-Dame de Grâce, Gosselies, [2] CHU de Charleroi Hôpital civil, Charleroi

L 12 **A boy with twice a bacterial meningitis with an underlying complement deficiency.**
S. A. Kluijfhout (1), P. Stordeur (2), S. Vermaning Sietske (1), F. Gordts Frans (1), M. Deneyer (1), M.Van den Akker (1), J. Van Der Werff Ten Bosch (1) / [1] UZ Brussel, [2] ULB Erasme, Brussels

Infectiology – I

Oral Presentations

I 01 **Lymphadenopathy caused by nontuberculous mycobacteriae in children: treatment and outcome.**
H. De Baerdemaeker, B. Meertens / UZ Gent

I 02 **Immunological and virological outcome in HIV-infected adolescents transitioning to adult care in Belgium.**
B. Mbiya (1), E. Tshibangu (1), T. Goetghebuer (2), D. Van der Linden (3) / [1] University of Mbujimayi, Democratic Republic of Congo, [2] ULB Saint-Pierre, Brussels, [3] UCL Saint-Luc, Brussels

Posters with short oral presentations

I 03 **Literature review of the burden of serogroup B meningococcal disease in Belgium. Meulemans, K. Billiaert, S. Klein, M. Moreira / GSK**

I 04 **Epidemiology and clinical features of Respiratory Syncytial Virus and Influenza viruses infections during the fall and winter period 2014-2015.**
J.I. Montero, T. Goetghebuer, P. De Backer, L. Busson, A. Tilmanne, E. Van der Kelen, J. Levy / ULB Saint-Pierre, Brussels

I 05 **Empiric treatment of febrile urinary tract infection in infants and children in Tournai-Belgique.**
M. Zingarelli, J.-P. Stalens / CHWAPI, Tournai

I 06 **Nontypeable Haemophilus influenzae meningitis causing a subdural empyema in a 6-month-old child.**
A. Wery, A.S. Haenecour / UCL Saint-Luc, Brussels.

I 07 **Menstrual Toxic Shock Syndrome in a young adolescent using menstrual devices.**
O. Polle, L. Boutsen, J-L. Hennecker / Clinique Notre-Dame de Grace, Gosselies

I 08 **Case-Report: Vasculitis in a 6-year-old girl with atypical clinical manifestations.**
M. Peers de Nieuwburgh (1), J.-P. Stalens (1), D. Van der Linden (2) / [1] CHWAPI, Tournai, [2] UCL Saint- Luc, Brussels

I 09 **Invasive group A streptococcal infections in a tertiary center.**
A.De Pryck, F. Zech, H. Rodrigues-Villalobos, D. Van der Linden / UCL Saint-Luc, Brussels

I 10 **Not always what it seems: acute otitis externa mimicking mastoiditis.**
E. Desclée, K. Poschet, A. Kurotova, T. Jonckheer, F. De Meulder / GZA Ziekenhuizen Campus Sint- Vincentius, Antwerpen

I 11 **Measles epidemic in 2017 at the CHR Verviers East Belgium: illustration by a clinical case.**
L. Zambelli, A. Fohn, T. Carvelli, K. Giebels / CHR Verviers

I 12 **Reduction of infections in Home Parenteral Nutrition with a simplified protocol: an 18-year study.**
M. Deltenre (1), R.Tambucci (1), F. Fusaro (2), D. Hermans (1) / [1] UCL Saint-Luc, Brussels, [2] Bambino Gesù Children's Hospital, Roma, Italy

I 13 **Neonatal suppurative parotitis: a case report.**
S. Schroven, E. Van Damme / UAntwerp, ZNA Jan Palfijn, Merksem

I 14 **Case Report: Kingella kingea spondylodiscitis in a 16-month-old child.**
A. Schmetz, T. Boulanger, I. De La Fuente, A. Biver / Centre Hospitalier du Luxembourg

I 15 **Extensive cervical spondylodiscitis with bone deformities and abscess formation in a 10-year-old boy: a case report.**
E. Feenstra, M. Claeys, F. De Meulder, T. Jonckheer, K. Poschet / GZA Campus Sint-Vincentius, Antwerpen

I 16 **Haemophilus influenzae meningitis in a two-year old child.**
L. Adouane, S. Noirhomme, V. Gilain, A. Lievens, G. De Bilderling / CHR Sambre et Meuse, Namur

I 17 **Scarlet fever? Kawasaki syndrome? Coxsackie infection? Report on a medical Odyssea.**
R. Kinuani, M. Hoyoux, J. Frère, M-C Seghaye / ULiège, CHR Citadelle, Liège

I 18 **Atypical right hip osteoarthritis: where is the cat?**
C. Martin, O. Chatzis, D. Van der Linden / UCL Saint-Luc, Brussels

I 19 **Abnormal psychomotor development revealing a HIV infection in a young boy.**
B.Nanga Diasi (1,2), A. Bocquet (1), C. Gernay (2,3), V. Schmitz (3), J.-P. Misson (1,3) / [1] CHR Namur, [2] Université de Liège (ULiège), [3] ULiège, CHR de la Citadelle, Liège

I 20 **Postnatally Acquired Neonatal Herpes Simplex Virus Infection: About Two Cases.**
S. Lommaert (1), J. Vanclaire (2) / [1] UCL, Saint Luc, [2] Clinique Saint Jean, Brussels

I 28 **The Belgian casopharyngeal carriage study of S. PNEUMONIAE in infants aged 6-30 months.**
I. Wouters (1), S. Desmet (2), L. Van Heirstraeten (1), A. Rahman (1), J. Verhaegen (2), S. Malhotra-Kumar (1), H. Theeten (1)/[1] U Antwerp, [2] UZ Leuven

Posters

I 21 **Peritonitis, could it be tuberculosis?**
ML. Godet (1), M. Barbier M (1), V. Selimaj (1), J. Vanclaire (1), M. Rezai Monfared (1), O.Chatzis (2), D. Van der Linden (2) / [1] Clinique Saint-Jean, Brussels, [2] UCL Saint-Luc, Brussels.

I 22 **An unusual cause of cytopenia and fever in a one-year-old child.**
A. Delfosse, G. Levy, M.-L. Colaiacovo, D. Van Der Linden, A. Van Damme, B. Brichard / UCL Saint-Luc, Brussels

I 23 **Acute abdominal pain as initial presentation of toxocariasis: a case report of a 12-year-old girl.**
L. Guerit (1), O. Chatzis (1), D. Van Der Linden (1), M. Maka (2), T. Moldovan (2) / [1] UCL Saint-Luc, Brussels, [2] CH EpiCURA, Hornu

I 24 **Acute mastoiditis and the importance of pathogen identification: Two case reports.**
G. De Crombrugghe, A. Nebbioso, A. Salas, E. Jonniaux, M. Gerbaux, E. Juvene, P.-Q. Le / Hôpitaux Iris-Sud, Site Etterbeek-Ixelles, Brussels

I 25 **A rare case of complicated sphenoidal sinusitis. Lemierre Syndrome or not?**
F. Kubat, D. Stroobant, M. Henin, M. Avram / GHDC, Charleroi

I 26 **Atypical gastroenteritis: a diagnosis not to be missed.**
T. Dutilleux, A. Fohn, T. Carvelli, K. Giebels / Regional Hospital Center East Belgium, Verviers

I 27 **From dental care to subdural empyema: a short step.**
Marcuzzi (1), A. Taxhet (2), J. Frère (2), M-C Seghaye (2) / [1] ULiège, [2] CHR Citadelle, Liège

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Intensive Care - IC

Oral Presentations

IC 01 **Acute hepatic failure in children: experience of a paediatric intensive care unit.**
V. Hermans, T. Detaille, A. Haenecour, E. Derycke, L. Houtekie, R. Reding, S. Clément de Cléty / UCL Saint-Luc, Brussels

IC 02 **Glomerular hyperfiltration: a new concept in critically ill children.**
T. Van Der Heggen, E. Dhont, H. Peperstraete, J.Delanghe, J. Vande Walle, P. De Paepe, P. De Cock / UZ Gent

Posters with short oral presentations

IC 03 **Small artery, big damage.**
M. Detienne (1), X. Beretta (1), R. Morais (2), D. Grimaldi (2), G. Boitsios (1) / [1] ULB HUDERF, Brussels, [2] ULB Erasme, Brussels

Neonatology - N

Oral Presentations

N 01 **Earlier achievement of full enteral feeding in ELBW neonates is not associated with growth improvement in the first two years of life.**
C. Brants (1), T. van Tienoven (2), M. Rayyan (1,3), K. Allegaert (1,4,5), A. Raaijmakers (1,3) / [1] KULeuven, [2] University of New South Wales, Sydney, Australia, [3] UZ Leuven, [4] Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands

Posters with short oral presentations

N 02 **Can an age-linked webapplication support parents of premature babies during 2 years and have impact on the child 's later development?**
M.-R. Van Hoestenberghe (1), K. Van Leeuwen (2) / [1] ZOL Campus Sint-Jan, Genk, [2] KULeuven

N 03 **Retrospective study on the medium-term outcome of children born with omphalocele or gastroschisis.**
C. Schmit, B. Van Grambezen / UCL Saint-Luc, Brussels

N 04 **Discordant pregnancy and intrauterine growth retardation: neonatal evolution of eutrophic twin.**
T. Thiry, C. Hocq / UCL Saint-Luc, Brussels

N 05 **Challenges of choanal atresia in an extremely low birth weight neonate.**
S. Verelst, A. Smits, A. Debeer, G. Naulaers, V. Vander Poorten, G. Hens / KULeuven, UZ Leuven

N 06 **Start Therapeutic Hypothermia in Neonatal Spinal Cord Injury: a «Hot» Topic.**
H. Hubinont, D. Avino, A. Vuckovic, AB. Johansson / ULB HUDERF, Brussels

N 07 **Irritability and tachypnea in the maternity ward: think metabolic emergencies.**
S. Del Re (1), O. Balasel (1), AB. Johansson (1), C. De Laet (1), A. Vicinanza (1), JP. Stalens (2) / [1] ULB HUDERF, Brussels, [2] CHWAPI, Tournai

N 08 **'Fear not" and give vitamin D and magnesium from the first day of hypocalcemia: a case report of neonatal hypocalcemia.**
E.I. Levy (1), D. Grossman (2), E. Boros (3), M. Closset (2) / [1] UZ Brussel, [2] CHIREC Site Clinique Edith Cavell, Brussels, [3] ULB HUDERF, Brussels

N 09 **Congenital Steinert's myotonic dystrophy: a case-report of a child born from in vitro fertilization (IVF).**
M.-E. Leboutte, M. Melchior, E. Gueulette / Clinique Sainte-Elisabeth, Namur

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N 10 **Subdural hematoma, thrombocytopenia and hepatic cholestasis: what they have in common.**
S. Tribolet (1), S. Merckx (1), F. Kubat (1), I. Kahn (1), T. Dienst (1), S. Smeets (1), A. Vervoort (1), A. Francois (1), A. Marguglio (1), FG. Debray (2), A. Destree (3), S. Colinet (4), N. Demonceau (4), P. Maton (1) / [1] CHC, Clinique Saint-Vincent, Rocourt, [2] CHC-CHU Liège, Sart-Tilman, [3] IPG Gosselies, [4]CHC, Clinique de l'Espérance, Montegnée, Liège

N 11 **Two cases of distal humeral epiphysiolysis in the new-born: diagnosis and management.**
HA. Bourgeno (1), K. Mathé (1,2), M. Bellemans (1), E. Damis (1,2), JMG. van Hout (1,2) / [1] ULB HUDERF, Brussels, [2] CHU Brugmann, Brussels

N 12 **Mitochondrial fatty acid beta oxidation disorders (FAOD) as a cause of sudden neonatal death.**
A.Blauen (1), I. Kahn (1), J. Bottu (2), E. Scalais / [1] UCL Saint-Luc, Brussels, [2] Centre Hospitalier du Luxembourg

Posters

N 13 **Neonatal brachial plexus palsy: a case report.**
E. Juvene, A. Nebbioso, E. Chevalier, G. de Crombrugghe, P-Q Le / Hôpitaux Iris Sud Etterbeek-Ixelles, Brussels

N 14 **Inside out.**
A. Berthold, J. Penninckx, C. Theyskens / ZOL, Campus Sint-Jan, Genk

N 15 **Congenital Arthrogryposis-Renal dysfunction-Cholestasis (ARC) syndrome.**
A.Colot, O. Balasel, A-B. Johansson, C. Vilain / ULB HUDERF, Brussels

N 16 **A rare case of neonatal respiratory distress.**
W. Kappers (1), B. Michel (1), C. Heinrichs (2), M. Flausch (1) / [1] CHIREC Site Clinique Edith Cavell, Brussels, [2] ULB HUDERF, Brussels

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S. Celen (1), N. De Vos (1), L. Cornette (2), J. Casselman (2) / [1] UZ Gent, [2] AZ Sint-Jan Brugge

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A.Guffins, N. Laval, M. Bache, S. Heck, W. Boehm / CHL Kannerklinik Luxembourg

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MKF. Docx (1), J. Vande Walle (2), A. Den Dooven (3), M. Helbert (4) / [1] ZNA Koningin Paola Kinderziekenhuis, Antwerpen, [2] UZ Gent, (3) UZ Antwerpen, (4) ZNA Middelheim, Antwerpen

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E. Lavrysen (1), T. Menovsky (2) / [1] UZ Gent, [2] UZ Antwerpen

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L. Dethioux (1) , G.Boitsios (2) L. Regal (2), F. Bugnon (1), A. Aeby (2) / [1] Centre Hospitalier Hornu- Frameries, [2] ULB HUDERF, Brussels

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J. Carpentier, L. Vega, C. Clees, E. Scalais / CHLuxembourg, Luxembourg

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B 09 **Peri-cerebral effusion in infant: diagnosis and management.**
G. Battisti, V. Somville, E. Gueulette, M. Deprez / CHU UCL site Namur

B 10 **Intracranial aneurysm in a 9-year-old girl: A case report and literature review.**
D. Mandelenaki, Lubicz , C. Fricx, F. Vermeulen / ULB Erasme, Brussels

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La solution est claire ou légèrement opalescente. **INDICATIONS THÉRAPEUTIQUES :** Synagis est indiqué pour la prévention des infections respiratoires basses graves, dues au virus respiratoire syncytial (VRS), nécessitant une hospitalisation chez les enfants à risque élevé d'infection à VRS : Enfants nés à 35 semaines d'âge gestationnel ou moins et de moins de 6 mois au début de l'épidémie saisonnière à VRS ; Enfants de moins de 2 ans ayant nécessité un traitement pour dysplasie bronchopulmonaire au cours des 6 derniers mois ; Enfants de moins de 2 ans atteints d'une cardiopathie congénitale avec retentissement hémodynamique. **POSOLOGIE ET MODE D'ADMINISTRATION** Posologie : La posologie de palivizumab recommandée est de 15 mg/kg, administrée une fois par mois pendant les périodes à risque d'infections communautaires à VRS. Le volume (exprimé en ml) de palivizumab à administrer à des intervalles d'un mois = [poids du patient en kg] multiplié par 0,15. Lorsque c'est possible, la première dose doit être administrée avant le début de la saison de l'épidémie à VRS et les doses suivantes, chaque mois pendant toute la durée de cette saison. L'efficacité du palivizumab à des doses autres que 15 mg/kg ou administré à une posologie différente du schéma mensuel pendant toute la saison à VRS n'a pas été établie. La majorité de l'expérience, études cliniques pivotales de phase III comprises, a été obtenue avec 5 injections de palivizumab pendant une saison (voir rubrique 5.1). D'autres données, bien que limitées, sont disponibles au delà de 5 injections (voir rubriques 4.8 et 5.1), par conséquent le bénéfice en terme de protection au delà de 5 doses n'a pas été établi. Chez les enfants traités par le palivizumab qui sont hospitalisés avec une infection à VRS, il est recommandé, pour réduire le risque de réhospitalisation, de poursuivre l'administration mensuelle des doses de palivizumab pendant toute la durée de l'épidémie à VRS. Chez les enfants ayant eu une chirurgie cardiaque avec circulation extra corporelle, il est recommandé d'administrer une dose de 15 mg/kg de poids corporel dès que l'enfant est stabilisé après l'intervention chirurgicale afin d'assurer des taux sériques adéquats de palivizumab. Les doses suivantes doivent être administrées mensuellement au cours de la saison restante à VRS pour les enfants qui continuent à être à haut risque d'infections à VRS (voir rubrique 5.2). Mode d'administration : Le palivizumab est administré par voie intramusculaire, de préférence à la face antéro-externe de la cuisse. Le muscle fessier ne doit pas être utilisé systématiquement comme site d'injection en raison du risque de lésion du nerf sciatique. L'injection doit être pratiquée selon les conditions habituelles d'asepsie. La dose doit être fractionnée si le volume à injecter dépasse 1 ml. Synagis solution injectable est une solution prête à l'emploi. Pour les précautions particulières de manipulation, voir rubrique 6.6. **CONTRE-INDICATIONS :** Hypersensibilité à la substance active ou à l'un des excipients mentionnés dans la rubrique 6.1), ou à d'autres anticorps monoclonaux humanisés. **EFFETS INDÉSIRABLES :** Résumé du profil de tolerance: Les effets indésirables les plus graves survenus avec le palivizumab sont l'anaphylaxie et d'autres réactions d'hypersensibilité aiguë. Les effets indésirables les plus fréquents survenus avec le palivizumab sont la fièvre, l'éruption cutanée et la réaction au site d'injection. Liste des effets indésirables: Les effets indésirables et les anomalies biologiques sont présentés ci-dessous, classés par systèmes d'organes et selon l'échelle de fréquence suivante (très fréquents ≥ 1/10 ; fréquents ≥ 1/100 à < 1/10, peu fréquents ≥ 1/1000 à < 1/100; rares ≥ 1/10000 à < 1/1000). Ils ont été rapportés au cours des essais cliniques menés chez les enfants prématurés et ceux atteints de dysplasie bronchopulmonaire ou chez les enfants atteints de cardiopathie congénitale. Les effets indésirables identifiés lors de la surveillance après la mise sur le marché ont été rapportés de manière volontaire à partir d'une population de taille inconnue ; il n'est pas toujours possible d'estimer de manière fiable leur fréquence ou d'établir un lien avec l'exposition au palivizumab. La fréquence de ces effets indésirables telle que présentée dans le tableau ci-dessous a été estimée en utilisant les données de tolérance des deux études cliniques du dossier d'enregistrement. Les incidences des effets dans ces études n'ont montré aucune différence entre le groupe placebo et le groupe palivizumab et les effets n'étaient pas liés à la prise du médicament. **Effets indésirables rapportés au cours des études cliniques * et après commercialisation chez les enfants** : - Affections hématologiques et du système lymphatique : Peu fréquent ; Thrombocytopénie# - Affections du système immunitaire : Fréquence indéterminée ; Anaphylaxie, choc anaphylactique (dans certains cas, des décès ont été rapportés.)# - Affections du système nerveux : Peu fréquent ; Convulsion# - Affections respiratoires, thoraciques et médiastinales : Fréquent ; Apnée# - Affections de la peau et du tissu sous-cutané : Très fréquent ; Eruption cutanée , Peu fréquent ; Urticaire# - Troubles généraux et anomalies au site d'administration : Très fréquent ; Fièvre , Fréquent : Réaction au site d'injection. *Pour une description complète de l'étude, voir la section 5.1 Etudes cliniques #Effets indésirables identifiés lors de la surveillance après la mise sur le marché. Description des effets indésirables sélectionnés : *Expérience depuis la mise sur le marché* : Les effets indésirables graves, spontanés et rapportés au cours d'un traitement par palivizumab entre 1998 et 2002, période couvrant quatre saisons d'infections à VRS ont été évalués. Un total de 1291 cas graves d'effets indésirables, dans lesquels le palivizumab a été administré selon les indications et pendant une saison ont été rapportés. Les effets indésirables sont apparus après la sixième injection ou les suivantes dans seulement 22 cas (15 après la sixième injection, 6 après la septième et 1 après la huitième). Ces effets sont qualitativement similaires à ceux rapportés après les 5 premières injections. Entre 1998 et 2000, le schéma du traitement par palivizumab et les effets indésirables ont été surveillés à l'aide d'un registre d'observance dans un groupe d'environ 20 000 nourrissons. Parmi eux, 1250 nourrissons inclus ont reçu 6 injections, 183 ont reçu 7 injections, et 27 ont reçu soit 8 soit 9 injections. Les effets indésirables observés chez les patients après la sixième injection ou les suivantes ont été qualitativement et quantitativement similaires à ceux rapportés après les cinq premières injections. Dans une étude de base de données, observationelle, post-commercialisation , une faible augmentation de la fréquence d'asthme a été observée chez les prématurés ayant reçu du palivizumab; cependant, le lien de causalité est incertain. Déclaration des effets indésirables suspectés : La déclaration des effets indésirables suspectés après autorisation du médicament est importante. Elle permet une surveillance continue du rapport bénéfice/risque du médicament. Les professionnels de santé déclarent tout effet indésirable suspecté via : **Belgique :** Agence fédérale des médicaments et des produits de santé, Division Vigilance, EUROSTATION II, Place Victor Horta, 40/40, B-1060 Bruxelles. Site internet: www.afmps.be, e-mail: adversedrugreactions@fagg-afmps.be. **Luxembourg :** Direction de la Santé – Division de la Pharmacie et des Médicaments, Villa Louvigny – Allée Marconi, L-2120 Luxembourg. Site internet: http://www.ms.public.lu/fr/activites/pharmacie-medicament/index.html **TITULAIRE DE L'AUTORISATION DE MISE SUR LE MARCHÉ** AbbVie Ltd, Maidenhead, SL6 4UB, Royaume Uni **NUMÉRO(S) D'AUTORISATION DE MISE SUR LE MARCHÉ :** EU/1/99/117/003 & EU/1/99/117/004. **STATUS LÉGAL DE DÉLIVRANCE** Sur prescription médicale **DATE DE MISE À JOUR DU TEXTE :** 08/2017 Des informations détaillées sur ce médicament sont disponibles sur le site internet de l'Agence européenne du médicament : http://www.ema.europa.eu

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Pulmonology - P

Oral Presentations

P 01 **A Novel Imaging Technique for Bronchopulmonary Dysplasia: Functional Respiratory Imaging.**
K. Vanhaverbeke (1), M. Slaats (2), M. Al-Nejar (1), N. Everaars (1), A. Van Eyck (1), B. De Winter (1), K. Van Hoorenbeeck (1), J. De Dooy (1), L. Mahieu (1), J. De Backer (3), W. Vos (3), B. Mignot (3), M. Lanclus (3), A. Mulder (1), S.L. Verhulst (1) / [1] U Antwerp, [2] UZ Antwerpen, [3] Fluidda, Kontich

P 02 **Intrapleural use of tissue plasminogen activator and dornase alfa are successful as treatment of pediatric empyema: a pilot study.**
M. Slaats, J. de Dooy, P. Lauwers, E. Duval, P. van Schil, S. Verhulst, J. Hendriks / UZ Antwerpen

Posters with short oral presentations

P 03 **A case report of a tracheoesophageal fistula successfully managed by Chemocauterization.**
J.C. Beghin (1), N. Lefevre (1), F. Carlier (1), H. Steyaert (1), M. Lopez (2), L. Hanssens (1) / [1] ULB HUDERF, Brussels, [2] University Hospital Vall d'Hebron, Barcelona, Spain

P 04 **Pulmonary embolism in childhood and adolescence: an often forgotten diagnosis.**
J. Lorand, N. Blavier, E. Bodart / CHU UCL Namur-Godinne.

P 05 **Severe paradoxical reaction during anti-tuberculosis therapy: a report of two related infants.**
E. Brandt (1), S. Pasdermadjian (1), O. Gilliaux (1), N. Delvaux (1), SE. Lali (1), V. Mathys (2), F. Mouchet (3) / [1] CHU de Charleroi Hôpital Civil / [2] Scientific Institute of Public Health, Belgian Reference Centre of Tuberculosis and Mycobacteria, Brussels [3] CHU Saint-Pierre, Brussels

P 06 **Diffuse alveolar hemorrhage in an infant: a case report.**
E. Gkogkou, M. Mastouri, H. Boboli, M-C Seghaye / CHR de la Citadelle, Liège

P 07 **Digital clubbing in a seven-year-old boy born in Burundi.**
I. Gonzales, A. Malfroot, C. Ernst, S. Allard, M. Deneyer, Y. Vandenplas, E. De Wachter / UZ Brussel

P 08 **Bronchiolitis with an atypical course: which differential diagnoses to consider.**
K. Van Mechelen,A. Trompenaars, S. Verhulst, K. Van Hoorenbeeck / UZ Antwerpen

P 09 **The prevalence of lower airway anomalies in children with Down syndrome.**
M. De Lausnay, S. Verhulst, L. Boel, M. Wojciechowski, A. Boudewyns, K. Van Hoorenbeeck / UZ Antwerpen

P 10 **Idiopathic acute eosinophilic pneumonia in a teenage girl: a case report.**
N. Blavier (1), M. Thimmesch (2), F. Lebrun (2), E. Bodart (1) / [1] CHU UCL Namur, Dinant, [2] CHC Clinique de l'Espérance, Montegnée

P 11 **Paradoxical response and hepatic dysfunction during anti-tuberculosis treatment.**
C. De Rongé (1), L. Lecomte (2), F. Mouchet (3) / [1] UCL, Saint-Luc, Brussels, [2] Centre hospitalier de Jolimont-Lobbes, La Louvière, [3] CHU Saint-Pierre, Brussels

C 01

The effect of weight loss on endothelial function and sleep-disordered breathing in obese children

M. Ysebaert (1), A. Van Eyck (1), L. Bruyndonckx (1), B. De Winter (1), A. De Guchtenaere (2), K. Van Hoorenbeeck (1), S. Verhulst (1) / [1] Antwerp University Hospital, Edegem, [2] Zeepreventorium VZW, De Haan

Introduction

Obese adolescents can exhibit impaired endothelial function, an early marker of atherosclerosis. Sleep-disordered breathing (SDB) is a prevalent condition in childhood obesity. Studies in normal weight children have shown that SDB is associated with endothelial dysfunction (ED). No studies have yet confirmed this finding in an obese pediatric population.

Aim

The objective of this study was to investigate the effects of an intensive weight loss treatment program on SDB and ED.

Methods

Obese adolescents, aged 11 to 19 years, were recruited at the start of an in-patient weight loss treatment program. All subjects underwent body composition measurements, a sleep screening using a portable device (ApneaLin TM, ResMed, Switzerland) and evaluation of endothelial function measured by peripheral arterial tonometry (EndoPAT 2000, Itamar Medical, Israel) at baseline and after 6 months of treatment.

Results

A total of 62 children were recruited at baseline. Mean age was 15.8 years (11.7 - 19.0), 68% of subjects were boys. BMI z-score at baseline was 2.86 0.41. In 39% of the children SDB was detected. After six months there was a mean decrease in BMI z-score of 0.8 or 26%. Eighty-six percent of cases showed resolution of earlier diagnosed SDB. All children showed significant improvement of endothelial function after an intensive 6 month period of weight loss regimen (p0.001). No correlations between the presence of SDB and improvement in endothelial function could be found. There was no difference in baseline endothelial function between children with and without SDB.

Conclusions

Endothelial function in obese youngsters is significantly improved after intensive weight loss treatment. In this population SDB could not be linked to endothelial function impairment.

C 02

Systemic to pulmonary shunts: morbidity, mortality risk factors and pulmonary tract development

FX. Van Vyve, A. Poncelet, S. Moniotte, J. Rubay, T. Sluysmans / UCL, Saint-Luc, Brussels

Introduction

Nowadays, systemico-pulmonary shunting is still the gold standard for the palliative treatment of congenital cyanotic heart diseases. Despite the progress of medical knowledge and the evolution of surgical techniques, shunt-related morbidity and mortality stay constant over time.

Aim

Our study aims to assess the impact of shunt diameter on such morbidity, mortality and vascular pulmonary tract growth.

Methods

We retrospectively analyzed the records of 138 patients operated at the Cliniques universitaires Saint-Luc (UCL), between 2000 and 2014. Complications, in-hospital mortality, interstage mortality and mortality risks factors have been studied. We also analyzed the growth of the pulmonary tract between palliative and curative surgery.

Results

135 patients undergone systemico-pulmonary shunt placement at a mean age of 182 days (mean weight: 4.6kg), with a mean "shunt-diameter/weight" ratio of 1.21 mm/kg and a mean "shunt index" of 69.2 mm^2/m^2. Most frequent early postoperative complications were the need for postoperative blood transfusion (28.9%), a postoperative infection (21.5%) and a shunt thrombosis (5.9%). Mortality rate up to the curative operation was 12.6% (8.9% for in-hospital mortality and 3.7% for interstage mortality). Significant in-hospital mortality correlated risk factors were female gender, prematurity, central shunt, sternotomy, per-operative use of cardiopulmonary bypass, per-operative use of inotropic drugs, post-operative low cardiac outflow and a highest lactatemia value within 24 or 48 postoperative hours higher than 2.2mmol/l. Up to curative surgery identified mortality risk factors were weight less than 3kg at palliative surgery, prematurity, central shunt, sternotomy, per-operative use of cardiopulmonary bypass, per-operative use of inotropic drugs and a highest lactatemia value within 24 or 48 postoperative hours higher than 2.2mmol/l. Concerning vascular pulmonary tract development, distal pulmonary arteries showed a significant growth at curative surgery (+2.9mm for right pulmonary artery and +3.7mm for the left one), correlated to a significant Nakata index increase of 88.2 mm^2/m^2.

Conclusions

Our study showed that our cohort of patients was operated at a relatively old age, with a trend to use rather large shunt diameters. However, morbidity, mortality and growth of the pulmonary tract were in line with data reported in the literature. Further studies are needed to compare the results of systemico-pulmonary shunts to the results of other alternative treatments becoming increasingly available.

C 03

Use of a biodegradable airway stent to manage airway compression in a child with ALCAPA.

O. Polle (1), A. Durward (2), A. Nyman (2), P. James (2) / [1] UCL, Saint-Luc, Brussels, [2] Evelina London Childrens Hospital, London, UK

Introduction

Anomalous Left Coronary Artery arising from the Pulmonary Artery (ALCAPA) is a rare congenital cardiac malformation where the left coronary artery arises from the pulmonary artery instead of the aorta. At birth the infant is asymptomatic but as the pulmonary artery pressure decreases during the neonatal period, desaturated blood flows under low pressure from the pulmonary artery via the left coronary artery to the left ventricle predisposing to myocardial ischaemia. Furthermore, collateral vessels develop between the right and left coronary arteries causing retrograde flow from the high-pressure coronary arteries to the pulmonary trunk. This is known as myocardial steal and further contributes to myocardial ischaemia which principally occurs in an anterolateral distribution causing global left ventricular dilation and dysfunction. Mitral valve regurgitation is common and secondary to papillary muscle infarction, mitral annular dilation, or both. Left atrial dilation and pulmonary venous congestion ensue. The condition is treated by anastomosis of the anomalous left coronary artery from the pulmonary artery directly to the aorta. Medical therapy provides a bridge to surgery and should be used to optimize the hemodynamics in the patient during the preoperative period. Compression of the airway by the enlarged left atrium can add significant morbidity and mortality, with recurrent chest infections, ventilator dependence and cyanotic death spells as frequent symptoms.

Aim

We report a case of ALCAPA with severe left ventricular dysfunction and mitral regurgitation where a biodegradable airway stent was used in the perioperative period to assist in optimization of the patient post-surgical correction of ALCAPA, to avoid the need for mitral valve repair and to shorten the ventilation period in the postoperative period.

Methods

A 9-month-old infant presented to her local A&E after a minor incidental head injury. A thorough history and examination by the medical team raised the suspicion of congestive cardiac failure as the infant had severe failure to thrive and a history of breathlessness and sweating with feeding. Clinical examination revealed signs of respiratory distress and a pan systolic murmur on auscultation. A chest x-ray showed cardiomegaly and ECHO an enlarged left ventricle with severely impaired systolic function and mitral regurgitation. She was urgently transferred by a specialist retrieval team to the Evelina London Childrens Hospital PICU. After intubation and ventilation a detailed ECHO revealed anomalous origin of the left coronary artery from the pulmonary artery. Urgent surgical correction was planned but delayed as she developed a temperature and had thick bronchial secretions. After a course of antibiotics and physiotherapy the patient underwent complete repair but needed left ventricular assistance for a period of 3 days postop. She was successfully decannulated with inotrope support. Serial echo's revealed slowly improving function. Once stable a bronchoscopy showed significant compression of the left main bronchus from the enlarged left atrium. Given the poor left ventricular function, the significant mitral regurgitation and the airway compression it was decided that extubation was not possible until the airway had been opened by the placement of an Ella biodegradable polydioxanone stent.

Results

Four weeks post ALCAPA repair, a 7 x 20 mm stent was placed successfully under fluoroscopic and bronchoscopic guidance.
She was extubated the day after stent insertion and managed a week off invasive ventilation. The mitral regurgitation did not improve with time and the patient had to undergo mitral valve repair 6 weeks post original surgery.
In 24 months, she underwent 6 stent changings. No complication was reported for the patient. She is now growing well.

Conclusions

Biodegradable stent is a good option for temporary clinical state needs. Studies show less complications when using biodegradable stent rather than metal stent. It must be mentioned that a tiny follow up by chest X-ray and bronchoscopy (after 10-12 weeks) is required as those stents are biodegradable. Complications such as chest infection, risk of stent migration and risk of granulomas have been described but not observed in our patient. Despite needing a mitral valve repair, stenting allowed us to decrease ventilation dependence time and thus, decreased long-term post-intubation complications.

C 04

Association between major sickle cell anemia and dilated cardiomyopathy: an unusual condition

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[2] CHR de la Citadelle, [3] UZ Leuven UZ Sint Pieter

Introduction

Cardiomyopathies (CM) in childhood are uncommon, the most frequent forms are dilated or hypertrophic CM. Among dilated CM, congenital forms due to genetic disorder predominate beside acquired forms due to exposure to infections, toxins or to ischemia.
Sickle cell anemia is associated to cardiac complications due to the hyperdynamic state, to myocardial fibrosis and iron overload, explaining the restrictive physiology. Usually, systolic function is normal.

We describe here the case of a boy with major sickle cell disease diagnosed soon after birth.
He received a treatment based on Folic Acid, Amoxicillin, Hydrourea, and vitamin D.
At the age of 16 months, he was hospitalized for a second vaso-occlusive crisis. In the course of the hyperhydration, he developed weight gain with generalized edema, global discomfort, hepatomegaly and dyspnea with grunting and abdominal bloating.
In this context, a cardiac ultrasound was performed and showed hypokinetic dilatation of the left ventricle with a non-compacted appearance: LVID 50 mm, EF max at 45%, SF max at 23%, IM estimated at ¼ and IT at ¼.
An electrocardiogram was also performed and showed a regular sinus rhythm at 140 bpm, a normal conduction and a diffuse end-stage alteration with signs of left overload. There was no sign of ischemia.
Blood concentration of BNP was increased (24,000 n/l).
A treatment with angiotensin converting enzyme inhibitor, diuretics and carvedilol D was introduced.
Examinations to exclude metabolic- or auto-immune diseases were performed and were negative. Thyroid function was normal. There was no serological argument in favor of a post-infectious disease.
Parents were screened with a normal cardiac ultrasound.
After a period of stabilization under anti-congestive treatment of 2 years, he showed an episode of acute cardiac failure.
Echocardiography demonstrated more extensive dilated cardiomyopathy with extensive right-sided involvement not previously described, with moderate to severe signs of pulmonary arterial hypertension.
An optimization of the drug treatment was therefore set up with close clinical and ultrasound monitoring.
In addition, an invasive assessment confirmed congestive cardiomyopathy with restrictive physiology and pulmonary arterial hypertension.
A myocardial biopsy of the right ventricle was taken for molecular-, histological-, and genetic analysis. The genetic results are pending. But the histology shows a myocardium within the limits of normal. There are no arguments for hypertrophy or iron overload.

Conclusions

Our case reports a rare association between major sickle cell anemia and dilated cardiomyopathy with systolic and diastolic dysfunction and pulmonary hypertension. Besides the deleterious effect of anemia, chronic tissue hypoxia might also be responsible for myocardial remodeling with loss of both systolic and diastolic function.

C 05

Cardiac papillary fibroelastoma of a bicuspid aortic valve: a case report and review of the literature

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Introduction

We report the case of a 15-year-old boy with papillary fibroelastoma on a bicuspid aortic valve, discovered accidentally during transthoracic echocardiography conducted for chest pain. The initial echocardiography, performed in 2012 for thoracic pain and palpitations, only showed bicuspid aortic valve without stenosis. However, on the recent echocardiographic examination bicuspid aortic valve was confirmed, and a round mobile mass, approximately 8 mm in diameter, on the ventricular side of the aortic valve, projecting at the free edge of the two leaflets was visualized. An ECG-gated cardiac computed tomography and cardiac magnetic resonance imaging confirmed the presence of a bicuspid aortic valve and showed a nodular lesion of 6x7 mm, evoking a fibroelastoma, just below the raphe connecting the non coronary and right coronary cusp. The patient is scheduled for elective surgery.

Aim

Case Report

Conclusions

Cardiac papillary fibroelastomas (CPFE) are rare primary cardiac tumors, arising from the cardiac endothelium and affecting primarily the heart valves. The pathogenesis of CPFE remains uncertain, but several possible explanations have been reported, including endothelial damage, iatrogenic factors, organizing thrombi, etc. Although papillary fibroelastomas are benign tumors, they have potential life threatening complications such as sudden death, stroke, and myocardial infarction. Historically, papillary fibroelastomas were discovered incidentally at autopsy or during heart surgery. With the advent of transthoracic and transoesophageal echocardiography, diagnosis of this lesion in living patients have been possible, and an aggressive treatment approach has evolved to prevent catastrophic cerebral or coronary embolization. In some cases, magnetic resonance imaging and/or ECG-gated cardiac computed tomography may be used to assist in the diagnosis of CPFE. Due to the higher risk for embolization in paediatric population, prophylactic tumor excision is considered to be the treatment of choice, even in asymptomatic patients.

C 06

Congenital cardiac malformation in spinal muscle atrophy: clinical case and review of literature

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Introduction

A new-born boy was transferred to our centre soon after birth due to profound hypotonia at birth. Cardiotocograph traces were normal. He was born at 38 weeks gestation by vacuum-assisted vaginal delivery needing ventilation from birth on for absent respiratory effort. Apart from the profound hypotonia he also had joint contractures and lacked primary reflexes. Due to the pronounced clinical picture a neuromuscular disease was suspected. The diagnosis of spinal muscular atrophy (SMA) type 0 was confirmed by multiplex ligation-dependent probe amplification showing a homozygotic deletion of exon 7 and 8 of the SMN-1 gene and a homozygotic co-deletion of the neuronal apoptosis inhibitory protein (NAIP) gene might explain the phenotype severity.

He was the second child to unrelated Caucasian parents with no family history of neuromuscular nor congenital cardiac problems. Fetal ultrasound at 12 weeks gestational age showed an increased nuchal skin fold thickness. Additionally, amniocentesis was performed and showed a normal micro-array. Fetal ultrasound at 34 weeks gestation showed an enlarged right atrial appendage with no other apparent associated defects. The pregnancy was further uneventful with normal fetal movements. Postnatal echocardiography showed a large atrial septal defect with a virtually common atrium, an enlarged right atrial appendage and an apical muscular ventricular septal defect.

In view of SMA type 0 a joint decision was made with the parents to discharge their child with an ambulant palliative care plan as these type of SMA usually die within 6 months postpartum. Our patient died due to respiratory insufficiency at the age of 16 days.

Aim

Aim of the study was to review the literature to identify all articles that could claim a potential link between SMA and congenital heart disease

Methods

We searched MEDLINE for articles on SMA and cardiac pathology published up to September 30th 2017, using a combination of the following terms: spinal muscular atrophy AND cardiac, heart OR congenital heart disease.

Results

With a live-birth prevalence of 1 in 6.000 SMA is the most common inherited motor neuron disease. More so, it is the leading genetic cause of infantile death. SMA is an autosomal recessive disorder due to homozygous loss of the survival of motor neuron-1 (SMN-1) gene on chromosome 5. The resulting reduced SMN protein levels lead to progressive muscular atrophy by loss of functional motor neurons and degeneration of the anterior horn cells of the spinal cord. In humans a copy gene, SMN-2, is expressed as result of inversion and duplication. SMN-2 is nearly identical to SMN-1, but cannot fully complement the SMN-1 deficiency in SMA because the majority of SMN-2 derived transcripts are spliced alternatively, leading to an unstable protein lacking the 16 amino acids encoded by exon 7 of chromosome 5q. Mutations in SMN-2 have no clinical consequence if intact SMN-1 is present. Complete loss of

SMN is embryonic lethal, as SMN performs a vital function in global gene expression through small nuclear ribonucleoproteins (snRNP) biogenesis in all tissues. So, defects not only confined to the motor neurons would be expected. SMA type 0 is characterised by fetal onset and the following clinical features at birth: areflexia and paucity of movement in limbs, face and trunk. Because of this there are congenital muscle atrophy and contractures. This severe type SMA requires mechanical ventilation support from birth on.

Originally, congenital heart disease (CHD) was regarded as an exclusion criterion for SMA. Though, recently there have been an increasingly number of case reports of co-existing CHD with severe SMA. The exact nature and cause of CHD in severe SMA remains unknown. The fetal akinesia in severe SMA could hypothetically lead to structural cardiac defects by means of altered expression of growth factors by changed cardiac flow. However, the heart is embryologically formed before fetal movements arise from muscular activity. SMN1 probably plays a more immediate role in cardiogenesis as SMN1 protein is expressed in heart muscle. Mouse models have shown that in a severe model (Smn-/-, SMN2+/+) the cardiac remodeling already initiates at the embryonic stage, before the motor neurons are seemingly affected. This link is not reported in milder forms of SMA. This difference might be attributed to the present number of SMN2 copies. So, further studies are required to investigate the role of SMN on cardiogenesis.

Conclusions

Complex congenital heart disease should be considered as an additional cause of morbidity and mortality in the severe SMA phenotype. Further studies are required to investigate the role of SMN on cardiogenesis.

C 07

Non syndromic supravalvular aortic-, supravalvular pulmonary- and peripheral pulmonary artery stenosis in an infant: a rare association

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Introduction

Case report:
Supravalvular (SV) aortic stenosis (AS), isolated or associated with SV pulmonary stenosis (PS)- and/or peripheral pulmonary arteries stenosis (PPAS), is typically encountered in patients with Williams-Beuren Syndrome (WBS).

Aim

We report here the case of an infant of Indian origin, without any contributive family history, in whom a heart murmur was identified after birth.

Methods

Investigation by heart ultrasound came back normal. The persistence of the heart murmur suggestive of an organic origin, led to a control examination at 2 months. Echocardiography showed then pathological PPAS.
3 months later, additional moderate to severe SVAS was diagnosed.
An angio-CT-SCAN confirmed echocardiographic diagnosis. Renal artery ultrasound was normal.

Results

Although the cardiac defect is typical of WBS, the infant does not display any facial stigmata. The boy has a round face, large eyebrows, normal iris, no hypertelorism, bilateral epicanthus, everted lower lip, normally positioned ears with mildly large lobules.
Genetic testing, by array-Comparative Genomic Hybridization (a-CGH) ruled out any microdeletion/microduplication, within the limits of +- 100Kb resolution.
At 9 months, the patient has a normal development but feeding problems (vomiting, gastro-esophageal reflux) that had been explored and treated medically. He also had a right-sided inguinal hernia for which he had surgical repair.

Conclusions

Discussion:
SVAS, SVPS associated with PPAS are different clinical entities but they underlie identical lesion phenotype. Indeed, both may be caused by elastine gene (ELN) haploinsufficiency and belong therefore to elastin arteriopathies. ELN is one of the 28 genes possibly deleted in WBS, and point mutations in this gene have also been identified in patients with sporadic and familial autosomal dominant SVAS. In both syndromic and non-syndromic cases, other arteries can also be involved (renal-, cerebral-, coronary arteries) but far less frequently. So far, no other gene has been involved in non-syndromic SVAS, but the genetic cause remains unknown for several families. In the absence of family history and clear dysmorphic features, the phenotype in our patient is suggestive of a de novo ELN point mutation.

C 08

Unusual cause of thoracic pain and raised cardiac markers: a case report

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Introduction

Thoracic pain is a common presenting symptom in pediatrics and mostly has a musculoskeletal origin. Only 1-5% of cases have an underlying cardiac cause, most commonly caused by peri(myo)carditis.

Aim

Review causes of thoracic pain in children with respect to our case.

Methods

A 14-year old boy presented at a local hospital with stabbing retrosternal pain without radiation with repetitive similar complaints for a year. This pain was unrelated to respiration, position or exercise. He had no history of palpitations, syncope, nor infection. Raised creatine kinase and Troponin T levels, respectively 4280U/L and 2536ng/L, were observed. ECG showed ST-elevations anterolaterally. Chest x-ray was normal. He was given acetylsalicylic acid as recurrent or chronic pericarditis was suspected.

Personal history included only ADHD, for which he took Equasym (methylphenidate) for 1 year as only medication. Family history was unremarkable.

He was transferred to our center and was hemodynamically stable on arrival with normal clinical examination. Echocardiography showed a structurally normal heart with slightly diminished systolic function based on septal hypokinesia and no pericardial fluid. To exclude drug-induced cardiotoxicity Equasym was discontinued. The day after admission chest pain worsened with rising cardiac enzyme levels. Coronarography showed no visible coronary disease. Endomyocardial biopsies showed no signs of myocarditis, nor inflammation. Further work-up could not withhold an infectious cause. Under acetylsalicylic acid the clinical picture improved with subsiding of the chest pain and lowering of cardiac enzyme levels.

Three months later, he represented with chest pain and raised cardiac markers. Slightly enlarged calves were noted, without exertional complaints. This clinical sign raised our suspicion of a muscular dystrophy. Genetic analysis confirmed Becker Muscular Dystrophy (BMD).

Results

BMD is a X-linked recessive defect of the dystrophin gene. In contrast to Duchenne Muscular Dystrophy were the dystrophin protein is lacking, in BMD this is partially functional, explaining the later and milder presentation in BMD.
The incidence of BMD is 1:19.000 male births. Mean age of onset is 12 years, usually with musculoskeletal symptoms. In rare cases cardiomyopathy may be preceding. Frequency of cardiac involvement is 60-75%, while the average age of first cardiac involvement is 28 years.

Conclusions

Cardiomyopathy may be the initial presentation of Becker muscular dystrophy, although rare.

C 09

Pheochromocytoma in a 11 year old girl with acquired long QTc and aortic root dilation

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Introduction

We report the case of a 11 year girl who has been presenting a severe alteration of her general state for one month with asthenia, orthostatic dizziness, headaches, abdominal pain.

Laboratory examination had revealed moderate inflammation (leucocyte count : 13.440/ml ; CRP : 30 mg/L) but increased sedimentation rate (68 mm), and slightly increased glycemia (106 mg/dl) with normal insuline concentration. Urine analysis showed bacteriuria. On that base, she received a treatment by sulfamethoxazol (Bactrim).

She did not improve and was referred to our institution for endocrinology and cardiology advice.
Physical examination confirmed recent weight loss (2,5 kg in 10 days), arterial hypertension (147/104 mmHg) in decubitus with lower blood pressure (80/60 mm Hg) in orthostasis, normal heart rate (HR : 70/min.), SaO2 : 99%.

The patient was pale with wet and cold extremities. Precordium was hyperactive, no murmure was auscultated, cardiac sounds were normal. Lung- and abdominal examination was normal.
ECG showed left ventricular hypertrophy (LVH) with non specific repolarisation disorder and markedly prolonged QTc (470 msec.).
Echocardiography demonstrated global LVH with dilated aortic root (Z-score : 2,5) and grade I aortic insufficiency.

Oral glucose tolerance test showed moderate hyperglycemia associated with hyperinsulinemia. Cortisol and thyroid hormone serum levels were normal. Urine catecholamines were strongly increased (urinary noradrenaline >711μg/ 24H, normetanephrine >9000 μg/24H).

Abdominal sonography showed normal kidney but, the presence of a right-sided adrenal mass wich was confirmed by magnetic resonance. MIBGI123 scintigraphy indicated fixation on the right adrenal gland.
The patient was scheduled for surgery and stabilised until then by beta-blockers and calcium chanel blockers, allowing to control blood pressure and to normalise QTc duration.

Cardiac examination performed 2 weeks after right sided adrenalectomy showed residual LVH but normalisation of the aortic root dimension (Z-score : 0,7).

Pheochromocytoma in children is a rare tumor the diagnosis of which might be difficult due to the aspecific and confusing clinical signs, as it is demonstrated by this case. In children, pheochromocytoma is more frequently associated with other familial syndromes, such as neurofibromatosis, von Hippel-Lindau disease, tuberous sclerosis, Sturge-Weber syndrome, or multiple endocrine neoplasia syndromes. The genetic diagnosis is crucial for further follow-up.

In our patient, from the cardiological point of view, arterial hypertension with orthostatic hypotension, prolongation of QTc , LVH and dilated aortic root, that we postulate to be secondary to the rise of systemic vascular resistances, were acquired alterations, secondary to huge catecholamine secretion.

Conclusions

In conclusion, our case demonstrate acquired electrophysiological and morphological cardiological complications due to catecholamine excess caused by a pheochromocytoma in a child.

D 01

Case report of a 5 year-old child presenting an idiopathic linear IgA bullous dermatosis.

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Introduction

Linear IgA bullous dermatosis (LABD) is a rare auto-immune bullous disease characterized by a linear deposition of IgA against antigens along the basement membrane zone, leading to subepidermal cleavage and appearance of tense bullous lesions with fluid content.

LABD can be idiopathic or triggered by a drug (most often vancomycin, but also nonsteroidal anti-inflammatory drugs, antihypertensives, antiepileptics ...).

With an incidence of 0.5 to 2.3 cases per million individuals a year, the disease is characterized by two peaks of onset : first peak between 6 months and 10 years, and second peak after the age of 60.

The clinical presentation is heterogeneous with skin lesions, mucosal lesions or both locations. Linear IgA bullous dermatosis in children most often shows widespread blistering lesions on healthy, erythematous or urticarial skin. New blisters often appear at the periphery of old bullae, resulting in annular marks, often described as « strings of pearls » or « crown of jewels » or « rosettes ». Distribution differs between adults and children. In childhood, the most involved areas are: limbs, perineum and lower abdomen. Other sites are: feet, hands and face.

The physiopathological mechanisms remain unknown but humoral and cellular immune response could be involved.

In order to establish LABD diagnosis, biopsies are made in lesional skin for histology and in peri-lesional skin for direct immunofluorescence. The histological findings are non-specific: subepidermal blisters with a neutrophilic infiltration. The gold standard for LABD diagnosis is direct immunofluorescence, which shows linear IgA deposits along the basement membrane zone. The research of circulating antibodies is inconsistently positive. If in doubt, immunoblotting and electronic immunomicroscopy can be used to confirm the diagnosis.

Concerning drug-induced LABD, stopping the triggering drug allows a quick healing.

The treatment of idiopathic LABD is based on dapsone. Colchicine, sulfapyridine and systemic corticosteroids are kept in case of dapsone failure or intolerance only. Some publications report the interest of first-line antibiotherapy on children.

Results

We report the case of a 5-year-old boy with a linear IgA bullous dermatosis.

As a first step, the patient sought medical attention at the pediatric emergency department of our hospital: he complained of bullous lesions mainly on the lower limbs and behind the ears, which had been lasting for a month. The child hadn't taken any medication during the days before the bullous eruption. The diagnosis of impetigo was made. In ambulatory care, a treatment by flucloxacillin was started because of the extent of cutaneous lesions.

As a second step, 5 days later, the clinical examination revealed an extension of the eruption. The patient showed several tense bullous lesions with clear liquid content

surrounded by an indurated erythema of a few millimeters on the hands, behind the ears and on the legs. The patient reported that they were painful and pruritic, especially during the night. Given the extent of the eruption, a biological assessment was carried out showing a slight increase of IgA to 2.5g/l (N: 0.25 - 1.6 g/l from 4 to 6 years old) but no sign of inflammation. A skin biopsy was made for histological analysis and for direct immunofluorescence test. The direct immunofluorescence showed linear deposit of IgA along the basement membrane and confirmed the diagnosis of linear IgA bullous dermatosis. A treatment with dapsone was started. The patient continues his follow-up in dermatology with frequent hematologic monitoring.

Conclusions

We report the case of an idiopathic LABD diagnosed on a 5-year-old child. The aim is to increase awareness of this rare disease. We discussed the diagnosis, physiopathology, triggering factors, clinical data and treatment of this pathology. In any case of LABD, a triggering drug must be sought and stopped. Dapsone is the reference treatment for idiopathic forms. However, it should be carefully used due to the risk of side effects. Therefore, frequent hematologic monitoring is necessary.

D 02

Acute febrile purpuric rash in young infants: if sometimes we should not fear for the worst?

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Introduction

Case report:
A 4 month-old boy was brought to the emergency department in our hospital by his mom with an acute rapidly progressive purpuric rash and a fever at 38.7°C. He remained in a good general status despite a previous admission to another hospital for 4 days for a viral bronchiolitis (influenza A virus found in naso-pharyngeal aspirate).

Aim

He was born at 37 2/7 weeks of gestation from a twin pregnancy, and has always been in perfect shape until last week when he has caught the first virus at daycare with his sibling. He received vaccinations on time, his growth was excellent and we did not deplore any medical history in the family.

Methods

His vitals in the emergency room were the following: Weight 7.6kg (P90-97), height 65cm (P90), cranial perimeter 43cm (P90), temperature 37,0°C, blood pressure 101/70 mmHg, heart rate 170bpm, SpO2 97%, respiratory rate 35/min. Physical examination revealed a polypneic, crying, not irritable and tonic infant, with normotensive fontanel, clear nasal discharge, red throat, bilateral serous otitis, numerous purpuric spots and necrotic areas on the ears and the feet with diffuse edema predominantly on the ears and the feet. Cardiopulmonary auscultation and abdominal examination were normal.
We performed a blood test: Coagulation was normal, platelets count was 654 000/μl, hemoglobin level was 12.1g/dl, WBC count 13 700/μl (42.9% PNN), CRP 28mg/l, albumin level 34g/l. We also performed 2 peripheric blood cultures followed by empiric antibiotherapy with Ceftriaxone and Clindamycin. He was transferred to Pediatric Intensive Care Unit for further surveillance. In the next days, our patient remained perfectly stable, did not present any more fever and the purpuric rash did not extent more. Blood cultures remained negative as well as the serologic tests for Cytomegalovirus and Epstein-Barr virus. The Urine sample did not show any proteinuria or any other abnormalities. He was discharged after 2 days of surveillance without any treatment and was followed up by a dermatologist who has seen the rash and the edema completely resolved in a few days.

Results

Discussion:
This 4 month-old boy presented a typical form of acute hemorrhagic edema of infancy without any further complication. It is a small vessel vasculitis of young infants, a benign disease with rare extra cutaneous involvement. The etiology of this pathology remains unknown but we note that there is often a viral trigger. It does not require any specific treatment but can be confused with meningococcemia or other severe bacteremia with the acute clinical presentation and rapidly progressive purpuric rash, an history of fever in the anamnesis, and always make us fear for the worst. Other differential diagnosis might be urticaria, Henoch-Schonlein purpura, erythema multiform and Kawasaki disease.

Conclusions

Acute hemorrhagic edema of infancy is an idiopathic affection, which is more and more described in the literature and is definitely a differential diagnosis that needs to be taken into account while working in a pediatric emergency department.

D 03

Infantile Digital Fibromatosis : A Rare Benign Fibroproliferative Tumor in Early Childhood.

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Introduction

Infantile digital fibroma is a rare benign tumor made up of mostly myofibroblasts. Approximately 200 cases were reported in the literature.This entity was first described by Reye in 1965 as recurring digital fibrous tumor of childhood. It appears almost exclusively on the digits of the hands and feet, rarely involving the tumb or big toe.

Aim

A 15-month-old preterm born Caucasian boy presented at the age of 6 months with two reddish, confluent, small painless, indurated, well-circumscribed nodules on the fifth digit of the left foot, which rapidly increased in size. There was no history of trauma or inflammation. The other foot and both hands were unremarkable. None of the family members had similar lesions. There was a slight functional impairment for walking. Futher clinical examination was normal except a prenatal known hydronephrosis of the left kidney.Rontgen examination revealed the cutaneous and subcutaneous location of the lesion without bone or joint involvement.

Methods

A biopsy of the lesion was performed. Skin biopsy consisting of epidermis and underlying dermis. The epidermis has a preserved layering and maturation. No cytonuclear atypia. The dermis contains a cell-poor coil cell proliferation of (myo) fibroblasts with an eosinophilic cytoplasm and intervening collagen. In the cytoplasm we find scattered eosinophilic (hyaline) inclusions. The cells contain a normochromatic, oval core without atypical features.
Immunohistochemical research:
- The cytoplasmic inclusions clearly turn red on a Trichrome stain, but do not color for PAS.
- The spindle cells of the lesion strongly and diffusely diffuse for alpha-SMA and desmin.
- They do not color for CD117 and we also do not see nuclear beta-catenin staining.

Results

We can conclude that the final diagnosis is infantile digital fibromatosis. A topical treatment with a steroid cream is prescribed. Conservative management is being followed.

Conclusions

Infantile digital fibromas are benign tumors that can appear worrisome. These lesions typically appear on the second to fifth digits on the hands and feet of children during the first 2 years of life. Microscopically, they usually have inclusion bodies, typically to identify this lesion as a benign type of fibromatosis. The inclusion bodies are made up of actin filaments. The best treatment is "wait and see", because of their propensity to spontaneously regress and the complications that are described by surgery. However in huge lesions , new intralesional injections with steroids appear to be promising for inducing faster regression.

D 04

Recurrent superficial lymphangitis after insect bites

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Introduction

Superficial lymphangitis is commonly described in association with acute bacterial infections such as Staphylococcus or Streptococcus infections and is treated with systemic antibiotics.
However, nonbacterial causes of lymphangitis exist and are underrecognized.

Aim

We would like to present cases of lymphangitis after insect bites, to broaden the clinician's differential diagnosis and avoid misdiagnosis and unnecessary antibiotics.

Methods

We report two cases of recurrent superficial lymphangitis after insect bites. Children were hospitalized in Grand Hôpital de Charleroi between 2016 and 2017.

Results

The first case affects a seven-year-old girl visiting our paediatrics emergency department for a linear eruption on her left arm after an insect bite on her left thumb. Besides, an important left periorbital oedema appeared after an insect bite localized around her eye. The linear eruption extended from the left thumb - corresponding to the insect bite area - to the left axillary fold. The site of the insect bite is pruritic, albeit not painful. Clinically, she had a good general state and did not develop fever. No lymphatic enlargement was noticed. Biology did not show any inflammatory syndrome either. After extended anamnesis, we noticed that it had been her third lymphangitis in three months. The two previous ones had also succeeded insect bites. During these eruptions she had also maintained good health without fever and had been treated with intravenous antibiotics (oxacilline), which had resulted in good recovery and the disappearance of the eruption after a few days.
After consulting literature, we thought of a nonbacterial cause of lymphangitis and decided to treat this patient with topic corticoids and antihistamines. The eruption disappeared in 24 hours and she maintained a good general state.
The second case affects a four-year-old boy who had an insect bite located on his fifth toe. Within a few hours, the redness of the bite grew to form a linear streak on the back of the foot. Except for the pain due to the bite, he had no complaints, an excellent general state and did not develop fever. Biology did not show any inflammatory syndrome or hyperleukocytosis. The boy has had no medical history apart from two similar lymphangitis after mosquito bites for the last two years. He had each time been treated with intravenous antibiotics. We also started with antibiotics and after 48 hours, the lymphangitis had disappeared. However, when considering the anamnesis, clinical exam and biology, it was most likely a second case of recurrent superficial lymphangitis and antibiotics should not have been used.

Conclusions

Superficial lymphangitis after an insect bite without any systemic signs, fever or lymph node enlargement and with normal C-reactive protein is probably the result of an immunoallergic reaction. Literature hypothesized that toxins are drained by the lymphatic system and migration of inflammatory cells induce a linear eruption mimicking acute bacterial lymphangitis. Biopsy can occasionally help to diagnose but

is rarely needed. Therefore, the use of antibiotics must not be considered for recurrent or multifocal superficial lymphangitis after insect bites without any systemic signs. Only a symptomatic treatment is helpful.

D 05

Cutaneous necrosis of the foot secondary to local Ketoprofen application

K. Farhat, A. Anthopoulou, M-C Seghaye / ULg, CHU Liège

Introduction

A 14 year old boy presented in the emergency department with cellulitis of the left foot.

Aim

Six days before, he went to a school race. A slight pain in his left foot appeared a few hours later without any visible wound. The next day, he underwent clinical examination and radiography of the foot that was normal. The patient was discharged with a local treatment by Ketoprofen (Fastum).

Methods

Two days later, he consulted his famiy doctor because of absence of an improvement, for the pain and appearance of redness on the foot. A blood test was performed that showed a slight inflammatory syndrome (Leukocytes: 7.000/mm³; CRP: 30mg/L) so a treatment with amoxicillin, paracetamol and ibuprofen was started.
Three days later, despite this treatment, the redness increased and the pain was still present. The child came to our pediatric emergencies. He had fever since the beginning of the day and a blister could be observed at the medial metatarso-phalangeal joint. Laboratory examination showed an increased inflammatory syndrome (Leukocytes: 7.860/mm³; CRP: 120mg/L). The blister was pierced and a sample was taken. The child was then hospitalized for dual intravenous antibiotic therapy with Clindamicin and Flucloxacillin in addition to local care.
The next day, the localized erythema increased up to the ankle and the palpation showed an accumulation of pus under the blister.The abscess was then unbridled by the surgeon.
Initially , a 25 cm isobetadine wick was needed for local care. Quickly, the gauze plugging of the wound decreased and the healing was evolving properly.

Results

The sample taken finally showed the presence of S. Pneumoniae in the wound.
An MRI was also performed during the patient's hospitalization in order to check the presence of underlying osteoarthritis. It was well present in the first 2 phalanges of the second ray of the foot.
Antibiotic therapy was then continued at home for 3 weeks in addition to local care.
Currently, antibiotic therapy has ended and local care needs to be performed on daily basis until complete healing.

Conclusions

We hypothesize that Ketoprofen gel caused cellulitis in our patient, since there was no open wound on his foot. Of course, a superinfection occurred. But also knowing that no study shows this side effect of the Ketoprofen gel, it would be prudent to remain alert to the use of this preparation in the pediatric population.

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Thursday March 8, 2018

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Room 201 A/B

Speaker: Anna Prugnola
Global Medical Education Lead GSK Vaccines

Moderator: Marta Moreira, MD
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M 01

Overweight and insulin resistance in metabolic diseases requiring a high carbohydrate diet.

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Introduction

In glycogen storage diseases (GSD) and fatty acids oxidation defects (FAOD), patients are treated with fasting avoidance and high carbohydrate diets to avoid hypoglycemia.

Aim

Our aim was to investigate overweight and insulin resistance (IR) as potential side effects of these dietary regimens.

Methods

We retrospectively analyzed data from 60 patients aged 5 months - 44 years (median 10 years), 33 with GSD and 27 with FAOD. Overweight was defined as ideal body weight percentage >110%, and obesity as > 120%. IR was defined as HOMA index >2.5 and/or plasmatic glucose/insulin ratio < 6.

Results

Overall, 13/60 (21.7%) patients were overweight/obese (11 GSD versus 2 FAOD; p=0.03). The prevalence of overweight in our cohort was similar to the Italian pediatric population (21.7% versus 27.2%; p=0.4), except for < 6 years GSD patients who presented more overweight (66.7%; p<0.01). IR was found in 9/29 patients (31%) (4 GSD versus 5 FAOD; p=1). Mean HOMA index in our overall cohort was comparable with Italian pediatric population for normal weight (1.79 ± 1.66 versus 1.49 ± 0.91; p=0.21), and for overweight/obese patients (4.06 ± 3.72 versus 4.18 ± 2.16; p=0.9). FAOD normal weight patients had a higher IR prevalence compared to Italian normal weight pediatric population (21.4% versus 2%; p=0.02).

Conclusions

High carbohydrate diets did not appear associated to overweight and insulin resistance in our overall cohort. However, GSD patients younger than 6 years showed more overweight compared to Italian children, while FAOD normal weight patients of all ages showed more IR.

E 01

Birth weight in the offspring of obese mothers: comparison of bariatric surgery pre-pregnancy to lifestyle intervention during pregnancy

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Introduction

Bariatric surgery before or lifestyle interventions during pregnancy can influence the birth weight in the offspring of obese mothers.

Aim

To compare the birth weights of the offpsring of mothers who underwent bariatric surgery before pregnancy to obese mothers who underwent a lifestyle intervention during pregnancy.

Methods

Secondary data analysis on combined, previously published study populations of PABAS (Pregnancy After Bariatric Surgery) and a Randomized Controlled lifestyle intervention during pregnancy for obese mothers was performed. Descriptive statistical analyses were complemented by one-way ANOVA and Chi-square tests.

Results

A total of 184 pregnant women with a mean age of 29.2 (+/- 4.3) years and pre-pregnancy BMI of 32.1 (+/- 4.9)kg/m² were included. Forty-nine (26.6%) underwent bariatric surgery before pregnancy, 88 (47.8%) participated in a lifestyle intervention and 47 (25.5%) underwent no intervention. Prevalence of smoking during pregnancy was significantly higher in women after bariatric surgery (24.5% vs 5.7% and 14.9%; p=0.007), contrary to prevalence of chronic (10.2% vs 18.6% and 24.4%; p=0.021) and pregnancy-related hypertension (0% vs 30.2% and 31.1%; p<0.001). Mean total gestational weight gain and rates of excess of the Institute Of Medicine (IOM) guidelines, mean gestational duration and parity did not differ significantly across the groups. Mean birth weight SDS was significantly lower in the offspring of women after bariatric surgery compared to the lifestyle intervention and control group (F(2,181)=5.34; p=0.006; -0.33 SDS vs +0.19 SDS and +0.12 SDS).

Conclusions

Bariatric surgery before pregnancy results in lower birth weight compared to a lifestyle intervention during pregnancy despite comparable gestational weight gain and lower arterial blood pressure. The long-term consequences on childhood body composition need additional investigation.

E 02

New algorithm for modification of insulinotherapy during exercise in MDI and insulin pump-treated children with type 1 diabetes

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Introduction

In type 1 diabetes (T1D), exercise is the third essential component in blood glucose (BG) regulation after insulin and dietary management [Dr Joslin, 1950s]. Although the evidence for a positive effect of exercise on glycemic control (i.e. HbA1C) is weak, there is growing evidence for benefits of regular physical activity on cardiovascular risk factors. Today, clear recommendations are lacking for insulin dose adaptation during physical activity, especially for children under insulin pump therapy. Furthermore, the available guidelines were not based on evidence arising from clinical trials and do allow individualization of care.

Aim

To determine the influences of algorithm-based insulin adaptation on the evolution of subcutaneous glucose (SG) after a standardized aerobic exercise in children and adolescents treated with continuous subcutaneous insulin infusion (CSII) or multiple daily injection (MDI) regimen.

Methods

Eleven CSII- and 13 MDI-treated patients performed two 30-minute sessions of moderate to vigorous (70% of age-based maximal heart rate) exercise on a treadmill under continuous glucose monitoring (CGM). First sessions were scheduled without insulin modification (TT#1) while patients performed second sessions (TT#2) after preemptive algorithm-based insulin dose modifications.

Results

CSII-treated patients had their glucose control improved during TT#2 (mean of 141 ± 56 mg/dL vs 144 ± 80 mg/dL in TT#1; $P<0.05$) with up to 86% of SG levels within targets during 16 hours post-exercise. Contrarily, SG levels did not normalize during TT#2 in MDI-treated patients who experienced higher rates of hyperglycemia during the afternoon snack. Insulin adaptations did not modify immediate post-exercise drops in blood glucose during TT#2 in either group. As compared to TT#1, CSII-treated patients had reduced rates of hypoglycemia during 4 hours post-TT#2 (from 19.5% to 2.1%; $P<0.01$) and had shorter duration of nocturnal hypoglycemia (35.5 ± 12.8 vs 204.7 ± 165 minutes; $P=0.04$) whereas in the MDI group no changes in percentages of hypoglycemia were observed during TT#2.

Conclusions

Our study shows the differences existing between pump and MDI-treated children and adolescents in their potential to bring glucose levels within therapeutic targets during and after aerobic exercise. Using tailored algorithmic adaptations of insulin administration, CSII users were more successful than MDI-treated patients in alleviating their rates of hyper- and hypoglycemia during most of the 24-hour periods following exercise. This advantage may partly be accounted on higher levels of precision in fine-tuning insulin adjustments under CSII therapy, as no quantitative and qualitative differences in self-monitoring and adjusted insulin dose were observed between groups.

E 03

A novel mutation of the AMHR2 gene in twin brothers with Persistent Müllerian Duct Syndrome

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Introduction

In 46, XY boys with bilateral cryptorchidism or with unilateral cryptorchidism associated with an inguinal hernia, the possibility of Persisting Müllerian Duct Syndrome (PMDS) should be considered. Anti-Müllerian hormone (AMH) gene and AMHR 2 gene mutations are the most frequent genetic causes of PMDS.

Aim

To report a different clinical presentation of a novel mutation in the AMHR 2 gene in MCDA twin boys.

Methods

Case report based on data from the electronic medical records.

Results

The MCDA twin brothers were born at 36 weeks after an uneventful gestation with a normal birth weight and length. Both consanguineous Turkish parents were healthy, but their two older female children have an unexplained retinitis pigmentosa. Bilateral cryptorchidism without penile abnormalities was noted at birth in both boys, but inguinal testes were suspected at ultrasound. No further examinations were performed. At referral at the age of 14 months, physical examination of the first boy revealed a normal scrotum and penile length, whereas the second boy had an underdeveloped scrotum, both in absence of inguinal hernias. Both infants had a body weight of 7.93 kg (-0.86 SDS), body length of 79.5 cm (+0.18 SDS) and a synophrys and slight hypertrichosis. Serum testosterone level (respectively 5.98 μg/L and 6.21 μg/L) as well as serum dihydrotestosterone level (0.50 μg/L and 0.56 μg/L) increased normally after hCG in both boys. A normal 46, XY karyotype was found. At laparoscopic exploration, a crossed fused ectopia of the left testis was found in the first boy, whereas in the second an atrophic vas deferens and a fallopian tube was discovered. A novel homozygous mutation (Asp491Glu) in the AMHR2 gene was found by Saenger sequencing in both boys. This mutation is probably responsible for the persistence of the fallopian tube, given the known pathogenic effect of a (Asp491His) mutation.

Conclusions

A crossed testicular ectopia and female type of PMDS was found in twin boys with a novel AMHR 2 gene mutation.

E 04

Integration Of Routine Parameters Of Glycemic Variability In A Simple Screening Method For Partial Remission In Children With Type 1 Diabetes

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Introduction

In type 1 diabetes (T1D), there is a longstanding autoimmune attack of pancreatic beta cells recognizable by seroconversion of specific antibodies, that develops on genetic susceptibility grounds and leads to symptomatic insulinopenia when beta-cell mass is drastically reduced. Since the fall of insulin stores is abrupt, it is thought that dysregulation of glucose homeostasis is contemporaneous to overt onset (i.e. polyuria and polydipsia) of the disease. Alleviation of hyperglycemia by administration of exogenous insulin is accompanied in about 60% of patients by a rapid reduction of daily insulin requirements (DIR) for maintenance of normal glycemia and HbA1C levels. This defines a transitory state of partial remission (PR) (or honeymoon period) with residual beta-cell function, improved insulin sensitivity and reduced risk of severe hypoglycemia (SH).
The definition of PR, being of particular clinical importance, has been variously addressed, and remains a matter of debate. The Hvidoere Study Group on Childhood Diabetes proposed the identification of remitters using the insulin dose-adjusted hemoglobin A1C (IDAA1C) formula, which strongly correlated with residual beta-cell function estimated by stimulated C-peptide levels during mixed-meal tolerance test, when being lower or equal to 9.
A common feature of clinically meaningful PR is that patients harbor low levels of glycemic variability (GV) (e.g., standard deviation, coefficient of variability, percentage of normoglycemia), which is a recognized feature of residual beta-cell function since more than three decades. As opposed to DIR, parameters of GV might per se represent a better assessment of PR since it only refers to objective measures, whereas for patients without electronic logs of insulin doses, correction units may not always be recorded.

Aim

In this study, we analyzed a retrospective cohort of patients with the aim to develop a definition of PR using parameters independent of DIR and which significantly correlates with hallmarks of beta-cell function.

Methods

The study was designed as an observational study with a retrospective cohort of 239 children and adolescent with T1D attending outpatient clinic in a tertiary health care center (Cliniques universitaires Saint-Luc) and followed in our pediatric diabetes clinic from diagnosis (from 1998 to 2013) to adulthood (18-20 years of age). The local ethical Committee approved the study protocol. T1D was diagnosed according to International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines and based on symptoms of insulinopenia, elevated blood glucose (expressed in mg/dL) and HbA1C, positive anti-islet antibodies (GAD65, IA2, insulin), and lack of family history of genetic diabetes. Biometrics and biological features were collected at diagnosis and at each consultation (post-diagnosis consultations occurred at 15 days, 1 month and then every 3 months; only fully adherent patients were recorded). At diagnosis, measures included screening of DKA (defined as pH <7.3 and/or bicarbonate <16 mM) and postprandial C-peptide levels, which were assayed every year. Z-scores for height and BMI were assessed using Belgian Flemish reference charts.
Insulin doses were adjusted for pre- and post-prandial glycemic targets according to ISPAD guidelines, when available, or to our institutional guidelines. Only patients that performed at least five measurements of capillary BG were included in the study.

Self-monitoring data were recorded during each consultation. PR was defined as IDAA1C (being inferior or equal to 9), according to definition by Mortensen et al.: A1C (%) + [4 x insulin dose (U/kg/day)].

Data were analyzed using the GraphPad and Sigmaplot softwares. Categorical variables were analyzed using chi-square test or Fisher exact test for small samples. Continuous variables were analyzed using unpaired t test or Mann-Whitney Rank sum test, according to the statistical distribution. ANOVA with or without R tests were used, according to the statistical distribution, when there was more than two groups. Normality of distribution was verified through Shapiro-Wilk testing. For continuous variables, data were expressed as mean +- standard deviation when normally distributed, and as median and interquartiles (q25% - q75%) when not. Correlation analysis was used to evaluate relationship between variables. When building logistic regression models, all significant variables in univariate analyses were entered into a multivariate logistic regression. Results are expressed as odds ratio (OR) with 95% confidence intervals. Logistic regression analyses were performed using IBM SPSS Statistics 21.0 software. $P<0.05$ was considered significant.

Results

Diabetic ketoacidosis and age at diagnosis, but no other clinical feature (e.g. gender, BMI, or levels of HbA1C, C-peptide, or anti-islet antibodies at diagnosis), influenced the occurrence of remission. We evaluated whether parameters of glycemic variability used in clinical routine may reliably define partial remission, as these would alleviate confounding factors related to insulin treatment. Using multiple linear regression, we observed that HbA1C levels and percentage of normoglycemia were efficient and sufficient to predict partial remission. These parameters were entered into a formula, called Glycemic Target-Adjusted HbA1C (GTAA1C), that corresponded to [HbA1C(%) - (3 x % of normoglycemic values(70-180 mg/dL)). With a threshold of 4.5, this alternative formula predicted partial remission with a sensitivity and a specificity of 72.3% and 92%, respectively, and yielded strong correlation with IDAA1C levels and BETA-2 score, which is a correlate of beta-cell function after islet transplantation.

Conclusions

We propose GTAA1C, based on routine and objective markers of glycemic variability, as a new alternative for definition of partial remission in T1D. GTAA1C showed strong correlation with parameters of beta-cell function. Longitudinal studies are now mandatory for external validation of the potential of GTAA1C to identify PR patients with new-onset T1D.

E 05

Rhabdomyolysis following the initiation of methimazole in a 14-year-old girl with Graves'disease

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Introduction

Graves' disease is the most common cause of hyperthyroidism in pediatric patients. There are three modalities of treatment: antithyroid drugs (ATD), radioactive iodine and total or near total thyroidectomy. ATDs are often recommended as first-line treatments. Methimazole (MMI) is preferred to propylthiouracil (PTU) because it causes less adverse drug reactions.

Aim

To describe an unusual case of rhabdomyolysis due to the initiation of methimazole in a pediatric female patient with Graves' disease, and to review the literature to identify predisposing factors to this condition.

Methods

We compare our case to three similar pediatric cases and discuss the contributing factors.

Results

We report a 14-year-old adopted Chinese girl with a recent diagnosis of Graves' disease. Within two weeks after the initiation of methimazole (30 mg/j), the patient developed diffuse acute muscular pain without a decrease in muscle strength. Her laboratory results showed increased levels of CK and a level of thyroid hormone within normal range. The myalgia resolved and CK levels returned to normal after the patient was switched to propylthiouracil with the addition of L-thyroxine and vitamin D supplementation. The most probable etiology appears to be an acute decrease of thyroid hormones resulting in a relative hypothyroid state in the muscles. This may have been aggravated by a vitamin D deficiency. However, a direct action of MMI on muscle tissue cannot be ruled out. Similar cases in children are rare and the mechanism has not yet been elucidated.

Conclusions

After the introduction of an antithyroid drug in a child with Graves's disease, we recommend looking for muscular symptoms. CK levels should be monitored in case of such symptoms and the addition of L-thyroxine should be rapidly proposed. We also recommend being more careful in patients with other risk factors of muscular damage such as vitamin D deficiency and certain ethnic backgrounds.

E 06

Early Cushing's syndrome: differential diagnosis and etiological exploration.

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Introduction

Cushing syndrome is a rare entity, especially in children. There are two main types: ACTH-dependent Cushing Syndromes where excessive glucocorticoid production is due to an exaggerated stimulation of the adrenal cortex by ACTH which may be paraneoplastic or related to pituitary (in Cushing's disease) or to ectopic and stimulating secretion of CRH. The second type of Cushing is independent ACTH where the adrenal glands secrete cortisol autonomously, and therefore inhibit endogenous ACTH by feedback control.

Aim

Case report:
A two-year-old patient was assessed after excessive weight gain, early onset and rapid progression under normocaloric conditions and worsening after a tonsillectomy procedure with a break in the growth curve. His weight was + 2.55 SD, size -2.12 DS. He is the second child of non-consanguineous parents, without any relevant pathology in the family. An exhaustive anamnesis revealed a normal stature-ponderal development until the age of 1 year, then an important weight gain associated with growth retardation.
At the sight of a frank cushingoid picture, several cortisol determinations demonstrated a hypercorticism of peripheral origin (low ACTH), independent of the ACTH secretion (dexamethasone positive braking test). The normal circadian rhythm in cortisol secretion was lost.
Regarding the clinical examination, we found the advanced Cuching syndrome stigmata (obesity android, bison neck, stretch marks, ...). There was no signs of hyperandrogenism.
He presented also a severe hypertension with a normal renal and cardiac ultrasound assessment.

Methods

Adrenal mineralocorticoid function was notably normal (renin and aldosterone) and tumor markers (AFP, NSE, beta-HCG) were negative.
A radiological assessment consisting of an abdominal ultrasound (US) and computed tomography (CT) showed normal adrenal glands and normal abdominal status. Bone scintigraphy was normal as well as thyroid assessment (biological and ultrasound). Testicular ultrasound showed two hypoechogenic bilateral testicular parenchymal lesions with fuzzy and irregular margins presenting a hyperechoic, hypervascularized center whose anatomopathological biopsy and genetic analysis are still in progress.
A thoracic CT was performed as part of a paraneoplastic assessment and showed no lesion.
Cushing syndrome in childhood usually results from the exogenous administration of glucocorticoids,
which was excluded in this patient.
Adrenocorticotropic hormone (ACTH) independent Cushing syndrome can also occur in 2 currently known genetic syndromes: Carney's Syndrome, resulting from an autosomal dominant mutation of the PRKAR1A gene characterized by pigment spots, myxomas, endocrine hyperactivity (acromegaly, giant cell testicular tumors). Existing cases are very rare before 4 years and after 40 years.
McCune Albright syndrome, due to somatic mutations of the GNAS gene, may associate Cushing's syndrome with bone dysplasia, coffee-milk spots, early puberty and other hypersecretory endocrinopathies (hyperthyroidism, excess hormone growth

and hyperphosphaturia).

Results

Therapy with mitotane, which is an adrenocytolytic agent, was used at the dose of 500 mg daily. The treatement was well tolerated given orally. We noted a progressive decrease of hypercortisolemia and almost normalization of blood pressure. PRKAR1A gene was sequencing and we didn't identify any mutation. Other rarer genes are still sequencing (PDE11A, PDE8B, MYH8). Further genetic analyses on the testicular biopsied material are performing, looking for a mutation in the GNAS gene.

Conclusions

We reported the case of an infant presented with severe Cushing syndrome, for whom metyrapone was effective. Genetic evaluation is in process to establish the diagnosis.

E 07

Stunted growth and alopecia totalis : A case report

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Introduction

Hereditary resistance to vitamin D (HRVD), formerly known as Vitamin D receptor resistance type II (VDRR II), is an autosomal recessive disease caused by mutations in the vitamin D receptor (VDR). It is a very rare form of rickets, with only about 100 cases reported. The typical clinical and biological signs are severe rickets, hypocalcemia, hypophosphatemia, secondary parathyroidism and markedly increased serum levels of calcitriol [1,25(OH)2D]. Children often exhibit growth impairment, poor bone structure (bowed legs, widening of the wrists, craniotabes...) and alopecia totalis (complete lack of body hair) in 2/3 of cases. The disease presents a broad clinical picture that largely depends on the genotype.

Aim

Case Report

Methods

The patient is a female infant whose parents continually sought medical advice regarding a marked alopecia. It was only when she reached the age of two, owing to relative psychomotor retardation and poor overall body growth, that the suspicion of rickets was raised. The clinical examination showed the typical signs of rickets: bowed legs, widening of the wrists, rachitic rosary and alopecia. X-ray examination confirmed a generalised lack of bone mineralisation and uncovered fractures of the distal forearms bilaterally. A blood test showing hypocalcemia, hypophosphatemia, excessive 1,25(OH)D, increased PTH levels and markedly high alkaline phosphatase strengthened the suspicion of HRVD. Genetic analysis uncovered a mutation in the coding region of the VDR gene, confirming the diagnosis. The treatment initiated was oral administration of calcium carbonate (1g three times a day) and vitamin D (25000 U/week). However, owing to poor response, it was switched to a daily intravenous administration of high doses of calcitriol and calcium. The patient was initially hospitalised for her treatment and later discharged with arrangements made for her intravenous infusions to be undertaken at home.

Results

The human VDR results from a single gene located on the chromosome 12(12q13-14), and mutations in the coding region of this gene lead to severe functional disorders. Among the diverse functions of vitamin D, calcium homeostasis is the most apparent one. Thus, malfunctioning VDR leads to poor calcium uptake by the digestive system. With a decrease in calcemia, the secondary parathyroidism that follows in turn depletes the calcium stock in the bones and favours phosphate excretion in the urine. While the physiopathology for the alopecia is still unclear, its presence indicates a more acute presentation of the disease. Treatment aims at enhancing growth, restoring normocalcemia and normal PTH levels, and improving bone mineralisation. Response however varies greatly and depends on the severity of the affection. HRVD patients presenting alopecia generally do not respond to oral treatment and intravenous infusions are therefore required.

Conclusions

This case illustrates a very rare and probably known-to-few affection of end-organ resistance to vitamin D, and depicts the cruciality of the latter for proper mental and

physical development. HRVD remains however a potentially treatable disease, as long as the diagnosis is early enough to reverse the clinical situation and correct the rachitic deformities. In the most severe cases, treatment is long, costly and tedious, lasting in most cases at least until puberty.

E 08

Type 2 diabetes in children and adolescents: experience in a single center in Brussels.

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Introduction

The incidence of type 2 diabetes (T2DM) among youths increases over the past decades all over the world, particularly among certain ethnic groups.

Aim

The aim of this study is to describe our clinical experience (epidemiology, clinical presentation, biochemical characteristics, initial treatment and first year metabolic control) with children and teens diagnosed with T2DM at the UZ Brussel.

Methods

Retrospective chart review of all newly diagnosed pediatric patients with diabetes mellitus at the UZ Brussel during the last 7 years.

Results

Of the 203 (80 Magreb) newly diagnosed children and adolescents (=< 16 years) with diabetes mellitus, T2DM was identified in 8 (7 females, 1 male). Their median age at diagnosis was 13 years (range 9.3 - 15.8 y). Two patients were prepubertal. All patients were obese with a median BMI SDS of 3 (range 2 - 4.2). Seven patients were diagnosed with primary obesity, whereas 1 patient had a previously diagnosed Prader-Willi Syndrome. All but one patient were from Magreb origin. Seven out of eight patients had a family history of T2DM. Three patients had mild typical symptoms (polyuria, polydipsia, weight loss) at diagnosis. In 5 patients physical examination revealed acanthosis nigricans. HbA1c at diagnosis was rather slightly elevated (mean 7.3% - ranged 6 - 10.7%). No type 1 diabetes-associated auto-antibodies were present. Six patients were started on metformin at diagnosis, whereas 2 patients, presenting with slight acidosis, received instant insulin therapy . These 2 patients achieved a faster optimal metabolic control (HbA1smaller or equal to 7.5% - within three months of treatment), but still received insulin therapy one year after diagnosis.

Conclusions

Currently T2DM makes up 3 % of newly diagnosed diabetic children and adolescents in our center and is characterized by an asymptomatic or mild presentation, a female preponderance, an onset during the second decade and a slightly elevated HbA1c concentration at diagnosis. Obese female adolescents of Magreb origin appear at highest risk, especially in association with a positive family history, justifying a regular screening for diabetes mellitus in this particular obesity patient group.
On the other hand diagnosis in pre-pubertal children is rather unusual and may therefore be missed.

E 09

Pituitary hyperplasia in a female adolescent: a challenging diagnosis

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Introduction

Pituitary hyperplasia is an uncommon and poorly understood condition that is difficult to diagnose and under-diagnosed (1). It is defined as a non-neoplastic increase in adenohypophyseal cell numbers and manifests itself radiologically as pituitary enlargement (2). Pituitary hyperplasia occurs in heterogeneous settings initiated by either physiological or pathological stimuli1. Increased awareness of physiological hyperplasia and its natural history in female adolescents, should circumvent unnecessary trans-sphenoidal surgery (1,2).

Methods

Case Report:
A 12-year-old girl was referred to the pediatric endocrinology clinic for pituitary enlargement discovered after neuroimaging in the work-up of frequent headaches, photophobia and the recent onset of concentration and memory problems. The headaches seemed to be triggered by stress and were treated by intermittent use of paracetamol or an NSAID. Additionally, the girl suffered from increasing fatigue following an atypical pneumonia (M. pneumoniae). A cranial CT scan hinted a pituitary microadenoma, but MRI provided diagnosis of a non-cystic macroadenoma. At physical examination weight was 82 kg (+2.2 SD), height 156 cm (0 SD), Tanner stage A2P3M4 and blood pressure 125/65 mmHg. Eye movements and visual fields were normal. Truncal white striae were present, but no hirsutism. Hormonal work-up showed an elevated IGF-1 for age, slightly elevated TSH (7.1 mU/L) and FT3 (6.1 pg/ml) levels, normal serum cortisol and urinary free cortisol excretion, as well as normal PRL, LH, FSH and estradiol levels for the pubertal stage. A GH-secreting pituitary adenoma was suspected. Indeed, in the past 2 years her weight had increased unexpectedly and her growth had accelerated. Since the last year her breast development had also started. A lifestyle weight management program had only transient success. Family history included paternal obesity, but no history of endocrine diseases. Repeated MRI of the brain revealed an enlarged anterior pituitary (maximal cranio-caudal diameter of 10.8 mm) with a slightly thickened stalk. The pituitary was isointense in T1 and T2, with homogenous enhancement after the administration of gadolinium. A suprasellar extension of the pituitary approached the optic chiasm, but there was no evidence of compression on the chiasm or the optic nerves. No pituitary hormone excess was concluded as elevated TSH and FT3 could be explained by obesity and elevated IGF1 by both advanced puberty and obesity. Bone age was slightly advanced (13 years and 3 months). Repeated basal GH values were normal. Screening for thyroid antibodies was negative, leaving two possible diagnoses for the pituitary enlargement: pituitary hyperplasia or non-secreting pituitary macroadenoma.

Her headaches remained unchanged despite maximal analgesia and her fatigue became especially debilitating with 3/5 days of homeschooling in the following months. The uncertain etiology of the pituitary enlargement, the possible future risk for compression of the optic chiasm, and the increasing severity of the headaches prompted the proposal of neurosurgical intervention. However, after multidisciplinary consultation a residential revalidation program, including a psychological and weight loss intervention was opted, as well as serial cranial MRI and hormonal status every 3 months. Weight loss resulted rapidly and menarche came after 6 months. Hormonal status remained stable, as did the structure and size of pituitary, which resulted after two years of follow-up in the diagnosis of pubertal, physiological pituitary hyperplasia.

Results

Discussion:
Normal pituitary dimensions have been empirically defined from limited radiological studies, showing greater dimensions in females than males and increasing up to the age of 20 to 29 years, but in generally remaining below 9 mm (1). Physiological pituitary hyperplasia by increasing gonadotrope cell volume occurs physiologically in adolescence and is important to consider in the evaluation, as it does not require medical intervention (2). Primary ovarian failure, producing gonadotrope hyperplasia with pituitary enlargement, can easily be detected at initial investigation (1, 3). In some cases, an association with polycystic ovary syndrome has been found (1, 3). Mutations in the PROP1 gene have also been associated with pituitary enlargement in adolescents, but this condition is usually identified by combined pituitary deficiencies (4).

Conclusions

The greatest pituitary heights are seen in young pubertal females (1, 2). The differential diagnosis of any pituitary enlargement should include physiological pituitary hyperplasia, even when mass-effect signs are present on neuroimaging. Clinical surveillance and treatment of any associated condition should be initiated. Surgery is to be avoided in the absence of urgent deficits since the pituitary enlargement rarely progresses.

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E 10

An adolescent girl with sudden weight gain and secondary amenorrhoea.

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Introduction

Rapid weight gain with a sudden onset in a child needs to alarm the clinician to investigate underlying organic disorders. These include endocrine disorders and genetic causes of obesity. The differential diagnosis of secondary amenorrhoea is broad and can range from endocrine disorders to environmental and psychological disturbances.

Aim

We present a clinical case from the obesity clinic with a rare outcome.

Methods

A 14-year old girl presented to our outpatient obesity clinic with recent, yet extensive weight gain (40 kg in 6 months) and amenorrhoea for 9 months. Her parents reported an abnormally increased appetite and mood swings. There were no headaches or blurry vision. She was not pregnant and did not take any medication. Physical examination was normal besides abdominal striae and mild systolic hypertension. Diagnostical work-up for rapid onset obesity and menstrual cycle disorder was performed and included a morning and fasting blood sample, oral glucose tolerance test and 24-hour urine collection. Screening of the hypothalamic pituitary adrenal (HPA) axis was normal apart from increased serum prolactin (PRL, >100 g/l, confirmed three times). Macroprolactinemia was ruled out. Other investigations showed no considerable metabolic disturbances. Coagulation screening was normal. After confirmation of raised PRL, magnetic resonance imaging of the pituitary gland was performed and showed a posterior pituitary microadenoma with a diameter of 3 mm. Two weeks after being diagnosed with microprolactinoma, the patient was started on a dopamine agonist (cabergoline) in order to reduce PRL levels. At submission of this abstract no follow-up information was yet available.

Results

Hyperprolactinemia is a rare endocrine disorder in childhood, which may result from pituitary adenoma. Other causes of hyperprolactinemia include idiopathic hyperprolactinemia, primary hypothyroidism and polycystic ovary syndrome in females. The most frequent symptoms of hyperprolactinemia in women are menstrual disorders, galactorrhea and infertility. The most common clinical presentations of hyperprolactinemia in children are growth and puberty disorders and obesity. Prolactinomas are pituitary adenomas that express and secrete prolactin. Retrospective studies show that prolactinomas in children are frequently associated with weight gain. The prevalence of obesity is four times higher in patients with prolactinomas than in patients with nonfunctional adenomas. If a prolactinoma progresses to a large size (10 mm or larger), it can impair surrounding structures, primarily the normal pituitary gland and optic pathways. The first one leading to hormonal insufficiency called hypopituitarism. Prolactinomas are treated with a dopamine agonist (DA) such as cabergoline or bromocriptine. Besides normalizing PRL levels, DA's have shown to reduce body fat and the consequent risk of developing the metabolic syndrome.

Conclusions

Weight gain in a child can be a clinical presentation of hyperprolactinemia.

Measurement of serum PRL should be included in the diagnostic work-up of children with obesity.

E 11

Cushing Syndrome and virilization revealing malignant adrenocortical tumor: Case report

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Introduction

Adrenocortical tumor are rare in children. Most of them are functional (80-90%) Virilization is the most common presentation (50-84%) and Cushing's syndrome (CS) only affects one third of the patients.
We report the unusual case of an 8-month-old infant who presented with CS and virilization, revealing a malignant adrenocortical tumor.

Results

Clinical case
A 8-month-old Moroccan girl presented with growth retardation, rapid weight gain and generalized hair growth of 2 months of evolution. She was born after 40 weeks of gestation from consanguineous parents (2nd degree). Clinical examination revealed round face, generalized obesity, buffalo hump, bloated abdomen, facial acne, severe hirsutism and clitoromegaly. She measured 61,5 cm (-3,5 DS). Her BMI was 22.4 kg/m2 (+2.7 DS). Blood pressure was increased at 91/69 mmHg (p82/p>99). She had biochemical hyperandrogenism with total testosterone at 432 ng/dl (N : <10 ng/dl), 17-hydroxyprogesterone at 1015 ng/dl (N: 13-106), DHEAS > 993.6 μg/dl (N : 5-48), and androstenedione at 3.55 ng/ml (N : 0.1-0.37). Morning serum cortisol was increased: 1169 nmol/l (N : 138-635), and didn't decrease after a midnight dexamethasone dose: 1197 nmol/l. ACTH level was normal-low: 6,2 pg/mL (N : 5-49), revealing an ACTH-independent form of CS. She did not have any clinical or laboratory sign of hyperaldosteronism. A concomitant pheochromocytoma was excluded through chromogranin A and urinary catecholamines determination. Abdominal ultrasound showed a left-sided adrenal mass. The abdominal MRI revealed an heterogeneous mass measuring 80 x 67 x 43 mm in the left adrenal gland, without metastases or local invasion of other organs. She underwent surgical resection with no complications. Hormonal levels normalized by 13 days postsurgery. A dramatic regression of virilization and CS features occurred after adrenalectomy. Pathological examination revealed a 176g mass with capsular invasion corresponding to an adrenocortical carcinoma grade III. Due to marginal resection, chemotherapy with cisplatinum, etoposide, doxorubicin associated with mitotane (inhibitor of steroidogenesis in adrenocortical cells) was therefore administrated (COG protocol ARAR0332), and hydrocortisone dose replacement increased. Genetic analysis of the TP53 gene did not show any mutation.

Conclusions

Although childhood adrenocortical tumors are rare, they should be always considered in the differential diagnosis of CS with important and rapid virilization. Complete surgical resection remains the most effective treatment. In case of residual tumor or metastatic lesions the prognosis is poor, and chemotherapy with mitotane may be considered. However, the intermediate groups, stages II and III as in this report, are heterogeneous and are linkely to include different prognostic categories. Only further international participation and collaboration can improved the outcome of these rare tumors.

E 12

Severe adrenal insufficiency in a context of fluticasone treatment

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Introduction

Adrenal insufficiency caused by high doses (< 500μmg per day for a child) of inhaled corticosteroids (budesonide, fluticasone, beclomethasone) has been illustrated in several studies. A review of the literature indicates that a majority of the cases of adrenal insufficiency in children involve fluticasone and can happen with doses lower than 500μmg.

The clinical case reported below concerns a 4-year-old boy who presented severe hypoglycaemia (10mg/dl) occurring in an infectious context. The biology performed during the hypoglycaemia revealed hypothalamic-pituitary-adrenal insufficiency in a context of chronic fluticasone treatment.

Aim

Causes of severe adrenal insufficiency in a context of fluticasone treatment and infection.

Methods

The first episode of severe hypoglycaemia (blood glucose: 10mg/dl) occurred in an infectious context and led to an alteration of consciousness. The 4-year-old patient was followed for asthma treated with fluticasone (250μmg twice a day) but did not present any other particular medical history. His growth and development were normal until then.
The endocrinological assessment performed during the hypoglycaemia (low cortisol and no hyperinsulinism) as well as a glucagon test (low ACTH and low cortisol, no GH deficiency, no hyperinsulinism) identified adrenal insufficiency.
Magnetic Resonance Imaging eliminated any hypothalamic or pituitary gland abnormalities.
A substitution therapy by hydrocortisone was therefore initiated with initial daily doses of 10 mg/m2 in 3 doses.

The patient had a second severe hypoglycaemia with obnubilation during the first night of a scarlet fever for which the parents had not increased the doses of hydrocortisone. This episode required the administration of hydrocortisone sodium succinate. Currently, fluticasone treatment has been progressively interrupted and the hydrocortisone substitution is progressively reduced.

Results

The endocrinological assessment performed during the first hypoglycaemia:
- Blood glucose: 10mg/dl
- Insulin: < 3,56 pmol/L (no hyperinsulinism)
- Cortisol: 132,8 ug/L (low for the blood glucose)
- Acetonuria +++

The glucagon test:
- Basal cortisol at 2ug/L (0 hours), maximum at 13,2ug/L (2 hours)
- Basal ACTH at 4,2ng/L (0 hours), maximum at 22,3ng/L.
- No hyperinsulinisme: 1336,2pmol/L
- No GH deficiency : 15,07ug/L

Conclusions

The risk of developing adrenal insufficiency associated with inhaled corticosteroids is difficult to predict at the individual level. The patient described in this abstract may have a high sensitivity to the inhibitory effect of corticosteroids. It is not currently possible to formally exclude a corticotrophic insufficiency of genetic origin revealed by the infectious episode, independently of the fluticasone treatment. This will only be ruled out after documentation of a normal adrenal function once the fluticasone and hydrocortisone treatment will be completely stopped. A review of the literature indicates that adrenal insufficiency caused by inhaled corticosteroids is rarely clinically symptomatic. As complications are potentially severe, the minimum dose of corticosteroids should be prescribed.

H 01

Clinical use of infliximab trough levels during maintenance in pediatric patients with inflammatory bowel disease

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Introduction

The role of therapeutic drug monitoring during maintenance treatment in paediatric inflammatory bowel disease (IBD) is poorly studied.

Aim

The aim was to determine whether infliximab (IFX) trough levels (TL) correlate with long-term remission in children receiving maintenance IFX.

Methods

In this cross-sectional study all children with Crohn's disease (CD) or ulcerative colitis (UC) receiving maintenance IFX at our referral centre were included. All children received pro-active drug monitoring with the therapeutic window defined between 3-7 μg/mL (conform adult studies). IFX TL were analysed using the Ridascreen IFX Monitoring ELISA. Demographics, disease activity indices, biochemical values and endoscopic reports were recorded retrospectively. Clinical remission was defined as PUCAI/PCDAI <10 and biochemical remission as CRP =<5 mg/L and ESR =< 20 mm/h. Patients were considered in deep remission if both criteria (clinical + biochemical remission) were met. Endoscopic remission was defined as absence of ulceration. Mann - Whitney U-test was used to compare responders from poor-responders and correlations were analysed with Spearman's rho. All data are presented as median [IQR] and alpha was set at 0.05.

Results

A total of 45 patients (30 CD and 15 UC; 47% male; median age of 15.4 years [12.2- 16.6]) and 617 IFX TLs (median 10 per patient [5.5- 21]) were included. Median age at start of IFX was 12.8 years [9.6- 15] with a median disease duration prior to starting IFX of 5.0 months [2.0- 9.5]. Mean administered IFX dose was 6.8 mg/kg [5- 10] and the mean maintenance interval 5.6 weeks [4- 6]. At start of maintenance 76% was on concomitant immunosuppressants. Median IFX TL during maintenance were significantly higher in children who were in clinical remission (5.4 μg/mL [3.8- 8.1] vs 4.1 μg/mL [2.6- 6.7], p= 0.0001), biochemical remission (5.2 μg/mL [3.7- 7.7] vs 4.2 μg/mL [2.5- 6.6], p= 0.0001), deep remission (5.7 μg/mL [3.9- 8.4] vs 4.2 μg/mL [2.6- 6.7], p= 0.0001) and endoscopic remission (6.2 μg/mL [3.9- 9.5] vs 3.2 μg/mL [2.3- 5.7], p= 0.005). With a median follow-up of 24 months [10- 40] under IFX, 36/45 (80%) patients were in clinical and 27/37 (73%) patients in endoscopic remission at last follow up. IFX TL correlated significantly with CRP, ESR, albumin and PUCAI/PCDAI (all p=<0.005).

Conclusions

In this paediatric IBD cohort treated with IFX maintenance, children who demonstrated clinical and/or endoscopic remission had significantly higher IFX TL. Our data support the value of proactive drug monitoring in children to improve long-term outcome. Whether the same therapeutic window as in adults needs to be pursued in children, needs to be investigated in prospective studies.

H 02

Sufficient exposure during induction is essential for a long and better response in paediatric patients with inflammatory bowel disease.

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Introduction

Loss of response (LOR) to biological therapies is a big concern in inflammatory bowel disease (IBD) management and especially among paediatric patients where treatment options are limited. Therapeutic drug monitoring has been proposed as one of the ways to improve outcome, but its role remains unclear.

Aim

The aim of this study was to determine whether infliximab (IFX) trough levels (TL) correlated with clinical and biological remission. We hypothesized that IFX TL after induction are predictive for IFX efficacy.

Methods

All paediatric IBD patients with IFX TL available at their first maintenance infusion and a follow-up of at least 54 weeks were included. IFX induction regimens could be intensified at the discretion of the treating physician based on disease severity. All children received pro-active drug monitoring in the maintenance phase with the therapeutic window defined between 3-7 μg/mL (conform adult studies). Demographics, disease activity indices and inflammatory biomarkers were recorded retrospectively. Clinical remission was defined as PUCAI/PCDAI <10 and biological remission as CRP =< 5 mg/L and ESR =< 10 mm/h at week 54. Patients were considered in deep remission if both criteria (clinical and biological remission) were met. IFX TL were measured by Ridascreen IFX Monitoring ELISA. Results were analysed using Mann-Whitney U-test. All data are presented as median [IQR] and alpha was set at 0.05.

Results

We included 25 children (15 with Crohn's disease and 10 with ulcerative colitis; 40% male). IFX was stopped in only 1 patient before week 54 due to LOR. Median age at start of IFX was 12.7 years [9.7-15.0] with a median disease duration prior to starting IFX of 7 months [4-12] and a median follow-up under IFX of 23 months [16-43]. At start of maintenance therapy, 76% was on concomitant immunosuppressants, which dropped to 36% at week 54. Median IFX TL at the time of the first maintenance infusion were significantly higher in children who were in clinical remission (3.4 μg/mL [2.4-6.0] vs 1.5 μg/mL [0.7-3.2], p=0.014), biological remission (3.8 μg/mL [2.7-9.0] vs 1.4 μg/mL [0.3-3.0], p=0.003) and deep remission (4.8 μg/mL [2.4-12.0] vs 2.3 μg/mL [0.9-3.2], p=0.008) at 54 week.

Conclusions

Paediatric IBD patients with enough exposure during induction therapy (deduced by the IFX TL at start of maintenance) have better chance for clinical and/or biological remission at week 54. This illustrates that sufficient exposure during induction is essential for a long and better response.

H 03

An adjusted Bristol Stool Scale for young, non-toilet-trained children: the Brussels Infant and Toddler Stool Scale (BITSS).

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Introduction

Although stools of infants and young non-toilet-trained children differ considerably from the illustrations in the Bristol Stool Scale (BSS) which was developed for adults, the BSS is widely used. The objective of this study is to validate an adjusted BSS based on photographs of infant stools in diapers.

Aim

To evaluate interrater reliability of stool consistency assessment between parents, nurses and medical doctors using the BITSS.

Methods

Seven photos of infant stools in diapers were selected and shown to 261 parents, 145 paediatricians and 160 nurses in paediatric departments throughout Belgium. They were asked to match the photos with the best corresponding BSS type.

Results

BSS types 1, 2 and 3 (hard stools) were assigned to the corresponding photos by over 98 % of parents, nurses and doctors. BSS type 4 (normal, formed stools) was matched with the corresponding photos by 92% of the observers. BSS type 5 and 6 (normal, loose stools) were assigned to the corresponding photos by 91% of the observers. BSS type 7 (watery stools/diarrhoea) was well recognized by all groups since 91 % classified it accordingly. Fleiss' kappa values (0.41-0.60: moderate agreement, 0.61-0.80: substantial agreement) were higher in paediatricians (0.67) and nurses (0.62) than in parents (0.58) (for each individual photo). When combined per consistency group, kappa values increased in all groups.

Conclusions

Our results suggest that the BITSS shows moderate agreement with the BSFS and that after grouping BITSS photographs together, this visual stool form scale is likely to prove useful in the assessment of stools of non-toilet trained children both in clinical practice and for research purposes.

H 04

Current practice of pediatric gastro-intestinal endoscopy in Belgium.

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Introduction

To improve and maintain paediatric endoscopic skills, current endoscopic practice in children needs to be monitored and a specific paediatric training curriculum should be developed.

Aim

We therefore tried to make an inventory of the number of diagnostic and therapeutic endoscopic procedures performed in Belgian children according to the central registration by the RIZIV (RijksInstituut voor Ziekte en Invaliditeits Verzekering)/INAMI (Institut National d'Assurance Maladie-Invalidité) in 2015.

Methods

Available data of all paediatric endoscopic procedures , diagnostic and therapeutic were retrieved from the RIZIV/INAMI database. . The last complete available data were from 2015. Besides number and type of procedure, registration number of the performing physician was also collected.

Results

Data on paediatric endoscopy by RIZIV/INAMI is divided in 2 age categories: <7 years of age and >7 years of age, including adults. Therefore we can only be certain that endoscopies performed in patients > 7 years of age and performed by paediatricians will be paediatric patients. It is uncertain how many adult gastroenterologists performed endoscopy in children. The most frequently performed procedures are esophago-gastro-duodeno-scopy (EGD) (n= 4410) and (ileo-) colonoscopy (n= 140) RIZIV registration showed following data for the year 2015:, 8 esophagoscopies (5 different paediatricians), 4410 EGD's (performed by 64 different paediatricians) of which 51% <7 years of age.
Next, 103 rectoscopies, 35 of them were carried out by paediatricians, the others by surgeons, 92% <7 years of age. Left colonoscopy/rectosigmoïdoscopy: 152 < 7 years, 135 performed by a paediatrician. In patients >7 years old: 117 left colonoscopy , 30 by paediatricians. In total, in 2015, 269 left colonoscopies performed by 32 different paediatricians. 71 total colonoscopies performed in children 23.9% in children under the age of 7. 69 ileocolonoscopies, performed by 10 paediatricians. 11.6% (n=8) < 7 years. Oesophageal dilatation was performed 26 times <7 years old, by 4 paediatricians. In children > 7 years of age, only 1 oesophageal dilatations was registered. Endoscopic treatment of oesophageal varices was only performed once in a child <7 years old, carried out by an adult gastroenterologist. Above 7 years of age, 4 ligations were performed by 2 paediatricians. Treatment of bleeding was only necessary in patients over 7 years old. In children under 7 years old, there was no need for this therapeutic intervention.

Conclusions

The most frequently performed endoscopic procedures in children were diagnostic EGD and colonoscopy Evaluation of the RIZIV/INAMI data makes us wonder whether all procedures performed in 2015 have been adequately registered. A more uniform and standardized registration would give us a more adequate idea about the current clinical practice in children. The fact that registration is divided in only 2 age categories

further complicates analysis of the gathered RIZIV/INAMI data.
This data shows that diagnostic and therapeutic paediatric endoscopy is performed in many centres in Belgium, challenging the quality of skill as fewer procedures are performed per paediatrician.
We can conclude that there is a need for subspeciality training and recognition, this by implying continuous education and training that will be warded by the government.

H 05

Triple A syndrome, a challenging race for the diagnosis in a deadly pathology: a case report

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Introduction

Background - The triple A syndrome (AAAS, Allgrove syndrome) is a rare disease characterized by the triad of esophageal achalasia, adrenal insufficiency and alacrima. Achalasia is a primary motor disorder with absence of peristalsis and incomplete relaxation of the lower esophageal sphincter (LES). There are few cases described in children and adolescents. The incidence varies according to the continents and is approximately 0,1/100,000. Diagnosis is often delayed in children because of lower incidence and unspecific symptoms.

Results

Case report - A 15-year-old girl, presented in our clinic for weight lost, postprandial vomiting, dysphagia since her third year of life and delayed puberty. Full term baby but with intrauterine growth restriction, she is the fourth child in five of a Moroccan family with consanguineous parents. Her younger brother died at the age of 13 presenting the same clinical symptoms. At the first clinical exam she was emaciated with muscular hypotrophy and dental cavities (anthropometric measurements: weight 28.7kg, height 140cm, BMI 14). The laboratory exams showed a primary adrenal insufficiency, anemia, hypoproteinemia, negative inflammatory bowel disease antibodies, negative celiac disease antibodies and normal thyroid function. The high resolution esophageal manometry showed no lower esophageal sphincter (LES) relaxation. The contrast study and upper gastrointestinal endoscopy showed a dilated and low peristalsis with delayed emptying of the esophagus. DNA sampling (AAAS gene, chr 12q13, mutation ALADIN) came positive for a mutation in the intron 14 c.1331 + 1G>A in the homozygous state (the most common mutation in North Africa). Proton pump inhibitors and adrenal supplementation was started. After a multidisciplinary discussion, a pneumatic dilatation of the LES and a feeding gastrostomy was proposed as a first line treatment.

Conclusions

Conclusion - Although its name connotes a triad, the syndrome is phenotypically heterogeneous; fewer than three features may be present. Additional features not originally identified, including progressive autonomic (central and peripheral) nervous system deficits, are associated with the syndrome. The etiology of achalasia in AAAS appears to be distinct from other forms of achalasia. Although it is a rare condition and epidemiologic data are scant, symptoms of swallowing difficulty and achalasia in AAAS usually manifests by the end of the first decade of life and can begin in infancy in contrast to idiopathic achalasia, where very small minority of patients manifest symptoms before 10 years of age. The gene AAAS, located at chr 12q13, account for the majority of cases. Consanguinity is often present in children of AAAS and the condition segregates in an autosomal recessive pattern. The penetrance with biallelic mutations in AAAS approaches 100%, though expressivity is variable, possibly due to allelic variation or the existence of as yet unidentified genes. Diagnosis is often delayed because of the poor specificity of symptoms (vomiting, dysphagia, weight loss, failure to thrive, chest pain, regurgitated food), lower incidence of achalasia then other more frequent pathologies (gastroesophageal reflux disease). The diagnosis must be as early as possible because achalasia is a deadly pathology. The workup includes radiography, esophageal manometry and upper endoscopy. The three primary types of treatment are pharmacologic, endoscopic (botulinum toxin injection into the LES, pneumatic dilatation and stenting, Per Oral Endoscopic Myotomy) and

surgical (Heller procedure with anti-reflux surgery and feeding gastrostomy). Patients must continue with regular follow-up to prevent progression toward a more serious disease (esophageal cancer) or motor disorders with malnutrition.

H 06

Role / impact of pediatric clinical studies in the pediatric gastroenterology and hepatology department of Saint-Luc University Clinics

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Introduction

Due to several legal, financial and ethical constraints, the setting up of clinical trials for a child population has provoked during many years debates on their objectives, effectiveness and limitations, while recognizing at the same time their necessity given the lack of availability of therapeutic options adapted to the pediatric domain. With the objective of obtaining marketing authorizations of new treatments for pediatric populations, the Authorities in charge of health agreed therefore on basic principles for the development of these trials; principally on safety and effectiveness of their conduct.

Aim

The aim of this thesis is two folds; (1) study and identify the effects of long-term experimental clinical trials on children from a medical, ethical, economic and psychosocial point of view and (2) assess the opinion of the families whose children were included in those studies.

Methods

This thesis is based firstly on the comparative analysis of 6 different clinical studies on the development of hepatitis B and C therapeutic options conducted worldwide and proposed to 20 patients treated in the pediatric gastroenterology and hepatology unit of Saint-Luc University Clinics. This analysis will help us primarily to determine if, comparing to a larger scale, those clinical studies offered a successful outcome for our patients, and more generally to what extend proposing an experimental clinical trial to the children has helped them medically. This analysis is completed by a collection of questionnaires proposed to the parents of these children, gathering their feelings and concerns regarding these experiences from a prospective point of view.

The survey developed in this thesis is composed of four parts: detailed understanding of the aims of the clinical trial proposed to the child, and both parents' and child's opinion on the quality of the documents received ; quality of the supervision during the experience ; potential impact on parents professional activities and children scholar schedule ; global opinion and parents' views aiming at improving the clinical trials experiments.

Results

For the retrospective analysis of this thesis, the experience has been positive for many of the children who accepted to participate to those studies (20 cases out of which 50 to 100% for the hepatitis C vs 25 to 100% for the hepatitis B trials who did the primary endpoint) with better control of the disease's progression (lower viral charge, regression of hepatic lesions), good tolerability to the products and an increased probability of healing profile (seroconversion has been detected for 5 patients suffering from hepatitis B).

As regards the prospective aspect of this study, 50% of parents agreed to complete the questionnaire proposed. The results are that 83.3% declared having been well-informed, 100% considered the documents to be clear for adults and 83.3% estimated that their child received a ludic and appropriate document for its age. 50% confirmed that their child beneficiated from a better medical care because he was

included in a clinical trial, while the other 50% considered that it didn't make any difference. 83.6 to 66.66% estimated that the child's clinical trial didn't have a significant impact on their daily lives but commented that adjustments were required. Finally, 33.3% declared that this experiment had an impact on their child's scholar activities. All in all, 100% expressed global satisfaction with these clinical trials.

Conclusions

This analysis allowed to conclude that as far as globally spread chronic diseases are concerned, these clinical trials represent an opportunity for therapeutic accessibility to new products not yet available to children or too expensive for them in long term use.

For a large proportion of the patients that have participated to these experiments, the access to the treatment has improved their clinical condition and in particular the progression of the disease.

These clinical studies have also provided future hope and an improved long-term prognosis for these children.

They have stimulated a feeling of satisfaction for the parents who expressed comfort to the idea that their child has new chances for recovery and in the meantime, a possible guaranteed follow-up.

However, these studies are costly. They request a daily adaptation for both the patients and their families for the application and follow up of the procedures required.

H 07

vWFpp/Adams 13 ratio is a usefull marker of thrombotic microangiopathy post liver transplant: A pediatric Case report.

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Introduction

Thrombotic microangiopathy (TMA) encompasses a process of microvascular thrombosis, with thrombocytopenia, macroangiopathic hemolytic anemia, and multiple organ failure following ischemia-injury. TMA has a large range of etiologies and clinical presentations.
Transplant-associated TMA has only, since recently, been recognized by the scientific community as a full entity. However, only a few pediatric cases have been reported after liver transplant. The diagnosis is often difficult and the treatment controversial.
We describe the case of a 5 years-old child diagnosed with TMA based on increased Willebrand Factor pro-peptid (vWFpp)/ADAMTS 13 ratio in the course of a living-related liver transplantation. Tacrolimus immunosuppression was replaced by sirolimus and mycophenolic acid, in combination with administration of fresh frozen plasma (FFP), and this led to recovery of the TMA.

Conclusions

We conclude that vWFpp/ADAMTS 13 ratio is a useful marker of liver transplant-associated TMA, and that the disease may be favored by Tacrolimus. Arrest of this drug can lead to recovery.

H 08

Severe enterocolitis, life-threatening presentation of Hirschsprung disease: case report

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Introduction

Introduction
Hirschsprung disease (HD) occurs in approximately 1 in 5000 live births. It is a motor disorder of the colon caused by the failure of neuronal crest cells to migrate completely during intestinal development. The resulting aganglionic segment of the colon fails to relax, causing a functional obstruction. HD is a debilitating disease that can be fatal.
The most important complications are mechanical intestinal obstruction and Hirschsprung-associated enterocolitis (HAEC).

Results

Case presentation
We report the case of a boy aged 1 with history of constipation in the last 4 days, presenting signs of viral gastroenteritis, without fever. After only 24h of liquid stools and vomiting, he started to have fecal vomiting and was admitted to the emergency department.
His personal and family medical history was no significant.
At the admission the patient was afebrile, stuporous and in circulatory and respiratory shock.
Chemistry results showed acute renal failure, liver cytolysis twice as normal and severe mixt acidosis.
Abdominal ultrasound and x-ray showed intestinal occlusion with numerous thin and distended loops filled with stool.
He was subsequently admitted to the pediatric intensive care unit (PICU) for the management of severe enterocolitis and shock.
The clinical state complicate rapidly with infectious ileus and protein loosing enteropathy. He received multiple fluid resuscitation (for a high output stool loose up to 6L/day) and broad-spectrum antibiotics due to a high inflammatory syndrome. The central and peripheral cultures were negative.
He was extubated the next day and his respiratory signs were stable thereafter. His mental state improved progressively and imaging by cerebral CT-scan and electroencephalogram were normal.
During his stay at the intensive care unit, the patient was fasted with nasogastric tube in discharge for 7 days and parenteral nutrition was started. After this period, the bowel movements came to normal, the stool output decreased and the refeeding was possible and tolerated.
He was discharged of the PICU after 15 days.
After discharge, constipation assessments showed a lack of ganglionic cells on 12 cm of the sigmoid colon the anal biopsy. The colic opacification confirmed HD with a transitional zone located in the middle third of the sigmoid. The rectal bulb had a normal caliber while the distal third of the sigmoid is narrow with thickened walls.
Sigmoid and rectal resections were performed 4 months later with good evolution (normal toilet training, regular and spontaneous bowel movements, fecal continence and growth improvement).

Conclusions

Conclusion
Any patient with severe constipation presenting in infancy, constipation refractory to standard medical interventions, and of course, intestinal obstruction should be

considered for HD
The absence of RAIR on anorectal manometry (ARM) is suggestive but not diagnostic of HD. Such patients should then undergo a full-thickness rectal biopsy to detect the absence of ganglion cells, the universally accepted standard to confirm the diagnosis of HD. ARM is considered an accurate, noninvasive screening test for HD particularly in children over one year old.
HAEC remains the principal cause of morbidity and mortality in children with HD. Early diagnosis of this pathology can help to prevent this severe complication but in some cases HAEC can be the presenting symptom and HD may not be immediately recognized due to the rarity of the pathology.

GP 01

Clinical outcome of children born to mothers living in social precarity in Brussels

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Introduction

Studying social determinants of health and their short and long-term consequences on children's health is not easy and demands a continuous re-evaluation because of their dynamic character.
International literature shows a connection between infant birth weight, vaccine coverage, risk of accidents, chronic illnesses, obesity, mortality rate, and social inequalities, linked to pre and postnatal exposure and factors.
Outcomes are different from one country to another, and from different social groups within the same country. It is then important to perform national studies in order to identify at risk groups.
In Brussels, 21% of pregnant women followed by O.N.E. (Office de la Naissance et de l'Enfance) had no Healthcare coverage (versus 8% in Belgium).
This implies financial limits in investigations during pregnancy. Fortunately some structures exist for supporting medical care of pregnant women in this situation, eg. ASBL Aquarelle includes midwives working with women without social security.
Nevertheless, this precarity could have important consequences on birth outcomes and early infancy follow-up.

Aim

The aim of our study was to evaluate if maternal social precarity is a risk factor for child health over the first 18 months of life.

Methods

Medical files of 217 children born at Saint Pierre Hospital in Brussels between January and August 2015 were analyzed.
We identified two groups: 117 children born to mothers with no healthcare coverage during pregnancy and 100 children born to mothers with regular access to healthcare (control group, followed up by the Aquarelle staff) matched by date of birth and sex.
Children followed-up by Kind&Gezin or outside Brussels region were not included.
We collected anonymously data (maternal socio-demographic, perinatal data) from hospital medical file and follow up data from medical file of Saint Pierre Hospital and O.N.E..
The study was approved by Saint Pierre Hospital and O.N.E. Ethical Committee.

Results

217 children were analyzed, 17 patients were excluded. The study population includes 100 children in each group.
30 O.N.E. Consultations were solicited, 19 (63%) of them provided medical files from the patients enrolled.
We managed to find follow-up data of 69 of the original 200 cohort (34,5%): 35 patients of the study group and 34 from the control group, without significant differences of male/female ratio.
Mothers living in social precarity were generally younger (median 28 years vs 32, p=0,006), mainly from Sub-Saharan Africa (43%, versus 47% of Maghreb origin for the control group), and arrived in Belgium less than 5 years ago (91% versus 11%, p=0,0001). Their level of education was lower (primary school or less in 40% versus 25%, p=0,003), only 23% of them had a regular income (vs 97%, p<0,0001), 94% were illegal in Belgium (versus 3%, p<0,0001) and 91% of mothers from the study

group had no access to healthcare in Belgium.
Pregnancy follow-up was irregular (at least 2 follow-up appointments missed) for 32% of them, versus a regular follow-up for all the mothers in the control group.
Despite these differences in maternal characteristics, we did not observe significant differences for in birth outcome (median gestational age, median birth weight, emergency C-section, perinatal antibiotherapy) nor at follow-up (re-hospitalizations during the first week of life, anthropometry, domestic accidents, ONE follow-up, emergency consultations, hospitalizations).
Maternal breast-feeding at birth was high (91%) but the mean duration of breastfeeding was only 3-4 months, as described in other Belgian studies with no significant differences between the 2 groups.
Vaccine coverage was good in both groups: only 4% (study group) and 9% (control group) did not receive vaccines according to the national schedule, the main problem being absence of Rotavirus vaccination (25% and 19%, respectively).

Conclusions

Our study confirms the presence of a precarious population in Brussels, as described by other national studies (41,5% of children in Brussels living below poverty level, versus 18,8% in Belgium). Women from Sub-Saharan Africa recently arrived in Belgium seems to be more fragile both in our study and in national literature.
Pregnancy follow-up seems less regular in precarious contexts. In contrast with international literature, we did not find significant differences in birth weight nor in gestational age, probably also thanks to specific programs offering pregnancy follow up for women with no healthcare coverage (eg.
ASBL Aquarelle, ONE).
The high frequency of maternal breast-feeding at birth in our samples underline the importance of reinforcing support after discharge in order to maintain the breastfeeding over the first year of life.
Vaccine coverage was good in both groups: vaccination was mainly provided by O.N.E.
Main limits of our study were the small number of our population, the high number of lost to follow up and the collection of data only from St Pierre hospital and ONE consultations.
In conclusion, we can confirm the existence of a precarious population in Brussels, but also the existence of effective measures for reducing their effects on newborn and infant's health, with a strong role played by Aquarelle and O.N.E.. We underline also the difficulty of making a link between hospital staff and preventive Pediatrics structures, which could be implemented for a better follow-up.

GP 02

A five-year-old girl with Henoch Schönlein purpura presenting with a rare cause of abdominal pain and vomiting

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Introduction

Gastrointestinal involvement is common in Henoch Schönlein purpura (HSP) and occurs in approximately two thirds of children with HSP. Abdominal pain is the most common gastrointestinal symptom in HSP and is typically severe and colicky. It is caused by oedematous haemorrhagic infiltration of the intestinal wall, secondary to small-vessel vasculitis. Complications of gastrointestinal involvement, including intussusception, bowel ischaemia and spontaneous perforation of the small bowel, occur in 4.6% of the patients.

Methods

We will describe a five-year-old girl with diagnosed HSP who was readmitted to the hospital with abdominal pain and vomiting.

Results

A five-year-old girl initially presented to our hospital with typical palpable purpura on the lower extremities accompanied by joint pain. She was diagnosed with HSP and was treated with a low dose of non-steroidal anti-inflammatory drugs (NSAIDs). After a stay of 2 days in the hospital she left the hospital in good condition and without further medication. However, three days later she was readmitted to the hospital with abdominal pain and vomiting. On clinical examination the abdomen was non tender and there was no guarding or rebound pain. There were increased purpuric lesions on the lower extremities. Blood analysis showed slightly elevated inflammatory markers and revealed a strongly elevated lipase. Additional abdominal ultrasonography confirmed the diagnosis of pancreatitis. Subsequently we started with the administration of intravenous fluid and pain medication. The inflammatory parameters, including the lipase, normalized during this treatment and the girl could leave the hospital in good condition after one week of hospitalisation.

Conclusions

Acute pancreatitis is a rare complication of HSP. This rare entity was first described by Toskin et al. in 1965 and since then a dozen or so cases in both children and adult were described. Although HSP is an usually benign cause of acute pancreatitis, it can be complicated with haemorrhage, necrosis and pseudocyst. In this case report we will further discuss the clinical features, presentation, treatment and clinical outcome of pancreatic involvement in HSP. To avoid unnecessary surgery, it is important to consider acute pancreatitis in children with HSP and persistent abdominal pain.

GP 03

Medical devices marketed as medicines: safety and regulatory concerns in children.

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Introduction

Some medical devices (MDs) claim safe, effective treatment by enteral barrier mechanisms, as if it were medicinal drugs, and are promoted to both paediatricians and patients. MDs enter the EU market for direct dispensing through (drug)stores and pharmacies as OTC products, through free movement of goods via CE-labelling, self-marked by the manufacturer, or after national notification via an EU-accredited notifying body (private companies contracting with manufacturers to supply certification to enter the market for a fee, assuring 'conformity'). They escape in-depth review by national medicinal authorities or EMA for regulatory medicinal approval and control of promotional claims.

Aim

To analyse the regulatory quality (non-clinical and clinical) of package inserts of 3 gastrointestinal products for paediatric use. For diarrhea: Tasectan®/Gelenterum® (gelatin tannate, GT) and Tasectan/Gelenterum Duo® (GT+tyndalized heat-killed probiotics; GTTP). For GORD: Ziverel®, Esoxx® (hyaluronic acid/chondroitinsulphate/poloxamer 407; HACDSPol)

Methods

Compare content of package insert with EMA standard. Literature search for published evidence at time of entering EU market.

Results

I. Product characteristics are inaccurately defined in the package insert: sachets GT contain 250mg powder, but the tannate is not specified (tannic acid (TA), gallic acid, bark gallotannins, Chinese, Turkish or other galls?), neither G bloom strength, ratio and free fraction of TA (added to 5 mL milk, 3 layers). GTTP powder additionally contains heat-killed L. acidophilus, L. plantarum, L. casei, L. rhamnosus, Bifidobacterium bifidum, Streptococcus thermophiles (units undisclosed). For HACDPol gel, the doses of HA, CS and Pol 407, origin (rooster comb/bacterial?) and polymerization grade of HA are missing. II. All leaflets allow unlimited use in children from birth onwards: GT and GTTP for effective relief of diarrhea of various origin within 12hrs, HACSPol for promoting mucosal repair/relieving GORD symptoms. Whereas medicines require placebo-controlled studies to support claims, overall clinical documentation was poor, even lacking for children with GTTP and HACSPol. For GT, efficacy was claimed based on 'observations' in 2 'cohorts' (97 children with acute diarrhea (>3months) receiving ORS+GT and 114 children on ORS) for 48hrs; antibiotic use was allowed but not documented, neither diarrhea diagnosis and rating scales; although groups didn't match for baseline stool number (ORS worse), efficacy at 12hrs was based on this parameter, yet no longer statistically significant at 24hrs. A poster disclosed observational data at 12hrs in 97 (same?) children. The only placebo-controlled study in adults (20/group) did not confirm the 12hr claim. For GTTP, studies in adults were even not retrieved; for HACSPol, gel or placebo was given add-on to standard-dose PPIs, even in PPI-naïve adults: there are no data confirming efficacy as single product, neither in comparison to PPI (so no rationale to

switch children from PPI to HACSPol). III. Safety: Rare AEs are difficult to detect if there is no prescription follow-up. MD leaflets mention "no known" or "no observed side effects". Yet, literature calls for attention: 1) GT: TA (μg range) is cytotoxic to intestinal cell lines and not chemically classifiable as safe with regard to carcinogenicity; 2) TPs were shown to give more diarrhea and AEs; 3) HA-dose is 5 to 20-fold the EFSA approved food supplement dose; oral experience with Pol407 (surfactant) is limited to ~5-6 mg/caps/day as excipient for delayed release tablets, yet surpassing >1000 mg/day in the gel [no chronic oral toxicity available; Pol407 abandoned in injectables, due to nephrotoxicity and effects on lipid balance]. Seprafilm® (HA 700mg/Pol407 300mg) sheets for 'single' use against surgical adhesions, were abandoned for gastrointestinal sutures due to increased abscesses, fistulae and sepsis. IV. None assessed or referred to potential drug-drug interactions: 1) TA is known to adsorb many drugs and identified as CYP450 and P-gp inhibitor; 2) HA/surfactant complexes change drug absorption; Pol 407 inhibits efflux transporters and can affect drug absorption.

Conclusions

EU regulation requires only national notification of MDs. This results in the marketing of poorly investigated and poorly labelled oral MDs claimed on 'barrier' effects, but hardly or not evaluated in children. They do not guarantee effective and safe 'medical' treatment of children, as for a medicinal drug registered though EMA or medicinal authorities. As a consequence, after launch of MDs in the EU, children currently serve as test subjects by direct exposure to these MDs, be it without effective pharmacovigilance.

GP 04

Medical devices in EU claiming oropharyngeal or gastrointestinal barrier action: barrier products or hidden pharmacological agents?

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Introduction

In deciding whether a product falls under EU drug regulations (EMA reviewed and approved) or EU medical device (MD) regulations (a national competence requiring CE certification only), the EU Directive states that particular account shall be taken of the principal mode of action of the product; in MDs, pharmacological actions are ancillary to the primary MD function. Hence 'medicine' products are increasingly launched in the EU as medical devices (MDs), claiming effective treatment primarily through a barrier function, while making multiple pharmacological claims.

Aim

To analyse the evidence for barrier and/or pharmacological actions of barrier-claiming MDs, by analysing package inserts, published evidence and promotional claims of 3 MDs and their ingredients: gelatin tannate (GT, Tasectan®,Gelenterum®) for diarrhea; hyaluronic acid/chondroitinsulphate/poloxamer 407 HACSPol (Ziverel®,Esoxx®) for GORD; glycerin/trypsine (GlyTS) oral mouth spray (Viruprotect®,Coldzyme®) for common cold

Methods

Extensive literature search on pubmed and internet in general (search strategy and reference list available upon request)

Results

None of the studies claiming barrier function were unambiguously conclusive: the claimed film effect was never observed/visualized. For all 3 MDs, mapping the experimental design illustrated that the claimed barrier was at the wrong side (contradicting pathophysiology): oral GT (=in gut lumen) was claimed to function as barrier against LPS toxins administered intraperitoneally (=serosal); HACDSPol reduced the protein extravasation from inflamed oesophageal wall to lumen (Evans blue used, instead of testing a bioadhesive barrier against luminal acid/pepsin diffusion/aggression as proven for alginates). It is recognized that Pol407 and modified HA/Pol407 composites can form (film)barriers by thermogelling (e.g. FDA-approved LeGoo® for endovascular occlusion on cardiac surgery and Seprafilm® against surgical adhesions, yet excluding GI-sutures); however, for thermogelling about 10-fold higher concentrations Pol 407 are needed; they are stable MDs requiring single application only; submucosal HACSPol(80%)-injected oesophageal cushions disappeared in 20 min. GlyTS, spayed in the throat, was claimed to form a barrier against rhinoviruses: however, rhinoviruses cause infection via nasal and not oral cavity, while glycerol is a good solvent mixing with water; 1-day prophylactic treatment with GlyTS could not prevent rhinovirus infection following nasal viral challenge. The assessed effects were always explainable by pharmacological actions of single ingredients, or physicochemical effects specific to the test model: 1) In GT models, effects were observed at caustic 37% HCl (tanning action; no significance at 3.7% - 10% HCl) or pH was close to the isoelectric point (iP) of G (pH 4.7) keeping GT precipitated, which however cannot guarantee barrier function at the pH range of human gut and its secretions: GT hydrolyses above and below iP. Tannins are

moreover hydrolysable and bacterially degraded, gelatine digested. Tannins have been found to exert many bio/pharmacological actions at (very) low concentrations (tannate-specific; range 0.1- 100 μg/mL; 0.1-1% of GT dose in the models): all but one model (using aberrantly high toxic TA doses) failed to validate the claimed barrier effect by including relevant TA controls. TA also precipitates dextran in presence of protein at iP 5 (= pH in mice gut), invalidating the GT dextran sulphate-induced colitis model. 2) For HACSPol, pharmacological actions of HA (fragments) can be mediated by binding to HA-binding receptors, abundantly present in the human oesophagus; they include angiogenic, immunostimulatory and anti-inflammatory actions (0.2% topical solutions heal buccal ulcers (= 6x less)). The effect may also be poloxamer-mediated alone, as Pols have been shown to reduce leakage by counteracting cell integrity deterioration, or simply to inhibit influx of Evans blue. 3) TS acts as signalling molecule on PAR in many complex processes of the body (including viral infection). For all MDs, pharmacological claims were made either in patent, developer-associated publications, leaflet or promotion, to support action and efficacy: a recent review listed HACSPol under 'Drugs' for GORD (Savarino 2017).

Conclusions

Evidence provided for barrier effect of MDs is non-conclusive. The barrier claim lacks either a scientific rationale (wrong barrier side), or is not tested in a validated model applicable in humans. As MDs escape claim control of medicinal drugs, vague barrier claims allow them making largely pharmacological and non-proven efficacy claims. Hence, CE marking of such MDs does not represent medicinal quality.

GP 05

EU medical device legislation (CE label) opens the door to unstudied products for OTC "medical" treatment of cough, based on "barrier" claim

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Introduction

A medical device (MD) means any instrument, apparatus, appliance, software, "material or other article", whether used alone or in combination,...to be used specifically for diagnostic and/or therapeutic purposes. Interpretation of "material" or "other article" as "sostanza o altro prodotto" in Italian (instead of "materiale y articulo"), "stof" in Dutch ("materiaal"), and "Stoffe" in German ("Material"), has led to the entry of oral medical treatmentfor children in the EU market by simple CE certification as a medical device, either self CE-marked by the manufacturer (CE without No.) or after certification by an EU-accredited notifying body (NB) (CE followed by identification No. of NB).

Aim

Identification and evaluation of sirups, sprays and lozenges, labelled in Dutch as MDs for "cough" and "throat(ache) + cough".

Methods

Google internet search (20/11/2017) for cough (+throat) and medical device was performed in Dutch, limiting the results to Flanders(BE) and the Netherlands(NL). Identification of composition, claims on mechanism of action, age of use, precautions and CE certification. Also several on-line pharmacies or drugstores were screened. Brands popping up with formulations not CE marked were excluded.

Results

30 products from 17 different companies were identified to be sold via (drug)stores (NL) and pharmacies online (BE,NL). Sometimes there was confusion on the MD status, 3 were subsequently identified as food supplement (1 'health product': 6.5% thyme syrup from age 0 onwards) and excluded. Twelve MDs were syrups, 8 sprays, 7 tablets/lozenges. Seventeen were manufacturer self-marked CE certified, one of which certified by another distributor (CE0459=G-MED,France), 5 were certified by Istituto Superiore di Sanita,Italy (CE0373), 4 by ECM, Germany (CE0481), 1 by MEDCERT GmbH,Germany (CE482). Umbrella branding together with medicines was common: e.g. Fabre markets BalsoKids® as MD with 2 Balsoclase® brands registered as medicines. Natterman lists 13 "effective" formulas for dry and congestive cough, 4 MD brands and 8 medicinal brands (1 undefined/lozenges). The manufacturing company often differed from the distributing company and these also could differ from the company dealing with information/questions. "Active ingredients" included "special formulations" or "powerful combination of 100% natural ingredients" (n=4), patented polymers (saccharides?) without any PuChem identification: Polysac-ActiveTM (n=5), Salvidol 2-LMF (n=3), and Poliflav (n=1), the latter described as a polysaccharide fraction of Plantago and flavonoid fraction of Thymus. Mel (honey, Apis mellifera) was claimed as active ingredient in 5, but present in 10 sirups claiming a barrier effect. Other additional active ingredients were herbal polysaccharides/herbs, such as Aloë vera, Thymus extract, Icelandic Moss, Althaea officinalis, licorice and Plantago, eventually specified to act in synergy. Glycerol (present in 2) was the single agent to claim a barrier in the throat in 1 syrup (yet being a good solvent). All other formulas

contained herbal medicines, or herbs, (gel, oil, concentrate, (dry) extract, root or leaves), such as Chondrus Crispus, Salvia Officinalis, Althaea officinalis radix, Verbascum Thapsus, Zingiber Officinale Root, Thymus Vulgaris, Salvia Officinalis, Glycyrrhiza glabra, Hedera helix extract, Grindelia, Malva, Illicium Verum Seed, Propolis,... Several of these herbs have been EMA reviewed as traditional medicines. For none of the ingredients, de mg-dose exposure was mentioned. All made claims of demulgent, lubricating and protective action, and effective relief of cough (for dry, tickle, congestive, allergic, mucous, burning or/and irritating cough, or for all types) +/- pain, linking the barrier effect also to recovery and protection against irritating substances (such as smoking). Age of use varied from birth till from 8 years onwards (one syrup = adults only). Many focussed on the pleasing taste for children. Some but not all listed precautions (allergy, breast-feeding, pregnancy, irritation for sprays). Most leaflets referred the child to the doctors after 7 to 30 days of use (some however referring also in case of lot of mucus and high fever). Some sprays warned not to breath during spraying, one warned to stop if irritation occured. All claimed to be generally well tolerated, and/or no adverse event was reported or expected. For none of the products, clinical studies or evidence for use were found or referred to.

Conclusions

Physicians should be aware of the increased over-the-counter availability of (unstudied) MDs for cough, containing (unknown) polysaccharides and/or glycerol, and most often other herbal substances, often in combinations. MDs present not only as syrup or lozenges, but also as sprays for children. MD regulation in the EU needs revision.

GP 06

Malnutrition in hospitalized children in Mayotte : prevalence and management

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Introduction

Malnutrition in hospitalized children is frequent and has several short and long term consequences. Mean prevalence in Europe in the last decade is about 10%.
In Mayotte, a French island in the Indian Ocean, the poor socio-economic conditions are responsible for a pediatric malnutrition that reach up to 7.3% of the general population.

Aim

The purpose of this study is to evaluate the prevalence and the management of the malnutrition among the children hospitalized in Mayotte. We also studied the efficiency of the Pediatric Nutritional Risk Score (PNRS) to assess the risk of malnutrition and the potential association between malnutrition and length of stay in the hospital.

Methods

We have made a prospective observational study in the pediatric unit of the only hospital of Mayotte (CHM). All the children admitted have been included between January 11th and April 4th, 2017. At the admission and at the discharge of each patient, nutritional and anthropometric information were collected through a standardized form completed by the pediatricians.

Results

380 patients have been included. Median age was 11 months old.
The prevalence of acute malnutrition, including mild stage(grade 1), was 40% according to the Waterlow score and 50% according to the Body Mass Index. Chronic malnutrition concerned 36% of the children. The nutritional status did not get worse during the stay, unlike previous studies. The PNRS was not predictive of a negative evolution for the children who were the most at risk of malnutrition. Median length of stay was 1 day longer for the undernourished patients compared to the well-nourished patients.

Conclusions

Acute and chronic malnutrition still is an endemic issue in Mayotte in 2017. However, the management of these patients in the pediatric unit is fairly good and sometimes even better than in European pediatric centers.

GP 07

Anisocoria: not always alarming - a case report

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Introduction

A 6-year old girl, with no significant medical history, presented with sudden onset right-sided mydriasis. History and clinical examination could not elucidate other accompanying symptoms. This raised great concern for the parents with fear of an intracranial mass. Establishing a correct diagnosis can be quite time-consuming and costly if pharmacologic mydriasis is not considered, especially in a young population. A detailed history is therefore crucial in the differential diagnosis.

Aim

Determining a work-up of unilateral mydriasis.

Methods

Recent literature was reviewed to determine a systematic approach to the work-up of unilateral mydriasis.

Results

A 4-year old girl, with no medical history, presented at the E&A department with sudden onset right-sided mydriasis. Accompanying symptoms of blurred vision, eye pain, diplopia or headache were absent. There was no recent trauma. Initially, no systemic medication was mentioned by the parents, but after thorough questioning, nebulized Ipratropium and Salbutamol appeared to have been used for wheezing bronchitis. General neurological exam was normal.
Upon clinical examination, a fixed dilated pupil was seen at the right eye. This right pupil was not responsive to light nor convergence, whereas the other demonstrated brisk constriction. General ophthalmic examination including visual acuity, extraocular motility, biomicroscopy and fundoscopy was unremarkable. Ptosis was absent.
In the work-up of anisocoria, the first step should always involve determining whether anisocoria is most notable in photopic or scotopic conditions. In this case, anisocoria was most pronounced in scotopic conditions. Therefore, the differential diagnosis should include ocular conditions that keep the large pupil from constricting (posterior synechia, previous ocular surgery, ocular trauma, ?), pharmacologic agents (atropine, tropicamide, cyclopentolate), Adie?s tonic pupil and third nerve palsy. Based on history and ophthalmic examination, ocular conditions can already be excluded from the differential diagnosis. Secondly, Pilocarpin 0.1% was instilled into both eyes. Bilateral absence of pupillary constriction as well as absence of convergent pupillary constriction were able to exclude Adie tonic pupil as the cause. Next, Pilocarpin 1% was instilled into both eyes. Upon instillation, only the ?normal? left eye constricted, while the right did not. This effectively excludes third nerve palsy as the cause of pupillary dilation. After this workup, it became clear that pharmacologic anisocoria has to be the cause of this sudden onset right-sided mydriasis.
During the diagnostic workup, the possibility of an intracranial cause was discussed with the mother as well as the possibility of neuro-imaging. Because of the mother?s pronounced fear of cancer, she demanded neuro-imaging to be performed, even when further workup excluded third nerve palsy as a possible cause.

Discussion
Unilateral mydriasis can be caused by several medical conditions. As demonstrated in this case, history is of the utmost importance. Since initially there was no mention of nebulized therapy, a diagnosis of pharmacologic mydriasis could have easily been

missed. Next, to differentiate between possible causes, one must determine whether anisocoria is most pronounced in scotopic or photopic conditions, since this will easily allow exclusion of a great deal of possible causes. In this case, Pilocarpin 0.1% and 1% instillation was used to further exclude Adie?s tonic pupil and third nerve palsy. In case of third nerve palsy associated symptoms are very important for diagnosis and localization of the lesion (nuclear, fascicular, basilar, intracavernous, intraorbital). Nonetheless, pupillary involvement may sometimes be the only sign of third nerve palsy, as seen in basal meningitis or uncal herniation. Therefore, it is recommended to perform an adjunctive Pilocarpin 1% test, even in the absence of other suggestive clinical signs. When this test suggests third nerve palsy, neuro-imaging should be performed.

Conclusions

Pharmacologic mydriasis is a possible cause of anisocoria. Carefull history and clinical examination are important in the differential diagnosis. In addition to the pilocarpine testing it could save from unnecessary neuro-imaging.

G 01

Confirmation of an Association Between CTNNB1 Mutations and Hyperekplexia

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Introduction

Hyperekplexia is a rare genetic pathology which can begin in the neonatal period. Hyperekplexia is characterised by a pathological startle reflex caused by an unexpected visual, auditory or tactile stimulus with generalized hypertonia. It is well known as a canalopathy involving the glycinergic pathway, with 5 genes described as causal: GLRA1, SLC6A5, GLRB, GPHN and ARHGEF9.

Aim

We describe a 4 month old male patient, with healthy parents, who presented hyperekplexia, microcephaly, bilateral palpebral ptosis, axial hypotonia and peripheral hypertonia. A genetic analysis for hyperekplexia (GLRA1, GLRB and SLC6A5) was not informative. The molecular chromosomal analysis was normal ((arr(1-22)x2,(XY)x1)). The evolution of this patient was characterized by developmental delay. The dysmorphological analysis evoked a beta-catenin pathway pathology. A gene panel analysis for neurodevelopmental disorders using a patient-parents trio revealed a de novo haploinsufficiency of CTNNB1 gene (c.1796_1799del).

Conclusions

By this case, we confirm the association of CTNNB1 mutations with hyperekplexia and extend the list of genes possibly associated with this rare pathology.

G 02

Isolated hyperferritinemia in a newborn revealing hereditary hyperferritinemia cataract syndrome

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Introduction

Hyperferritinemia may suggest hemochromatosis with the potential cardiac-, hepatic- and endocrine complications.

Aim

We describe here a case of isolated neonatal hyperferritinemia due to an autosomal dominant hyperferritinemia cataract syndrome.

Methods

In a blood analysis performed because of the mother's HIV seropositivity, isolated hyperferritinemia (1492 μg / L, N: 11.5-327) was found in a 1-month-old infant of African origin.

Results

The clinical examination of the neonate was normal, in particular, there was no hepatosplenomegaly or jaundice. Blood analysis did not reveal any sign of hepatic pathology (transaminases and free- and conjugate bilirubin were normal for age). Blood count and LDH were normal, without any argument for a lympho-proliferative syndrome or peripheral cytolysis. There was no inflammatory syndrome and HIV PCR was negative. The analysis of the martial parameters showed normal serum iron concentration and normal total transferrin binding capacity. This led to question the diagnosis of hemochromatosis that was initially suspected.

The analysis of the mother's medical chart revealed a similar martial status, with isolated hyperferritinemia (640 μg / L, N: 13-150). The hemoglobin analysis gave normal results.

All these elements led to suspect a hereditary hyperferritinemia cataract syndrome. This was confirmed by the identification of the heterozygous mutation c.-171C> G of the FTL gene (coding for the L subunit of ferritin) in the mother and the patient. An ophthalmological assessment is planned for both, in order to detect early cataract. No further investigations are planed. Indeed, in the absence of iron overload, there is no visceral pathology associated, except the cataract.

Conclusions

In neonates with isolated hyperferritinemia, the diagnosis of hereditary hyperferritinemia cataract syndrome must be evoked. It is essential to look at family members who may have hyperferritinemia, associated or not with early cataract. The only necessary follow-up is an ophthalmological one. Phlebotomies are useless and contraindicated.

G 03

Whole exome sequencing identifies atypical progeroid syndrome due to a recurrent LMNA mutation

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Introduction

A 16-year-old Dutch boy presented to our clinic with walking difficulties and stiff joints. He was born at full term pregnancy with caesarean section because of difficult labour and had a normal birth weight of and length. There were no perinatal complications. His neuromotor development was normal. Problems started around the age of 6 years when parents noticed an abnormal gait and stiff joints. He is currently not able to completely stretch the fingers and flex the knees what causes him difficulties when performing gymnastics at school. Furthermore he has normal intelligence and no significant medical history apart from a surgical correction for an unilateral inguinal hernia at the age of 5 years. He is the first son of non-consanguineous parents, his father has colitis ulcerosa, his 2 years younger brother is healthy and already taller than him. There are no other relatives with similar problems. Physical examination at the age of 16 years and 11 months reveals a height of 158.5 cm (-2.7 SD), a weight of 34 kg (-5.7 SD) and occipito-frontal head circumference of 57.5 cm (+0.6 SD). He has a round face with small pointy chin that is accentuated in profile view by a prominent nose with high nasal bridge. He has also has large ears and dental crowding. The thorax appears very narrow with drooping shoulders. He has little muscle bulk. There is no lipodystrophy. Hands are short with broad interphalangeal joints and broad thumbs. There is bilateral pes planus with broad halluces and bilateral coxa valga. Extension of the fingers is limited with also a limited supination of the hands and flexion of the knees. Because no clinical diagnosis could be made, whole exome sequencing (WES) was performed and revealed a de novo heterozygous missense mutation in exon 1 of the LMNA gene (c.331G>A; pGlu111Lys). This mutation was already reported by Garg A et al. in 1 patient with an atypical progeroid syndrome showing similar features as is seen in our patient [1]. Subsequently, additional investigations to look for signs of a progeroid syndrome were performed. Radiographs did not show signs of acro-osteolysis in the hands and distal parts of the clavicles. Cardiac ultrasound and electrocardiogram revealed a normal heart and rhythm. Biochemical analysis revealed normal results and no evidence for diabetes mellitus and hyperlipidemia.

Results

Mutations in the LMNA gene can cause a wide variety of clinical phenotypes including neuromuscular diseases, cardiac disorders, lipodystrophy and premature aging disorders such as classical progeroid syndrome (Hutchinson- Gilford progeria syndrome, HGPS). Heterozygous LMNA mutations can also cause an atypical progeroid syndrome (APS) as is seen in our patient. Only a small number of patients with APS have been described in the literature. Garg et al. described 11 unrelated patients with heterozygous missense mutations in LMNA causing an atypical progeroid syndrome phenotype characterized by growth delay, short stature, small mandible, overcrowding of the teeth, beaked nose, thin lips and a generalized progeroid appearance with reduced fat and muscle mass. Also mild flexion contractures are seen in the majority of patients. Onset of symptoms seems to be slightly delayed compared to patients with HGPS who usually show symptoms before the age of 1 years. Garg et al. also noted marked phenotypic variability in degree of lipodystrophy, insulin resistance, hyperlipidemia, osteoporosis and cardiac valvular anomaly. To our knowledge
there is only one previously reported case with the same mutation as in our patient (c.331G>A; pGlu111Lys). Interestingly, in both cases there were no biochemical signs of lipodystrophy.

Conclusions

We present a case of atypical progeroid syndrome caused by a de novo heterozygous missense mutation in exon 1 of the LMNA gene (c.331G>A; pGlu111Lys). To our knowledge it is only the second case with this mutation. Phenotype is very similar and so contributes to the further characterization of these patients. In addition, our case illustrates the power of WES in patients with an unclear clinical diagnosis.

G 04

Early onset epileptic encephalopathy caused by a 'de novo' KCNQ2 gene mutation in a boy: from phenotype, genotype and treatment

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Introduction

Early onset infantile epileptic encephalopathies refer to a wide spectrum of conditions whereas seizure onset occur within the first few months of life together with motor and cognitive severe involvement (Ohtahara, Dravet and West syndromes) represent the most frequent. Similarly a wide spectrum of EEG pattern, cortical brain malformations and chromosomal anomalies may be identified. Large genetic heterogeneity exists since mutation in one of these genes may be identified: ARX, CDKL5, SCN1A, STXBP1, MAGI2, SC25A2, PCDH19, SPTAN1. KCNQ2 gene encodes for the member 2 of the potassium channel protein family that regulate cell ability to generate and transmit electric signals in brain neurons.

Aim

Through precise phenotype description to complete genotype identification, better delineate natural history inside this large category of early onset epilepsies, possible targeted treatment and precise genetic counseling

Methods

GENETIC ANALYSIS: After rule out for CDKL5 gene mutation, a NGS approach (gene panel) allowed to identify presence of the c.820A>G in KCNQ2 gene. This change was confirmed by Sanger sequencing to the patient. 'De novo' occurrence was established since investigation to both parents did not show presence of the mutation.

Results

We report the case of 5 years old boy with early infantile epileptic encephalopathy (EIEE) Our patient was born at term from non-consanguinous parents. There is no previous family history for congenital malformation, epilepsy or cognitive anomaly. Pregnancy and delivery were uneventful (Apgar score 5/ 9 at 1 and 5 minutes). Birth parameters were along 50th Centile. During the first month of life, he had no fever but frequent cry. Gastroscopy showed grade A esophagitis. At age of 2 months, although treatment for reflux was continued, he was admitted for hypotonia and opisthotonos. Metabolic screening and neuroimaging were negative. EEG video showed a marked discontinuous pattern with excess of diffuse slow elements together with occipital bilateral spikes and sublclinic crises. Axial hypotonia, peripheral hypertonia and absence of eye contact were noted as oculogyric crisis. Pyridoxine test was not contributive. Sabril and Rivotril were not able to control the crisis for the first 9 months. Due to refractory epilepsy (Topamax, Valproate, Cetogene diet, Keppra and Frisium), switch to Carbamazepin allow to control seizure for 2 years. Secund brain MRI showed loss of white matter with widening of furrows and ventricles, thinner corpus callosum (aspecfiic images encoubntered also metabolic disease. He developed severe psychomotor delay and quadriplegia.

Conclusions

KCNQ2 mutation was described in benign familial neonatal seizures and recently in epileptic encephalopathy.). The phenotype and EEG pattern classification are very important for a better understand of epilepsy. Knowledge of genetic cause of epilepsy

should improve management and open for precise genetic counselling (index patient as his family

G 05

Variable presenting symptoms of Costello syndrome

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Introduction

Costello syndrome is one of the RASopathies, a family of genetic developmental disorders caused by mutations in the RAS/MAPK signaling pathway. It is an autosomal dominant disorder, characterized by facial dysmorphisms, hair and skin abnormalities, congenital heart defects, musculoskeletal defects and developmental delay.

Aim

Based on a two case reports we aim to illustrate the variability in initial clinical presentation of neonates subsequently diagnosed with Costello syndrome.

Methods

Case 1: A girl, born at a gestational age (GA) of 38 weeks with birth weight (BW) 3860g (>p95), length 49cm (p50) and head circumference 37cm (>p95), was transferred to the neonatal intensive care unit due to suboptimal drinking and dysmorphic features. Apgar scores were 6, 9 and 9 at 1, 5 and 10 minutes respectively. The pregnancy was complicated by thickened neck fold on prenatal ultrasound. A non-invasive prenatal test for trisomy 21 was normal. Postnatal clinical examination revealed macrocrania, macroglossia, large lips, wide nasal bridge, downslanting of the eyes, unilateral ear crease, pectus excavatum, finger pads, loose soft skin with deep palmar and plantar creases. In the first days of life glycemic values were around 40mg/dL with one documented hypoglycemia of 22mg/dL.
Case 2: After spontaneous premature rupture of membranes at a GA of 34 weeks and 1 day, a boy with BW 3000g (p95), length 47cm (p75) and head circumference 33cm (p75) was delivered. Apgar scores were 3,5 and 8 at 1,5 and 10 minutes respectively. The pregnancy was complicated by polyhydramnios and by gestational diabetes treated with insulin. Prenatal chromosomal screening by array CGH revealed no pathogenic variants. At birth he presented with macrosomia, coarse facial features, macroglossia, large lips, wide nasal bridge and bilateral ear crease. He was admitted to the neonatal intensive care unit due to respiratory distress needing nasal continuous positive airway pressure. Glycemic controls were at the lower normal range (45-55 mg/dL). During the neonatal period he had excessive vomiting and feeding difficulties. Neonatal convulsions were documented on postnatal age 22 days and treated with phenobarbital and levetiracetam.

Results

In both cases, a normal methylation on chromosome 11q15 was documented, advocating against Beckwith-Wiedemann syndrome. The diagnosis of Costello syndrome was confirmed with a de novo heterozygous c.34G>A (p.Gly12Ser) mutation in the HRAS gene in both patients.

Conclusions

Based on 2 case reports of neonates diagnosed with Costello syndrome, we aimed to illustrate that besides the dysmorphic features, the initial presenting symptoms (i.e. hypoglycemia, respiratory distress, convulsions) can be variable. When hypoglycemia or convulsions are accompanied by severe feeding difficulties, coarse facial features, hypotonia, deep palmar and plantar creases or neonatal arrhythmia in the neonatal

period, Costello syndrome has to be considered. Multidisciplinary follow-up on growth and development as well as parental support is of utmost importance.

G 06

One diagnosis for twins

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Introduction

VACTERL is the acronym of Vertebral, Anal, Cardiac, Tracheal, Esophageal, Renal and Limbs abnormalities. The diagnosis is defined by the presence of at least three of the above described congenital malformations.
The etiology of this syndrome is unknown but the inherited component is described.
We report the case of twins presenting abnormalities of this syndrome at different severities.

Aim

Case report

Methods

Case report:
The pregnancy is spontaneous, bi amniotic and with a suspicion of monochorionicity. The parents are non consanguineous and with no specific medical history. The fetuses are two girls. Twin one developed a severe intra uterine growth retardation (IUGR) with a congenital cardiopathy. Twin two presented a renal defect.
Due to the IUGR of twin one, the delivery is planned at 34 weeks of gestational age. At birth, twin one weighed 700 g and displayed multiple malformations: esophageal atresia type three operated at day zero of life, a duodenal atresia operated at day two, a large cleft palate, two hemi vertebras and a large cardiac ventricular septal defect. Twin one have three clinical criteria for the VACTERL association. Twin two weighed 1800g and presented an unilateral megaureter and an ostium secundum defect. Twin two present only two criteria for the VACTERL association.
During the pregnancy, the amniotic fluid punctures revealed a normal Fluorescence In Situ Hybridization (FISH) and a normal Array Comparative Genomic Hybridization (CGH) (resolution : 44 K Kilobases). At delivery the bichorionicity is clear and ABO-Rhesus blood groups the same.
Due to clinical severity, a second CGH (resolution180 K ISCA) is done on twin one. It shows three variants of DNA non significant for the VACTERL association. Twins zygosity determination is particularly important in this case of twins with shared pathology for easier identification of a genomic mutation.
A quad mendeliome of parents and both twins (included zygosity determination) is planned.

Results

Comments :
The antenatal ultrasound diagnosis of the VACTERL syndrome can be difficult as some defect are less detectable. A deep clinical investigation at birth is required further to confirm the association.
Approximately 90% of cases of VACTERL association appear to be sporadic, with little increased risk of having multiple affected individuals within a family. In this case, it is uncommon to found for all affected individuals all criteria of VACTERL, as an eventual mutation can be clinically differently revealed. The usual genetic work up can be normal.
Zygosity determination in the case of dichorial twins is complicated as one-third of monozygotic twin pairs have separate placentas.
The mendeliome is the part of the nuclear DNA containing all the genes already

known to be at the origin of rare genetic diseases (actually a library of ~4000 genes).

Conclusions

The familial genetic study using a mendeliome quad (the two parents and the twins), will be interesting for determination of zygosity and agnostic detection of pathogenic variants. Twins are a precious source in genetic research.

G 07

Suspicion of Infantile Cortical Hyperostosis or Caffey disease : A case report.

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Introduction

Introduction
Infantile cortical hyperostosis (ICH) or Caffey disease is a rare genetic disorder caracterized by an infantile episode of massive subperiosteal new bone formation. All bones can be involved but the mandibular involvement is caracteristic and is an essential diagnostic criterion (present in 75-95% of cases). Radiological aspect is typical. Soft tissue swelling, fever and unusual irritability can be part of the clinical presentation. Lab tests can show inflammatory syndrome. Differential diagnosis includes post-traumatic lesions (especially child abuse given the young age of the patients), metabolic disorders, tumoral, infective or inflammatory process. ICH is a genetic condition linked to a mutation in the COL1A1 gene (encoding alpha 1 chain of type I collagen) and is transmitted as an autosomal dominant trait. Family history can be missing because of incomplete penetrance or neomutation. It's a self-limiting condition that usually begins in the first 6 months of life and resolves after 2 years. The only treatment consist in pain management.

Clinical case
Our patient, a 3 month-old baby boy, is brought to the emergency room for painful swelling and reduction in mobility of his right wrist and forearm, without fever and without any history of trauma.
Past medical history revealed dystocic delivery at 37 weeks of gestational age with brachial plexus palsy, and an episod of painful swelling and reduction in mobility of left leg after 1 month of life. X-ray showed then important hyperostosis of left tibia, credited to an old fracture due to the labour dystocia.
There's no particular familial past medical history. He's the only child of two parents who seem to be adequate when interacting with the child.
Clinical examination showed only a painful swelling of the right wrist and forearm without redness or warm, and a palpable bone callus of the left leg.
X-Ray revealed an important hyperostosis of the right radius, comparable to the one found previously in the left tibia.
Laboratory tests were normal (full blood count normal, no inflammatory syndrome, blood alkaline phosphatase normal, normal kidney function).
Additional radiological assessment (whole skeleton x-ray) is required because of a suspicion of child abuse, and showed multiple hyperostosis with a typical involvement of mandible, allowing us to suspect ICH. Symptomatic management with acetaminophen was installed.
The baby was sent to the genetic department. COL1A1 mutation research is still in progress.

CONCLUSION :
ICH is a rare genetic condition causing multiple hyperostosis in infant. This condition must be suspected on a clinical and radiological basis, and confirmed by genetic analysis. Differential diagnosis includes post-traumatic lesions (especially child abuse), tumoral, metabolic, infectious or inflammatory disorders. Although the picture of hyperostosis can be very impressive, this is a completely benign condition, with a complete resolution within the first two years of life in most cases.

O 01

The link between neurocognitive functioning and health-related quality of life in pediatric brain tumors

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Introduction

Thanks to medical advances during the last decades, children with a brain tumor reach adulthood more often. Measurements of health-related quality of life (HRQOL) and neuropsychological functioning have therefore become increasingly important.

Aim

Our study aimed to examine the impact of neurocognitive functioning on HRQOL in patients, both immediately after diagnosis and in follow-up.

Methods

Children diagnosed with a brain tumor at the University Hospitals Leuven, were followed with neuropsychological assessments. In total, 49 patients (mean age at diagnosis 8.91 ± 4.18 years) were included, diagnosed with pilocytic astrocytoma (n=25), medulloblastoma (n=9), ependymoma (n=3), craniopharyngioma (n=3) and atypical brain tumors (n=9). Neuropsychological assessments were acquired within maximum six months after diagnosis, as well as after two years. Assessments included objective measurements of cognition (intelligence, memory, visual-motor functioning, attention and executive functioning) and subjective measurements of HRQOL (PedsQLTM Brain Tumor Module). Paired T-tests and pearson correlations were used to assess relationships between the neurocognitive variables and HRQOL in this population.

Results

Based on paired T-tests, attention ($t(48)=-3.39$, $p=0.001$) and executive functioning ($t(48)=-2.27$, $p=0.03$) declined over time. Consistent with literature, we found few significant correlations between the neurocognitive variables and the general measure of HRQOL. At diagnosis, a significant association between memory and patient-reported HRQOL was found ($r=0.453$, $p<0.05$). Interestingly, the follow-up measurement showed different correlations. More specifically, parent-reported HRQOL was correlated with both performance intelligence and executive functioning ($r=0.410$, $p<0.01$;$r =-0.323$, $p<0.05$). Correlations between subscales of HRQOL showed at diagnosis an association between verbal intelligence and parent-reported cognition ($r=0.427$, $p<0.05$) and at follow-up between attention and parent-reported cognition ($r=-0.356$, $p<0.05$).

Conclusions

Newly arising correlations after two years suggest a stronger link between attention and executive functioning, most strongly declining neurocognitive functions in our population, and subjective measurements of HRQOL. Possibly, parents' expectations of daily life functioning also change throughout time.

O 02

Assessment of pulmonary function in a cohort of children with sickle cell disease

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Introduction

Pulmonary complications of sickle cell disease (SCD), such as chronic sickle cell lung disease and acute chest syndromes (ACS), are important causes of morbidity and mortality. Since the highest incidence of ACS occurs during childhood, lung alteration may start early in life.

Aim

The main aim of our study was to assess the prevalence of pulmonary function alteration in children with SCD followed at our hospital. The secondary aims were to look for association between altered pulmonary parameters and potentially deleterious variables, in order to identify potential risk factors.

Methods

We retrospectively reviewed the files of the 168 children with SCD followed in our hospital and recorded their pulmonary parameters, as well as anthropometric data, biological variables and clinical events. We then assessed their pulmonary function and looked for association with the recorded data.

Results

We found a very high proportion of patients with severe phenotype (hemoglobin SS or Sb0) and treated with daily hydroxyurea in our cohort. More than half of the patients (55%) presented a ventilatory function alteration, of which 38% are obstructive and 17% restrictive. Lower oxygen saturation, higher white blood cells, as well as a higher number of vaso-occlusive crises (VOC) were found in the group presenting an obstructive lung alteration. A significant negative correlation between the white blood cells count and the FEV1/FVC as well as the FEF25-75 was revealed; supporting the hypothesis that chronic inflammation could be responsible for obstruction of the small airways. A history of severe ACS was significantly correlated with a worse FEV1, FEV1/FVC, FVC and FEF25-75. The number of severe ACS and the length of stay were also significantly correlated with lower FEV1 and FEV1/FVC.

Conclusions

Pulmonary function alterations seem to start early in childhood of patient with SCD, and be associated with clinical events such as ACS and VOC.
Young children being more likely to present ACS, and recent data showing a greater rate of decline of pulmonary function in young children, our results support the fact that screening for lung alterations should begin early in childhood, as well as asthma diagnosis and airway hyperresponsiveness detection, to prevent serious acute and chronic effects in children with SCD.
However, further prospective studies are needed to confirm the link between ACS and obstruction of the small airways in children with SCD.

O 03

Prognostic value of molecular alterations in infantile spindle cell rhabdomyosarcoma

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Introduction

Childhood rhabdomyosarcoma (RMS) is classified as embryonal (ERMS), alveolar (ARMS), or spindle cell (SRMS). SRMS is an uncommon subtype of RMS with age-dependent genetic characteristics, and recent studies on the molecular analysis of infantile SRMS (i.e. =<12 months of age) have correlated the presence of NCOA2 and/or VGLL2 rearrangements with good prognosis.

Aim

In this retrospective monocentric study, we sought to identify the presence of these molecular aberrations in infantile SRMS and investigate their correlation with observed clinical outcome.

Methods

The tumor samples from infantile RMS patients diagnosed between 1990 and 2016 at our hospital were analyzed with fluorescence in situ hybridization (FISH) and/or array-CGH, and correlated with clinicopathological characteristics and survival.

Results

Nine patients were diagnosed with infantile RMS, and three patients were histologically identified as infantile SRMS. Sites of primary disease of infantile SRMS patients included paravertebral, gluteal and periscapular muscles, with FISH analysis revealing absence of NCOA2 and/or VGGL2 rearrangements. Patients were allocated to RMS 2005 protocol (subgroup D); following chemotherapeutic course, two infantile patients diagnosed with SRMS underwent surgical removal and subsequently received 4 months of maintenance therapy (cyclophosphamide+vinorelbine). One patient did not require surgery nor maintenance therapy, and none required radiotherapy. Treatment-related toxicities (nephrotoxicity and temporary neurotoxicity) were documented in two patients. To date, all infantile patients diagnosed with SRMS are alive and well compared to infantile ERMS (66.7% survival) and ARMS (33.3% survival) patients. No patients diagnosed with SRMS developed local recurrence nor distant metastases.

Conclusions

The absence of NCOA2 or VGGL2 rearrangements in infantile SRMS patients did not affect the overall good prognosis. Further studies are needed to identify novel molecular aberrations in infantile SRMS that could correlate with prognosis and event-free survival.

O 04

Individual pain management in vaso-occlusive crisis in pediatric sickle cell disease.

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Introduction

Vaso-occlusive crises (VOC) are deleterious events for pediatric sickle cell patients. Management of acute vaso-occlusive pain is complicated because of the subjective nature of the painful experience. Assessment of pain intensity is a crucial step that must be accurate and systematic.

Aim

- To assess analgesic management and evolution of pain course during a VOC according to the initial pain score.
- To define points of improvement in the management of pain in sickle cell children during painful crises.

Methods

Retrospective study of pain management in sickle cell patients hospitalized for a VOC between January 2009 and March 2017 in two pediatric departments.

Results

We included 101 episodes of VOC for 27 patients. The average age was 7,8 +/- 4,3 years. 43,5% of VOC episodes analyzed occurred in children of 10 years or older. The parameters analyzed were: pain, analgesic management and length of hospital stay. The average duration of hospitalization is 5,8 days +/- 2,7 days. The time required to reach the therapeutic treatment threshold (TTT) (threshold above which the World Health Organization recommends analgesic treatment) was 3,8 +/- 2,7 days. 43,6% of painful episodes present with intense to very intense pain at admission. The pain score was elevated until the resolving phase, which is the time needed to reach the TTT. The intensity of the pain on admission determined the prescription of morphine during hospitalization (p=0,003). The initial pain was influenced by age: more intense in children over 10 years of age (p=0,001). Morphine treatment correlated with longer hospitalization time (p=0,00003), which was 2,28 +/- 3,57 days longer in the case of complications (p=0,016), and 1,29 +/- 2,89 days longer in the case of intense to very intense pain at admission (p=0,008). The time required to reach TTT is negatively influenced by intense to very intense pain on admission (p=0,010), age (p=0,016), and prescription of morphine (p=0,0002). The average time between arrival at the emergency department and administration of the first analgesic treatment is 69,5 +/- 81,1 minutes. The average time between the first two pain assessments is 109,3 +/- 68,7 minutes.

Conclusions

According to our findings, prescription of morphine increases the time needed to reach the TTT and the length of stay. Several explanations for this counter-intuitive finding are possible:
- the child does not respond well to the antalgic treatment received,
- the child has an increased plasma clearance for opioids,
- the child presents with intolerable pain and is first undertreated with a step 1 or 2 analgesic,
- the child presents with tolerable pain in the emergency room, and subsequently

develops intolerable pain during hospitalization.
This study confirms findings described in the literature regarding the characteristics of VOC pain. It highlights the difficulty of pain management in pediatric sickle cell patients during a VOC in an efficient and uniform manner. Indeed, VOC pain in is highly variable due to the multifactorial origin and individual pain tolerance and response to treatment.

O 05

Diagnosis and management of CLOVES syndrome

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Introduction

Congenital Lipomatous Overgrowth, Vascular malformations, Epidermal nevi, and Spinal/skeletal anomalies (CLOVES) syndrome is a newly described, rare, non-hereditary overgrowth syndrome. This disorder is caused by somatic mutations in the PIK3CA gene. These mutations abnormally activate the PI3K-AKT-mTOR cell-signaling pathway. Diagnosis is based on physical examination. Most of these anomalies are present at birth and should be detected in order to recognize this overgrowth syndrome.

Aim

This abstract will provide a review of the diagnosis and management of a rare syndrome: the CLOVES syndrome. Given the limited coverage in recent literature about this disease, this paper will serve as a first guide to the readers interested in the topic.

Results

Case report

Our patient is a 3-week-old girl, born at term with a perfect Apgar score and a weight of 3970 gr (P90). Gestation was normal, except for the detection, on regular ultrasound follow-up, of a possible lymphedema of the left lower limb at 20 weeks of gestation. At birth, physical examination revealed a large port-wine stain spreading along the anterior and lateral side of the left lower limb, from the buttock to the foot. In addition to this capillary malformation, there were some purple microcystic dermal lymphatic vesicles. Overgrowth of the left leg and foot, both in volume and length, was also seen. The volume overgrowth is most likely caused by abnormal and excessive veins and fat tissue. No other signs were noticed. Given the presence of the lipomatous overgrowth, mostly on the sole of the foot, the diagnosis of CLOVES syndrome was made.
The blood test revealed a localized intravascular coagulopathy, with increased D-dimers at 1800ng/ml (normal reference is <500ng/ml) but with a normal fibrinogen level. This coagulopathy is frequent with venous malformations and has no consequences for her daily life. Although, if surgery is necessary, a prophylactic treatment must be given to avoid a per-operative bleeding. A Doppler ultrasound should be done to detect some possible vascular anomalies. The patient must be followed by a pediatric orthopedic surgeon, who will monitor the leg's growth and may plan surgery (soft tissue debulking and epiphysiodeses) if necessary.

Conclusions

When a new-born presents an overgrowth syndrome and vascular malformations, it is a challenge to diagnose the correct overgrowth syndrome. Sometimes, patients with CLOVES syndrome are misdiagnosed as having other similar syndromes, such as Proteus syndrome or Klippel-Trenaunay syndrome. The diagnosis can be made at birth and is based on physical signs and symptoms. The patients will not have all the signs, but rather a combination of abnormalities. Presence at birth of one of the following symptoms should alert the pediatrician of a possible CLOVES syndrome: lipomatous overgrowth (trunk and limbs), vascular malformations (capillary malformations, lymphatic malformations, venous malformations, and sometimes fast-flow malformations, such as arterio-venous malformations), epidermal nevus, and

musculoskeletal anomalies (wide hands or feet, limb asymmetry, macrodactyly, scoliosis).
The diagnosis is also based on imaging: radiography of the extremities, MRI of the whole body, Doppler ultrasound for vascular malformations. A blood test (D-dimer and fibrinogen) is also necessary to look for a possible coagulopathy and a venous component. The confirmation of the diagnosis is possible with molecular testing for the PIK3CA gene mutation.
The purpose of the treatment is not to eliminate the malformations, as elimination is currently impossible. Nevertheless, this is a syndrome that should be managed by a multidisciplinary team to enhance the patient's quality of life. Each type of anomalies must be treated by the correct specialist, such as orthopedist, plastic surgeon, dermatologist, haematologist... Clinical trials with mTOR kinase inhibitors, such as sirolimus, are undertaken, since the discovery of a relationship between the PIK3CA mutation and the overgrowth syndromes. Even if the results appear to be encouraging, they don't yet display reliable proof of improvement in patients with CLOVES syndrome.

O 06

Retrospective study of a series of acute infant leukemia

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Introduction

Acute infant leukemia (AIL) is a very rare and aggressive form of leukemia with poor outcome, representing 5 to 10% of pediatric leukemias. It is characterized by a high frequency of rearrangement of KMT2A (11q23, KMT2A-R), resulting from a chromosomic translocation with several partner genes (of which AFF1 is the most frequent). This leads to higher transcription levels of certain genes and blocking of differentiation of hematopoietic progenitors.

Aim

The aim of the study was to properly characterize the cases of infant acute leukemia recorded in two Belgian reference centers. We specifically focused on three sub-groups. The first consisted of patients with an equal reciprocal translocation (KMT2A-AFF1). The second concerned infants lacking the reciprocal KMT2A translocation (KMT2A-G), which is usually related to a better outcome. The third group consisted of neonatal leukemias (diagnosed in the first month of life), which is related to a poor prognosis.

Methods

We retrospectively studied the characteristics of 20 patients from 2 Belgian reference centers. Thirteen cases were treated in the Cliniques Universitaires St Luc (Brussels, UCL), while 7 cases were treated in the Hôpital Universitaire des Enfants Reine Fabiola (Brussels, ULB). We analysed available information from patient files from patients diagnosed between 2000 and 2017. We recorded clinical, biological and genetic data. Patients with Down syndrome were excluded, as they represent a very peculiar case of infant leukemia.

Results

We identified 14 cases of infant acute lymphoblastic leukemia (ALL), 2 cases of biphenotypic leukemia (presenting surface antigens of both lymphoblastic and myeloblastic lineage) and 6 cases of acute myeloblastic leukemia (AML). Survival was 50% for both subgroups.

Among the 20 patients studied, 8 displayed the same reciprocal translocation (KMT2A-AFF1), known for a poor prognosis. Five patients in this subgroup died. A younger age at diagnosis (< 6 months) and high white blood cell (WBC) count (>100 000/μL) and central nervous system (CNS) involvement were identified as poor prognostic factors. Patients presenting these features suffered from an aggressive disease that caused early relapses, leading to death.

Five patients were not carrying KMT2A-R (KMT2A-G). This subgroup was more heterogeneous, and consisted of 1 ALL-B, 1 unusual ALL-T, 2 AML M4 (eosinophilic leukemia) and 1 AML M7 (megakaryoblastic leukemia). They globally had a lower WBC count at diagnosis than patients with KMT2A-R, 6 out of 7 patients are presently in clinical remission. Both patients with AML M4 presented a genetic abnormality associated with favourable prognosis (inversion between MYH11 and CBFB genes on chromosome 16), and are both alive. The 1 patient who presented with AML M7 had a normal karyotype (no trisomy 21) but died of an Acute Respiratory Distress Syndrome associated with Parainfluenza and Streptococcus oralis during his treatment.

Finally, 7 patients suffered from neonatal acute leukemia (< 1 month at diagnosis). Six patients died. The cause of death is frequently a consequence of the disease itself and toxicity of treatment. Interestingly, we identified one patient with AML M5 (monocytic leukemia) whose grandmother had been exposed to diethylstilbetrol (DES) during her pregnancy. As a consequence, the patient's mother was carrying gynecologic malformations and went through in vitro fertilization (IVF). The role of IVF and DES in leucemogenesis is currently unknown.

Conclusions

Age younger than 6 months at diagnosis, WBC count above 100 000/μL and CNS involvement seem to be poor prognostic factors. It would have been interesting to know if patients who relapsed and died were also carrying mutations of the PI3K/RAS pathway, supposed to be linked with a higher risk of relapse. KMT2A-G patients had a better outcome associated with a lower WBC count, and (inv)16 for those who were specifically suffering from LMA M4. Finally, AIL diagnosed in the first month of life have a dismal prognosis probably linked to their young age. AIL prognosis remains poor but progress should be made in the future with targeted therapies.

O 07

Recessively pathogenic MSH2 missense mutation causing biallelic mismatch repair deficiency syndrome

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Introduction

Biallelic mismatch repair deficiency syndrome (BMMRD) results from a biallelic mutation in DNA mismatch repair (MMR) genes MLH1, MSH2, MSH6 and PMS2. This syndrome results in the formation of early onset malignancies, because of a constitutional genetic instability.

Aim

This is the first report of the implication of hMSH2 c.1667T>C (p.Leu556Ser) in a BMMRD syndrome.

Methods

We present the case of a 14 year-old boy of Turkish origin of consanguineous parents. His oldest sister had been diagnosed in childhood with an aggressive brain tumor and died rapidly at the age of 5 years old. Two other sisters, a pair monozygotic twins, both developed multiple colon polyps, colic and/or small bowel adenocarcinoma and glioblastoma and died of glioblastoma before the age of 20 years. His youngest sister and his parents are in good health. The proband developed an adenocarcinoma in situ of the caecum and a high-grade infiltrating adenocarcinoma of the stomach at the age of 9 years, followed by multiple adenomatous polyps, treated by hemicolectomy, gastrectomy and multiple polyp resections. At age 13 years, he developed a bilateral glioblastoma multiforme (GBM). Initial glioblastoma treatment consisted of complete surgical resection and focal radiotherapy (60 Gy). Glioblastoma relapse occurred 7 months after initial treatment and polyp surveillance revealed in situ adenocarcinoma of the colon at the same time. Immunotherapy with Nivolumab was initiated, which has reported good response in BMMRD related malignancies. He developed severe intracranial hypertension with edema as a side effect of the immunotherapy, for which treatment with corticosteroids was unavoidable. The tumor continued to progress during immunotherapy and the patient died one year after glioblastoma diagnosis. The family history is very suggestive of a mutation in one of the DNA mismatch repair genes. Germline analysis revealed a homozygous hMSH2 c.1667T>C (p.Leu556Ser) mutation.

Results

The clinical history suggested a PMS2 mutation, because of the "late onset" BMMRD (5y.-20y.), the predominance of brain tumors (4/4), the presence of Lynch Syndrome-associated cancers (colorectal, small bowel and stomach cancers) and because of 3 of the 4 BMMRD patients were affected by a 2nd malignancy. Furthermore, PMS2 mutations in heterozygous carriers possess a low penetrance. However, germline genetic analysis ded not confirm the PMS2 hypothesis. Biomolecular analysis showed a class 3 VUS hMSH2 c.1667T>C (p.Leu556Ser), which is a missense mutation giving rise to the pathogenic state (BMMR-D) in case of homozygous genotype, but which does not cause Lynch Syndrome in heterozygous carriers.

Conclusions

Biallelic mismatch repair deficiency syndrome (BMMRD) should be considered in patients who present early onset cancer, multiple cancers, a strong family history of cancer and cutaneous features similar to neurofibromatosis type I. Genetic analysis revealed a mutation of the hMSH2 c.1667T>C (p.Leu556Ser), for which the proband and his twin sisters are homozygous carriers. The clinical presentation of the oldest sister is also highly suspicious for a homozygous genotype but DNA samples were not available to demonstrate this.
The mutation, hMSH2 c.1667T>C (p.Leu556Ser) shows a particularity in the presentation of the heterozygous carriers. Heterozygous germ-line mutations in DNA mis-match repair (MMR) genes usually result in Lynch syndrome, which is the most common inherited colorectal cancer syndrome in adults. Whereas colorectal polyps and cancer did occur in the proband and affected his sisters, no polyps have been detected in the heterozygous carriers in this family.

O 08

Clinical response and Pharmacokinetics Profiles of Hydroxyurea in Children with Sickle Cell Disease

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Introduction

Hydroxyurea (HU) is an important drug for sickle cell disease (SCD) that improves clinical outcome and survival. However, its pharmacokinetics (PK) and pharmacodynamics (PD) are highly variable. HU has an excellent oral bioavailability, with half-life of 2-4 hours and renal elimination. Two oral absorption phenotypes have been identified: slow phenotype with a peak concentration reached after 60 to 120 minutes and rapid phenotype with a peak at 15 to 30 minutes. These phenotypes seem to be linked to the maximal tolerated dose of hydroxyurea and could affect the response to HU.

Aim

The aim of this study was to explore the possible correlation between clinical and biological response to HU and PK and PD parameters.

Methods

This study was conducted at Hopital Universitaire des Enfants Reine Fabiola (Brussels, Belgium) and included SCD children older than 7 years, regularly followed for more than 3 years. PK samples (salivary and plasmatic) were collected at 0, 30, 60 and 180 minutes after oral HU intake. Patients have been classified as good (GR) or poor responders (PR) to HU according to the absence of recurrence of acute chest syndrome on HU and the number of vaso-occlusive crisis (VOC) and hospitalization days on HU. Changes in biological parameters were assessed after 1 year on HU. Chi square test was used for the comparison between good and poor responders on HU. Paired T test was used to compare biological effect of HU for each oral absorption phenotype and ANOVA to compare PK profile among them.

Results

Thirty-one patients with a median age of 15 years (Range: 6-20,4) have been included in this study. On HU, a significant decrease of the number of VOC and hospitalization days was observed with an improvement of biological parameters. The numbers of VOC and hospitalization days were significantly lower in girls compared to boys on HU (0.33 vs. 0, P=0.02 and 3.17 vs. 1.33, P = 0.02 respectively). However, except for reticulocyte count, biological data, age, dose of HU or PK parameters were similar in both sexes.
Eighteen patients have been classified as GR (14 girls) and 13 as PR (5 girls). Their demographic characteristics and biological values (pre and on HU) were not significantly different, except a higher change of HbF level in GR compared to PR (+13% vs. +3.7%; P=0.034). Girls had a non-significant trend to belong to the GR group (P = 0.059).
The median plasmatic peak concentration (Cpmax) was 42.25mg/l (Range: 14.8-62), the median salivary peak concentration (Csmax) was 19.54 mg/l (Range: 5.03-124.43) and the median AUC was 4650mg.min/l (Range: 1197-8742). AUC was similar in both sexes (4650mg.min/l vs. 4666mg.min/l; P=0.79). Except for salivary concentration at 60 minutes (10,3mg/L for GR vs 27,4mg/L for PR; P=0,043), all PK parameters were not significantly different between the GR and PR. No significant correlation was found between peak concentration and demographic parameters.
We identified 3 absorption phenotypes with a Cpmax reached at 30, 60 and 180

minutes for rapid, intermediate and slow absorbers. Six patients have been classified as rapid absorbers, 5 patients as slow absorbers and the 20 others as intermediate absorbers. Biological changes on HU were similar among the 3 phenotypes, but did not reached statistical signification in slow absorbers. 16/18 GR patients reach Cpmax at 30 and 60 minutes compared to 10/13 for PR (P=0.63). The AUC in the 3 absorption phenotypes was not significantly different (P=0.069). No correlation was found between salivary and plasmatic concentration at time-points studied.

Conclusions

No correlation between the absorption phenotype and the clinical response to HU could be found. No correlation was found between AUC, Cpmax and clinical response. Nevertheless, our study has limitation due to the limited sample size. Salivary measurement did not provide reliable information and cannot be used instead of plasmatic samples. The gender is the only factor identified that can predict the biological response to HU (with a trend to a better clinical response in girls) despite similar AUC and PK parameters. This finding may reflect the better adherence to treatment in girls compared to boys. The variability of the clinical response to HU remains to be elucidated.

O 09

MTHFR polymorphisms and susceptibility to methotrexate toxicity : a literature review

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Introduction

CASE 1 : A 13-years old Turkish girl treated for very high-risk (VHR) B-cell acute lymphoblastic leukemia (ALL) developed an acute myelopathy with severe polyneuropathy during reintensification. The neurotoxicity was attributed to methotrexate intrathecal injections. She was tested for methyltetrahydrofolate reductase (MTHFR) 677 polymorphism TT homozygosity, which was not present. Methotrexate therapy had to be discontinued for the remaining of treatment and central nervous system (CNS) prophylaxis was achieved through methylprednisolone-only intrathecal injections.

CASE 2 : A 7-years old caucasian boy was diagnosed with VHR T-cell ALL. The first months of therapy were uneventful, but he experienced severe prolonged myelosuppression following high dose-Methotrexate intervals in reintensification, responsible of consequent treatment delay. Still, there was no delayed methotrexate excretion nor abnormal requirement of folinate rescue nor methotrexate-induced acute kidney failure (AKF). The research for MTHFR 677 polymorphism TT homozygosity was positive. Consecutive dose of Methotrexate during reintensification were reduced to 2mg/m2. Simultaneously, 6-mercaptopurine doses were reduced by more than 75%.

The two patients mentioned above experienced different kind of methotrexate toxicity during reintensification with high dose Methotrexate : neurotoxicity and blood toxicity. None presented with delayed methotrexate excretion or AKF. Status for MTHFR polymorphism was different in those patients. Management of ALL in the setting of such toxicity require dose or schedule adaptation which can alter treatment aggressivity and disease prognosis.
We questioned the interest of MTHFR 677 TT homozygosity research in clinical practice and its implications for management of ALL in patients with methotrexate-induced toxicity.

MTHFR is an enzyme catalysing the reduction of 5,10-methyltetrahydrofolate to 5-methyltetrahydrofolate, the support for conversion of homocysteine to methionine. Methionine is then converted to S-adenosine-méthionine and acts as a substrate for purine synthesis through an enzyme named TPMT, which is involved in 6-mercaptopurine (6-MP) metabolism. Methotrexate inhibits the conversion of dihydrofolate to tetrahydrofolate, thus raising homocysteine levels and blocking purine synthesis and DNA replication. Due to their synergic effect on DNA synthesis, Methotrexate and purine analogs are often administered concomitantly in ALL therapeutic protocols.
MTHFR enzymatic activity is thought to influence methotrexate excretion and, in consequence, cytotoxic effects. Patients with a reduction of enzymatic activity are postulated to be at increased risk of developing toxicity. Three variants exist for MTHFR 677 gene : TT (8-20%), CT (40%), CC (40-52%). Patients harboring homozygosity for MTHFR 6877 TT are described to have a 60% reduction of activity in their enzyme activity.

Methods

We reviewed 53 papers published between 2002 and 2017 in order to determine 1) if MTHFR CC, CT, or TT genotypes interfered with Methotrexate excretion and seric concentrations 2) if carriers of some variants in MTHFR 677 gene were at increased

risk of toxicity (blood toxicity, hepatotoxicity, mucositis) 3) if there were difference in terms of prognosis (event-free survival, relapse rate) for carriers of variants of the gene 4) if carriers of variants had increased susceptibility to leukemia. 5 of these 53 studies were meta-analysis, 2 were reviews.

Results

First striking finding is the high discordance of results, probably due to the high variability of population studied (child/adult, leukemia risk group), of interventions (treatment protocol, different doses and interval between doses, concomitant drugs employed,...) and of definition of outcome (definition of toxicity, treshold for cytopenia). Yet, Methotrexate concentrations appear to be higher in patients homozygous for 677 TT polymorphism (5 studies against 3).
11 studies found an increased rate of toxicities in patients bearing the TT genotype. But 16 studies found no correlation whereas 2 of them found a protective effect of this genotype. Prognosis was described as unchanged in 5 studies, better in one study, and worse in 4 of them. Relapse rate was found higher in 7 studies, and equal in 1. Overall, no increased susceptibility to ALL was found in patients with MTHFR 677 TT genotype (3 studies with no association, 3 studies highlighting a protective effect of MTHFR 677 TT genotype and one study where ALL incidence was found higher in carriers of this variant).

Conclusions

This literature review highlights the heterogeneity and the discordance in data regarding the interest of MTHFR polymorphisms in childhood ALL therapy. Nevertheless, data seems consistant in finding higher methotrexate concentrations and higher risk of relapse in patients harboring MTHFR 677TT polymorphism. Yet, no reproductible association with toxicity has been highlighted.

O 10

Vascular tumors of infancy: from the good diagnosis to the good treatment. A retrospective monocentric study.

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Introduction

Vascular tumors of infancy include a wide range of entities with proper behaviours, complications and treatments. Complementary evaluations are advised to help clinicians making an accurate diagnosis. Nomenclature confusion is frequent despite the International Society for the Study of Vascular Anomalies (ISSVA) classification.

Aim

To give a global overview on the management of non malignant vascular tumors, and enlighten their specific diagnoses, complications and treatments. Also, we wanted to demonstrate that ISSVA classification is still poorly used outside reference centres.

Methods

We made a retrospective, monocentric study on patients from the Dermatology or Oncology departments between 2010 and 2016. A total of 167 patients (216 lesions) were included. The use and respect of the ISSVA classification was compared between our centre and peripheral hospitals. Patients with and without complementary evaluations were compared. Diagnosis methods, complications and treatments were reviewed.

Results

We included 169 infantile hemangiomas (IH), 14 congenital hemangiomas (CH), 5 kaposiform hemangioendotheliomas (KHE), 1 tufted angioma (TA) and 5 pyogenic granulomas (PG). Male to female sex ratio approached 1:1 in most tumors, except for IH patients which involved significantly more girls (sex ratio 1:3). Median age was 3.7 (2.5-6.5) months at first visit. Eighty-five patients (51%) were addressed by a clinician to the reference centre, mostly for diagnosis and management. ISSVA classification respect was significantly higher ($p<0.01$) in the reference centre. Complementary evaluations were ordered for 141(65%) lesions, generally in case of less accurate diagnosis ($p<0.01$). They included mostly Doppler ultrasonography, MRI studies (in order to assess the loco-regional tumor involvement) and histopathological examinations when clinical aspect was unusual or suggested an intermediate or aggressive tumor. These investigations helped the clinicians to obtain a reliable diagnosis ($p<0.01$), and had no deleterious impact on compliance and evolution of the lesions, nor did delay treatment instauration ($p>0.05$).
Most infantile hemangiomas were treated with propranolol at 3mg/kg/day. In order to minimize relapses, treatments were continued until at least one year of age. Median treatment duration (13 [10.00-16.93] months) was expectedly longer than usual, but relapse rates (3%) were lower than expected. Topical timolol was used for superficial small lesions.
Congenital hemangiomas were treated by surgery, topical timolol or propranolol. Surgery was the preferred option if tissue biopsy was required. Beta-blockers were effective and lesions regressed under treatment.
Pyogenic granulomas were treated by surgery or silver nitrate.
Aspirin 2mg/kg/day was used for uncomplicated KHE.
Rates and types of complications differed between tumor subtypes.
Overall, IH patients had 22% complications, including ulcerations and functional

impairment but also life-threatening complications requiring intensive care unit management (n = 3). Symptomatic treatment and propranolol was an efficient therapy for all patients.
Fourteen percent of CH had ulcerations.
Kasabach Meritt Phenomenon occurred in 4 KHE with a platelet count under 35,000/mm3 for all and below 10,000 for 3. One patient was treated with prednisolone alone, one with prednisolone combined with vincristine and the two others received sirolimus at 1,6 mg/m2/day. Response delay to reach 60,000 platelets /mm3 was more than 30 days for the two first patients, whereas it was 3 days and 9 days for patients treated by sirolimus.
Fourty percent of PG were complicated by ulceration and bleeding.

Conclusions

Nomenclature confusion and inadequate classification is frequent for vascular tumors, as proven by our study. We have demonstrated concretely that ISSVA classification is better used in a reference centre. Complementary evaluations are recommended to establish an accurate diagnosis and were shown to be significantly useful for the clinicians. They are also harmless in the management of vascular tumors, with no impact on the patient's compliance or the treatment delay. This study also shows our management for vascular tumors. We advice to treat longer the infantile hemangioma (at least up to one year of age) to avoid relapses. Timolol gel can be an alternative treatment for superficial lesion. We had also good results with propranolol and timolol for CH. IH can have severe complications but propranolol is still effective in those cases. KHE can develop severe KMP and our results confirm that sirolimus is much more effective than other therapies.
This study gives an overview on the management of non malignant vascular tumor from their diagnosis to their treatment with concrete results to support the actual recommendations.

O 11

Gardner Fibroma during childhood: a benign disease?

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Introduction

Fibroblastic and myofibroblastic tumors, a subset of mesenchymal neoplasms, are a relatively common children's disease. Their incidence is about 12% of all pediatric soft-tissue masses. They encompass a broad spectrum of benign to malignant tumors, including myositis ossificans, myofibroma, fibromatosis colli, lipofibromatosis, desmoid fibroma, low-grade myofibroblastic sarcoma and fibromyxoid sarcoma. The clinical manifestations and imaging appearance of these entities are often nonspecific and their histopathologic manifestations may overlap. However, considering the wide array of prognoses and differences in treatment for these different tumor types, an accurate diagnosis is essential.

Aim

We will hereafter report the case of a child who presented an important mass on the left side of his neck in the neonatal period.

Methods

A boy of nonconsanguineous parents presented a left-sided neck soft tissue tumor measuring 23 x 29 x 26 mm at birth. The boy was otherwise healthy. Ultrasound was performed and showed a dense masslike focal structure thickening the left sternocleidomastoid. The child was admitted in our outclinic department at the age of 3 months because of an increased mass volume associated with lateral neck flexion and rotation to the contralateral side. Analysis of the family history revealed that some family members are affected by adenomatous polyposis (FAP). This concerns the father, the paternal grand mother, the paternal uncle and 2 paternal cousins. One of the cousins also had maxillary osteomas. Complete work-up, including blood and urinary data were normal. A second ultrasonography showed a mass within the left paraspinal muscle resembling a hematoma or a tumor. Magnetic resonance imaging (MRI) showed a large fibrous lesion in latero cervical posterior revealing a fibroma. Finally, the biopsy performed 2 months later histologically confirmed a GF. Molecular genetic analysis of the APC gene by polymerase chain reaction is still pending. The clinical and sonographic course was good. The family prefers the option of a conservative treatment with regular follow-up until a surgical intervention can be considered.

Results

Gardner fibroma (GF) is a benign soft tissue lesion, described as a poorly circumscribed tumor-like lesion with particular histologic features. It predominantly affects young children. The majority of cases occur in the 1st decade of life; rare cases of neonatal onset were reported. It typically manifests itself as a paraspinal mass. GFs are associated, in 70% of the cases, with APC gene mutations and therefore with FAP. The association of GF and FAP is part of the Gardner syndrome, which is the association of a FAP with maxillary osteomas, osteomas of the skull, dental anomalies, epidermoid cysts or fibromas. GF can precede intestinal adenomas. The type of APC mutation probably plays a role in the evolution of the fibroma. The optimal treatment for patients with GF is not yet defined. Most patients undergo surgical excision.

Conclusions

Given the high likelihood of APC gene mutation in individuals with GF, continued follow-up of young patients, to check for the later development of intestinal adenomas, is necessary. Examination of the patient's parents and siblings, to check for APC mutation and FAP, is strongly advised as well. Furthermore, clinicians should always give a special look at the family history when facing that kind of fibroblastic mass, especially because of the lack of specificity of their imaging appearances. Finally, depending on tumor site and growth, individual therapeutic options must be thoroughly considered.

O 12

Hypereosinophilic Syndrome in Children : a case report

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Introduction

Hypereosinophilic syndrome (HES) is a rare disorder that can occur at any age. Hypereosinophilia is classified in mild - moderate - or severe depending on the absolute peripheral eosinophil count (AEoC) (>350/uL - >1500/uL - or >5000/uL). HES can be subdivided into three main categories: Monoclonal (myeloproliferative malignancy with clonal eosinophil expansion), secondary (reactional) and idiopathic hypereosinophilic syndrome (IHES). The presentation varies from an asymptomatic disease to severe life-threatening multisystemic disease.

Aim

The aim of this case is to highlight the differential diagnosis and management of HES.

Methods

This is a case report of a 5 years-old boy who was diagnosed with hypereosinophilia in a secondary center in 2017.

Results

Case:
A 5 years-old boy initially presented with persistent fatigue, recurrent upper respiratory symptoms and a history of bilateral wrist swallowing a week ago. He had no fever, no sweating and no knowledge of body weight loss. He had no particular background except for known dust mite allergy and recurrent bronchiolitis in early childhood.

Clinical examination was normal, with a weight of 20 kg (percentile75). Neither lymphadenopathy, nor hepatosplenomegaly nor bone tenderness were highlighted. Laboratory investigations revealed a severe hypereosinophilia (AEoC 17.950 cells/uL), without any abnormality of other blood lines (Hb 11.8 g/dL - platelets 383 x103/uL - total white blood cells 24.26 x103/uL - absolute neutrophil 2.890/uL - lymphocytes 2.010/uL) and no blasts on peripheral smear. C-reactive protein and erythrocyte sedimentation rate were 22,9 mg/L and 15 mm/h respectively. Liver test, renal function, LDH and alkaline phosphatase level were in normal range. ANCA and ANA were negative. Immunoglobulines where in normal range except for IgE at 967 KU/L. Chest X-ray and computed tomography scan were normal. Abdominal ultrasound showed no lymphadenopathy or hepatosplenomegaly. Echocardiography was normal. The complete workup for helminthic and parasitic etiology including stool studies and blood serology was also negative.
Bone marrow biopsy revealed large eosinophil excess (19.6% of eosinophilic line), without monoclonal expansion, no sign of myelodysplasia and with proportionately representation of other hematologic lines. No clonal disorder was revealed on peripheral and medullar immunophenotyping. The diagnosis of IHES was then considered. He is actually still in good general state, with persistent hypereosinophilia and is being closely followed-up.

Conclusions

HES is a rare disease in children that can be subdivides in monoclonal, reactive or idiopathic.

First investigations target the main reactive causes of HES, including allergy, infectious disease (mainly parasitic infections), drug reaction, inflammatory disease (including collagen vascular disease such as ANCA-associated vasculites), nonmyeloid malignancies (lymphoma and solid tumor) and immune deficiency. Secondary examination should exclude clonal disorders including bone marrow biopsy, immunophenotyping and molecular examinations.
In the event of persistent HES without primary or secondary cause, a diagnosis of IHES can be done. Organic involvement should be identified, including regular echocardiography, and biopsy should be performed in presumed damaged tissues. HES is associated with multisystemic damage mediated by the eosinophil tissular infiltration that can cause severe complications, highly increased in the absence of treatment, including cardiac involvement that can be fatal and needs to be quickly detected.
Systemic corticosteroid therapy is the first-line treatment and should rapidly be started with close biological and clinical monitoring. In case of failure, other treatment options such as Hydroxyurea or biological therapies could be added.

This case highlights the need for a complete workup for children presenting with hypereosinophilia. Exclusion of primary and secondary causes is essential in order to offer the best available care for each patient. Long-term follow-up is still needed with particular caution for the risk of hematologic malignancy development.

O 13

Cerebellar mutism syndrome in posterior fossa tumors: a better understanding for a better counseling. A retrospective analysis of pediatric patients from 1990 to 2015.

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Introduction

Cerebellar mutism syndrome (CMS) consists of mutism, emotional lability, hypotonia and ataxia. It is induced by resection of midline posterior fossa tumors. Little is known about the risk factors of this syndrome in children and about the intelligence outcome.

Aim

The main purposes of our retrospective analysis were identification of a risk profile for CMS, determination of the reported prevalence of CMS in our hospital and investigation of the correlation of early postoperative symptoms and long-term intelligence outcome.

Methods

The patient database of the University Hospitals Leuven was interrogated for pediatric patients diagnosed between 1990 and 2015 using terms as 'posterior fossa tumor', 'mutism' or 'cerebellar syndrome'.

Results

75 posterior fossa interventions. Median age at resection was 5.73 (0.30-18.43) years. Postoperative mutism was reported in 26.6%: 'Mutism Group' (MG). In 73.3%, mutism was not reported: 'Non-Mutism Group' (NMG). The medulloblastoma tumor type and preoperative ataxia can be withhold as significant risk factors to develop mutism after posterior fossa surgery ($p = 0.006$ and $p = 0.009$ respectively). Average age in the MG was 6.85 years (0.30-14.74), in the NMG 6.09 years (0.48-18.43). A telovelar surgical approach was used in 38%, a transvermian in 18%. Postoperative mutism occurred in 28.5% and 30% in both groups respectively. In the MG 75% of the patients received adjuvant therapy, in the NMG this was only 52.5%.Total IQ points compared between intervention and after 2 years (tested in 11/73 patients) is significantly lower in the MG (Total IQ 97.2 vs 83.6; $p = 0.043$, Verbal IQ 97.6 vs 92.2 and Performance IQ 95 vs 78.2; $p = 0.042$). IQ in the NMG did not differ (Total IQ 101.8 vs 105.5, Verbal IQ 103.2 vs 109.8, Performance IQ 102.5 vs 102.5).

Conclusions

CMS is a frequent postoperative syndrome occurring in 26.6% of the studied interventions. The medulloblastoma tumor type and preoperative ataxia can be withhold as significant risk factors to develop mutism after posterior fossa surgery. Our data indicate that children with CMS have a more impaired neuropsychological outcome.

O 14

Long-term outcome in survivors of pediatric low-grade glioma: the Leuven database

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Introduction

Children with pediatric low-grade glioma (PLGG) have excellent overall survival rates. However, less is known about the long-term outcome. We identified patients diagnosed with PLGG between 1 January 1979 and 31 December 2010 at the University Hospitals Leuven, Belgium.

Aim

To analyze long-term outcome in survivors of PLGG and determine factors associated with primary and secondary outcome.

Methods

194 patients with PLGG and at least 5 years after diagnosis were analyzed retrospectively. Kaplan-Meier curves for overall survival (OS) and progression-free survival (PFS) were generated. Long-term endocrine outcome, sensory loss and development of secondary malignancies were also analyzed. Factors associated with survival and secondary outcome were identified. Comparisons between factors was performed using log-rank tests.

Results

At a median follow-up of 10.30 years, 16 patients deceased. The 20-year OS was 87.6% (95% CI 79.8% - 95.4%) and 20-year PFS was 58.1% (95% CI 48.9% - 67.3%). Both OS and PFS were associated with extent of resection and treatment type, furthermore PFS was associated with tumor location. Patients with cerebellar tumors had the best PFS. Until at least 20 years from diagnosis, the incidence of secondary outcomes, such as visual and hearing impairment, endocrine deficits and epilepsy, continued to increase. Eight out of 194 (4.12%) patients developed a secondary malignancy. Secondary malignancies were significantly associated with radiation therapy with a remarkable increase after 25 years from diagnosis.

Conclusions

The excellent OS and PFS in PLGG patients creates a population at risk for developing long-term side effects such as secondary malignancies, sensory and endocrine deficits. An organized long-term follow-up program could detect these secondary outcomes and improve the prognosis in these cases through early detection and treatment.

O 15

A SERTOLI- LEYDIG TUMOR IN A 3-YEAR-OLD GIRL: A CASE REPORT.

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Introduction

Sertoli Leydig tumor is a gonadal tumor and more specifically a sex cord tumor and account for less than 0,5% of ovarian tumors. The benign or malignant behaviour depend on the degree of differentiation. This tumor occur often in women under the age of 30 years.

Aim

We report the case of a 3-year-old girl hospitalized for gastroenteritis.

Methods

She presented with abdominal pain,vomiting, diarrhea and fever. Biology showed an inflammatory syndrome with a CRP at 57.2 mg/L and white cells count at 18100/mm3 with 73% of polyneutrophiles. In the second day, we observed an unproductive diarrhea and rectal
tenesmus. An abdominal ultrasound was realised and showed a mass above the bladder with a contact with the appendix which was dilated. The abdominal CT scan confirmed a liquid, multilobar, heterogeneous 88X55X65mm mass suggestive of appendicitis complicated by an abscess of the left annex. We begun an antibiotic therapy and a laparoscopic surgical exploration was planned.

Results

Laparoscopy revealed a cystic and hemorrhagic mass suspicious of a necrotic and twisted left ovarian teratoma. A left annexectomy and appendectomy were performed. The anatomo-pathology diagnosis was a Sertoli - Leydig tumor. The immuno-marking was positive for inhibin and a mutation for DICER gene was found. The KI67 rate was inferior of 1%. A regular monitoring by abdominal ultrasound was programmed.

Conclusions

Sertoli - Leydig tumor is a rare ovarian tumor in pediatric. This case shows that we have to make the differential diagnostic with gonadal tumors for a girl with an abdominal mass. The first diagnostic is made with abdominal ultrasound and has to be complete with an IRM or abdominal CT scan. The final diagnostic depends of the anatomo-pathology analyze.

O 16

Neonatal renal vein thrombosis : about a case.

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Introduction

Neonatal renal vein thrombosis (RVT), is the most common site of spontaneous venous thrombosis in neonates although incidence is as low as 0.5 0/00 among NICU admissions. Literature is very poor compared to thrombosis of the renal vein in adults. Diagnostic presumption is based on the association of a palpable flank mass, micro or macroscopic hematuria, and thrombocytopenia. Doppler-Ultrasonography is the procedure of choice to confirm the diagnosis of RVT. Although there is no evidence-based consensus on acute management, everyone agrees on the need for long-term follow-up because of the significant morbidity.

Methods

We report the case of a full term male newborn of Maghrebian origin admitted to our neonatology department for respiratory distress. There was no consanguinity in the family. Shortly after birth, he presented thrombocytopenia with palpable mass in the right hypochondrium, but without macroscopic hematuria, arterial hypertension or renal dysfunction. Doppler ultrasound confirms unilateral RVT with no extension into the inferior vena cava. A limited prothrombotic laboratory evaluation is performed during the neonatal period. An empirical treatment with low molecular weight heparin (LMWH) is rapidly initiated. The immediate clinical course seems to be favorable with a lack of thrombus extension, a decrease in kidney congestion and a normalization of blood platelet count. Longer term evolution is unknown.

Conclusions

From this clinical observation and review of the literature, we conclude that:
- Neonatal RVT is a rare condition that can be associated with significant morbidity.
-The diagnosis should be made in the presence of thrombocytopenia, hematuria and abdominal mass. The triad is however rarely complete.
-In the absence of strong scientific evidence and with regards to the potential harms of anticoagulation in neonates, the clinician faces a dilemma. LMWH therapy might be warranted to limit thrombus extension. This attitude should ideally be supported by evidence-based data. Although survival is good in unilateral RVT, this pathology requires long-term monitoring of renal function.

O 17

A big belly like no other

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Introduction

Lymphangioma, newly called lymphatic malformation, is a very common pediatric pathology. It is often benign and usually appears in the head and neck area that makes the diagnosis obvious. However, in some rare cases the diagnosis can be challenging because of its deep location.

Aim

We report here the case of a 20-months-old girl with a giant abdominal cystic lymphangiomas who presented with isolated ascites.

Methods

The toddler was admitted to our pediatric emergency room for progressive abdominal bloating during the last 6 months and increased episodes of overnight crying for the past 3 months without fever or any other major symptoms. Her body temperature and vital parameters were normal. Physical examination revealed a shifting dullness of the flanks and abdominal ultrasound confirmed the presence of ascites. Biological data were unremarkable including no sign of inflammation, normal Pro-BNP value, and absence of neoplasic markers. Ascitic fluid showed signs of non-specific inflammation with reactional mesothelial cells, as well as negative tuberculosis PCR and negative culture. A thoracic canal agenesia was suspected but the 99mTc scintigraphic peritoneography performed was inconclusive because of the numerous septa in the ascites. Finally, the laparoscopic abdominal exploration including peritoneal biopsy revealed a voluminous liquid mass, compartmentalized by septa and enclosed by a thin and translucid membrane. The peritoneal biopsy showed only congestive fibro-adipose tissue without any sign of malignancy. The diagnosis of giant cystic lymphangioma was confirmed.

Results

Abdominal cystic lymphangioma is a rare disease and usually become symptomatic around the age of 2. It is more frequent among boys. The clinical presentation can be of various expressions: abdominal pain, ascites, abdominal mass, or with its most common complication, the volvulus. The mecanism leading to abdominal cystic lymphoma formation is poorly understood. Treatment goes from simple follow-up to invasive surgery. Some spontaneous regressions have been reported.

Conclusions

In conclusion, visceral lymphangioma is a rare disease in childhood and could be the cause of acute abdominal pain but the differential and preoperative diagnosis is not always possible especially when it is very large and fills the entire abdomen.

O 18

Jaundice and unexplained cholestasis as the first presenting symptoms in a child with mature B cell non-Hodgkin lymphoma

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Introduction

Lymphoma is the third most frequent cancer in children. Its variety of symptoms and its atypical presentation can be the reason for delay in diagnosis.

Aim

A 13-year-old boy presented at the emergency department on notice of the family physician for recurrent abdominal pain. He complained about pain since 10 days especially after having meal and during the night. He also describes a pruritus and strong sweating when pain occurs. He had discoloured faeces and dark urines. His two uncles suffered from vesicular gallstones. The blood sampling shows hepatic cytolysis (GOT 142 UI/L) and a cholestasis (total bilirubin 2.56 mg/dL; direct bilirubin 1.97 mg/dL; GGT 320 UI/L). Hepatic serologies were negative as well as the autoimmune workup (ANA, ANCAs). The abdominal ultrasound reveals a dilatation of intra-hepatic biliary tracts without dilatation of the common duct and without any obstacle or identified mass. At this point, the diagnostic hypothesis was a vesicular gallstone evacuated spontaneously. The pain came back one month after this first hospitalization. An endoscopic retrograde cholangiopancreatography shows some measure's irregularities between the distal, the proximal and the right intrahepatic biliary tracts with also some sludge in the gallbladder. After a large endoscopic sphincterotomy, an endoprosthesis was placed in the Wirsung canal.

Methods

One month later, the boy came back to the hospital because he developed some uncontrolled pain with extreme fatigue. He also complained about back pain especially in supine decubitus with a feeling of abdominal gravity. He lost four kilograms and presented incoercible vomiting. At the same time he discovered a small mass in front of his xiphoid appendix. The biology revealed hepatic cytolysis associated with strong cholestasis (total bilirubin 2.4 mg/dL; direct bilirubin 2.1 mg/dL; GGT 469 UI/L). All tumor markers were negative and LDH's level was normal. At that moment chest X ray showed mediastinal enlargement. Abdominal MRI showed an extrinsic mass compressing the common biliary duct. An anterior mediastinal mass and abnormal subcutaneous infiltration of the anterior chest wall were confirmed on chest CT. Bone marrow biopsy was negative. The 18F-FDG PET-CT confirmed abnormal uptake in the anterior mediastinum, the abdomen and in the nodule in front of the xiphoid appendix. The biopsy of this cutaneous nodule showed mature B cell non-Hodgkin lymphoma with normal cytogenetic, Cmyc negative, TdT negative and high Ki67 (97%).

Results

The presenting signs and symptoms of lymphoma in children depend mainly of the site and the extent of the tumor. The tumor compression resulting in obstructive jaundice is uncommon and usually a late presentation. It is very rare in children but already described in a few cases in the literature. In contrast, rhabdomyosarcoma appears to be the most common solid tumor causing biliary obstruction in children. Idiopathic cholestasis is also described as a paraneoplastic phenomenon that comes from a release of toxic cytokines from lymphoma cells without any associated compression.

Conclusions

Lymphoma is the third most frequent cancer in children especially in the young boy. Non-Hodgkin lymphoma in children are usually highly aggressive with a rapid evolving course. Usually the diagnosis is done quickly but sometimes the evolution can be more indolent and the presenting unusual symptoms may delay the diagnosis. Some cases of lymphoma with cholestatic liver disease at presentation have already been described. Our patient highlights that children with unexplained cholestasis must be explored in dept.

O 19

Desmoid pancreatic tumor in a 12-years-old child

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Introduction

Pancreatic desmoid tumors are extremely rare in the child and there are no definite guidelines on their treatment.

Aim

In this cas report, we aim at presenting a case of pancreatic desmoid tumor that was treated successfully with surgery only.

Methods

A 12-year-old caucasian boy without significant medical history was referred for a left abdominal mass, which had appeared three months before admission and had a rapid growth. The patient with good general status only complained of pain during mobilization. Examination revealed a firm and painful mass of around 10cm of diameter under the left costal margin. Lansky score was of 100%.
Abdominal ultrasound and CT-scan revealed a voluminous retroperitoneal mass, seemingly from the tail of the pancreas. 18-FDG-PET-CT showed an increased metabolism in the tumor, without secondary localization. Pancreatic origin was confirmed by cholangio-MRI. Finally, needle biopsy was performed and diagnosed a fibromatous desmoid tumor.
Surgical resection was decided. The surgery confirmed the pancreatic origin with a very adherent and inflammatory tumor. A wide surgical removal consisted in a resection of the tail of the pancreas, of the spleen, of a part of the stomach and of the left colon.
Anatomopathology confirmed the diagnosis of a fibromatous desmoid tumor and the pancreatic origin. Spleen, stomach, colon and surgical margins were free of tumor cells. Genetic analysis in the child excluded APC mutation.
The patient had no complication of the surgery and is well 1 year after surgery with no relapse.

Results

Desmoid tumor is an uncommon diagnosis in the adult population and is even scarcer in children. Although histologically benign , these tumors are locally invasive and have an unpredictable clinical course. The morbidity and mortality come from their local invasive potential and high local recurrence rate. Symptoms are commonly scarce and non-specific and are mainly due to localization.
Pancreatic locations of the desmoid tumors are extremely rare. They are mostly localized in the tail of the pancreas and are usually asymptomatic for a long period.
Many issues regarding the optimal treatment of patients with desmoid tumors remain controversial, however, surgery is the therapeutic mainstay, except if mutilating and associated with considerable function loss. Watchful waiting may be the most appropriate management in selected asymptomatic patients because of the heterogeneity of the biological behavior of desmoid tumors, including long periods of stable disease or even spontaneous regression. This attitude could however not be chosen for our patient because of the growing rate of the lesion and therefore, the treatment of choice was a complete resection.
Postoperative radiotherapy reduces the local recurrence rate and can be proposed in selected cases with involvement of the surgical margins.

Conclusions

This case reported a very rare abdominal tumor. The first problem was the difficulty to assess the origin of the tumor, considering its unusual localization. Secondly, the choice of treatment was difficult to make because of the balance between the histologically benign nature of the tumor and the morbidity of the surgery. The expectative attitude was not suitable in this case, because of the fast-growing lesion. Although surgery implied wider resection than expected, it was complete and therefore the patient needed no adjuvant treatment.

O 20

Diarrhea-negative Hemolytic Uremic Syndrome: about a case.

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Introduction

Introduction :
Hemolytic uremic syndrome (HUS) is defined by the triad « hemolytic anemia, thrombocytopenia, acute kidney injury » and is responsible for most cases of acquired acute kidney failure in young chidren (under five). Traditionnally HUS is divided into typical or diarrhea-positive HUS (D+ HUS) and atypical or diarrhea-negative HUS (D- HUS). D+ HUS follow thus (bloody) diarrhea, and is classically caused by shiga toxin-producing E.Coli (STEC). D- HUS include various etiologies like complement dysregulation, other infection (eg pneumococcal or HIV infection) or drug toxicity, and requires thus more investigations. We report on the case of a seven-year old girl who developped HUS without any diarrhea.

Case report :
The patient was admitted to the emergency room with a 48h history of vomiting, pallor, weakness and oliguria after a school trip to the seaside, without any fever, diarrhea or respiratory symptoms.
Physical examination was normal excepted for general weakness, pallor, mild jaundice and moderate signs of dehydration. Laboratory findings showed hemolytic anemia (Hb 5.1 g/dL, LDH 1710 UI/L, hyperbilirubinemia), severe thrombocytopenia (10 000 platelets) and kidney failure (urea 144 mg/dL serum creatinine 1.20 mg/dL). Blood smear revealed schistocytes. Coombs test was negative. After 6h without urination, an urinary sample could finally be collected and showed hematuria and proteinuria. The child was admitted to the pediatric intensive care unit with diagnosis of « atypical HUS », for close monitoring and supportive management. A blood cells transfusion was necessary on day 2. Owing to the lack of diarrhea, further investigations were started : ADAMTS13 activity, complement proteins levels, hemoglobin electrophoresis, pyruvate kinase activity and serum antibodies levels appeared all normal, and no Paroxysmal Nocturnal Hemoglobinuria clone was founded by immunophenotype. Owing to the absence of stool, a rectal smear must be done. After 4 days this rectal smear came positive for an O157:H7 E.Coli and shiga toxin was found by PCR, changing our diagnosis into « typical HUS ». Clinical evolution was favourable with a rapid restauration of diuresis without dialysis, progressive increase of platelet count (normalization on day 8) and stable moderate anemia after transfusion (Hb 8 g/dL on day 8, when she was discharged). The child never had any diarrhea ; she was rather constipated with several days without any stool.

Conclusion :
The association of hemolytic anemia, thrombocytopenia and acute kidney failure in children point to the diagnosis of HUS. This syndrome was classically divided into « typical » (STEC-linked) or « atypical » (various etiologies) according to the presence or absence of diarrhea. However, our case illustrate that the lack of diarrhea doesn't exclude the diagnosis of STEC infection ; and conversely diarrhea can be present in non-STEC HUS. A new classification based on pathogenesis distinguishes primary HUS (complement-mediated) from secondary HUS (due to infections - included STEC -, drugs, systemic or metabolic disorders).
A STEC research should be done in all patient with suspected HUS, and more investigation are needed when diarrhea is missing to exclude other etiologies of HUS or other thrombotic microangiopathy like thrombotic thromocytopenic purpura.

L 01

Is the Concept of Rheumatogenic Group A Streptococcus a Myth? A Systematic Literature Review from 1944 to 2016 and a Molecular Analysis of the M-Protein

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Introduction

Group A Streptococcus (GAS; Streptococcus pyogenes) infections, are a major cause of morbidity and mortality throughout the world. The number of deaths due to this bacterium is estimated at over 500 000 each year, mainly in low and middle-income countries. The highest mortality rate associated with GAS infections is due to Acute Rheumatic Fever (ARF) and its chronic sequela, Rheumatic Heart Disease. Those are the principal causes of acquired cardiac illnesses in children, adolescents and young adults in developing countries. The concept that a minority of GAS emm-types are more rheumatogenic than others is widely disseminated. However, there has only been one single review of predominant serotypes involved in streptococcal outbreaks associated with ARF between 1939 and 1971. This review of US studies found the following emm-types to be associated with ARF: 1, 3, 5, 6, 14, 18, 19, 24, 27 and 29. A review of GAS emm-types associated with ARF in endemic regions has never been undertaken and some recent publications from low and middle-income countries suggest an association between ARF and non-classical strains. Recently, a new functional classification divided the numerous GAS emm-types into a limited number of emm-clusters containing emm-types with closely related M proteins.

Aim

The objective of this review is to provide a comprehensive list of ARF-associated strains and analyze their genetic diversity.

Methods

Reports of original research in the Pubmed and Embase database, from 1st January 1944 (first publication of Jones criteria) to 31rd December 2016 were used as sources to identify cases of ARF. All articles reporting ARF-associated strains or ARF-associated emm-type-specific antibody responses were selected. The revised Jones Criteria (American Heart Association, 2015) were used to define ARF and a maximum time-period of four weeks between microbiological characterization and ARF onset was accepted. A database of 175 M-protein sequences was used to analyze the genetic diversity of ARF-associated emm-types in a PhyML phylogenetic tree. Geneious software was used to search for the presence of putative ARF-associated motifs (PARF motif and two proposed rheumatogenic peptides).

Results

Thirty-seven relevant studies were identified among 840 publications. 464 ARF-associated isolates belonging to 66 different emm-types were included in the analysis. The classical rheumatogenic emm-types represented 40% of the 464 ARF-associated isolates and 14% of the 66 identified emm-types. When the classical rheumatogenic emm-types were mapped by specific clade onto the emm-cluster-type phylogenetic tree, ARF-associated emm-types were disseminated along the tree suggesting ARF-associated emm-types belong to various genetic backgrounds. ARF-associated motifs (PARF or rheumatogenic peptides) were present in only 23 and 15% of the ARF-associated isolates and emm-types, respectively.

Conclusions

The ten classical rheumatogenic emm-types were associated with ARF in our systematic review. However 56 non rheumatogenic emm-types, belonging to various genetic background and currently circulating worldwide were also associated with ARF. The concept of rheumatogenic emm-types should therefore probably be extended to include emm-types other than those classically described. These results should inform GAS vaccine development and highlight the need of a better understanding of ARF physiopathology.

L 02

Pediatric systemic lupus erythematosus presenting with pancytopenia and retinal vasculitis.

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Introduction

Pediatric systemic lupus erythematosus (pSLE) is a relatively uncommon auto-immune disorder that may affect multiple organ systems. The exact etiology remains largely unknown, although it is characterized by the production of a wide spectrum of auto- antibodies. The disease follows a relapsing and remitting course. The presenting manifestations of pSLE are divers. The most common initial symptoms are fever, weight loss and malaise. Often, a malar rash or discoid skin lesions are seen. Children also may have renal disease and small joint arthritis. Hematologic abnormalities are common in the pediatric population with SLE. SLE- associated retinopathy appears to be less common in children. To our knowledge, there are no published incidence studies.

Aim

Presentation of a pediatric case with SLE to illustrate the diverse manifestations and challenging diagnostics involving multiple medical specialists.

Methods

An 11-year-old girl of African origin presented at the pediatric department with a 4-week history of discoid skin lesions on the face, ventral thorax and tips of fingers and toes. The patient complained of pain and morning stiffness in both wrists and PIP joints. She reported malaise and fatigue. There was no history of fever. Skin examination revealed numerous discoid, erythematous lesions involving the face and ventral thorax. These lesions were not itchy nor flaking. On the ventral thorax, several purpura were found. On the tips of fingers and toes, the same lesions were seen as well as several petechiae. Additionally, oral ulcerations were seen. There was no hepatosplenomegaly. Laboratory evaluation revealed a pancytopenia (Hb 10.9 g/dl, thrombocytes 77 10^9 /μL and white blood cell count 1.4 10^9/μL) and the patient was referred to the department of Paediatric Haematology- Oncology because of the suspicion of a malignancy. However, bone marrow aspirate showed a normal cellularity without increased blasts. Additional laboratory tests showed an elevated sedimentation (106mm/u), a hypocomplementemia (C3, C4, CH50) and a hypergammaglobulinemia. The patient was found to be ANF positive, with positive antibodies to dsDNA, SmD and RNP. Hence, the diagnosis of pSLE was made. Ocular fundus examination at diagnosis showed a vascular tortuosity and the presence of cotton-wool spots, a marker for micro-angiopathy.

Results

Treatment was started with high-dose glucocorticoids and hydroxychloroquine. Within weeks, a favorable decrease in skin lesions was observed and the patient's pancytopenia gradually resolved. Then, azathioprine, a steroid-sparing agent, was added to reduce glucocorticoid use and avoid its toxicity. Nevertheless, it had to be discontinued and replaced by mycophenolate due to azathioprine associated leukopenia. On ophthalmologic follow-up, the patient's vasculitic changes almost completely resolved. Today, she remains stable and continues to be treated with glucocorticoids, hydroxychloroquine and mycophenolate.

Conclusions

Pancytopenia may be a presenting manifestation of pSLE. A less common manifestation is retinal vasculitis. Treating the systemic disease may result in improvement of ocular disease. The mainstay of treatment for SLE retinopathy is similar to the treatment of SLE in general. It involves the use of immunosuppressive therapies as glucocorticoids and DMARDs. Once disease control is attained, low-dose systemic glucocorticoids and hydroxychloroquine are often continued long-term to potentially prevent flares of disease.

L 03

LEOPARD SKIN-LIKE COLITIS

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Introduction

We report a case of special colitis in a chronic granulomatous disease (CGD) patient.

Aim

We will discuss work up needed to make the diagnosis of colitis in CGD, the typical endoscopic image of the pathology, the treatment of the disease and recent advances in this area.

Methods

A 10-year-old boy, from non cosanguinous parents, has a diagnosis of chronic granulomatous disease since the age of 2 years following adenitis and anal abscesses with fissures. Antifungal and antibiotic prophylaxis was initiated since diagnosis.
He was suffering from abdominal pain and diarrhea since many years. A first work up showed calprotectin levels at the upper limit of normal, IgE mediated allergy for milk and positive ASCA. Symptoms resolved under diet without milk until 2017 when the child had a reccurence of diarrhea. He also had recurrent oral aphtosis. We performed colonoscopy which revealed diffuse colitis with brown dots distributed across a yellowish edematous mucosa. This endoscopic image has been described recently as "Leopard sign" (Obayashi, N., et al., J Pediatr Gastroenterol Nutr, 2016. 62 (1): p.56-9). Histopathological features of the colonic mucosa showed normal crypts with normal distribution, and excess of macrophages sometimes slightly tinged brownish (pigment - laden macrophages). No granuloma were found. This confirm a type of inflammatory bowel disease associated with CGD. Treatment with Mesalazine (60 mg/kg/day) did not resolved the symptoms of diarrhea. Subsequently, Budenoside (5 mg/day) was tried and the symptoms was resolved. The dose was halved because of steroids impregnation symptoms. The diarrhea disappeared as the abdominal pain. The oral aphtosis did not recur. No compatible hematopoietic cell donor for our patient was found.

Results

Chronic granulomatous disease is an inherited (X-linked or autosomal recessive) immunodeficiency disorder due to a defect in the phagocyte nicotinamide adenine dinucleotide phosphate oxidase (NADPH). This disorder is characterized by reccurent, severe, life-threatening infections because of inability of phagocytes to kill ingested bacterial (catalase-positive) and fungal pathogens. The global incidence of CGD is estimated at 1/120.000 to 1/250.000 live births.
About 30 to 50% of patients with CGD have gastrointestinal symptoms but these are often nonspecific (fever, abdominal pain, stomatitis, nausea and vomiting, weight-loss, diarrhea). Gastrointestinal manifestations associated with this condition include esophageal stricture, gastric outlet obstruction and colitis.
To orient us towards the diagnosis, additional examinations must be carried out including digestive endoscopy with biopsy samples.
The endoscopic evaluation allows the demonstration of a unique mucosal appearance of brown dots distributed across a yellowish edematous mucosa. A recent scientific article termed this endoscopic image "Leopard sign". The histology of the colonic mucosa with this specific features revealed many pigment-laden macrophages in the yellowish area. Other features that distinguish CDG colitis from other forms of chronic colitis are a paucity of neutrophils and an eosinophil-rich inflammatory process in the

lamina propria. The macrophages can form clearly defined granuloma but this aggregates are not seen in all patients. Another gross finding in CDG is the relative localization of severe disease to the distal colon while, for example, Crohn disease tend to have more global gastrointestinal involvement.
The lifelong antifungal and antibacterial prophylaxis (itraconazole and trimethoprim-sulfamethoxazole) recommended in patients with CGD has significantly improve the prognosis. Oral glucocorticoids are the most common therapy used for inflammatory manifestations of CDG especially chronic colitis. Glucocorticoid-sparing therapies include long term anti-inflammatory treatment such as sulfasalazine, azathioprine.
Hematopoietic cell transplantation is the only cure therapy currently but gene therapy approach are under development and may eventually replace HTC. These new therapies would offer new perspectives for patients with chronic granulomatous disease.

Conclusions

Colitis in chronic granulomatous disease must be part of the differential diagnosis of bowel inflammatory diseases.
Inflammatory bowel disease has to be in mind in CGD patients even with mild symptoms (in contrast with diffuse colitis in our case).
Treatment remains classic with some immunosuppressants and needs to be discussed with the team of immunologists.

L 04

STEM CELL TRANSPLANTATION IN A PATIENT AFFECTED BY A PURINE NUCLEOSIDE PHOSPHORYLASE DEFICIENCY

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Introduction

Purine nucleoside phosphorylase (PNP) deficiency is a rare autosomal recessive metabolic disease, leading to primary immunodeficiency. PNP is a key and ubiquitous enzyme involved in purine metabolism. Besides primary immunodeficiency symptoms, PNP deficiency is characterized by autoimmune disorders and neurological impairment. We present a 4-years old girl with neurological symptoms as gateway to the disease. For now, hematopoietic stem cells transplant (HSCT) is the only curative treatment.

Results

We report the case of a 4-years old girl with neurological symptoms in the foreground. The patient had an important delay in the acquisition of motor skills. The anamnesis revealed repeated infections, mainly during her two first years.
The physical examination showed an axial and peripheric hypotonia, ataxia and balance disorders. There was no failure to thrive.
Laboratory investigations only revealed a lymphopenia (290 lym/μL) and low uric acid (0.3 mg/dL).
A genetic analysis by exome sequencing was performed and higlighted two mutations in the PNP gene leading to a PNP deficiency.
Afterwards, we performed a HSCT from an unrelated donor, with a myeloablative conditioning regimen according to the protocol A from the 2017 EBMT/ESID guidelines. The first signs of engrafment appeared on the 12th day after the procedure.
Four months after the HSCT, the patient has shown neurological improvement and better motor skills. She did not present severe complication except a minimal veno-occlusive disease and a mild thrombotic microangiopathy which both have been rapidly resolved.

Diagnostic of PNP deficiency can be done in different ways. First, by highlighting a low or absent PNP activity. Genetical analysis can also be performed. Based on lymphopenia and low uric acid, a PNP deficiency can be suspected in a neurological context. Newborn screening on dried blood spots would also be a possibility and would allow an early diagnosis.
Nowadays, the only curative treatment is HSCT which is curative for the immune deficit but do not resolve the neurological impairment. For now, research have been focused on gene and enzyme replacement therapies. The research results for this latter revealed a long-term efficiency for the immune deficiency improvement. Moreover, it has been shown that the replacement enzyme pass through the blood-brain barrier.

Conclusions

Most of the patients with PNP deficiency present with immune symptoms at the first sight but it is also important to discuss this diagnosis for patients with unexplained neurological impairment. Blood tests can help to the diagnosis before genetical analysis or PNP activity measurement.
PNP-deficiency is a very rare disease, but early diagnosis and therapy increase the efficiency of the treatment and allow a stabilisation of neurological impairment.

L 05

An unusual manifestation of Behcet's disease.

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Introduction

Behcet's disease (BD) is a chronic multisystemic variable vessel vasculitis characterized by recurrent oral and genital ulceration associated with uveitis, cutaneous, articular, neurological and gastrointestinal involvement. The complete disease expression is rarely seen before the age of 16 and its diagnosis remains therefore challenging. We report hereafter an unusual case of an Armenian teenager suffering from a newly discovered BD.

Aim

A fourteen-year-old Armenian girl was admitted to our pediatric emergency room for fever with chills, nausea and severe vulvar pain for four days. An abscess of the labia majora was diagnosed and treated by intravenous antibiotics and surgery five months before. She reported also history of monthly recurrent febrile throat infection and abdominal pain. A previous test for family Mediterranean fever returned negative. Physical examination showed flanks pain and two minor erythematous spots on the labia minora. Imaging studies were normal. Blood tests revealed hyperleucocytosis (14,135/mm3), increased CRP (142.3mg/L), negative serologies for Epstein-Barr and Herpes viruses and no sign of immunodeficiency or autoimmunity. During the hospital stay, she remained febrile and nauseous for two days. Vulvar lesions became larger, deeper, necrotic and ulcerated. She did not present any oral ulcer or arthralgia. Further investigations such as ophthalmological examination, cardiac ultrasound turned out negative. A vulvar biopsy performed on the sixth day of her hospital stay showed strong suggestive images of BD with leucocytoclastic vasculitis, vascular necrosis and inflammatory infiltrates. Intravenous ceftriaxone and clindamycin were initiated followed by methylprednisolone for a total duration of respectively 10 and 21 days during acute phase. Corticosteroids were tapered and colchicine was introduced 3 weeks later. The recovery was achieved 2 weeks after the introduction of corticosteroids.

Conclusions

According to the new consensus classification criteria for paediatric BD published by the Paediatric Behcet's Disease study in 2015, three of six items are required to meet the diagnosis of paediaric BD. It includes recurrent oral aphthosis, genital ulceration or aphthosis, skin and ocular involvement, neurological and vascular signs. Our patient only showed oral and genital features macroscopically. But thanks to the performed biopsy, skin signs with necrotic folliculitis were also demonstrated, helping to narrow the diagnosis.
Due to the rarity of the condition and its non-specific presentation, the diagnosis of BD is very challenging for paediatricians, and could therefore delay the diagnosis. One should think of the utility of the biopsy to demonstrate the skin involvement necessary into the determination of diagnostic criteria of BD.

L 06

ABSENCE OF B-CELLS & NK-CELL LYMPHOPENIA MIMICKING PRIMARY IMMUNE DEFICIENCY IN NEONATAL PERIOD DUE TO ANTI-LYMPHOCYTE MATERNOFETAL ALLO-IMMUNISATION

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Introduction

Neonatal cytopenias due to allo-immunisation are common, and affects predominantly platelets, red blood cells and neutrophils. In case of neonatal alloimmune thrombocytopenia (NAIT), anti-HLA type I antibodies can be found with debatable role in disease.
Lymphopenia at birth is always suggestive of primary immune deficiency, and should prompt further evaluation.

Aim

We here describe a newborn boy, with total lymphopenia, no B cells, low NK cells, thrombocytopenia, due to maternofetal immunisation to HLA class II antigens.

Methods

Laboratory work-up and follow-up of this case includes repeated complete blood counts ; serial flow cytometry immunophenotyping (including CD3, CD4, CD8, CD19, CD20, CD22, CD31, CD45RA, CD45RO, CD16, CD56, HLA-DR staining) ; lymphocyte proliferation assay ; KRECs/TRECs determination on dried blood spot ; antiplatelets antibodies determination ; anti HLA type I and II determination (ELISA)

Results

FACS	Day 5	Day 15	Day 45
Total Lymphos	2470	4890	4950
CD19 (/µl)	10	150	680
CD3 (/µl)	2290	4410	3910
CD3/CD4 (/µl)	1900	3510	3130
CD3/CD8 (/µl)	390	840	680
NK cells (/µl)	70	250	240
CD3/HLA DR (/µl)	0	50	50

Naive T cells subsets were normal for age. Proliferation assays were normal. KRECs/TRECs analysis are pending.
Both antiplatelets and anti HLA class II were present in mother's serum

Conclusions

This is the first case of a transient lymphopenia due to anti-HLA type II antibodies. As expected in this setting, B cells and NK cells, that express constitutively HLA-DR antigen were the most impacted cell types. Resolution occurs within 3 months, as in other allo-immune neonatal cytopenias

L 07

Severe combined immunodeficiency and metaphyseal osteochondrodysplasia: A case report

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Introduction

We report a case of opportunistic infection in a patient with severe combined immunodeficiency (SCID) associated with metaphyseal osteochondrodysplasia. Clinical features and etiologic assessment suggest the diagnosis of Cartilage Hair Hypoplasia (CHH).

Results

Case report: A 8-month-old Romanian girl is admitted to the pediatric emergency department for fever and cough progressing for the last 48 hours. She was born in Italy with a neonatal diagnosis of dwarfism. Her medical past is confused, with poor information available. Family medical history seems irrelevant. Initial assessment shows a febrile infant weighing 4 kilograms, with short-limbed dwarfism and fine silky hair. Clinical examination reveals upper respiratory tract infection, multiple lymphadenopathy and hepatosplenomegaly. Blood tests show increased level of CRP, moderate thrombocytopenia, lymphopenia and moderate hyper-gammaglobulinemia. Abdominal and cervical ultra-sonographies confirm acute adenitis and micronodular splenomegaly. Skeleton radiography shows short limbs bones with severe curving of femoral diaphysis and metaphyseal flaring. Lymphocyte phenotyping reveals a severe T helper lymphopenia with inversion of the CD4/CD8 ratio and low level of T cells proliferation. She is rapidly managed with empiric broad spectrum intravenous antibiotherapy due to immunodeficiency. However, her clinical course evolves towards a respiratory deterioration. Common or opportunistic infections are searched for in the context. A broncho-alveolar lavage is performed revealing a high level of human cytomegalovirus (CMV) DNA. Final retained diagnosis is CMV infection with multiple lymphadenopathy, hepatosplenomegaly and respiratory tract involvement evolving towards pneumonia in a patient with severe combined immunodeficiency (SCID) and metaphyseal chondrodysplasy. Clinical findings, SCID with CD4 lymphopenia and radiological features suggest the diagnosis of Cartilage Hair Hypoplasia (CHH). Gene panel analysis for osteochondrodysplasia and especially research of RMRP gene mutations are pending.

Discussion: Severe combined immunodeficiency (SCID) is a genetic disorder characterized by a disturbance in the development and function of T and B cells, resulting in heterogeneous clinical presentations. Classics manifestations are recurrent infections, either with common viral pathogens, or opportunistic infections (e.g. pneumocysticis jirovecii), persistent candidiasis, infections caused by attenuated vaccine organisms (e.g. rotavirus, BCG), chronic diarrhea or failure to thrive. Even if the past medical history was not suggestive of immunodeficiency, the presentation combined with clinical and biological findings raised the alarm for underlying condition. Differential diagnoses were HIV infection, miliary tuberculosis, other acquired immunodeficiency syndrome, malabsorption and severe malnutrition.

Conclusions

Cartilage Hair Hypoplasia (CHH) is a skeletal disorder characterized by metaphyseal chondrodysplasia associated with variable phenotypes of severe immunodeficiency. This rare disease arises from RMRP gene mutations. Clinical and biological findings in this patient strongly suggest the diagnosis. We need to remain alert to signs and symptoms of rare diseases in common practice.

L 08

Cerebral venous sinus trombosis as the presenting symptom for Behçet's disease in a 15-year old boy.

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Introduction

Behçet disease is a rare auto-immune vasculitic disorder characterized by recurrent oral and genital ulcers, ocular disease and skin lesions. Central nervous system involvement has been reported at variable rates, including either a meningo-encephalitis or vascular involvement. Cerebral sinus venous thrombosis has been reported as a rare complication.

Results

A 15-year old Ghanaian boy presented at the emergency department with persistent headaches with nausea and morning vomiting since 2 months. There was no history of recent travelling. He had no particular medical history or maintenance therapy. Brain MRI revealed a thrombosis of the left sinus transversus and of the left temporal cortical vein. Treatment with low-molecular weight heparine, guided by frequently control of factor anti-Xa levels, was started. Laboratory work-up showed an elevated erythrocyte sedimentation rate, but no evidence of a hypercoagulation disorder. Because of increasing headaches one week after admission, brain MRI was repeated and showed extension of the thrombosis to the transversus sinus, despite adequate heparin therapy, with therapeutic anti-Xa levels. For this reason, intravenous heparin therapy was initiated. During hospital admission, the patient developed oral ulcerations, which by specific history taking seemed to be recurrent since a few months. He also developed a papulopustular rash surrounding the injection area of a tuberculine test. Based on the clinical presentation Behçet's disease was suspected and systemic corticosteroid therapy was initiated, followed by prompt clinical improvement. Baseline immunosuppressive treatment with azathioprine was initiated one week after steroids were started.

Conclusions

DISCUSSION: We present a 15-year old boy with prolonged headaches and a cerebral venous sinus thrombosis accompanied by oral aphtosis and pseudo-folliculitis. Based on the International Study Group Criteria, the diagnosis of Behçet disease was made. Primary neurological involvement in children is exceptional and available literature is limited. Systemic corticosteroids and/or immunosuppressants are essential for management.

CONCLUSION Behçet's disease is uncommon and difficult to diagnose in children. Neurologic involvement as a first presentation is rarely described, but may be underestimated. Careful history taking and physical examination provide important clues to diagnosis facilitating early identification and aggressive treatment essential for optimal prognosis.

L 09

Hereditary angioedema in two sisters due to parental mosaïcism

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Introduction

Hereditary angioedema (HAE) is a heritable disorder that is phenotypically characterized by the appearance of recurrent, circumscribed, non-pitting, non-pruritic, but often painful subepithelial swellings of sudden onset, that fade during 48-72 hours, but can persist for up to 1 week. Patients with HAE experience angioedema because of a defective control of the plasma kinin-forming cascade. Various types of HAE have been described of which type I and II HAE are autosomal dominant conditions resulting from mutations in the SERPING1 gene that encodes the serpin peptidase inhibitor (C1 esterase inhibitor - C1-INH).

Aim

Here we report the occurrence of type I HAE in two sisters with unaffected parents. Both affected sibs experienced attacks of spontaneous oedema and had very low C4, C1-esterase inhibitor function and C1-esterase inhibitor plasma concentrations, consistent with a type I HAE. In contrast, the parents and the non-affected sister displayed normal C4 and C1-esterase inhibitor plasma concentrations.

Methods

The SERPING1 gene was analysed (bidirectional Sanger sequencing and MLPA analysis) in a blood sample of the two affected sisters and in a sperm sample of the unaffected father. Deletions, nonsense or frameshift mutations in SERPING1 usually result in HAE type I.

Results

In the two affected sisters our analysis did not show evidence for deletions or duplications but revealed the heterozygous presence of a single nucleotide change in exon 3 predicted to result in a threonine to isoleucine substitution at residue 179 (c.536C>T;p.Thr179Ile) of the protein. This particular missense mutation has not been reported in databases of normal variation (ExAC, 1000 genomes, GoNL) but was previously identified once in our cohort of 50 patients analysed because of HAE. Subsequently, we examined the sperm of the father. This analysis clearly showed the presence of the p.T179I mutation in a fraction of the sperm cells. The mutation was undetectable in his lymphocytes which explains the absence of clinical signs and laboratory abnormalities.

Conclusions

Somatic and gonadal mosaicism are uncommon. Nevertheless, the diagnosis of an autosomal dominant disorder in two children from unaffected parents should prompt the clinician to consider the possibility of somatic or gonadal mosaicism in one of the parents. Correct diagnosis is important since it affects further family planning. Individuals with germline mosaicism should be counselled about the increased risk of having multiple affected children despite the autosomal dominant character of the disorder and the absence of clinical signs and detectable germline mutations in the parent(s).

L 10

The good and bad sides of Intravenous Immunoglobulin Therapy

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Introduction

Immune thrombocytopenia (ITP) is an acquired autoimmune disorder that is characterized by isolated thrombocytopenia in the absence of other causes or disorders that are associated with thrombocytopenia. Its incidence is estimated to be 2.9-5.3 per 100,000 persons per year in Europe. First-line therapy options for acute ITP are well defined with commonly chosen agents such as intravenous immunoglobulin (IVIg), anti-D immunoglobulin, and corticosteroids. Neurologic complications, including aseptic meningitis caused by IVIg, could occur in the management of patients with ITP.

Aim

We will hereafter report the case of a child who presented an aseptic meningitis caused by IVIg.

Methods

A 6-years-old girl was admitted via the emergency room for diffuse petechial rash, without fever, associated with thrombocytopenia (44 000/μL). ITP was diagnosed after a complete work-up. Treatment with IVIg was administered. The next day, she presented headache, nausea, vomiting and fever. Clinical examination showed neck stiffness and positive Brudzinski sign. Laboratory findings revealed leucocytosis (24 500/μL) with a majority of PN (20 000/μL) and a normal rate of platelet. The lumbar puncture performed demonstrated pleocytosis (1720/μL) with a predominance of neutrophils (86%), high level of protein (0,551 g/L) and normal level of glucose. Cerebrospinal fluid and blood culture were normal. Intravenous ceftriaxone was given with dexamethasone. She recovered rapidly and the antibiotic was stopped one week later when the second lumbar puncture of control was perfectly normal.

Results

Several mild and serious adverse events are known to be associated with IVIg therapy, occurring in 20% to 50% of patients. They are subdivided in different types: a) Immediate reactions (60%), which occur within 6 hours of an injection. They include head and body aches, chills and fever. They are usually mild and readily treatable. b) Delayed reactions (40%), which occur 6 hours to 1 week after an injection. The most common delayed reaction is persistent headache. Less common but more serious reactions include aseptic meningitis, renal failure, thromboembolism, and hemolytic reactions. c) Late reactions, which occur weeks and months after an injection. They are rare (less than 1%) but can be serious, including lung disease, myocardial infarction and stroke.
Aseptic meningitis syndrome after IVIg injection manifests itself by a persistent headache accompanied by neck stiffness, photophobia, fever and severe myalgia. Lumbar puncture in early cases discloses cerebrospinal fluid pleocytosis (both granulocytic and lymphocytic), elevated cerebral spinal fluid protein, and sterile viral or bacterial cultures. The cause of aseptic meningitis is not known but its occurrence with high IVIg dose suggests that the CNS inflammatory response may result from small quantities of IgG in the cerebrospinal fluid, causing inflammation and osmotic shifts of the meninges. Treatment consists of analgesics, anti-emetics, and anti-migraine therapy. If IVIg must be continued, injections should be given in smaller increments, at a slower rate and with a different IVIg brand.

Conclusions

In conclusion, knowledge of the IVIg's side effect profile is important due to the increasing number of clinical indications. Hence, IVIg should be used cautiously and judiciously with well defined pathologies.

L 11

Case report of systemic juvenile idiopathic arthritis

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Introduction

Systemic juvenile idiopathic arthritis (sJIA), also called "Still's disease" or "systemic juvenile rheumatoid arthritis", is officially classified as a subset of juvenile idiopathic arthritis by the International League of Associations for Rheumatology. Adult-onset Still's disease is probably a similar disease when it begins in patients more than sixteen years old.

We would like to report a case of a sJIA and its successful management with nonsteroidal anti-inflammatory drugs and glucocorticoids.

Results

Case report
A fourteen-year-old Belgian girl presented paediatric emergencies for rash, sore throat, diffuse muscle aches and joint pain in her wrists and ankles. The eruption started abruptly two days before. It was pruritic, located at hands and thighs, associated with a swelling of the lower lip, in a context of ingestion of pistachio milk product. First, a diagnosis of allergic reaction was made and a treatment with antihistamine and low-dose corticosteroids had been started, allowing a temporary improvement of the symptomatology.

On physical examination, she had a fever at 38°C, a heart rate of 120 beats per minute and a blood pressure of 119/59 mmHg. She developed a maculo-papular salmon-pink rash on her face, wrists, belly, thighs and ankles and very painful arthralgia on wrists and ankles without swelling or redness.

During the hospitalisation, she presented a daily fever mainly in the afternoon and the evening. During febrile peaks, the arthralgia and the rash increased. By the third day, she developed a hepato-splenomegaly and a meningeal syndrome with cervical pain and stiffness.

The laboratory studies were remarkable for an elevated white blood cell (WBC) count of 17 500 cell/mL, a ferritin level of > 2000 μg/L, an elevated erythrocyte sedimentation rate of 50 mm/h, an increase of CRP from 31 to 198 mg/L and the presence of anti-mycoplasma antibodies. Other rheumatologic and infectious studies, including FAN, anti- citrulline (CCP3), antibodies against toxoplasmosis, EBV, CMV, parvovirus, borrelia burgdorferi, rickettsia conorri and typhi, revealed no abnormalities. A throat swab and lumbar puncture were performed and revealed to be sterile.

Finally, the patient was diagnosed with Still's disease and referred to a rheumatologist. She was treated by nonsteroidal anti-inflammatory drugs per os (Indomethacin® 30mg Q 8H), glucocorticoids per os (Medrol® 64mg Q 24H) and a low salt and carbohydrate diet. The evolution was favourable: the child didn't present any severe complication, the symptoms gradually faded and the biologies normalized.

Discussion
Still's disease is an autoinflammatory systemic disease. Its aetiology remains unknown and there is no specific diagnostic test. Therefore, the diagnosis is usually based on clinic findings.
Yamaguchi et al (J Rheumatol, 1992, 19) proposed major diagnostic criteria including high fever for more than one week, arthralgia for more than two weeks, leukocytosis

and « typical » rash (an evanescent salmon pink or urticarial skin eruption), and minor diagnostic criteria including sore throat, lymphadenopathy, splenomegaly and absence of ANA and rheumatoid factor. Fautrel et al (Medicine, 2002, 81) have also added glycosylated ferritin level as a major criteria.

The blood tests showed various abnormalities including a leukocytosis, an elevated erythrocyte sedimentation rate and an extreme hyperferritinemia, relatively correlating with disease activity.

The prognosis is variable: monophasic, polycyclic or persistent course.
Serious systemic complications include pulmonary hypertension, macrophage activation syndrome (MAS), thrombocytopenic purpura, diffuse alveolar haemorrhage and amyloidosis (Sun et al, J Am Acad Dermatol, 2015, 73).

The treatment is mainly based on the control of the inflammation. The guidelines vary according to the clinical presentation and presence or absence of active systemic features. The principal immunosuppressants are glucocorticoids, mehotrexate, tracolimus, cyclosporine, anakinra and IL-1 inhibitor.

Conclusions

Systemic juvenile idiopathic arthritis is an autoinflammatory disorder characterised by a diagnostic triad : daily spiking fevers, rash and arthralgia. There is no specific diagnostic test. Due to systemic complications and potential toxicities of the drugs, children with sJIA should be referred to a rheumatological centre and require close supervision and careful monitoring. The treatment is based on immunosuppressants.

L 12

A boy with twice a bacterial meningitis with an underlying complement deficiency

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Introduction

The complement system is part of the innate immune system. The complement system plays an important part in defence against pyogenic organisms. It promotes the inflammatory response, eliminates pathogens, and enhances the immune response. Complement deficiencies are said to comprise between 1 and 10% of all primary immunodeficiencies.
Patients with deficiency of a complement pathway protein are susceptible to recurrent sinopulmonary bacterial infections, bacteremia, and/or meningitis. The pathogens most commonly implicated are encapsulated bacteria, such as Streptococcus pneumoniaem Hamophilus influenzae type b, and Neisseria meningitidis.

Aim

Not applicable

Methods

Case: A 3 year old boy presents with a meningitis due to streptococcus pneumoniae. He is from Mediterranean origin and the parents are consanguineous. There was a history of dental abscesses with hospitalisation in the past. The boy was treated with antibiotics intravenous during 14 days for his meningitis.
One year later he presents again with a meningitis (started with an otitis) due to streptococcus pyogenes. A CT scan of the temporal bone showed a probable dura leak. Neurosurgical exploration showed a chronic mastoiditis instead of a dura leak. An immunologic workup was done because the child was presenting again with a bacterial meningitis. Immunoglobulins were normal, as were lymfoctes and neutrophil counts. Investigation of the complement system reveals reduction of the classical pathway, alternative pathway and low C5 and C8 values. More specific testing of the complement system of the boy lead to the final diagnosis of a factor I deficiency, the confirmation that he has a complement deficiency. Human complement factor I is a plasma serine proteinase that plays an essential role in the modulation of the complement cascade. Factor I cleaves the alfa chains of C4b and C3b and thereby is involved in the regulation of both the classical and alternative C pathways. The clinical manifestations usually begin in early childhood and consist essentially of severe recurrent pyogenic infections mainly caused by Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenzae, as well as an increased incidence of glomerulonephritis and systemic lupus erythematosus-like illness. Complement factor I deficiency is inherited in an autosomal recessive pattern. Both parents and a younger sister were genetically tested, results are still awaited.
A few weeks after his second meningitis he presents with a bacterial pneumonia. For that he received antibiotics intravenous for 14 days and he was strictly followed and started with orally prophylactic antibiotics (amoxicillin). Also he received influenza and pneumococcal vaccine.

Results

Discussion: We present a 3 year old boy with twice a meningitis because of an underlying complement deficiency. Because of the severity of the infections an immunological workup was done and, although a complement deficiency is rare, it was

found in this boy. More precisely he had a factor I deficiency which explains his recurrent infections . Strict follow up, antibiotic prophylaxis and additional vaccinations were provided.

Conclusions

Complement deficiency is quite rare but should always be kept in mind for a patient with recurrent severe bacterial infections (eg meningitis) in a young child and should be part of the immunological workup.

I 01

Lymphadenopathy caused by nontuberculous mycobacteriae in children: treatment and outcome.

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Introduction

Nontuberculous mycobacteria (NTM) can cause chronic, localised cervicofacial lymphadenopathy in children. There is no clear consensus in the literature on how to deal with this disease. Patients affected by this disease have been successfully treated at University Hospital Ghent (UZG) for years now.

Aim

The aim of this paper is to describe the results of this treatment and to compare them to the results described in the literature.

Methods

This retrospective study is focused on a sample of 30 children diagnosed with NTM infection that were treated between January 2000 and June 2017.

Results

The patient population consists of 16 boys and 14 girls. Almost all patients (96.7%) had taken medication prior to the first medical visit at UZG. In addition, 16.7% had already received surgical treatment in a regional hospital.
Of the 30 patients who were operated in UZG , 93.3% initially underwent a curettage and only 2 patients (6.7%) underwent a complete excision. The lymphadenopathy of these last two patients was in an early stage and the lymph nodes could be easily removed. No complications were reported.
In 15 patients (50%) the first operation was successful. The remaining 15 patients underwent a second curettage and 2 of them had to undergo a third curettage. In 3 patients a scar resection was necessary for aesthetic reasons.
The median healing time for the group undergoing a complete excision (2 patients) was 13 days. In the patients who underwent curettage (28 patients), a median healing period of 10.9 weeks was observed.
All patients received a local treatment after the operation: 28 patients received a sponge dressing dipped in a rifamycin solution (Rifocine®), while the remaining 2 patients received an sponge dressing dipped in betadine. In addition, 18 patients (60%) received oral medication at the start of the therapy. On the basis of the type of antibiotic, patients can be divided into the following groups: neomacrolide with rifampicin (40%), B-lactam antibiotics (13.3%), isoniazid (3.3%) and clindamycin (3.3%). Adverse reactions were reported in 33,3% (6/18) of patients receiving antibiotics, mainly in the group who received a neomacrolide with rifampicin (5/12).

Conclusions

Early diagnostics are crucial in the treatment of lymphadenopathy caused by NTM. The choice of treatment is determined by the stage at which the diagnosis takes place, which in turn impacts on the treatment outcome and healing time.
Our study shows that complete excision in an early stage of disease achieves the highest degree of healing and involves the shortest duration of healing process. For more advanced stages (lymph node liquefaction or adhesion to the surrounding tissue) it is preferable to opt for curettage. Despite the lower healing rate, complete healing can be obtained in a reasonably short period of time and this treatment also has good results in the field of wound healing.

Any residual disease can be tackled by means of a medication therapy. Local antibiotic therapy in the form of a rifamycin sponge dressing can be chosen. This is a safe option that avoids systemic side effects. In therapy resistant cases, a neomacrolide with rifampicin can also be administered orally.

I 02

Immunological and virological outcome in HIV-infected adolescents transitioning to adult care in Belgium

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Introduction

There are scarce data regarding health outcome of HIV-infected adolescents after their transfer from pediatric to adult care.

Aim

To assess the immunological and virological outcomes of HIV-infected patients 2 years after transfer to adult care.

Methods

This study included patients from nine pediatrics centers transferred to adult care between 1st January 1996 and 31st December 2013. Socio-demographic, clinical, immunological, and viral loads (VL) have been recorded at the time of the transfer and 2 years after transfer. A multivariate logistic regression model was used to identify factors predicting a poor immunological status at two-years post transfer. Loss to follow-up after transfer was not assessed.

Results

A total of 70 HIV-infected patients were transferred during the study period. The median age at transfer was 18 years (range: 15-25) with a sex-ratio of 1:1. At the time of transfer, 83% of HIV-infected adolescents were on cART. The median number of T lymphocytes was higher after transfer (p=0.04) compared to before, but the median CD4 cell count did not differ before and after transfer. However, the proportion of patient with CD4 < 200/mm3 (Low CD4 cell count) increased from 12.7% to 18.7% after transfer towards adult care but the difference did not reach significance (p= 0,366). Low CD4 cell count after transfer was associated with detectable VL before transfer (aOR=16,4 [2,1-27,2]; p = 0,0073), detectable VL 2 years post transfer (aOR=15,5 [2,1- 17,5]; p = 0,0054), and female gender (aOR=0,02 [0,002- 0,3]; p = 0,004). However, it was inversely associated with history of depression (aOR=9,2 [1,2-68,7]; p = 0,03). Factors associated with detectable viral load at 2 years post-transfer were the concomitant low CD4 cell count (aOR=11.0 [3.4-35.4]; p=0.0001) and African origin (aOR=1.8 [1.1-3.0]; p=0.0315).

Conclusions

Among the patients who transferred from pediatric to adult care, the proportion of patients with virological suppression and preserved immune function was not different before and after transfer. African origin, female gender and detectable VL at the time of transfer might serve as markers for patients requiring more careful attention by health care providers.

I 03

Literature review of the burden of serogroup B meningococcal disease in Belgium

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Introduction

Invasive meningococcal disease (IMD) is an alarming illness with rapid onset, progression, and high rate of sequelae and mortality. The surveillance of IMD in Belgium is based on the mandatory notification of the disease to the regional health authorities and to the Belgian Meningococcal Reference Centre that characterizes isolates from peripheral laboratories since 1971. Although IMD is considered a rare disease in Belgium, it is a public health priority due to its high morbidity and mortality. Meningococcal disease due to serogroup B (MenB) is endemic in many European countries, causes the majority of IMD in Europe and is responsible for unpredictable outbreaks. Protein-based vaccines against MenB are available to prevent this disease. Encouraging vaccine effectiveness post-dose 2 (83%) has been observed in England after the introduction of MenB vaccine in the national paediatric immunization calendar in 2015 (co-administered with other routine vaccines at 2, 4 months with a booster at 12 months). Target proteins derived from serogroup B meningococci included in these MenB vaccines may be shared by strains belonging to other serogroups. Adequate protection against MenB by the vaccines likely depends on the circulating meningococcal strains.

Aim

As MenB data in Belgium is dispersed, the aim of this literature review is to provide an overview of the national burden of the disease in the advent of meningococcal vaccines.

Methods

MEDLINE, Belgian Journal of Paediatrics and reports from the Scientific Institute of Public Health (WIV/ISP) were searched for MenB-related publications (disease, treatment, prevention) in Belgium.

Results

Incidence: As of 1969, an increase of MenB cases was observed in Belgium (highest incidence in 1971-1972 with 5 cases/100,000), followed by a decline as of 1975. Incidence of IMD rose in the nineties (1995-2001; 2.0-3.7 cases/100,000) to level off at around 1/100,000 (0.8-1.6/100,000) over the 2004-2016 period. This latter showed a predominance of MenB (63-87% of the cases). Available surveillance data from the WIV/ISP for 2012-2016 reports 87-134 IMD cases per year, in which 63-78% were due to MenB. There has been variation in the last 10 years with number of MenB cases ranging from 60 to 140 cases per year. The 2016 inter-epidemic incidence shows 0.96 cases/100,000 in all ages (108 cases).
Age: As in other European countries, the age groups in which IMD occurs most frequently in Belgium are children <5 years and adolescents 15-19 years old (27-39% and 13-18% of cases per year for 2012-2016 respectively). Infants <1 year are at highest risk (MenB incidence of 21.8 and IMD incidence of 15.6/100,000 inhabitants in 2009-2010 and 2012 respectively). Notably, the nasopharyngeal carriage of MenB is more prevalent in adolescents than in the rest of the population.
Strains virulence/diversity: The outbreak of MenB that occurred in the seventies (1969-1975), was predominantly caused by serotype B:2b:P1.2. From 1991 to 1996, incidence rose again due to expansion of a B:4:P1.4 clone. More recently

(2006-2009), out of the 513 IMD strains typed at the National Reference Centre, 431 strains belonged to serogroup B and 45 (10.4%) were identified as B:NT:P1.14. Most cases were geographically clustered in the northern part of the country. The majority of the 1,933 IMD strains analyzed from 2000 to 2010 were susceptible to antibiotics that are currently used for the treatment and prophylaxis of IMD, but a decrease of penicillin G susceptibility of the analyzed strains was observed over the years. The continuous monitoring of the susceptibility to antibiotics remains important. Importance of antibiotic prophylaxis for close contacts of cases: The Walloon Agency for Quality of Life (AViQ) and the Flemish Agency for Care and Health advice the administration of one dose per os of ciprofloxacin 15 mg/kg (max. 500 mg) to close contacts up to 7 days post last contact. Close contacts include those living in the same house, intimates, persons sharing same kindergarten classroom or specialized schools, persons being in close contact with the respiratory secretions of the index case (medical entourage).

Conclusions

In Belgium, MenB cases have decreased in the last ten years. Nevertheless, disease outbreaks are unpredictable and IMD case fatality remains around 5-10%. Accordingly, the implementation of MenB protein-based vaccines has the potential to decrease the disease incidence in the vaccinated children. Adequate follow-up of vaccine effects require intensive epidemiological surveillance.

I 04

Epidemiology and clinical features of Respiratory Syncytial Virus and Influenza viruses infections during the fall and winter period 2014-2015

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Introduction

Respiratory syncytial virus (RSV) and Influenza viruses A and B are major causes of hospitalization for lower respiratory tract infection (LRTI) in young children.

Aim

The main objective of this work was to compare the epidemiological and clinical characteristics of pediatric hospitalizations for infections by one of these viruses.

Methods

The evaluation was conducted between 2014/09/29 and 2015/04/31. Children under 16 years of age with a positive rapid lateral flow chromatography test or cell culture for RSV or influenza A or B on nasopharyngeal samples were included. They were identified by the microbiology laboratory of the CHU Saint Pierre. The medical charts of these children were reviewed. Influenza A and B infections were included in a same group and compared with the RSV group.

Results

RSV or influenza viruses infections were diagnosed in 781 patients among which 262 were hospitalized. Hospitalization rate was 43% in patients infected with RSV (196/453) and 20% in children infected with an Influenza (66/328). The seasonal distribution revealed distinct peaks of incidence for the two groups with an overlap between the two epidemics. Children hospitalized for RSV infection were younger, and more dyspnoeic, requiring more frequent respiratory support and longer hospitalizations than those hospitalized for an Influenza infection. Non-invasive ventilation was required in 23% of children hospitalized with RSV infection, but in none of those with an Influenza and 9% of children with RSV were transferred to ICU compared to none in the group with an Influenza infection (p-value <0.0001 and 0.009 respectively). Children hospitalized with an Influenza infection presented more febrile seizures, abdominal or gastro-intestinal complaints.

Conclusions

During 2014-2015 fall and winter seasons, RSV represented the major burden of viral respiratory disease with a high rate of hospitalization for LRTI. Children hospitalized with RSV infection were younger and they suffered from more severe respiratory distress than children hospitalized for an Influenza infection.

I 05

Empiric treatment of febrile urinary tract infection in infants and children in Tournai-Belgique

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Introduction

Resistance pattern of bacterial pathogens responsible for febrile urinary tract infections (UTIs) shows inter-regional variabilities.

Aim

The aim of the study is to analyse the susceptibility of the germs causing UTIs in symptomatic infants and children admitted in the paediatric unit of CHwapi- Tournai in order to propose an optimal empiric treatment pending cultures and susceptibilities in our area.

Methods

During a three-year-period (30th July 2014-29th July 2017), we collected prospectively data of 233 patients, (31.4% males, 68.6% females) presenting in our paediatric unit with symptoms compatible with the diagnosis of febrile UTI and confirmed by suprapubic aspiration or bladder catheterization in children younger than 3 years and by clean void or bladder catheterization in children >= 3 years of age. UTI was confirmed in case of any growth in samples obtained by suprapubic aspiration, >= 10.000 colony-forming units in urine obtained by bladder catheterization and >= 50.000 colony-forming units in urine obtained by clean void. Identification and antibiotic susceptibility of the pathogens were performed according to standardized procedures in the laboratory of microbiology of our hospital. Results were analysed regarding age-groups (0-2 months, 2-36 months, and >= 36 months), known urologic abnormalities at the time of UTI diagnosis and number of episodes of UTI (first or recurrence). The resistance pattern of E.coli and « pathogens other than E.Coli » was also reported.

Results

In the group with no known abnormality at the time of the diagnosis of febrile UTI, there were 157 patients with a first episode. Resistance is 49.68% to ampicillin, 13.38% to amoxycillin-clavulanate and 25.48% to co-trimoxazole. It is 3.82% to cefuroxime, 1.27% to ciprofloxacin, and 0% to temocillin and amikacin. In the same group, but with recurrence (46 patients), the resistance increases to 63.04% to ampicillin, 15.22% to amoxycillin-clavulanate, 30.43% to co-trimoxazole, 10.87 % to cefuroxime but is only 4.35% to ciprofloxacin, 2.17% to amikacin and 0 % to temocillin. These data analysed in the 3 age-categories have the same trends if it was a first episode of UTI and if it was a recurrence for patients >= 2 months of age but were not statistically acceptable for analysis in the group of patients < 2 months with recurrence of UTI.

In the group with an abnormality known at the time of the diagnosis, there were 30 patients (9 with a first episode and 21 with recurrence). In case of a first episode (9 patients), resistance is 44.4 %, to ampicillin, 11.11 % to cefuroxime, 33.33 % to co-trimoxazole, 0 % to ciprofloxacin, 11.11% to temocillin and 0% to amikacin. In case of recurrence (21 patients), the rate of resistance increases to 66.67 % to ampicillin, 23.81 % to cefuroxime, 33.33 % to co-trimoxazole, 14.29 % to ciprofloxacin, 9.52 % to temocillin and 4.76 % to amikacin. Because of the small number of patients, these results are only trends not statistically significant.

E. coli is the most common pathogen isolated in our study (86.7%). 6 are ESBLs and 5 of them occured in cases of recurrence of UTI. Resistance rate of those ESBLs E. Coli is 100% to ampicillin and cefuroxime but 0 % to temocillin and amikacin.

Conclusions

If a child is admitted with the diagnosis of UTI, it is crucial to know if it is a first episode versus recurrence and if there is any known abnormality of the urinary tract.
In case of a first episode with no known abnormality of the urinary tract, cefuroxime is our first choice to initiate the empiric antibiotic treatment pending the cultures and susceptibility of the germ isolated because the resistance rate in this group is only 3.82%.
But in case of a first episode of UTI in an infant or a child with a known abnormality at the time of the diagnosis of UTI, and in case of recurrence with or without known urinary tract malformation, resistance tends to increase and amikacin becomes our first choice as an empiric treatment pending the results of the urine culture. The study is going on and more data will be available soon to precise those recommandations.

I 06

Non typeable Haemophilus influenzae meningitis causing a subdural empyema in a 6-month-old child

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Introduction

NTHI is frequently held responsible in otitis media, sinusitis and bronchitis. It can also occasionally be found in rare cases of invasive diseases such as meningitis or sepsis, particularly when associated with risk factors such as head trauma, cerebrospinal fluid leak or immune deficiency.

Aim

The purpose of this case report is to underline the grown relevance of Nontypeable Haemophilus Influenzae (NTHI) which is a commensal host-bacteria present in the nasopharyngeal bacterial flora of 40 to 80% of the population, all age groups included.

Methods

We report the case of a healthy 6-month-old female patient who, although vaccinated in accordance with the immunisation schedule, presented a Nontypeable Haemophilus Influenzae meningitis complicated by a subdural empyema treated with Cefotaxime and neurosurgical drainage.

Results

Our discussion focuses on the increased importance of NTHI in Haemophilus Influenzae (HI) meningitis and the current paths in vaccine research and development. We also address subdural empyema occurring in the context of bacterial meningitis in children and its neurosurgical treatment. Finally, we discuss the infectious risk associated with neutropenia in a previously healthy child.

Conclusions

Given the rising implication of NTHI in HI-related diseases since the implementation of the anti-HIB vaccine, capsular typing has proven its interests in NTHI-related conditions in order to broaden the existing epidemiological data about this pathogen involved in such a wide range of diseases, and to study the benefits of a vaccine.

I 07

Menstrual Toxic Shock Syndrome in a young adolescent using menstrual devices

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Introduction

Menstrual toxic shock syndrome (mTSS) is a life-threatening affection which needs to be early diagnosed among women wearing menstrual devices and presenting flu-like symptoms. The two main toxin-producers pathogens are Staphylococcus Aureus and Streptococcus pyogenes (group A), the former being involved in more than 95% of menstrual toxic shock syndromes. TSS comes from toxin ability to act as a super antigen, activating more than 20% of host T-cells resulting in a cytokine storm.
While pathogenesis of TSST-1 Staphylococcus-associated toxin gets better understood, medical management remains symptomatic including a supportive treatment and a large spectre antibiotherapy during first line management (intravenous immunoglobulins being only used under special conditions). We report a case of a young adolescent presenting to local A&E for rash and orthostatic hypotension manifestations since the afternoon of the same day.

Methods

A 13-years-old-girl presented late in the afternoon with one-day history of fever. Upon arrival, she complained of headache, sore throat, orthostatic malaise and recent appearance of a rash. She had her periods since a year and was using menstrual devices since a month. She was menstruating when she consulted and had the same tampon for 26 hours.
On physical examination, she was febrile and had a heart rate of 130 beats per minute with diminished heart sounds, respiratory rate of 30 breaths per minute, blood pressure of 84/54 mmHg, capillary refill time at 3 seconds, conjunctival erythema and erythematous maculopapular rash on the whole body like a sun burn.
A blood test shows increased inflammatory syndrome with CRP at 80 mg/L, increased neutrophils at 23400/microliter and a platelet count at 225000/microliter. Coagulation screening shown altered INR at 1,61. The rest of the blood test shows no hypoglycaemia, normal renal function and no rise of hepatic enzymes. Initial blood gas shows no alteration of acid-base blood balance, normal electrolytes and increased lactate levels at 2,7mmol/L.
At the admission at patient inward, she needed initial fluid resuscitation at 20mL/kg followed by 400mL of SSPP. An empiric antibiotherapy was started with Vancomycine and Clindamycine. Due to persistent hemodynamic instability, despite fluid administration, inotropic support by noradrenaline was started. Afterwards, she remained tachycardic and hypotensive. She was transferred to PICU.
The vaginal swab culture was positive for Multi-sensitive Staphylococcus Aureus with positive genetic testing for TSST-1 toxin.
Blood cultures remained sterile.

Results

mTSS has been first described in the 1980s among women using highly absorbent tampons, which were removed from stores afterwards, reducing incidence at 0,9-3,6/100.000 persons per year nowadays. As described above, the main pathogen is Staphylococcus Aureus which produces TSST-1 endotoxin. It can be found in 1-5% of healthy women vaginal mucosae microbiota. After being secreted, TSST-1 toxin crosses the mucosae barrier by itself. Once in the bloodstream, most people produce anti-TSST1 antibodies which neutralize the toxin. In populations developing mTSS, 95% lacked this immunoglobulin. Moreover, even after mTSS, less than 50% produce it explaining increased risk of further recurrences in the same patient.
Toxin acts as a super-antigen, binding MHC of class II receptor, which is expressed by

antigen-presenting cells and TCR. This new complex first induces excessive and non-conventional T-cell expansion leading to overproduction of multiple cytokines by T-cells and antigen-presenting cells. They amplify the recruitment of other lymphocytes, increasing pro-inflammatory molecules secretion (Lappin E., & Ferguson A. J., The Lancet infectious diseases, 2009, 9(5), 281-290) and finally leading to toxic shock. It was recently shown (Dixit S., Fischer G. & Wittekind C., Australasian Journal of Dermatology, 2013, 54(4), 283-286.) that oestrogens and progesterone are also playing a role in the non-conventional inflammatory response.

Conclusions

TSS is a rare life-threatening emergency that needs to be recognized fast in first-line hospitals. Physicians need to be alerted by healthy women presenting flu-like symptoms and hypotension during their peri-menstrual period. The cutaneous and conjunctival rash are clinical signs orienting the diagnosis. Treatment is symptomatic and must include a bacterial toxic antibiotic in association with Clindamycine which neutralizes the toxin. Permanent restriction of using tampons as menstrual devices must be transmitted to patient as they present an increased risk of recurrence.

I 08

Case-Report: Vasculitis in a 6-year-old girl with atypical clinical manifestations.

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Introduction

Vasculitis in children is a rare disease described by an inflammatory process of one or several types of blood vessels accompanied by modifications in the blood vessel wall structure. It can either be a primary process or secondary vasculitis. A wide variability of symptoms is observed depending on the type and extent of the inflammation and the size and location of the blood vessel affected, in turn, determining which organ will be affected. The treatment will depend on the type of vasculitis and the severity of the affection.

Aim

The aim of this case-report is to remind that even though some vasculitides with common clinical and biological manifestations have been classified into "syndromes", about 30% of the vasculitides found in children remain unclassified and therefore harder to diagnose and to treat.

Methods

A 6-year old girl was brought to our pediatric emergency center for a high fever, limping and swelling of the left cheek and the back of the left foot. The limping and the fever started 2 days before admission. Her parents noticed the swelling of the left cheek the day of the admission. Her general practitioner diagnosed tonsillitis 5 days before admission and treated her with Amoxicillin/Clavulanic acid. She did not present any respiratory, digestive or neurologic symptoms. Her clinical examination showed hypertrophic and inflammatory tonsils with a mild trismus. The cardio-respiratory and abdominal examination was normal. We noticed a swelling of the left cheek and back of the left foot, both without inflammatory signs but painful when palpated. No open wounds were found on the body. Over time, the swelling on the foot became red evolving to a pearly purple color to become necrotic and more painful. New lesions appeared, over a few days, in the same order covering the fingers, legs, ribcage, forearm and face (i.e. nose and chin) with progressive desquamation of the old lesions. The lesions varied in size. The fever increased over time reaching up to 40°C several consecutive days.

Results

The inflammatory syndrome increased every day with a CRP at 95mg/L on admission day up to 245 mg/L after 4 days and was accompanied by a neutrophilic hyperleukocytosis. Complementary exams showed elevated ASLO and IgA, negative ASCA and ANCA, positive IgM and IgG for Toxoplasma Gondii with low avidity and a polyclonal elevation of gammaglobulines. The blood culture, urine culture and throat swab were negative. The urine sample showed glycosuria, microscopic hematuria, and an elevated proteinuria. Chest radiography, abdominal and cardiac ultrasounds were normal. The head CT-scan showed hypertrophic tonsils. A suspicion of dental abscess motivated the removal of 2 teeth. The MRI and eye fundus were normal. The PET-CT showed signs of multiple septic emboli in the muscles without any source determining its origin. Finally, the skin biopsy showed signs of necrotic vasculitis. The patient was treated with Amoxicillin during 24 hours, Amoxicillin/Clavulanic acid for 2 days and Piperacillin/tazobactam during 4 days without improvements of her condition or lowering the fever. She was then further treated with a first dose of IV Methylprednisolone (20 mg/kg) when the skin biopsy results were obtained. The

treatment resulted in a rapid improvement of the skin lesions with no emergent lesion observed. A immediate disappearance of the limping was noticed. The blood sample showed an important decrease of the blood CRP, and a normalization of the blood IgA. Methylprednisolone (1 mg/kg/day) was started orally and our patient went home after a total of 17 days of hospitalization.

Conclusions

Due to the atypical presentation of our patient's vasculitis, it could not be classified into a known "vasculitis syndrome" such as Kawasaki Syndrome or Henoch-Shonlein vasculitis.
Because of the wide variability of symptoms, some vasculitis with more subtle clinical manifestations can be misdiagnosed and treated with unnecessary medication. Furthermore, a half to a third of children with systemic vasculitis can not be classified as typical vasculitis and are therefore easily mistreated.

I 09

Invasive group A streptococcal infections in a tertiary center

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Introduction

Group A B-hemolytic streptococcus (GAS) is an human pathogen responsible for a wide range of clinical manifestations. Invasive GAS infections are rare, an increase has been described since the mid 1980s in developed countries and they cause high morbidity and mortality.

Aim

To describe the incidence, predisposing factors specific to each age group and clinical characteristics of patients with invasive GAS infection, as well as to analyze risk factors associated with bacteremia and mortality

Methods

Retrospective and descriptive study through systematic analysis of medical records of all hospitalized patients for an invasive GAS infection in the Cliniques universitaires Saint-Luc (CUSL) between 2011 and 2016. We split the cohort into two groups to compare pediatric and adult populations.

Results

Sixty-height patients were included (26 children and 60 adults). Childrens' median age was 1,6 years old and 66,1 years old for adults. In the adult population, 90% had 1 to 4 predisposing factors (median of 2 factors) in contrast 70% of children did not have any documented risk factor but 19% developed a GAS infection following chickenpox. The most common clinical manifestations were occult bacteremia (31%; n = 31), bone and joint involvement (27%; 9 arthritis, 10 bursitis and 8 osteitis), necrotizing fasciitis (14%; n = 14), pneumonia 13%; (n = 13) and pleural empyema (9%; n = 9). Thirty cases of STSS were recorded (36%). Streptococcus pyogenes was isolated from blood cultures in 70% of case. The average length of stay in the hospital was 19,4 days. Early fatality rate (< 10 weeks) was 18,4% (12% in pediatrics and 21% in > 18 years old). We found a predictive value of positive blood culture; elevated LDH, CPK, GOT, GPT and urea on mortality. Thirty-six percent required a surgical treatment and 25% have benefited from dual therapy clindamycin-penicillin.

Conclusions

Invasive GAS infections are rare. However the clinical progression is rapid and the mortality is significant. A risk factor is more common in adults but chickenpox is the main risk factor in children.
Early diagnosis and management is crucial to improve the outcome and limit the complications. Blood culture and elevated LDH, CPK, GOT, GPT and urea could be used as warning factors for aggressive management. Clinical outcome was similar in children and adults in our study. Meningitis and pleural infections were specifically pediatric presentations.
Mortality and morbidity related to invasive GAS infections could be potentially prevented in the future by a vaccine and current reseach in this field must be encouraged.
Antimicrobial prophylaxis is indicated in persons in close contact with a patient infected with invasive SBHA.

I 10

Not always what it seems: acute otitis externa mimicking mastoiditis

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Introduction

Acute otitis externa (AOE) is a common condition in the paediatric population which usually presents with pain, itch, ottorhea or fullness of the ear, with or without hearing loss. The key physical finding in AOE is tenderness to traction on the pinna or palpation of the tragus. Initially the skin of the external auditory canal is oedematous and erythematous, but as the infection progresses, swelling of the ear canal may occur leading to narrowing of the auditory canal with accumulation of debris in the canal.

Aim

/

Methods

We will describe the case of an eight-year-old boy who was initially diagnosed with acute mastoiditis based on a strongly suggestive, but seemingly misleading clinical presentation of mastoiditis.

Results

An eight-year-old boy presented with unilateral otalgia, profuse purulent discharge from the ear, subfebrility and postauricular swelling, tenderness and redness with protrusion of the auricle. The day before presentation he already presented to the general practitioner because of unilateral otalgia since one week. Assuming an ear plug he rinsed the ear, which subsequently led to aggravation of the redness and pain. Although this clinical presentation was strongly suggestive for mastoiditis, computed tomography (CT) revealed no signs of mastoiditis and adequate antibiotic treatment did not improve his condition. Therefore we contacted otorhinolaryngology for further advice. On direct otoscopy, the external ear canal seemed inflamed and oedematous with bullous epidermolysis and the presence of granulation tissue. A foreign body was removed from the ear. Thus, although the clinical presentation was strongly suggestive for mastoiditis, CT and direct otoscopy surprisingly revealed an AOE associated with erysipelas, secondary to a foreign body. Treatment was adjusted and the boy recovered quickly.

Conclusions

In severe cases of AOE complete obstruction of the ear canal by seropurulent material may occur, and the condition may be then associated with fever, regional (cervical) lymphadenitis and cellulitis of the periauricular skin, thus sometimes mimicking the clinical picture of acute mastoiditis.

I 11

Measles epidemic in 2017 at the CHR Verviers East Belgium: illustration by a clinical case

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Introduction

CASE REPORT
A male infant of 9 months is hospitalized in our service for fever since four days, with cough, coryza and conjunctivitis. He is apathetic, has a maculopapular rash, which started on his face two days ago, and a diarrhea since two days.
A week ago, in our institution, he was in the same waiting area than a child who had measles, but no contact was noticed.
At the clinical examination, he has a generalized maculopapular rash, a bilateral conjunctivitis, an erythematous pharynx and Koplik's spots.
Biologically, he has a mild inflammatory syndrome, a transaminasis elevation and the LDH count is of 1984 mU/mL.
The presence of anti-measles IgM and a positive salivary PCR confirmed the diagnosis of measles. The infection was complicated by an otitis, but the evolution was favorable after five days of hospitalization.

DISCUSSION
Measles is a highly contagious viral illness characterized by fever, cough, coryza and conjunctivitis, followed by an erythematous, maculopapular rash which begins on the face and spreads cephalocaudally two to four days after the onset of fever. It is transmitted by the nasopharyngeal secretions or by direct contact, and can lead to death in 1/1000 cases due to its complications as pneumonia or encephalitis. In our institution, we had 53 cases of measles (36 confirmed, 13 probable and 4 possible) between February and April 2017. 70% needed a hospitalization, for a median stay of 4 days. 56% were pediatrics patients (<15 years old), 30% of them were younger than 1 year and weren't already vaccinated. Patients were mostly from romani community, medical staff, poor people or persons who had a recent contact with a case of measles at the hospital. Serology (anti-measles IgM) or PCR on nasopharyngeal aspirates have been used for diagnosis of measles virus infection. Preventive measures have been taken at the hospital, mainly at the emergency department, the pediatric ward and the walk-in consultation of pediatrics, and have been managed by a coordination cell.

CONCLUSION
We should enhance the vaccinal coverage to avoid other measles epidemics, which are a public health problem because of the major contagiousness of the disease, as illustrated by our case report. 95% of coverage of the population with the 2 doses of vaccine is needed for the EU to become measles-free, which is the OMS aim for 2018. The emergency department and the walk-in consultation of pediatrics are the front door for a local epidemic, and the medical staff has a main role to declare any clinical suspicion of measles, and to take hygienic measures for the patient and the family to avoid the spread of the disease.

I 12

Reduction of infections in Home Parenteral Nutrition with a simplified protocol : a 18-year study

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Introduction

Home parenteral nutrition (HPN) is a life-saving procedure for children with intestinal failure. This requires long-term central venous catheter placement and its related complications, including catheter-related infection (CRI), and particularly Catheter-related-bloodstream-infections (CRBSI), which leads to an increase morbidity and mortality rate in children dependent on parenteral nutrition (PN).

Aim

We prospectively analysed the impact of a standardised simplified central venous catheter (CVC) home care protocol on the incidence of post-discharge CRIs and CRBSIs in a paediatric HPN population.

Methods

In a single-centre study, patients followed up from November 30th 1999 to March 1st 2017 in the HPN program are reported. A standardised tunnelled catheter home care protocol focusing on rigorous asepsis and reduced manipulations was adopted by all parents and healthcare providers. The incidence rate of CRIs was analysed and categorised as either catheter-related bloodstream infection (CRBSI) or tunnel infections. HPN indications were short bowel syndrome (n=25), chronic intestinal pseudoobstruction (n=2), malabsorption (n=7), and chronic chylous ascites (n=1).

Results

Overall 35 consecutive children were studied over 96.6 catheter-years. Sixteen CRIs were observed in ten patients, namely twelves CRBSIs and four tunnel infections. The mean infection incidence was 0.5 ± 1.2 CRIs/1000 catheter days (interquartile range: 0.0- 0.4), of which there were 0.3 ± 0.9 CRBSIs/1000 catheter days (interquartile range 0.0 - 0.0).

Conclusions

This very low CRI incidence may be explained by the strict educational program, leading to improved compliance and observance, along with reduced manipulations. CRI and CRBSI might be prevented by optimal catheter connector antisepsis based on Chlorhexidine 0,5% combined to a "no-touch technique". Simplifying standard procedures is thus achievable without increasing the risk of complications and, moreover, improve the patient chances of recovering intestinal function.

I 13

Neonatal suppurative parotitis: a case report

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Introduction

Acute suppurative parotitis is a very rare condition, with only 44 reported cases in the English literature since 1970 (Ismail et al, Pediatrics International, 2013, 55, 60-64). The most common complaints on presentation are irritability, unilateral swelling, erythema and tenderness. Pus exuding from the Stensen duct is pathognomonic. Less than one half of the affected neonates presents with fever (47%). Most of the cases were male (77%), one third of the patients were premature babies.
The most frequent causative agent was Staphylococcus aureus (61%), but also other Gram-positive, Gram-negative or anaerobic organism have been found in cultures. The organisms can reach the parotid gland either via the Stensen duct or, less frequently, by the haematogenous route in case of a septicaemia. Positive blood cultures were found in 35% of patients studied.
Risk factors for developing neonatal suppurative parotitis are insufficient breast-feeding, prematurity, hot weather, nasogastric tube feeding, excessive oral suctioning, maternal breast abscess in a breast-fed infant. Dehydration seems to facilitate ascending of the infection through the Stensen duct, by reducing salivary flow.
Most of the cases were treated with only antibiotics, but sometimes surgical drainage was needed (23%). Usually, a combination of an anti-staphylococcal agent with an aminoglycoside or a third-generation cephalosporin was used as antibiotic treatment.

Results

Case report:
A 11-day-old breast-fed girl presented with a history of fever (38.2°C) since that morning, poor sucking and left pre-auricular swelling, redness and tenderness. She was born at term after an uneventful pregnancy with a birthweight of 3075 g. On admission the baby looked well, rectal temperature was 37.2°C. Her weight was 3050 g. Clinical examination showed a left pre-auricular swelling with local redness, warmth and tenderness. Further examination showed no abnormalities.
Laboratory tests showed a haemoglobin of 16.8g/dl; white blood cell count 31 500/mm³ with a differential of 50.2% neutrophils, 37.1% lymphocytes; 12.7% monocytes; a C-reactive protein of 22.4 mg/L. Kidney function and serum electrolytes were normal. Bilirubin levels were also measured and were well under the limit for starting phototherapy (12.1 mg/dL).
Ultrasonography of the parotid gland showed a moderate oedematous infiltration of the subcutaneous fat in the left pre-auricular region and a heterogeneous hypoechoic area (2.4 x 1.4 x 2.5 cm) in the parotid gland, suggestive of an acute parotitis with periparotitis.
Although no pus was visible, a culture from the Stensen duct after parotid massage and a blood culture were obtained. After the collection of the cultures antibiotic therapy with Flucloxacillin (100mg/kg) and Cefotaxime (200mg/kg) was started intravenously. Both cultures showed positive for Staphylococcus aureus, with the same resistance pattern (Clindamycin and Erythromycin resistant). After three days Cefotaxime was stopped and only Flucloxacillin was continued intravenously for a total of seven days. After one day of intravenous antibiotic therapy the swelling was almost completely gone and the baby remained afebrile after submission. After 7 days of intravenous therapy the baby was discharged and the parents were asked to continue oral Flucloxacillin for another three days.
Follow-up examination demonstrated no residual abnormalities.

Conclusions

Discussion

If we compare our case with literature data, we find a lot of similarities between our case and the most common complaints (unilateral swelling, erythema, tenderness). Though the pathognomonic sign of pus exuding from the Stensen duct was absent in our case, the oral swab after parotid massage did show positive for Staphylococcus aureus, from which we can deduce that S. aureus was present in the parotid gland. Our patient was being breast-fed, which is considered to be a risk factor.
Our patient also had a positive blood culture, which is only found in approximately one third of the cases described in literature.
In this case, we saw a fast improvement with intravenous antibiotic therapy, without the need of surgical drainage.

Conclusion
Neonatal suppurative parotitis is a rare disease, but it should be suspected in all patients presenting with a pre-auricular swelling with or without fever. Antibiotic therapy is usually sufficient for treating a suppurative parotitis, though sometimes surgical drainage is needed.

I 14

Case Report: Kingella kingea spondylodiscitis in a 16-month-old child

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Introduction

Kingella kingae is a germ increasingly found in the osteo-articular pathology of young children.

Aim

Discuss the most appropriate management of spondylodiscitis in young children

Methods

Case report

Results

Case presentation: A 16-month-old boy presenting to the emergency department for an acute, atraumatic refusal of walking. It has peaks of fever and at admission its biology shows leukocytes in the norm but a slight increase in C-reactive-Protein at 11.7 mg/L, Procalcitonin is at 0.12 ng/mL. The initial assessment by medical imaging with
radiology of the lower limbs, hip ultrasound, MRI and scintigraphy does not detect any lesions. The bone marrow puncture does not show any haematological malignancy. In view of this negative assessment, after one week of symptom progression a PET-CT is performed, which shows a hyper-metabolic focus at the level of the first sacral vertebra compatible with an infectious phenomenon. The diagnostic of spondylodiscitis is confimed by MRI and CT-guided percutaneous spine biopsy. Only the 16S PCR on spine puncture showed Kingella kingea, while all microbiological cultures remained sterile. Under intravenous antibiotic therapy with Cefazolin, clinical improvement was observed.

Conclusions

Spondylodiscitis is a rare pathology in children but important to recognize because the potential complications can be serious and are related to a delay in diagnosis. The diagnosis is difficult because the clinic is not always specific and the early imaging can be negative. In this case, do not hesitate to repeat the tests or to ask for an F18-FDG-PET-CT, which seems to be more sensitive than the MRI during the first two weeks of evolution. The culture remains frequently sterile so molecular identification techniques can be a valuable aid.
Between the ages of 6 months and 4 years, the most common cause of spondylodiscitis is Kingella kingae. As a result, empirically initiated antibiotic therapy should cover this bacterium. The throat swabs in search of Kingella kingae can also give an important clue to the germ in question. For the treatment of Kingella kingae spondylodiscitis, there are few Evidence Based recommendations. Studies are needed to define standardized management of this condition.

I 15

Extensive cervical spondylodiscitis with bone deformities and abscess formation in a 10-year-old boy: a case report

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Introduction

Spondylodiscitis is a simultaneous infection of a vertebral disc and the adjacent vertebral body and is not very common in children. It involves most frequently the lumbar part of the spine, followed by the thoracic part and in a few cases the cervical part.

Methods

We will describe a 10-year-old boy with cervical spondylodiscitis.

Results

A 10-year-old boy presented to our hospital with high back pain of sudden onset, the pain was continuously present and increased during physical activity. There was no history of trauma, no systemic or neurological symptoms and notably no fever. The physical examination was normal and subsequently the boy was sent home. Five and a half weeks later the boy presented back to our hospital because his symptoms did not improve, furthermore he developed radiation pain in his arms and paresthesia in his left pink. A blood test showed slightly elevated inflammatory markers. The MRI showed an extensive spondylodiscitis from C5 to T2 with collapse of the vertebral body C7, erosion of the antero-caudal part of the vertebral body C6 and less pronounced erosion of C5, T1 and T2. Besides, there was an abscess formation anterior from C3 to T3 and posterior through the neuroforamina into the spinal canal from C6 to T1 with localized pressure on the spinal cord. The boy was admitted to our hospital, his neck was immobilized and intravenous antibiotic treatment was started. The hemocultures and a local biopsy stayed negative. In total the patient was treated with intravenous antibiotics for 40 days and orally for another 14 days. The inflammatory parameters normalized during this treatment. The most recent scan, two weeks after the stop of the antibiotic treatment, showed the known vertebral bone deformities with further improvement of the inflammation and complete remission of the abscess formation.

Cervical spondylodiscitis in children is a rare infection. It can be caused by hematogenous spread or by contiguous spread of another infection. The hematogenous spread spondylodiscitis occurs almost all at younger age, while the contiguous spread -mostly after ingestion of a foreign object- occurs at younger and older ages. The rarity makes it difficult to describe a symptom pattern typical for cervical spondylodiscitis. The main treatment is immobilization and the administration of antibiotics.

Conclusions

This case learns that continuous neck- or high backpain in children, without a previous trauma or ingestion of a foreign object and without any red flag symptoms, can be the chief complaint of cervical spondylodiscitis. Cervical spondylodiscitis is rare but can cause seriously bone deformities and neurological complications and should be considered in cases with persisting and unexplained neck- or high backpain.

I 16

Haemophilus influenzae meningitis in a two-year old child.

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Introduction

Haemophilus Influenzae type b (Hib) meningitis is a life-threatening medical emergency. Historically causing significant mortality and morbidity, it was the leading cause for bacterial meningitis in children under 5 years of age. Its frequency has dramatically decreased worldwide, and it became extremely rare with the introduction of the Hib vaccine (1993 in Belgium). Rapid and accurate evaluation is essential to guide further specific investigations and to start treatment as soon as possible.

Methods

We describe the case of a two-year old child without any previous personal or familial history, who presented with meningitis. He had a delay in his booster vaccinations. An Haemophilus Influenzae type b grew both in blood and cerebrospinal fluid (CSF).

Results

A two year old boy was brought up in the emergency room for uncontrollable vomiting and fast worsening of his general state in the 48 hours prior to his admission. His clinical condition then quickly declined adding new symptoms: headaches and the inability to hold the upright sitting posture. Upon examination, the child was slightly pale and seemed uncomfortable and irritable. Clinical examination showed no fever, an erythematous pharynx and mucosal dryness. Photophobia, a nuchal rigidity with positive Kernig and Brudzinski signs were noted. Blood test showed a predominantly neutrophilic inflammatory syndrome (White Blood Cells: 30750/μl, CRP: 46,6mg/dl). CSF analysis was highly suggestive of bacterial meningitis (23052 leukocytes/mm3 including 77% neutrophils, proteins: 178mg/dl, glucose: 1mg/dl). Both blood and CSF cultures grew an Haemophilus Influenza type b. He received IV doses of steroids during the first 72 hours and ceftriaxone 100mg/kg/j. After improvement in his general condition, ENT symptoms such as walking difficulties, imbalance and a slightly hearing loss were discovered. A thorough investigation revealed bilateral labyrinthitis with slight cochlear ossification requiring a close ENT follow-up and vestibular physiotherapy.
Evolution was slow and IV antibiotherapy was prolonged for a total of 21 days. ENT symptoms resolved very progressively.

Conclusions

A reemergence of severe infections due to Hib has been identified in the last few years, due to different factors including a reduction in indirect protection or herd effect, a decrease in antibody titers among children vaccinated before 1 year of age who did not receive a booster dose, and the emergence of more virulent, contagious strains. In our patient, we concluded that the meningitis was a consequence of the loss of immunity in light of the lack of vaccine booster. Antibody titers in children vaccinated before one year of age have a tendency to decrease more rapidly.
Any bacterial meningitis and in particular meningitis due to Hib infection requires a careful ENT examination to detect early signs and symptoms of complications due to damage in the inner ear. An initial ENT evaluation must be performed and reassessed on a regular basis during and after treatment. One of the most feared complications is the cochlear ossification which - if it goes undetected - becomes irreversible and does not allow cochlear implant.

I 17

Scarlet fever? Kawasaki syndrome? Coxsackie infection? Report on a medical odyssea

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Introduction

The association of fever and rash is common in children and may have several etiologies (infectious, autoimmune, allergic ...). However, in the presence of persistent fever for more than 5 days associated to skin rash and skin desquamation, the diagnosis of Kawasaki disease may be considered unless clinical or biological signs suggest another disease such as scarlet fever or coxsakie infection.

Results

We report the case of a 7-year-old girl who was referred to our Pediatric Infectious Disease Unit for the exploration of a recurrent fever persisting for 20 days.
Day 0: Diagnosis of scarlet fever based on fever the last 48 hours with pharyngitis and typical skin rash. Treatment by amoxycillin was carried out.
Day 4: Hospitalization for persistent fever, increased rash, glossitis and cheilitis. However, during hospital stay, she was afebrile for 48 hours. Laboratory investigation was normal but slightly increased liver transaminases. She was discharged with the antibiotic treatment.
Day 8: Re-hospitalization for brief recurrence of fever. The rash was still present with desquamation of the palms of the hands. Fever disappeared for 4 days. There was no significant biological inflammatory syndrome, but persistent slight alteration of liver tests and positive IgA against the coxsackie virus. Antibiotics were discontinued.
Day 18: Second re-hospitalization for recurrence of fever and conjunctivitis. Kawasaki syndrome was evoked and patient received intravenous immunoglobulin. Despite this, fever persisted and significant inflammatory syndrome was objectivated in the laboratory tests. ?Furthermore, 2 throat swabs went back positive with the presence of staphylococcus aureus. Blood cultures were negative. A second dose of immunoglobulin was then given and anti-inflammatory doses of aspirin introduced. In the next 24 hours, fever had disappeared and the patient improved continuously and could definitively be discharged.
Echocardiography and abdominal sonography were both normal.
Given this clinical presentation, several differential diagnoses were considered including scarlet fever and coxsakie infection. Treatment with antibiotics did not resolve the symptomatology. As the diagnosis of Kawasaki disease was not excluded, an immunoglobulin challenge treatment was therefore administered, and finally, symptoms disappeared.
Kawasaki disease mainly affects children under 5 years. It is an extended vasculitis of unknown origin with particular tropism for the coronary arteries. The diagnosis is based on clinical criteria associating a set of symptoms: a fever evolving for 5 days at least, a desquamation of the palms of the hands and soles of the feet, a diffuse eruption, a cheilitis, a conjunctivitis, and cervical lymphadenopathy. Laboratory tests indicating inflammation, thrombocytosis, cytolysis and cholestasis are not specific but, in the clinical context may contribute to the diagnosis.
In addition to the classical form, an atypical form is described which represents 15-20% of cases, for which the presentation includes an incomplete association of clinical signs.

Conclusions

The diagnosis of Kawasaki disease can sometimes be difficult to establish formally, especially in its atypical form. However, after exclusion of other differential diagnoses or following immunoglobulin challenge, the diagnosis of Kawasaki disease can be suggested as exclusion diagnosis in our patient.

I 18

Atypical right hip osteoarthritis: where is the cat?

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Introduction

Bartonella henselae is the agent of cat-scratch disease (CSD). This bacteria transmitted by cats, mainly causes subacute, self-limited regional lymphadenitis. However approximately 10% of patients with CSD may develop extranodal manifestations. Osteoarticular infections, one of these manifestations, are uncommon and represent a real diagnosis challenge.

Results

Case Report:
A 12 years old girl presented right inguinal pain radiating to the lateral side of the thigh for five weeks, associated with high fever and walking difficulties. She has been transferred to our tertiary center with right hip osteoarthritis, confirmed by magnetic resonance imaging and bone scan. Despite standard empirical treatment with flucloxacillin, she did not show any significant clinical improvement.
Physical examination revealed painful mobilization of the right hip in abduction and adduction but without others local signs of inflammation. Blood test showed inflammatory syndrome (CRP: 179 mg/l, white blood cells 7950/μl) and mild anaemia (Hb: 9.6 g/l). Blood cultures were negative. The hip ultrasound revealed a coxofemoral synovium's swelling and a joint effusion.
Synovial fluid punction showed the presence white blood cells (15814/μl, 84% of neutrophils) but standard cultures and bacterial broad range PCR 16S remain negative. Intravenous flucloxacilline was continued. In view of the persisting fever and joint pain, a magnetic resonance imaging was repeated and showed the recollection of a large joint effusion. However, no abscess was detected. An arthrotomy was performed with washing of the joint and synovial extraction. This intervention had a successful outcome with pain and fever decrease, walking improvement and progressive extinction of the inflammatory reaction. Standard Cultures were negative on surgical samples. In order to define the causative agent of this clinical picture, others analyses as Bartonella henselae serology and specific PCR were realised. Both tests highlighted the diagnostic of CSD arthritis. A complement of history revealed a contact with a kitten. Moreover, the patient's sister developed a typical lymphadenitis due to Bartonella henselae few months ago. The patient was discharged from the hospital with a long term intravenous treatment with a first generation cephalosporin. Even if this treatment is not the recommended one in CSD, the clinical condition of our patient improved why we didn't change the antibiotherapy. The one month follow-up showed a symptom-free outcome and a new ossification of the osseous lesions at the hip radiography.

Conclusions

Discussion and conclusion:
This case illustrates the potential of Bartonella henselae to affect joints and more specifically coxofemoral joint. The uncommon clinical presentation and the difficulties to isolate the bacteria are challenges to do the diagnosis. Blood serology and specific PCR on synovial specimen allow the diagnosis. Despite the diagnosis delay, the patient's clinical progress was favourable. Osteoarticular manifestation in CSD is rare and specific guidelines for management and treatment are lacking. The most effective antibiotics are trimethoprim and sulfamethoxazole, rifampicin, ciprofloxacin, gentamicin. Usually patients have a good clinical evolution whatever the treatment used. Spontaneous complete recovery is also described.
Bartonella henselae hip osteoarthritis is rare and probably misdiagnosed but it deserves to be looked for especially in case of non-typical progression on

conventional antibiotic treatment and contact with kitten.

I 19

Abnormal psychomotor development revealing a HIV infection in a young boy.

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Introduction

Due to preventions measures, HIV infections in infants became very much uncommon over the past decade in our countries. This is rewarding as such transmission can be responsible for several dramatic infectious disorders as well as cerebral and development disturbances.

Aim

N/A

Methods

We report here the case of a 14 month-old boy sent to the pediatric neurology clinic for a developmental delay and EEG analysis. The mother reported that the boy couldn't hold a sitting position and even less a standing position. The neurological examination was pathological showing significative axial hypotonia and abnormal head lag during the pull-to-sit test and lack of movements. General physical observation revealed a very pale and grumpy boy. The abdominal palpation detected a splenomegaly around 5 centimeters under the costal edge.

Results

Retrospective anamnesis and medical record analysis revealed that the boy was born through a vaginal birth from an HIV positive and Hepatitis C positive mother who wasn't regulary taking her medication for a year. On the day of the delivery she had an undetectable viral load (HIV-PCR < 40 copies) as well as her boy was negative for HIV-PCR. No other blood samples was ever done since then.

The abdominal ultrasonography confirmed a splenomegaly measured at 8,4 cm, and showed multiples hypertrophic peri-aortic, peri-splenic and mesenteric lymph nodes. The initial blood sample showed an iron deficiency anaemia (haemoglobin (Hb) 5.6 g/dl, ferritin (Fe) 8.3 μg/L, total iron-binding capacity (TIBC) 5%), EBV VCA-IgM and IgG were positives, a positive detection of p24 Ag and anti-HIV antibodies, positive IgG Coombs's test, an increased CD3 cell count (3.819.000/μL, a low CD4 cell count (4,2%), and a low CD4/CD8 ratio (0.09). The Serum Protein Electrophoresis (SPEP) showed a polyclonal increase of the gamma fraction.The second blood sample showed a persisting iron deficiency anaemia (haemoglobin (Hb) 5.5 g/dl, ferritin (Fe) 7.9 μg/L) but the PCR for the HIV viral load identified 1 million copies/ml. The requested EEG showed no irritative signs but diffuse slow activity. Cerebral MRI revealed diffuse cerebral atrophy.
At this point, the boy and her family have been refered to the CHR-CHU HIV reference center to initiate an ARV therapy.

Conclusions

This case is a typical case of post-partum HIV contamination which could have happened due to a non-recommended and unsupervised breast-feeding. It also shows the importance of a regular follow-up with blood tests for children born from HIV positive mothers. For those children, the HIV-PCR should be tested at birth, at fifteen days, at 1 month and at 3 months of life. Early diagnosis of HIV children promotes

their immediate access to treatment with ARV therapy in order to prevent general and neurolgical complications.

I 20

Postnatally Acquired Neonatal Herpes Simplex Virus Infection: About Two Cases

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Introduction

Herpes Simplex Virus (HSV) is a well known pathogen involved in serious neonatal infections, in which mortality rate reaches 40% if untreated; furthermore, morbidity can be considerable even in promptly treated newborns. The spectrum of clinical presentation includes muco-cutaneous, neurological and disseminated forms. In the latter two cases, cutaneous lesions are not constant, sometimes leading to belated diagnosis. Transmission of HSV to the newborn typically occurs during the per-partum, most frequently following a recent genital primo-infection of the mother; type 1 and 2 are involved.
However, postnatal (horizontal) transmission to the newborn via the parents, relatives or medical staff is another possible route of contamination, though less frequently evoked, that might potentially result in equally serious infection. Few cases have been reported as opposed to materno-foetal infection, and there is a lack of knowledge about the comparative severity of the disease and its prognosis.

Aim

To add experienced cases to the pool of reported patients having suffered from postnatally acquired neonatal HSV infection, and so broaden the experience of, and bring awareness to readers regarding this alternative route of potential contamination by HSV in neonates.

Methods

We report two cases of postnatally acquired HSV in infants aged respectively 2 and 4 weeks, term-born following an uncomplicated pregnancy. The following cases were encountered by the author in a secondary care hospital in two month's time. Anamnestic, clinical and biological data were partly prospectively acquired, and partly retrospectively collected from the patient's hospital medical files.

Results

The first patient presented with peribuccal and oral clusters of erythematous vesicles, some of which being covered with a yellowish crust. She was feeding well, was apyretic and had an otherwise normal clinical and neurological examination (CNE). Similar lesions were found on the mother?s breasts and attributed to impetigo. The child and mother had been treated by topic fusidic acid for the previous three days, unsuccessfully; a further extension of the eruption prompted the parents' visit to the ER. Viral culture on cutaneous swab from mother and child's lesions showed the presence of HSV type 1; serologic tests for HSV-1 and 2 were negative - demonstrating the primo-infection in both. PCR for HSV-1 and 2 was negative on the cerebrospinal fluid (CSF). Eventually, the father reported a small cluster of vesicles in the process of healing on his nasal ala, a recurring location in his case, which has been hypothesized as the origin of the infection in both child and mother. No swab could be taken at this late stage to identify the virus and its type, but paternal serology showed evidence of recurring HSV infection. In this infant, the HSV infection was limited to muco-cutaneous form; she was treated with 2 weeks of IV acyclovir and presented a small local recurrence of clustered vesicles at 6 months of age, with spontaneous fast resolution. Psychomotor development proved normal until at least 9 months of age.

The second child presented with moderate fever following four days of a subfebrile state. The parents reported one episode of vomiting and only a slight alteration in general state. CNE revealed a grayish, pale skin, a full anterior fontanelle, an adequate axial tonus and slowed capillary refill. No muco-cutaneous lesion was found. Cultures on blood, urine and CSF were obtained and treatment with ampicillin and cefotaxime initiated. CSF showed the presence in moderate amount of WBC, mainly lymphocytic, and of RBC, thus PCR for HSV was requested; nevertheless, no antiviral therapy was added. The child was apyretic from the day following the admission to the pediatric unit and the negative cultures resulted in discontinued antibiotherapy. PCR for HSV-1 on CSF was soon positive and from then IV acyclovir was given for 3 weeks, followed by oral therapy for 6 months as a prophylaxis, given the neurologic form of the primo-infection. A labial cluster of healed vesicles was found on mother's examination. Mucous and cutaneous swabs for viral culture were taken on the newborn and proved negative. CNE remained normal and psychomotor development adequate until at least 4 months.

Conclusions

In conclusion, neonatal HSV infection is a well known disease with potential morbidity and mortality, for which a treatment exists, although insufficient to prevent those consequences. More prevention and awareness in parents, relatives and medical staff is needed regarding the impact of this infection and the facility with which it is transmitted, in order to minimize the risk of contamination of newborns with this widely-borne virus. Furthermore, studies are needed to compare the characteristics of the materno-foetal and the postnatally acquired infection, and to assess the potential severity of the latter.

I 21

Peritonitis, could it be tuberculosis ?

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Introduction

Tuberculosis (TB) is one of the top 10 causes of death worldwide. The incidence varies from 0 to 10/100000 in industrialised world to 500/100000 in developing countries. Belgian incidence is around 8,8/100000/year (and 3 times higher in Brussels region). Due to population migration and more frequent use of immunosuppressant therapy, TB still remains an important cause of disease in children.
Abdominal TB is an uncommon presentation of TB and is challenging to diagnose due to its insidious onset. It can have different presentations but the most common forms in children are peritonitis and lymphadenitis.

Aim

A 13-years-old girl was admitted to our hospital for unspecific symptoms including abdominal pain for one month, important weight loss (11kg), prolonged fever, walking difficulties and confusion. Physical examination peritoneal guarding, decreased bilateral air entry, asthenia and bradypsichia. She was native of Congo but has been living in Belgium for five years. None in her household presented such symptoms. Blood tests showed important inflammatory syndrome (CRP : 115 mg/L), microcytic anemia (Hb 8,7 g/dl, MCV 73 fL), hyponatremia and normal renal and liver functions. Serologies (HIV, HBV, CMV, EBV) were negative. Ascites, adenopathies and peritoneal nodes were identified on abdominal computed tomography (CT) and a bilateral pleural effusion on chest CT. Due to her neurological symptoms, an electroencephalography and a brain CT were performed showing a slow cerebral activity without signs of TB meningitis. Lumbar puncture was negative. A peritoneal tuberculosis was highly suspected and the patient was transferred to a tertiary care center.

Methods

A surgical lymphnodes biopsy and an ascites tap were performed, confirming an abdominal infection by Mycobacterium tuberculosis. The culture and the polymerase chain reaction (PCR) were positive on the samples. The Mantoux-test was also reactive.
She started on antituberculous treatment : isoniazide, ethambutol, pyrazinamide, rifampicine for 2 months followed by rifampicine and isoniazide for 4 months. In the context of important weight loss and inadequate nutritional status (pain, abdominal distension), a parenteral nutrition was also started for 3 weeks. After a 1 month of hospitalisation, she was discharged with a close follow-up. Her clinical condition progressively improved with complete resolution and weight recovery after 2 months of treatment.

Results

Abdominal TB is an uncommon cause of acute abdomen in resource-rich countries. Nevertheless, the diagnosis should be considered in case of chronic abdominal pain, especially in children coming from countries with high TB incidence. Contamination can result from swallowing infected sputum, ingestion of contaminated product or haematogenous spread from another organ. The symptoms are insidious : weight loss, chronic abdominal pain, diarrhea. Four clinical presentations of abdominal TB

were described : tubercular lymphadenopathy, peritoneal TB, gastrointestinal TB and visceral TB. The patient can also present an acute complication such as an intestinal occlusion or perforation. Lymphadenopathy is the most common presentation, due to the drainage of the affected organs. Peritoneal TB may be divided in three forms, however a combination of features is usually noted : wet ascitic type, fixed fibrotic type, dry plastic type. For the gastrointestinal TB, all the digestive tract can be involved but the most common location is ileocecal. Visceral TB can involve the genitourinary system but also liver, spleen and pancreas.
Diagnosis is based on histopathological and radiological findings. First line imaging includes ultrasound is useful to look for nodes, ascite or peritoneal thickening. CT provides imaging in depicting various forms of abdominal TB.
A specific PCR amplification on biopsies confirms the diagnosis quicker than conventional mycobacterial cultures.
The treatment includes a 6-month therapy and a close follow-up. Surgery is rarely needed, only in cases of non resolving intestinal obstruction, perforation or abscess. There are three types : bypass the involved segments, radical resection or conservative surgery like a stricturoplasty.

Conclusions

Abdominal TB has to be suspected in any child with abdominal distension, chronic abdominal pain especially in patients coming from endemic settings with positive Mantoux test. Clinical, laboratory and imaging findings are unspecific and diagnosis is confirmed by microbiological findings on biopsy. Response to medical treatment is generally favorable.

I 22

An unusual cause of cytopenia and fever in a one-year-old child

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Introduction

Febrile neutropenia is a medical emergency but the field of its triggers is broad.

Aim

In this case report, we aim at showing that some aetiologies of febrile neutropenia might be easily diagnosed and treated.

Methods

A one-year-old child of Caucasian origin, with no specific medical history was admitted for fever and deterioration of the general status. He had persisting fever exceeding 40°C over three days with abundant sweating, he was irritable and refused every food or drink. Moreover, he vomited the day before admission. He was weak, grumpy and seemed painful. On clinical examination, he was pale. Hepatomegaly was felt at 3 cm and splenomegaly at 2 cm under the costal margin; there were no swollen lymph nodes. Complete blood count revealed microcytic anaemia (7.4g/dL) with low reticulocytosis and thrombocytopenia (87000/microL). White cells were at 6780/microL (neutrophils 2014/microL and lymphocytes 4461/microL). LDH were increased at 1355UI/L. Serum creatinin and complete ionogram were normal. Liver enzymes were increased with GPT at 101UI/L but without cholestasis. Inflammation serum markers were high with (CRP at 192mg/L and hyperferritinemia at 19567ng/mL (normal >400ng/mL). A bone marrow aspiration was performed to investigate this central cytopenia. Cytology showed the presence of multiple Leishmanian-Donovan bodies in macrophages, and therefore polymerase-chain-reaction was performed to identify the species of Leishmania (Leishmania infantum).

Results

The diagnosis of visceral leishmaniasis (VL) was retained. Retrospectively, the parents had travelled with their baby to the South of France (Haute-Provence) the month before the beginning of the symptoms and identified a dog as probable carrier. Treatment was thus given according to the guidelines of the Infectious Disease Society of America (IDSA). It consisted in 3mg/kg/day of the liposomal form of amphotericin B (AmBisome), on days 1 to 5, 14 and 21 for a cumulative dose of 21 mg/kg. Treatment allowed quick recovery with disappearance of the fever after four days and of the hepato-splenomegaly within two weeks. Complete blood count normalised after eight days.

Conclusions

This case points out the fact that febrile cytopenia encompasses multiple differential diagnoses. Some diagnoses are rare and very easy to cure as VL. In these cases, a thoroughful anamnestic interview might be the key-point. This child contracted the disease in the south of France, which cannot be considered as an atypical travel destination. However, this area not far from Belgium, as the whole Mediterranean Basin, is yet an endemic area for Leishmania infantum, which is transmitted by mosquitoes to mammalian hosts such as dogs or humans.

I 23

Acute abdominal pain as initial presentation of toxocariasis: a case report of a 12-year-old girl

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Introduction

Toxocariasis is a helminthozoonotic disease caused by larvae of Toxocara canis and Toxocara cati. There are two principal clinical syndromes of the disease: visceral larva migrans (VLM) and ocular larva migrans (OLM), but there is a third category, 'covert or common toxocariasis'.

Aim

We report the case of a 12-year-old girl with acute abdominal pain as initial presentation of toxocariasis.

Methods

The patient was diagnosed and followed in Centre Hospitalier EpiCURA (Hornu, Belgium) and went to Cliniques universitaires Saint-Luc (Brussels, Belgium) to meet an ophthalmologist and a specialist in infectious diseases. The blood samples were sent to Institut de medecine tropicale (Anvers, Belgium) for parasitic serologies.

Results

The 12-year-old girl came to EpiCURA's emergency department. She complained about acute abdominal pain, nausea and diarrhea. The pain was localized in right loin and right iliac fossa. At the physical examination there was a tenderness in right iliac fossa, a Mc Burney's sign and a psoas sign. There was no fever. Two laboratory tests were performed spaced in time by almost 24 hours and there was no sign of biological inflammatory syndrome. However, there was an eosinophilia (2.5 x 10^3/microL), representing 12,5% of the circulating leukocytes. The appendix was not seen at two echography controls. Due to the suspicion of appendicitis, a laparoscopic exploration and appendectomy were performed. The appendix was not inflamed.
She returned home the day after the surgery, but, one day after, she came back to the hospital because of persistent abdominal pain. She developed hematuria, but she thought it was menarche. She also complained about arthralgia localized in right knee. When asking, she said she had a dog at home. She mentioned soft stools for one month. She had no medical background, but her mother had a Crohn disease.
We performed some extra laboratory tests: stool, urine and blood tests. Stool tests showed Charcot Leyden crystals, but no pathogenic parasite was found. Urine tests showed a macroscopic hematuria associated with proteinuria for two days, then proteinuria disappeared but hematuria remains. Dysmorphic red blood cells were seen in one urine sample. There was no argument for a Crohn disease or another autoimmune disease in the blood tests. Serology for Toxocara was positive. The anatomo-pathology showed a nematode in the appendix and a focal lesion of intra-mucosal appendicitis.
While waiting for the results of serologies and anatomo-pathology, she developed four petechiae in abdomen and thighs. We thought wrongly she had an atypical form of Henoch-Schonlein purpura.
After diagnosis of Toxocariasis, a dilated fundus examination was done. There was no sign of ocular toxocariasis. There was no eosinophilia in the blood test control anymore, so we decided not to treat the infection.

Toxocariasis is a parasitic disease caused by dogs and cats roundworms. The

incidence and prevalence of the disease are unknown. Children are more frequently infected because of their proximity with puppies and kittens. Symptoms are various. VLM and OLM are the two principal presentations of the disease. The third category of Toxocara infection, the 'covert toxocariasis', is characterized by mild nonspecific symptoms, such as abdominal pain, fever, anorexia, headache, ... Due to this presentation of the disease, Toxocara infection can be difficult to diagnose. Lots of healthcare providers are unfamiliar with this disease.
There are some case reports in literature about acute abdominal pain associated with Toxocara infection by children. We only found one case report about false diagnosis of acute abdomen and unnecessary operation. If there are other symptoms in addition of acute abdominal pain like hematuria, headaches, diarrhea and if the blood tests are not in favor of an appendicitis, laparoscopy should be delayed, and other extra tests should be realized. Diagnosis is confirmed by serology.
Treatment with a benzimidazole is controversial if patient is asymptomatic or presents mild symptoms. Risks and benefits must be considered. Mild Toxocara infection often goes away without treatment.

Conclusions

In conclusion, a parasitic infection, especially Toxocara infection, must be evocated if acute abdominal pain and mild nonspecific symptoms are associated with high eosinophilia and if the blood tests are not in favor of an acute abdomen. Appendectomy should be delayed, and some extra tests should be performed to avoid useless surgeries.

I 24

Acute mastoiditis and the importance of pathogen identification: Two case reports

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Introduction

Acute mastoiditis is a complication of acute otitis media. Middle ear and mastoid cavities are continuous and purulent material from the middle ear may accumulate within the mastoid cavities, causing mastoiditis. Complications are related to the spread of infection to contiguous structures or into systemic blood circulation.
The clinical spectrum of acute mastoiditis ranges from an absence of symptoms with spontaneous resolution to progressive disease with life-threatening complications.

Aim

The aim of this study is to highlight the importance of specimen identification in acute mastoiditis.

Methods

We describe hereby two cases of bilateral mastoiditis in two 8 months-old children. These patients were admitted in the pediatrics department of a secondary Center in Brussels, Belgium, within a two weeks interval in October and November 2017.

Results

Cases :
Both patients presented the same clinical features at admission: fever, retroauricular tenderness, erythema and swelling as well as protrusion of the auricle. The first case showed elevation of C-reactive protein (CRP) at 34 mg/L but no increase of white blood cells (WBC) and the second case showed elevation of CRP at 202mg/L and 16 400/uL WBC.
Both case were diagnosed with acute mastoiditis and were treated by intravenous 3rd generation cephalosporin.
Our first case was admitted on a Friday night, when no ENT (ear-nose-throat) specialist was available. Acute mastoiditis was diagnosed based on clinical findings and the antibiotherapy was directly initiated. The patient presented an adequate treatment response, becoming afebrile and presenting a decrease of the retroauricular swelling within the first 24 hours following antibiotic administration.
At the admission of our second case, ENT specialist was available and proceeded to a tympanocentesis in order to isolate infecting pathogen before starting antibiotherapy. This patient however did not show adequate treatment response within 48 hours post antibiotic administration and continued with high fever, a toxic aspect and the apparition of a macular rash with redness, tenderness and heat of the upper and lower limbs.
The ear puss culture has returned positive for Group A Streptococcus (GAS, Streptococcus Pyogenes). We considered the erythematous macular rash and swelling as suggestive for a Streptococcal toxic shock syndrome with diffuse capillary leak and added Clindamycin to the treatment. The response to the bitherapy was favorable with rapid apyrexia as well as decrease of the rash and biological inflammation.

Conclusions

Bacteria most often implicated in acute mastoiditis are Streptococcus Pneumoniae,

Streptococcus Pyogenes and Staphylococcus Aureus.
As this case reports show, it is crucial for a proper therapy of acute mastoiditis, to identify the pathogenic cause by means of a specimen culture. Given the variety of organisms that can cause acute mastoiditis and the potential for antibiotic resistance of S. pneumoniae and S. aureus, the importance of isolating the germ cannot be overemphasized.
Specimens should be obtained from the middle ear by tympanocentesis through an intact eardrum or by aspiration through a tympanostomy tube or perforation. Cultures obtained from the external canal may be contaminated with P aeruginosa or S aureus.

Streptococcal toxic shock syndrome is the result of diffuse capillary leak and tissue damage due to release of inflammatory cytokines induced by streptococcal toxins that act as superantigen. The estimated incidence of GAS bacteremia and/or invasive infections in children is 2 to 3 cases per 100,000 per year. The incidence is greatest in children < 1 year (4 to 9 cases per 100,000).
In patients with invasive GAS infections, in which a large number of bacteria may be present, therapy with a beta-lactam plus Clindamycin is recommended. Clindamycin should not be used as single agent because it is not bactericidal and because GAS resistance increases in some geographic regions.
Patients with acute mastoiditis should demonstrate clinical improvement within 24 to 48 hours of adequate antimicrobial therapy.
Imaging of temporal bone is not necessary to make the diagnosis of acute mastoiditis in children with characteristic clinical findings. However, it may be opportune to confirm diagnosis in children without characteristic findings, determine the stage of infection or evaluate suspected complications.

This case report highlights the importance of isolating the pathogen in acute mastoiditis in order to guide appropriate antibiotherapy.

I 25

A rare case of complicated sphenoidal sinusitis. Lemierre Syndrome or not?

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Introduction

Sphenoidal sinusitis belongs to the posterior group of sinusitis. This rare condition represents about 3% of acute sinusitis. Sinus cavities growth depends on the facial growth. Symptoms are generally nonspecific. Complications are not frequent and sometimes the only way to rule out the diagnosis. Intracranial complications are particularly challenging.

Aim

We describe the case of an acute sphenoidal sinusitis complicated by aseptic meningitis and a cervical thrombosis in a 13 years old teenage.
Etiologies, pathophysiology and treatment are discussed here.

Methods

Clinical case:
A 13 years old teenage presented to the emergency service for 11 days of high fever, with headaches and asthenia. He only presented nonspecific symptoms: odynophagia, clear rhinitis. No clinical argument for a Kawasaki Disease. Nobody was sick at home. No recent trip abroad. Biology showed an inflammatory syndrome (CRP 167 mg/L [0 - 10], VS 43 mm/h [1-15], leucocytes: 21500/l [4000-11000], neutrophil: 89.9% [40-75]), a moderate hyponatremia (Na+ 131 mmol/L), and a cholestasis. Blood culture and urine were sterile. Viral, parasitic and bacterial serology were negative. Chest radiography was normal. We ran a second line of additional tests to found the etiology of this fever: cardiac and abdominal echography didn't show any sign of deep infection or Kawasaki disease. Intradermoreaction was also negative. At day 15 of fever, the boy still complained about headaches. Lumbar puncture was done and showed an aseptic meningitis. A cerebral MRI confirmed the meningitis and showed a left sphenoidal sinusitis and a cervical thrombosis. Our main hypothesis became a sphenoidal sinusitis complicated by meningitis. But is there a bone erosion and a communication between the supra-sellar region and the sphenoidal sinus, or is this case a Lemierre Syndrome? A cervical echography confirmed the cervical thrombosis. A CT was performed showing a 2 to 3 mm sphenoidal erosion as the origin of the meningitis. Coagulation assessment was normal. Patient was treated by low molecular weight heparin for ten days. We observed a thrombus regression. Surgery drainage was performed and parenteral broad spectrum antibiotics administered for 6 weeks. The patient was initially treated by Acyclovir for 48 hours and Cefotaxime. We added Oxacillin on day 4 of hospitalization and Metronidazole on day 5, knowing respectively Staphylococcus Aureus and anaerobic bacteria implicated in bacterial sinusitis. Intra operative smears were positive for Streptococcus Intermedius sensitive to Ampicillin and Cephalosporin. We finally decided to treat the patient for 6 weeks with Ceftriaxone and 4 weeks with Metronidazole. We rapidly observed a good outcome. Patient was afebrile 72 hours after surgery and 8 days after antibiotics beginning. CRP was normal on the third post-operative day. No clinical sequelae are observed 4 months later.

Results

Discussion:
Sphenoidal sinus growth is completed between 13 and 18 years old. Due to its location, symptoms are generally nonspecific. The only symptoms we initially had was 11 days of high Fever of Unknown Origin, asthenia, sometimes headaches. There was no sinusitis pain, only a clear rhinitis.

Sinusitis' complications are not frequent. These complications can be extracranial or intracranial. Intracranial complications may result from anatomical proximity of the sinuses to the brain or orbit, or by progression of septic thrombi. Lemierre Syndrome is a thrombophlebitis of the intern jugular vein with disseminated septic embolies. CT or MRI are useful tools in ruling out the diagnosis. The difficulty in this case report was the presence of both cervical thrombus and meningitis. Bone erosion reversed Lemierre Syndrome hypothesis. The presence of the thrombus can be explained by a state of hypercoagulability in this very ill patient.
The exact incidence of sinusitis complications is not known. They are more frequent in older children. Mortality rates of 10 to 20%. Long term neurologic deficits occurs in 13 to 35% of survivors. Diagnosis and management could be challenging like in this case. It requires collaboration among specialists and the respect of a precise algorithm. Treatment of these complicated sinusitis require broad spectrum antibiotics. Surgery drainage should be discussed with specialists.

Conclusions

Intracranial complicated sphenoidal sinusitis is a rare entity. Symptoms are poor and nonspecific due to its location, especially in children. Clinicians should consider sinusitis as a cause of intracranial infection even in the absence of sinus history. Complications can be life threatening. CT or MRI are useful tools in ruling out the diagnosis. Prompt diagnosis and treatment are required.

I 26

Atypical gastroenteritis: a diagnosis not to be missed.

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Introduction

Introduction:
Malaria is still the number one killer in paediatric population and caused one death per minute in the world. Malaria is endemic in tropical and subtropical regions, where majority of the cases are composed of children aged from 6 months to 5 years.
Malaria is less common in Belgium. However, we must not forget to think about it.

Case report:
A 11 years old girl was seen at the emergency for fever since five days, with febrile peak at 40°c and poor response to antipyretic.
She also complained about vomiting and diarrhea for three days.
Parents found her more apathetic with a lack of appetite.
They travelled to Senegal one month ago and they came back in Belgium ten days ago. She took Lariam as prophylaxis, but she forgot to take once she came back in Belgium.
What about her family history: one little brother with sickle cell disease, and about her personal history: asthma.
Chronic treatment: Rupatall 10 mg 1x/day, Relvar 1 puff 2x/day.

At clinical examination the girl was eutrophic.
Pulmonary, cardiac, neurologic and abdominal examinations were normal. There were no signs of deshydratation.
The blood test showed:
- Haemoglobin 13,4 g/dL, thrombocytopenia 67000/mm*3.
- Leukocyte 7,9 10*3/mm*3, CRP 111mg/L.
- Increase liver test: total bilirubin 3,8mg%, LDH 2722 mu/ml, GOT 356 mu/ml, GPT 268 mu/ml.
- Acute renal failure: creatinine 1,5mg%, urea 58m%, uric acid 8,3 mg%.
- Thick blood smear positive.
- Thin blood smear positive for plasmodium falciparum (parasitaemia index 16%).

The diagnosis of Malaria with acute renal failure was posed. The patient was transferred to intensive care.
The abdominal ultrasound did not show splenomegaly, hepatomegaly or other abnormalities.
Co-infection, that would have required antibiotic therapy, was excluded.
Treatment by malarone was introduced and normalization of parasitaemia have been noticed after four days of treatment.
Prerenal acute renal failure, supported by intravenous hydratation, standardized quickly.

Conclusion:
Malaria is a disease that often mimics other common childhood illness like meningitis/encephalitis, pneumonia and in this case gastroenteritis. Fever is the main symptom.
It should be considered in case of travel in an endemic area, even if a prophylactic treatment has been carried out.
The most common complications are severe anaemia, impaired consciousness and respiratory distress.
Early diagnosis allows for better management and reduces complications.
Note that a Belgian vaccine, Mosquirix, will be introduced in Africa in 2018.

I 27

From dental care to subdural empyema: a short step

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Introduction

Subdural empyema is a rare but potentially fatal complication of sinusitis or dental treatment. It must therefore be considered as a neurological emergency. We report here two cases who initially showed some similarities but rapidly evolved in different ways.

Aim

The first case is a 10-year-old child admitted to emergency room for headache, vomiting, fever, and right periorbital swelling. The CT scan shows a right anterior frontal periosteal abscess, an anterior frontal subdural empyema and segmental thrombophlebitis of the upper longitudinal sinus. The retained diagnosis of gram positive cocci septicaemia secondary to a pansinusitis complicated by a subdural empyema was made. The child was rapidly put on intravenous antibiotic therapy consisting of a third-generation cephalosporin, a glycopeptide antibiotic and metronidazole. A antrostomy to quickly drain the sinus is performed by the ENT. Unfortunately, after more than one month of conservative treatment, the radiological progression renders the neurosurgical intervention necessary. Empyema drainage is performed via frontal craniotomy. The child has evolved very favorably in the aftermath of the intervention.
The second case is a 13-year-old girl presenting to the emergency department for swelling in the left hemiface with fever occurring 3 weeks after tooth extraction. The diagnosis of acute pansinusitis of odontogenic origin is retained. Broad spectrum antibiotics composed of thirdgeneration cephalosporin, glycopeptides and metronidazole are started intravenously. A few days later, she presentes an inaugural epileptic seizure. Radiological examinations show a left frontal subdural empyema complicated by purulent meningitis, requiring neurosurgery. Empyema drainage was performed via frontal craniotomy. Current evolution is favorable.
In both cases, aggressive antibiotic therapy associated with ENT- and neurosurgical interventions had to be implemented. Both cases were managed using a multidisciplinary approach including pediatric infectious disease specialist, ENTs and neurosurgeons.

Results

Sinusitis are rare diseases in Pediatrics, however older children and adolescents can encounter such pathologies especially after dental cares or in the course of sinusitis. Intracranial complications of sinusitis have become rare because of the early and judicious use of antibiotics. However, once the infection spreads, it can infect different structures such as orbits, underlying bones, meninges, adjacent veins, and the brain. The clinical feature of subdural empyema is often explosive with occurrence of seizure or focal signs. These symptoms must suggest complications and lead to further medical work-up.

Face to such a case, the brain scanner is the first test to be done for a quick diagnosis. The CT scan shows a subdural collection or extra-dural hypodense with contrast enhancement peripheral. MRI has become the test of choice now especially in front of scattered small empyema, both for diagnosis and follow-up. Conservative management with antibiotics and follow up imaging is recommended if there are no focal deficits, change in mental status or if the patient is responding well to antibiotics. Alternatively, craniotomy is warranted in addition to antibiotic therapy. The results are generally good thanks to rapid and effective antibiotic treatment.

Conclusions

Sinusitis is a infection that is often trivialized. However, it must always be borne in mind that this can quickly evolve into an intracranial complication. Mortality and morbidity are directly related of diagnostic delay. A multidisciplinary management multidisciplinary therapeutic management is necessary.

I 28

THE BELGIAN NASOPHARYNGEAL CARRIAGE STUDY OF S. PNEUMONIAE IN INFANTS AGED 6-30 MONTHS

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Introduction

The Belgian infant pneumococcal conjugate vaccine (PCV) programme changed from PCV13 to PCV10 in 2015-2016. In March-June 2016 (Y1) and in November-May 2016-2017 (Y2), we monitored S. pneumoniae colonization in infants residing in day-care (DCC) or presenting with acute otitis media (AOM) at their physician. The yearly sample size of this 3-year study was calculated to detect a 3% change of the combined prevalence of serotypes 6A and 19A.

Methods

Infants (6-30 months) residing in one of 85 (Y1) versus 112 (Y2) randomly selected day-care centres (DCC), or visiting one of X (Y1) versus 55 49 (Y2) trained physicians for AOM, were approached to take part in the study. Recruitment was planned between January and June in 2016 (Y1) and between October 2016 and June 2017 (Y2). The target number aimed for was 700 infants in Y1 for each setting separately and 900 in Y2. In participating infants, a single nasopharyngeal (NP) swab was taken and transported in STGG medium to the Pneumococcal Reference Centre at KULeuven, either fresh (AOM) or frozen (DCC) within 24 hours. S. pneumoniae were cultured, screened for antibiotic resistance (5 antibiotics), and serotyped (Quellung). Additional PCR-analysis was set up at the Laboratory for Medical Microbiology (LMM), Universiteit Antwerpen. Demographic and clinical characteristics and vaccination status were collected via a questionnaire in both infant populations. In infants with AOM, additional clinical data about the AOM and its treatment were collected and AOM recurrence was checked during a phone call after one month. Infants who returned to their physician within a month with remaining or recurrent AOM were asked for a second NP sample.

Results

In year 1, 760 infants from DCC were included and 39 infants with AOM; in year 2 inclusion rate increased to 1096 DCC- and 122 AOM infants. Pneumococcal carriage was frequent in both populations in each collection period: in DCC (68.2%, Y2) and (60.8%, Y1); in AOM (69.2%, Y2) and 64.8%, Y1).
Among carriers in DCC, PCV13 serotypes were identified at low frequency (3.5% in Y2 and 5.4% in Y1), and dominated by 19F, followed by serotype 14 in Y1 and by 19A in Y2. Culture-based prevalence of PCV13-non-PCV10 serotypes (3, 6A, 19A) altogether was not significantly higher in year 2 (1.6%) than in year 1 (0.9%).
In infants with AOM, findings were similar with PCV13 serotype carriage in 7.6% (Y2) versus 7.7% (Y1). Predominant non-vaccine serotypes in both populations were 23B and 15B in year 2.
Among detected strains, resistance to at least one of five tested antibiotics was 41.3% (Y2) versus 42.4% (Y1) in DCC and 49.4% (Y2) versus 48.1% (Y1) in AOM and was most frequent against cotrimoxazole. Culture-based pneumococcal carriage was related to region, year of sampling, having siblings, history of AOM, signs of common cold and antibiotic treatment within 3 months prior to sampling (P-value $Chi^2<0.05$). Further PCR-based analysis is still ongoing.

Conclusions

Both during and one year after the PCV13-to-PCV10 switch in Belgium, culture-based PCV13 serotype carriage in infants was found low without significant increase. Since half of the infants participating in year 2 had been vaccinated before the switch, further monitoring is necessary.

IC 01

Acute hepatic failure in children: experience of a paediatric intensive care unit.

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Introduction

Pediatric acute liver failure (PALF) is a rare but severe condition characterized by rapid progression of hepatic dysfunction and occurrence of a multisystem organ failure (MOF) in previously healthy children. It represents several clinical challenges, one of them being to identify the children who won't recover without liver transplantation (LT).

Aim

This study aimed to review our experience and to identify mortality risk factors. The results might also improve our reflection about living donor liver transplantation (LDLT) and its indication in the difficult context of PALF.

Methods

Retrospective data collection of all children admitted with PALF from March 1989 to December 2016 to our paediatric intensive care unit. Demographic, clinical, laboratory and short-term outcome data were recorded. Statistical analysis was performed to identify mortality risk factors.

Results

100 children (54 girls) were included; mean age was 59.9 months with 40% of the children being younger than 2 years. Hepatic encephalopathy, shock and respiratory failure were diagnosed in respectively 73, 39 and 32 patients. Main causes of PALF varied with age; aetiology remained undetermined in 35 % of cases. 14 children had contraindications to LT and died. 24 did not meet our criteria for LT; 22 survived. 62 children were considered as candidates for LT; 36 of them received a deceased donor liver and 3 underwent LDLT. 11 patients died on the LT waiting list and 12 were withdrawn from this list because of spontaneous recovery. Overall survival was 61%; survival after LT was 69%. Statistical analysis identified respiratory failure (OR= 2.9), acute renal failure (OR=2.9) and lactatemia (OR =1.5) as significant mortality risk factors. A risk staging system was developed based on these three factors to predict mortality in children (AUROC =0.83 [0.74 - 0.91] $p<0.001$). Mean waiting time before LT was 2.0 days. When comparing two periods, 1989-2002 (n=33 children) and 2003-2016 (n=6), we observed an increase in the mean time spent on the waiting list, from 1.5 to 4.8 days. Children died on average 6 days after being registered on the LT waiting list.

Conclusions

Our results confirm the poor outcome of PALF and suggest adding respiratory and acute renal failure to LT criteria. Since the majority of children, candidates for LT, died from MOF and since waiting time seems to increase, LDLT could be proposed 2 to 4 days after the child met the criteria for LT.

IC 02

Glomerular hyperfiltration: a new concept in critically ill children.

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Introduction

Glomerular hyperfiltration (GHF), defined as an elevated glomerular filtration rate (GFR), induces the enhanced elimination of circulating solute by the kidneys. Recently, this phenomenon has received increasing attention in critically ill adults. The incidence in this setting is high, 28-65% depending on the cut off used for definition and the patient selection. In case of treatment with renally eliminated drugs, like some frequently used antibiotics, GHF suggests that these patients may be at risk for subtherapeutic drug concentrations when using standard dosage schedules.
In critically ill children, evidence about GHF is limited and incidence data are still scarce.

Aim

The primary objective of this study was to investigate the incidence of GHF in critically ill children. Secondly, risk factors for the development of GHF are evaluated.

Methods

This study was a single center, prospective, observational study, conducted at the pediatric intensive care unit (PICU) and the cardiac surgery intensive care unit (CSICU) of the Ghent University Hospital, Belgium, Patients beween 1 month and 15 years of age were enrolled, if having a urinary bladder catheter in place. Glomerular filtration rate (GFR) was measured by means of a calculated 24 hours creatinine clearance (24h ClCr). Creatinine in serum and urine were determined using Jaffe's reaction, and corrected for interfering total protein concentration. GHF was defined as a GFR exceeding normal values for age plus two standard deviations. Logistic regression analysis was used to identify covariates for GHF.

Results

Data were collected from 65 patients (median age 1.7 years, IQR 3.0). Overall, 84.6% of patients expressed GHF. GHF patients had a median ClCr of 181.8 ml/min/1.73m² (IQR 78.9). Lower body surface area (BSA) and the absence of vasopressor support were found as independent associated factors with the development of hyperfiltration.

Conclusions

The incidence of GHF in critically ill children seems even higher compared to adults, using an age dependent definition. As GHF may lead to subtherapeutic treatment of renally eliminated drugs, early detection of patients at risk should be of main importance at every PICU.

IC 03

SMALL ARTERY, BIG DAMAGE

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Introduction

We present a unique case of vertebral artery (VA) blunt injury following a penetrating neck trauma.

Aim

Clinical presentation
A 13 year-old boy passed accidentally through the shower screen and presented two penetrating wounds in the left part of the neck and axilla. At the arrival in Emergency Department, he presented an haemorrhagic shock despite direct compression of the bleeding. Hemodynamic state deteriorated quickly requiring massive transfusion. Computed Tomography Angiography (CTA) showed a left VA dissection and a pseudaneurysm associated with contrast leakage. Endovascular occlusion was emergently performed. Multiple thrombotic emboli in the cerebral posterior territories occurred causing a complete blindness that was fortunately completely reversible in few weeks.

Methods

We realised a litterature review using Pubmed.

Results

VA blunt injury is a rare condition (0,01%) among head and neck trauma. Most frequent cause is motor vehicle accident. No similar case has been reported in the literature in the paediatric population. According to Majidi et al. (Neurocritical Care, 2014, vol 21, 253-258) only 6 cases due to a penetrating injury among 84 cases of VA dissection (VAD) are reported. The most frequent entry locations are the C6 transverse foramen and the C1-C2 level. Digital angiography is the gold standard for VAD diagnosis, but CTA is the preferred technique. Stroke is observed in 5% of patient. Six patients with VAD required an endovascular treatment.

Conclusions

Embolization treatment was the only therapeutic option in this rare life-threatening paediatric case of a penetrating vertebral artery injury.

N 01

Earlier achievement of full enteral feeding in ELBW neonates is not associated with growth improvement in the first two years of life

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Introduction

Feeding strategies during neonatal stay may affect growth in the first years of life. Moreover, limiting the number of days until achievement of full enteral feeding in extremely low birth weight neonates (ELBW; <1000 g) might affect growth. Strategies to achieve full enteral feeding earlier were implemented, but data on the impact on subsequent growth after discharge are limited.

Aim

This study compared the Z-scores in growth over time of two cohorts of ELBW neonates that were comparable on maternal and neonatal characteristics and characteristics of hospitalization, but differed in enteral feeding strategy during neonatal admission.

Methods

The current study compares two cohorts of extremely low birth weight neonates (ELBW; <1,000 g) all born in the University Hospitals of Leuven, Belgium. The collected data included maternal and neonatal characteristics as well as characteristics of hospitalization. Anthropometrics were also collected at the corrected ages of 9 and 24 months (chronological age minus degree of prematurity). The Leuven neonatology department changed its feeding strategy from delayed to earlier initiation of enteral feeding. This provided us with the opportunity to explore and compare growth patterns post discharge in a more recently (2010-2014) admitted cohort of ELBW neonates compared to the cohort described earlier.

Results

There were only minor differences in the maternal characteristics and characteristics of hospitalization in both cohorts. There was no statistically significant interaction between different strategies in days until enteral feeding on weight over time (F=2.181, P=0.14), on height over time (F=1.280, P=0.28), or on head circumference over time (F=1.104, P=0.32). In the 2010-2014 cohort, full enteral feeding was achieved on average 14 days earlier than in the 2000-2005 cohort. In both cohorts, weight, height and head circumference were recorded at birth and at the corrected ages of 9 months and 24 months. A two-way repeated measures analysis of variance showed no significant effect of different strategy in achievement of full enteral feeding on any anthropometric Z-scores over time.

Conclusions

We investigated two hypotheses in this study. First, we investigated if both cohorts differed mainly and significantly on the strategy in days until enteral feeding and not or only marginal on other characteristics. Second, we tested if there was any effect of different strategy in days until enteral feeding on growth in the first two years of life. The main difference between the 2000-2005 and 2010-2014 cohorts of extremely low birth weight neonates (ELBW; <1000 g) born in the University Hospitals of Leuven,

Belgium was indeed the number of days until full enteral feeding was achieved. Although full enteral feeding was achieved earlier in the 2010-2014 cohort this was not associated with growth patterns during the first two years of life. We conclude that early enteral feeding strategies do not necessarily improve growth during the first two years of life.

N 02

Can an age-linked webapplication support parents of premature babies during 2 years and have impact on the child 's later development ?

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Introduction

Premature born children are at high risk for developmental delay. This delay can have important consequences for the quality of life of these children later on. The primary goal in neonatal intensive care is to optimize the development of immature newborns as much as possible . NICU-Interventions, such as NIDCAP and FCC (family centered care) support parents and try to reduce stress in order to increase positive parent-child interaction, a very important contributor to a healthy infant development. Many of those interventions proved to be effective. Nevertheless, very few interventions focus on continued coaching of parent-child interaction after NICU-stay. Although there is still opportunity to have further impact during the first 2 years of life . In this time span there is a very active process of formation and modelling of synapses in the brain. Environmental factors influence which synaptic connections remain and which ones disappear by pruning and apoptosis. The parent (as primary caregiver) is the most important environmental factor in pre-school children and plays a key role in further stimulation of brain development. The intensive support in the NICU has to be followed by a parent empowerment intervention in the preschool period.

Aim

An age-linked webapplication was developed for parents from 0 up to 2 years of age. This program targets at enhancing developmental parental interaction with the child, diminishing parental stress and empowering parenting skills. By optimizing the parent-child interaction in the home situation, this program hopes to improve the developmental outcome of these vulnerable children.
The primary study goal is to investigate the clinical effectiveness of this intervention program. Secondly we evaluate the use of a digital communication system with parents and their adherence to it. Using a web application is a fairly new challenge in preventive medicine but seems the preferable option for young parents, who grew up with digital communication. It is an advantage for parents (who are already very busy taking care of their vulnerable child) to be able to access supportive intervention that is available all times without the need of transport.

Methods

In our single center interventional prospective study we evaluate stress, parent empowerment and the developmental outcome of 3 cohorts of children. The first cohort is a group of babies under PMA of 32 weeks whose parents did not have access to the web application (NICU control group). The parents in the second cohort of babies less than 32 weeks are offered an age-linked web application from the first weeks of hospitalisation until the childs' corrected age of 2 years (Intervention group). The application contains visual information on developmental stimulation and practical issues at specific ages. It also provides peer support through testimonies of other parents. To correct for normal postpartum stress a third cohort of term babies was included (Term control group).
Recruitment started in February 2016. Meanwhile, about 50 children are included in both the premature control group and the intervention group. Recruitment of term babies is ongoing, since it is more difficult to recruit those children, due to the short-stay in the maternity.
On 6 specific moments, until the corrected age of 5 years old, stress and parent empowerment are measured by validated questionnaires. The developmental scores (Bayley III and WIPPSI) are obtained only in the 2 premature cohorts.

Results

We present the study design and some preliminary data on parental stress and empowerment until the corrected age of 5 months.
The 2 year follow-up data will be available in May 2018 and February 2020 for the NICU control group and intervention group respectively. All 5 year follow-up data will be available from February 2023 onwards.

Conclusions

This intervention is the first that targets to support parents of premature born babies until their childs' corrected age of 2 years old. To our knowledge, it is also the first intervention that uses an age-linked webapplication for this purpose. The study will show the impact of prolonged supportive intervention on the parents' stress experience and parenting skills and possibly on the babies development. It will also point out the difficulties in using web communication with parents and hopefully open the perspective to other digital systems to optimize the communication between care provider and parents.

N 03

Retrospective study on the medium-term outcome of children born with omphalocele or gastroschisis

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Introduction

The most frequent congenital anomalies of the anterior abdominal wall found in newborns are omphaloceles and gastroschisis. A prenatal diagnosis is often possible. Omphaloceles are present in 1 in 4000 live births whilst gastroschisis are found in 1 to 5 live births out of 10 000.

The omphalocele is a central anomaly of the anterior abdominal wall, it can be located in the epigastric, the umbilical or in the hypogastric region. The small intestine, and sometimes other abdominal organs (liver, stomach, spleen, genital organs, bladder), may be found inside a sac covered by a membrane derived from the peritoneum and the components of the umbilical cord (Wharton jelly and the amnios). The umbilical cord attaches itself to the top of the sac containing the abdominal organs.

The gastroschisis differs from the omphalocele on various aspects. In this case the anomaly is paraumbilical (more often seen on the right side of the umbilicus) and all the layers that constitute the anterior abdominal wall are impaired. There is no membrane present to contain the organs in a secondary pouch, and the bowels float freely in the amniotic fluid (there is often a malrotation associated and a lack of fixation to the posterior abdominal wall), and the umbilicus is normally inserted.

Aim

To study the evolution of children born with gastroschisis or omphalocele, especially looking at the general, digestive and neurological outcome; and to examine the medium term outcome. It would seem that children born with an omphalocele, even if isolated, have an uncertain prognosis. This study aims to look at the outcome of children born with an isolated omphalocele and those born with syndromic omphalocele, as well as the outcome of children born with gastroschisis.

Methods

Retrospective study on 22 cases of gastroschisis, 13 isolated omphaloceles and 20 syndromic omphaloceles admitted at the Cliniques universitaires Saint-Luc, in the neonatal and/or obstetrical units, between 2005 and 2014. This study used obstetrical and paediatric information.

Results

All the children born with gastroschisis had a normal development and 15% of our study population had a delay in growth. All the children born with an isolated omphalocele had a normal development and their growth wasn't hindered. 3 children born with syndromic omphalocele had developmental delays: two children had a general delay requiring a specialized education, the third had severe learning difficulties without language problems.
There were 2 deaths in the neonatal period during the duration of the study. A child born with gastroschisis died at 10 days due to multi-organ failure; a child born with syndromic omphalocele died on the eighth day after the decision to start palliative care given the multiple anomalies diagnosed after birth.
There were statistical differences between the different groups for the language development which was significantly delayed in children with syndromic omphaloceles compared to children with isolated omphaloceles ($p<0,02$). There were statistical

differences for the general development after the main motor steps, with the development of intellectual delays during school years requiring specialized education in the group of children born with syndromic omphalocele.
We noticed as well that the follow up rate of our patients after 3 years is relatively low: 33% for children born with gastroschisis, 60% for children born with isolated omphaloceles and 86% for children born with syndromic omphaloceles.

Conclusions

In our cohort of patients, those born with an isolated omphalocele seemed to have a good prognosis in terms of developpement and on the digestive level. The most important elements to determine the prognosis of infants born with gastroschisis are the state of the bowels at birth and the rate of prematurity. Children born with syndromic omphalocele, when compared to children born with an isolated omphalocele, had the most psychomotor complications, their prognosis will mostly be determined by the presence of associated anomalies and their impact on the neurological and the vital prognosis. There are statistical differences for the language and development at medium term between these two groups.
The rate of follow up at 3 years is relatively low but is most important with children presenting with syndromic omphalocele.

N 04

Discordant pregnancy and intrauterine growth retardation: neonatal evolution of eutrophic twin.

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Introduction

Twin pregnancies frequently contain a weight discordance between the twins. In monochorionic pregnancies, several possible causes can explain this discordance, for example the twin-to-twin transfusion syndrome. However, in dichorionic pregnancies the discordance explanation comes mainly from a difference in uteroplacental blood distribution between the two twins. The presence of a weight discordance with or without intrauterine growth retardation is known to increase the risk of neonatal complications in hypotrophic twins at different levels (digestive, neurological, hemodynamic, etc.). While in the eutrophic child, an increased risk of respiratory complication is rarely described.

Aim

The aim of the study is to shed light on the neonatal outcomes of the eutrophic twin from a diamniotic-dichorionic twin pregnancy in which the second twin had an intrauterine growth retardation (IUGR) and for which there was an indication to prematurely trigger the delivery.

Methods

Three groups were compared: the first group was composed of eutrophic twins (study group), the second group included eutrophics twins born from diamniotic-dichorionic twin pregnancies not containing delay IUGR (control group) and the third group encompassed hypotrophic twins (IUGR group). For every subject of the study group, two control infants of the same gestational age was selected. This analysis was performed on eight items (respiratory, neurology, digestive, infectious, metabolic, hemodynamic, ophthalmological and growth) between January 1st, 2006 and December 31st, 2015 in the Cliniques universitaires Saint-Luc.

Results

In this research, there were 21 subjects in the study group, 42 in the control group and 20 in the IUGR group (there was one intrauterine death). The median of gestational age was 34 weeks. A significant difference was found in the analysis of the respiratory help during the neonatal period between the study group and the IUGR group ($p = 0,0116$), but none between the study group and the control group ($p = 0,2801$). No significant difference was found between the study infants and the eutrophic control infants when the digestive, neurology, hemodynamic, infectious, ophthalmological and growth items were analysed. It was observed, however, that the IUGR infants were significantly more likely to develop metabolic disorders.

Conclusions

It appears from this study that eutrophic twins, whose birth was triggered prematurely following the indication of foetal distress from their hypotrophic twins, have a similar evolution to eutrophic twins born from pregnancies that do not contain IUGR and have the same gestational age. Thus, they do not develop additional complications than those caused by the prematurity. On the other hand, the hypotrophic subjects have a better respiratory outcome than the eutrophic subjects.

N 05

Challenges of choanal atresia in an extremely low birth weight neonate

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Introduction

Choanal atresia (CA) is an uncommon disorder. It occurs in approximately 1/6000 to 1/10000 live births. Reports on preterm neonates with CA are even limited to 9 published cases. Clinical presentation can differ depending on uni- or bilateral CA, or associated airway abnormalities. The diagnosis should be suspected in case of failure to pass a small suction or nasogastric tube through both nares into the nasopharynx. Subsequent confirmation by transnasal endoscopy and computer tomography (CT), as standard diagnostic tools, is requested.

Aim

Based on a case report we aim to illustrate the challenges of bilateral CA diagnosis and management in an extremely low birth weight (ELBW, <1000g) neonate.

Methods

After premature rupture of membranes at a gestational age of 28 weeks and 3 days, a boy with birth weight 820 g (p10), length 33 cm (p3-10) and head circumference 24 cm (p10-25) was born. Apgar scores were 2,5 and 8 at 1,5 and 10 minutes respectively. During resuscitation at birth he was intubated orally due to failure of nasal passage of the intubation tube. He was ventilated and admitted to the neonatal department of the University Hospitals Leuven. Clinical examination further revealed hypospadias, pectus carinatum, clinodactyly, small ventricular septal defect and minor facial dysmorphisms.

Results

The diagnosis of bilateral CA was suspected after birth and confirmed by transnasal endoscopy on postnatal age (PNA) 2 days. High-resolution CT-scan could be performed on PNA 25 days, after sufficient weight gain and stable clinical condition. Bilateral CA due to medialization of the bilateral posterior maxillary wall was documented. Due to his prematurity with ELBW, therapeutic options were only possible after some weeks. Continuation of mechanical ventilation was therefore requested. According to literature, the smallest neonate undergoing surgery had a weight of 1120g.
On PNA 44 days he underwent an endoscopic transnasal resection of the atresia. Perforation of the atretic palate was performed using a Holmium YAg laser Auriga XL fiber 365 μm at a setting of 10 Hz, 0,50 J/pulse, guided through a 1,6 mm Marchal Sialendoscope (Karl Storz, Tüttlingen). Postoperatively a nasal portex tube size 3 mm was left in the left nostril for respiratory support and stenting. Surgery due to restenosis was needed on PNA of 88, 123, 133 and 151 days. In between, continuous nasal stenting was performed with portex tubes. These tubes were definitively removed on PNA 179 days. Genetic testing revealed a normal male karyotype and absence of pathogenic mutations in the CHD7 gene, hereby excluding CHARGE syndrome.

Conclusions

Bilateral CA in ELBW (<1000g) neonates is uncommon and challenging. Based on a case-report we highlighted the diagnostic difficulties and the therapeutic limitations related to the small patient size. Multidisciplinary management, with prolonged

endotracheal ventilation until surgery can be performed is mandatory. In addition, an increased risk of restenosis by synechiae and granulation tissue has to be taken into account in ELBW neonates. Due to the complexity of the disease and the limited case reports, a multidisciplinary approach and follow-up is of utmost importance.

N 06

Start Therapeutic Hypothermia in Neonatal Spinal Cord Injury : a «Hot» Topic

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Introduction

Neonatal spinal cord injury (SCI) is an extremely rare and serious complication and the diagnosis could be delayed by the hypoxic ischemic encephalopathy (HIE) that is often associated with it.

Aim

For the treatment of HIE, therapeutic hypothermia is widely recommended but its effect on the SCI is still not well known.

Methods

A female infant was born from a G1P1 mother at 39 weeks of gestation. The parents were unrelated and there was no family history of neurological disease. The pregnancy was uneventful. The delivery was initially assisted by vacuum device and then by forceps associated with a Mac Roberts maneuver. At birth she required an invasive respiratory support due to respiratory failure and hypotonia. The Apgar scores were 1 at 1 min, 3 at 5 min and 4 at 10 min. She was then admitted in the neonatal intensive care. All the criteria of severe HIE were present : the physiological and neurological markers like metabolic acidosis (pH:6.88), Apgar score (less than 5 at 10min) and the need for mechanical ventilation after 10 min and pathological EEG. Therefore a total body therapeutic hypothermia was started 1 hour after admission which lasted for 72 hours. After 24 hours the biological parameters were normal and the EEG improved but the neurological evolution was still a concern. No spontaneous respiration appeared. Only facial movements were present with normal pupillary light reflex. The presence of a flaccid quadriplegia (absence of extremities movements and deep tendon reflex) led us to perform a CT-scan of the head and the cervical spine. This exam did not show any lesion. At the end of hypothermia, no clinical improvement occurred and an MRI was achieved. An ischemic lesion on cervical spinal cord (C1-C2) was revealed without brain lesion of HIE. Given the pessimistic issue and the absence of treatment, a palliative care was performed and she died at 9 days old.

Results

During neonatal HIE, SCI should be considered as a differential diagnosis if there is an absence of spontaneous respiration and severe hypotonia with EEG and biological improvements, particularly in an assisted delivery. The best exam to confirm the diagnosis is MRI.
At birth the clinical presentation of SCI can mimic a HIE. In case of severe HIE, therapeutic hypothermia must be performed in a maximum delay of 6 hours.
In adults (and in animals) some authors reported the neuroprotective effect of the therapeutic hypothermia in SCI. Nowadays, we need more studies to understand how and when to perform it.

Conclusions

The worsening of the clinical neurological evolution and the unexpected improvement of EEG and biological parameters should lead to perform an MRI promptly and to diagnose SCI earlier. Starting a therapeutic hypothermia is not a mistake, in any case. Due to the very poor prognosis of SCI, an earlier diagnosis should be an ethical issue for the family and the neonatal team.

N 07

Irritability and tachypnea in the maternity ward: think metabolic emergencies

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Introduction

Introduction
We report 3 newborns with irritability and tachypnea in the maternity ward. Their gas analysis revealed a respiratory alkalosis which leads to the diagnostic of 3 different enzymatic defects in the urea cycle.

Aim

Early diagnosis and management is the key to minimizing neurologic sequellae in infants presenting with hyperammonaemia in general and more specifically in infants with urea cycle defects.

Methods

The case report

The first patient is a boy born full-term of non-consanguineous parents. The pregnancy was properly monitored and without any specific event. He is the couple's first child, the maternal half-sister and the 3 paternal half-brothers are healthy. On the first day of life he was admitted in the non-intensive neonatal care unit (NINCU) for irritability and poor feeding. The infectious laboratory work-up was negative. On day 2, he developed lethargy with respiratory alkalosis. He is transferred to the neonatal intensive care unit (NICU) and the suspicion of hyperammonaemia is confirmed at 1086mcg/dl. The first line of treatment consisted in invasive respiratory support, parenteral nutrition with glucose, sodium benzoate and arginine. A supply of carglumic acid did not improve ammonaemia. Continuous venovenous hemodiafiltration(CVVHD) was rapidly initiated and maintained during 5 days. The high level of urinary orotic acid and the low plasma levels of citrulline and arginine suggested the ornithine transcarbamoylase (OTC) deficiency; this diagnosis was confirmed by genetic analysis. The patient developed seizures responsive to phenobarbital. The treatment at discharge was: a low protein diet associated to sodium benzoate, L-citrulline, arginine, phenobarbital, and assisted enteral feeding. His neurologic development was delayed at 8 month age.

The second patient is a boy born full-term of non-consanguineous parents. At the first day of life he was admitted in NINCU for irritability, poor feeding and sepsis screening. On day 2, he developed lethargy with respiratory alkalosis. The patient was admitted in the NICU and the suspicion of hyperammonaemia was confirmed at 739mcg/dl. The same initial conservative treatment was started and he also required CVVHD during 2 days. The normal levels of urinary orotic acid and the low blood levels of citrulline and arginine revealed the carbamoylphosphate synthetase(CPS) deficiency. The patient developed seizures responsive to phenobarbital. The treatment at discharge was a low protein diet associated to sodium benzoate, L-citrulline, arginine, phenobarbital, and assisted enteral feeding. . The clinical neurologic evolution was favourable at 6 month age.

The third patient is a late preterm girl born at 36 week of non-consanguineous parents. On the 7th day of life she presented lethargy. A sepsis was excluded. On the 8th day of life her neurological state worsened and a respiratory alkalosis appeared. The hyperammonaemia was confirmed at 1185mcg/dl. The initial conservative treatment was initiated and she also required CVVHD during 2 days. The high levels of urinary orotic acid and plasmatic citrulline revealed the argininosuccinic acid synthetase deficiency. The treatment at discharge was a low protein diet associated to sodium

benzoate and arginine. Her neurologic evolution was satisfactory at 1 month age.

Results

Comments:
The earliest presentation of hyperammonaemia was irritability, poor feeding and tachypnea which evolved to lethargy with respiratory alkalosis. The diagnostic latency was of 1 day. Seizures were present in 2 patients and responsive to general and specific treatment. Hyperammonaemia was refractory to the initial medical treatment and a CVVHD was needed and performed. Hence, the ammonaemia exceed 1000mcg/dl for less than 24hours. Their neurologic evolution is to be followed.

Conclusions

Conclusions:
Ammonaemia should be measured in all newborns with unexplained symptoms such as poor feeding, irritability, lethargy, particularly in presence of tachypnea and respiratory alkalosis. The CVVHD limits the exposure to hyperamonaemia if the therapeutic response to sodium benzoate, arginine and carglumic acid is delayed.

N 08

"Fear not" and give vitamin D and magnesium from the first day of hypocalcemia: a case report of neonatal hypocalcemia

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Introduction

The incidence of neonatal hypocalcemia has decreased with routine supplementation of vitamin D during pregnancy and in infant formulas. Here we report a case of neonatal hypocalcemia detected early and unexpectedly during investigations for hypoglycemia. We emphasize that, during investigation of hypocalcemia, genetic analysis should be included and vitamin D and magnesium therapy should be started early.

Methods

A baby boy was born to a non-diabetic mother at 37.5 weeks by normal vaginal delivery. His Apgar score was 9/10/10 and birth weight was 4060g. The mother was of Belgium ethnic origin and pregnancy was unremarkable.
The blood glucose was checked due to macrosomia and the level was 34 mg/dL. On day-3 repeat blood investigations including serum calcium showed hypocalcemia (1,65mmol/L (2,25-2,75 mmol/L) and ionized calcium level the following day was 0,8 mmol/L (1-1,6mmol/L). On day-5 serum calcium (1.57 mmol/L (2,25-2,75 mmol/L) and ionized calcium (0,71 mmol/L (1-1,6mmol/L)) decreased further. Despite the initiation of therapy, hypocalcemia (1,91mmol/L (2,25-2,75 mmol/L) persisted on day-9 with hypomagnesemia (0,57 mmol/L(0,62-0,91mmol/L)) and hyperphosphataemia (1,28 mmol/L (1,25-2,25mmol/L)). Further investigations showed low parathyroid hormone (PTH) and hypercalciuria. Maternal investigations done on day-15 showed vitamin D deficiency in the mother with a low 25-hydroxy vitamin D level (9ng/ml), and normal PTH, calcium, phosphate and magnesium levels. The underlying cause of the hypocalcemia in the baby was identified after the genetic analysis revealed type 1 mutation in CaSR gene. This is a Familial autosomal dominant type 1. The mutations lead to an overactive CaSR that is more sensitive to low calcium levels, The parathyroid hormone release is blocked due to overactivity of CaSR gene mutation, which prevents the release of calcium into the blood.
The infants hypoglycemia was managed with 10% dextrose infusion for four days. The hypocalcemia was treated with 10% calcium gluconate orally together with breast milk supplemented with intravenous calcium (50mg calcium/kg/day). Due to persisting hypocalcemia and hypomagnesemia, vitamin D3 (cholecalciferol (D-cure®:12 drops) and magnesium (100mg/day) was added. Despite 9 days of treatment, calcium levels remained low and 25-hydroxycholecalciferol (Dedrogyl®:2x2drops/day) was started. By day-20 the infant showed improvement with near normal calcium levels and decreased calciuria. At this stage 25-hydroxycholecalciferol and magnesium was discontinued and he was started on Alfacalcidol (1-alfa- (OH)hydroxyvitamin D: 1-alfa-leo®: 5 drops/day). Following this change, serum calcium levels decreased, and calciuria increased. The treatment was changed to vitamin D3 with magnesium and the child was discharged with follow-up arranged. During his stay in hospital the child showed no clinical signs of hypocalcemia (jitteriness, seizures or muscle twitching etc). The mother was started on vitamin D3 and magnesium supplements when her vitamin D status was known. A renal ultrasound scan performed at 2 months of age showed nephrocalcinosis.

Results

In this case hypocalcemia was detected on the second day of life and managed as a case of early onset hypocalcemia. This delayed us investigating the mother and testing the baby for late onset causes of hypocalcemia. Nevertheless, by starting

treatment early we may have prevented hypocalcemia induced convulsions. Vitamin D administration was delayed until day 7, because of the misconception that if given together with calcium, it may further aggravate hypocalcemia. However, in hindsight we were treating a case of hypocalcemia due to a genetic cause, which would more commonly be diagnosed as a late onset hypocalcemia. In such cases vitamin D supplementation is the management needed to help absorb oral calcium. While the type of vitamin D supplement is debatable, D3 is required to restore vitamin D deficiency with simultaneous addition of Alfacalcidol (1-alfa- (OH)hydroxyvitamin D) in late onset cases. The downside of long term use of Alfacalcidol is the risk of developing nephrocalcinosis for which regular calciuria checks are recommended. To get optimum benefit of vitamin D supplement, magnesium should be started concurrently, otherwise hypomagnesemia could lead to PTH resistance and affect the metabolism of vitamin D.

Conclusions

In our case, hypocalcemia was detected prior to the onset of symptoms, although the underlying cause was of genetic origin. The response to treatment and progress observed in the hospital suggests that we should consider investigating metabolic or genetic causes early. The therapy should include the appropriate vitamin D derivative with simultaneous supplement of magnesium started early without reservations.

N 09

Congenital Steinert's myotonic dystrophy: a case-report of a child born from in vitro fertilization (IVF).

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Introduction

Steinert's myotonic dystrophy is a rare genetic disease with autosomal dominant transmission. Its worldwide incidence is about 1/20 000 births. Two forms can be distinguished: a congenital form with early neonatal manifestations and childhood forms (infantile, late-infantile and juvenile). The diagnosis can be confirmed at any age by genetic analysis.

Aim

We report the case of a girl born at 40 weeks 1/7 by emergency c-section for a decrease of fetal movements, bradycardia at the monitoring and meconial amniotic fluid.

Methods

case-report in CMSE hospital.

Results

At birth, she presented a perinatal asphyxia with an Apgar score of 0/1/4. Her weight was 2.440 kg (<P3), her height was 50.5 cm (P25) and her head circumference was 33 cm (P5). The child was born after a medically assisted pregnancy by IVF. It was a bi-chorial bi-amniotic twin pregnancy with involution of the first twin during the first trimester. The antenatal story was marked by a polyhydramnios at 34 weeks 2/7 that led to an amniocentesis (PLA) of 1,2 L. The analyses performed on the PLA (electrolytes and CGH-array) were negative. Antenatal echography showed feet in extension, a mega-bladder and an absence of swallowing. The screening smear for group B streptococcus was negative and the rupture of membranes was less than 12 hours before birth.
At one minute of life, the initial care consisted in perinatal resuscitation (cardiac massage and mask ventilation) with a good response. The newborn presented a slow cardiac rhythm without respiratory movement. After stabilization, a ventilation by neopuff was continued for the first 20 minutes of life. A high flow nasal therapy was maintained during 3 days (FiO2 max 0.32) because of persistent tachypnea. Clinically, a 2/6 left parasternal systolic heart murmur and several dysmorphic features were observed (ogival palate, bulging front, eye revulsion, hypertelorism, marked orbital arches and micrognathia). From a neurological point of view, the child had her feet positioned in equine varus and a hypertonia of the lower limbs. She presented axial hypotonia associated with peripheral hypertonia. Furthermore, suction was weak and ocular contact was poor. An extensive paraclinical assessment including blood tests, cardiac and abdominal ultrasounds, magnetic resonance, electroencephalogram, ear tests, eye fundus and genetic were performed. Genetic molecular biology results showed a CTG-triplet amplification with high number of replication that confirmed the clinical suspicion of Steinert's congenital myotonic dystrophy. Since then, genetic analysis of the mother was carried out and the results are also positive for Steinert's disease.
The neonatal evolution of the child was marked by an exclusive parenteral fluid maintenance until day 4. Then, an enteral feeding with maternal milk by nasogastric tube was maintained until day 19. The full autonomous nutrition was acquired after 20 days. Antibiotics (Amikacine and Ampicilline) were stopped after microbiological results came back negative. Vomiting and delayed gastric emptying were treated with

domperidone. A cardiorespiratory monitor has been given to return home as well as daily physiotherapy.

Conclusions

This case-report demonstrates the main antenatal and neonatal symptoms and signs of congenital myotonic dystrophy also called Steinert's disease. It also reminds of the frequent discovery of previously unknown maternal form of this disease. The evolution of the neonatal form can be either marked by the death of the child or by a slow improvement of the symptomatology towards the classical form. However, cognitive prognosis remains often reserved in the neonatal forms.
In case of IVF, preimplantation diagnosis of the disease by molecular biology must be discussed in genetic consults for affected women because CGH-array performed on the amniocentesis fluid is not able to diagnose the disease. However, a prenatal diagnosis is possible on amniotic cells or trophoblast biopsy by Southern blot or Polymerase Chain Reaction (PCR).

N 10

Subdural hematoma, thrombocytopenia and hepatic cholestasis: what they have in common

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Introduction

We report the case of a 34-week-old boy born by emergency C-section for decreased fetal movement and altered monitoring. His father is Egyptian and healthy, and his mother, who is Belgian, suffered from congenital unilateral cataract, due to a congenital rubella. This first pregnancy was well monitored, the recurrent TORCH serologies were negative and ultrasounds were normal till the week.
At birth, the newborn developed a Respiratory Distress Syndrom stabilized by nCPAP. The initial pH showed an important respiratory acidosis (pH 6.98, pCO2 90 mmHg, lactate 9 mmol/l) confirming the diagnosis of fetal asphyxia. The blood analysis revealed a severe thrombocytopenia (21000/mm³). Apnea and tonico-clonic movements appeared this is why he was transferred to our intensive neonatal care unit.
The clinical examination was normal, with no dysmorphia and no hypotonia. The newborn was eutrophic (Fenton charts) with a weight of 1950 g (P27), a height of 45 cm (P3) and a cranial perimeter of 30 cm (P3).
Platelets were transfused and they corrected the platelet level. Transient coagulation abnormalities disappeared in the same time. Antiplatelet antibodies were negative (no immunization). He was offered parenteral alimentation and fed with breastmilk.
At 48 hours of life, seizures with severe apnea and tonico-clonic movements appeared. The electro-encephalogram showed generalized seizures from the left occipital lobe. This status epilepticus was treated with phenobarbital, phenytoin and midazolam, along with respiratory invasive support.
The MRI revealed bilateral and symmetric subdural hematoma in the occipital area, with edematous cerebral parenchyma compressed and delimited by calcifications. Surgical drainage was performed. While it was initially discontinuous, the electroencephalographic pattern improved slowly but with persistent paroxystic plurifocal activity. Midazolam was stopped at day 6 and phenytoin at day 22. Parenteral alimentation was perfused till day 10 (lipids from day 6 to day 9).
At day 17, some tonico-clonic movements were suspected and a lumbar puncture was performed. It revealed the presence of 1000 leucocytes with 69% of monocytes. The cerebrospinal fluid culture was negative. Antibiotic treatment by vancomycin and cefotaxime was administered during 5 days.
At the same time, hepatic cholestasis developed. Blood analysis showed a total bilirubinemia of 8.9 mg/dl with 8 mg/dl of conjugated bilirubinemia, increasing transaminase and GGT, hypercholesterolemia, hypertriglyceridemia, hyperferritinemia and transitory hyperammonemia. Three abdominal echographies were normal. A treatment by ursodeoxycolic acid was started and bilirubinemia slowly decreased. Extensive etiological research was launched. Alloimmune diseases were excluded, as well as bacterial infection. Research of TORCH, listeria, BK, enterovirus, parvovirus, Zika virus, herpes simplex, chickenpox, HHV6 and parechovirus were negative. The metabolic workup (galactose, orotic and glutaric acid, acylcarnithin profile, asialotransferrin level, organic and amino acids in urines, very long chain of fatty acids, alpha-1-antitryspin, alpha-fetoprotein...) was normal. CGH array was normal too and COL4A1 mutation research is still in progress. Complex molecular studies have been started, including Mendeliome analysis by NGS, with a special focus on OCLN, USP18 and JAM3 genes, as well as in genes implicated in Aïcardi-Goutières syndromes.
As for now, the central diagnostic hypothesis is a pseudo-torch syndrome.

Results

We did not found this association of antenatal subdural hematoma, thrombocytopenia and cholestasis in the literature. Even if our diagnosis is still unclear, we thought it was very interesting to discuss its differential diagnosis and his etiological path. After exclusion of alloimmunization, infectious and metabolic disease will be searched. In a second time, genetic syndrome can be researched (including mitochondrial pathologies).
In our case, the diagnosis of pseudo-torch syndrome, also called Baraitser syndrome, subsists. Its diagnosis is only based on clinical features: intrauterine growth retardation, hepatosplenomegaly, hyperbilirubinemia, thrombocytopenia, cerebellar hypoplasia or atrophy, and congenital cataract. He can't be posed till an intrauterine infection is excluded. Its etiology is unknown, but several familial cases have been reported and are compatible with an autosomal recessive pattern of inheritance. Treatment is only symptomatic and prognosis is variable, with some patients dying before one year.

Conclusions

We report the diagnostic pathway of a late-preterm where antenatal subdural hematomas were discovered in a context of epilepticus status. The association of initial thrombocytopenia and conjugated hyperbilirubinemia in a second time leads us to formulate the hypothesis of a pseudo-torch syndrome.

N 11

Two cases of distal humeral epiphysiolysis in the new-born: diagnosis and management.

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Introduction

Distal humeral epiphysiolysis in new-born, also known as a fracture-separation of the distal humeral epiphysis, is a rare entity, with an incidence of 1: 35,000 births. The radiological diagnosis is sometimes difficult, especially when there is only little displacement. The X-ray can be suggestive of luxation, but at this age this doesn´t exist. The literature agrees that this pathology is in most cases associated with traumatic childbirth.

Aim

The role of this two-case report is to show the clinical elements that should make one think of epiphysiolysis and to give a prognostic long-term outcome to the parents.

Methods

Recently we diagnosed two cases of distal humeral epiphysiolysis in our maternity. We will describe them here.

Results

The first case, a girl from a twin pregnancy born at 37 weeks gestational age, second twins, pregnancy with gestational diabetes under diet. Delivery extracted vaginally in left vertex with left arm forward and an umbilical cord prolapse. Childbirth requiring a large extraction, reported as difficult, Apgar 8/8/10, birth weight 2340g. Physical examination at day 0 shows an uncomfortable baby with mobilization of the left upper limb, arm in extension, medial deviation of the left elbow in the frontal plane, Moro incomplete left arm, grasping and mobilization of the fingers are symmetrical, no vascularization disorder. The twin sister presents a normal physical examination. X-ray of the left arm showed a medial displacement of the left physics and posterior displacement of the olecranon. The patient was treated by orthopaedic reduction and immobilization by plaster splint, followed by X-ray control after reduction and pain control by analgesic treatment.

The second case, a boy from a single pregnancy born at 39 4/7 weeks gestational age, pregnancy with gestational diabetes under diet, born by spontaneous vaginal delivery, no dystocia reported during childbirth, no sutured D1, Apgar 9/10/10, birth weight 3540 g. Physical examination shows asymmetry in the right upper limb, presence of swelling in the right elbow, reflexes present, rest of the physical examination without particularity. X-ray of the right arm showed a medial displacement of the right physics and posterior displacement of the olecranon, and was identically treated as the previous case.

Conclusions

In the maternity of our hospital we saw this relatively rare entity. The frequent clinical signs that must lead one to the path of this pathology are limb deformity, pseudo articular paralysis and swelling associated with pain. It is important to recognize this pathology although it is rare, even in the context of an uncomplicated childbirth. In both cases, orthopaedic examination, physical examination and radiography were sufficient to make the initial diagnosis. The literature suggests that ultrasound seems a

more specific and sensitive examination, because it allows to see precisely the cartilage. We didn´t initially perform ultrasound in our hospital, because the diagnosis was clearly made by physical examination and X-ray.
In the literature it is suggested, by some authors, that reduction and pinning is necessary. However, pinning could be a possible cause of deformity, causing growth arrest at the distal physics. In our opinion, initial treatment should be as minimally invasive as possible while ensuring optimal reduction of the epiphysiolysis.

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N 12

Mitochondrial fatty acid beta oxidation disorders (FAOD) as a cause of sudden neonatal death

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Introduction

Inherited FAOD consist of a group of 21 diseases of defects in fatty acid transport and mitochondrial beta-oxydation. They are inherited as autosomal recessive disorders. FAOD are more frequent in Caucasian population with an incidence of 1:9300.
Fatty-acid beta-oxydation (FAO) is an important fuel source for the heart and skeletal muscle, particularly in the new born with low glycogen reserve. FAO is essential during catabolic stress such as fasting or febrile illness. There is a wide range of clinical presentations, including i.e. hypoglycaemia, cardiomyopathy, hepatic encephalopathy, metabolic acidosis, or sudden death, from neonatal onset to later onset or remaining asymptomatic. Usually, the first symptoms occur during a viral infection between the age of 3 months and 5 years, but 12% have neonatal symptoms.
Many DFAO are included in the neonatal screening program performed, on a guthrie paper, at day 2-3, by tandem mass spectrometry (MS/MS). Symptomatic or screened patients need laboratory investigations as plasma acyl carnitine, urine organic acid and DNA analysis or enzyme assay to confirm the diagnosis.

Aim

The aim is to present two neonatal cases of FAOD to illustrate the neonatal screening limits and the importance to include these disorders in the differential diagnosis of sudden neonatal death.

Methods

We report two newborns of respectively 4 and 2 days, with a normal pregnancy and delivery, presenting with cardio respiratory arrest

Results

The first patient was a full term healthy breastfed new-born. He had two unremarkable physical examinations at day one and three performed by neonatologists at the maternity. The mother noticed that her baby drank less during the latest night. However, he was discharged home on day 3. During the following night, he slept all night long without any awakening for feeding. In the morning, he was described by the parents as less tonic and he refused to drink. He was found an hour later in cardio respiratory arrest. Despite aggressive resuscitation maneuvers at home by the SAMU, he died.
The same day, we received his day 3 neonatal screening's results which were highly suggestive of MCAD deficit (Medium Chain Acyl coA Deshydrogenase)
The post mortem blood samples and the autopsy confirmed the diagnosis, and the genetic analysis highlighted a K329E homozygous mutation, which occurs in about 90% of patients with MCAD deficit.
The second patient had a severe life threatening event at the maternity on day 2 at about 40 hours of life which required assisted ventilation, chest compressions and intra tracheal adrenaline. The ECG monitoring showed ventricular tachycardia (VT), his initial laboratory showed hypoglycaemia of 3 mg/dl (0.16mmol/l), hyperlactatemia of 3.9 mmol/l with compensated acidosis, normal sodium, hyperkalaemia of 7.8 mmol/L ,severe rhabdomyolysis (CK 1803 U/L), with normal kidney function. IV glucose 20%, calcium gluconate, amiodarone and dobutamine reversed the initial VT to sinusal rhythm. Secondarily, he had generalized seizures related to hypoglycaemic

encephalopathy, controlled by Phenobarbital and Levetiractam. His plasma acylcarnitine profile is highly perturbed with high C4, C5, C6, C6-DC, C8, C10, C12, C12:1, C14, C16, C18 and C18:1 and high dicarboxylic acids (C6, C8, C10), suberylglycine, lactate and ketones bodies in the urine. His enzyme activity of the beta-oxidation, in vitro, in fibroblasts is suggesting a multiple acyl-Coa dehydrogenase deficiency. Genetic analysis is in progress. He recovered slowly, with regular feeding, with a normal neurological exam at day 6 after the event. Actually, he's 2 months old; he's avoiding fasting period and gets riboflavine as treatment. His neurological exam isn't strictly normal and he needs a close follow up.

Conclusions

These clinical cases remind us the time limitation of the neonatal screening. We need to stay aware in the presence of the clinical signs and be alert to red flags like inappetence, somnolence, hypotonicity when the babies are at the maternity and before the screening results. We also need to educate the parents to be alert to those signs. Whereas it's not recommended for any newborn it's even more dangerous for this kind of patients to experience fasting.
Moreover, we need to have these diagnosis in mind when a baby is presenting with an apparent life threatening event. The earlier is the diagnosis, the better is the prognosis.

N 13

Neonatal brachial plexus palsy : a case report.

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Introduction

Introduction
Neonatal brachial plexus palsy (NBPP) is not a rare problem with an incidence varying from 0.5 to 3.0 cases per 1000 live births. The clinical picture itself depends on the localization of the lesion. The majority of NBPP is related to brachial plexus stretching during the delivery. Birth weight is the most important fetal risk factor for NBPP, and it is clearly related to shoulder dystocia. Other risk factors include maternal diabetes mellitus, obesity, short stature as well as previous shoulder dystocia and forceps extractions.

Aim

Case report
This is a case of a 41-weeker baby boy, born by caesarean section in emergency after failure of suction cup and pair of forceps of assistance for acute fetal suffering. He is the first child of a young and no consanguineous Caucasian couple. The evolution of the pregnancy was normal. The Apgar score was 4 at 1, 5 at 5 and 7 at 10 minutes after birth. Birth weight, length and head circumferences were 3.62 kg, 48.5 cm and 36.5 cm respectively. Immediately after birth, the newborn was pale, floppy with absence of spontaneous breathing and moderate low heart rate between 60 and 100 beats by minute. He was successfully resuscitated but showed no movement of the left arm. The Moro reflex is absent in the affected side, but the grasp reflex is normal. During the hospitalization, the metabolic acidosis with hyperlactatemia due to the neonatal asphyxia quickly disappeared as well as transient acute renal failure and hypoglycemia. Empiric antibiotic treatment was applied and discontinued after 72 hours. Magnetic resonance imaging revealed an extradural hemorrhage in the right parietal lobe that was measured 10 mm at its greatest diameter size. There was no mass effect and no ischemic injury. The evolution was favorable with a better motility of the left arm and he was discharged from the hospital 7 days after the delivery.

Results

Discussion
NBPP is a common situation but its incidence is not declined during the last decades despite the advances in modern obstetrics practice. Standard treatment involves careful clinical examination, needle electromyography follow-up and surgical treatment in the absence of spontaneous recovery. Data about NBPP prognosis is surprisingly variable with the proportion of patients having complete recovery varies among from about 10% to 90%. Recent studies indicate a more balanced perspective: about 50% of the patients will be completely recovered while about 15% will be severely handicapped. The remaining 35% of the patients will have a satisfactory outcome, but with some shoulder functional limitation. Nevertheless, data are emerging to suggest that central and peripheral adaptation may play a role in the recovery.

Conclusions

Conclusion
Forceps extractions are related to a higher risk for NBPP; however, it is not clear if this is due to fetal traction or just an associated factor present in a difficult delivery situation. The indication of cesarean section for macrosomic babies would be a rational approach for prevention of such complication. Infants who sustain NBPP have

an overall optimistic prognosis, with the majority recovering adequate functional use of the affected arm. In case of the absence of spontaneous clinical improvement after a couple of weeks, early referral to specialized centers with multidisciplinary approach is mandatory.

N 14

Inside out

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Introduction

Introduction: Classic bladder extrophy is a rare condition, without a clear cause. Prenatal diagnosis is difficult, and it can easily be missed at prenatal ultrasonography. Due to the infrequency it is important to realize that this condition needs specialized care in a center with expertise.

Aim

Case description: A 26-year old woman (G3P2A0) gave birth after a uncomplicated pregnancy of 41 weeks. Prenatal follow up was without particularities, ultrasound was normal, no consanguinity of the parents. During delivery a call for the pediatrician was made because of meconial amniotic fluid. After birth she made a good start, with an Apgar score of 9 and 10, at respectively 1 and 5 minutes. During clinical examination an abdominal wall defect was noticed, a round, bulging defect, no visibility of intestines, umbilicus was not involved in the defect and had a normal position and form. The female genitals were placed anteriorly and there was a doubled clitoris. In between both sides of the clitoris a orifice was seen. The defect was examined by a joined force of the pediatric abdominal surgeon and the pediatric urologist. The aspect of mucosae was suggestive of a bladder exstrophy, and ureters were found with the use of a Ch 3 umbilical artery catheter. The neonate was transported to UZ Gent, expertise centre for the bladder exstrophy and epispadias complex (BEEC), for instructions of the parents and planning of the surgeries. Repair is done in several times, firstly a reconstruction of the bladder (if necessary with osteotomies). In further surgeries a reconstruction of the bladder neck is pursued. Continence is achieved in 60-80% with or without chronic intermittent catheterisation.

Methods

A review of the literature was performed with the use of Pubmed.

Results

Discussion: This case illustrates the possibility of severe congenital defects not seen on prenatal follow-up before. Treatment of this condition should be guided by specialised caregivers in expertise centra. Finding of a BEES should be handled with care. Covering of the abdominal wall with a plastic film is advised to prevent dehydration and damage to the bladder mucosae. Profylactic antibiotics are not necessary, except when there are other risk factors for a neonatal infection.

Conclusions

Conclusion: BEES is a rare condition, but a basic knowledge of it's treatment helps to give qualitative patient centered care.

N 15

Congenital Arthrogryposis-Renal dysfunction-Cholestasis (ARC) syndrome

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Introduction

Introduction: We present the case of a newborn post-term with joint malformations in the limbs.

Aim

During our examination, we highlight a renal and hepatic dysfunction, which will lead us to suspect an ARC syndrome.

Methods

Case report: The patient is a boy born full-term of non-consanguineous parents. The pregnancy was properly monitored and without anything particular to report. It is the couple's third child; the other two children are in good health. At birth, cardiopulmonary resuscitation was performed during the first 5 minutes of life due to perinatal asphyxia. The child had morphologic abnormalities: restriction of growth (weight <P3), amyotrophia, excessive laxity of the ankles and wrists. The early post-natal biologic assessment revealed refractory cholestasis to ursodeoxycholic acid and adapted milk formula treatment and tubular acidosis resilient to sodium bicarbonate supplementation. The global neurologically impairment with global hypotonia, lack of archaic and deep tendon reflexes, oral feeding difficulties lead to chronic nasogastric tube feeding. The check-up sheet will also reveal bilateral deafness and dysgenesis of the corpus callosum. During his hospitalization, the newborn presents chronic pyrexia without an identified infectious focus. In view of this multi-malformation clinical picture (arthrogryposis, cholestasis and renal dysfunction), an ARC syndrome was suspected. A genetic test has been done and we will confirm this syndrome.

Results

Comments: ARC syndrome is the association of arthrogryposis, cholestasis and renal tubule dysfunction. It is a rare autosomal recessive syndrome but fatal in the neonatal period. There is no specific treatment for this syndrome.

Conclusions

Conclusion: The combination of cholestasis, renal dysfunction and arthrogryposis should be reminiscent of ARC syndrome and genetic analysis should be performed.

N 16

A rare case of neonatal respiratory distress.

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Introduction

Respiratory distress in the neonatal period is commonly due to respiratory distress syndrome, transient tachypnea of the newborn, pneumonia, pneumothorax or interstitial lung disease. Non-pulmonary causes include cyanotic congenital heart disease, anaemia, polycythaemia, metabolic acidosis or neuromuscular problems. Endocrinological problems, although rare, can also present with severe respiratory distress as we describe in this case report.

Aim

Presenting a case of neonatal respiratory distress due to hypopituitarism.

Methods

A term girl was born at 38 weeks+ 5/7 gestational age after a caesarean section for fetal distress and breech position. At birth, the infant showed signs of respiratory distress and required support with nasal CPAP and a maximal FiO2 of 0.6. The child was transferred to the neonatal unit for further management. She had mild hypoglycaemia on admission and received a bolus of glucose followed by a perfusion of intravenous glucose. There were no signs of maternal or neonatal infection and no signs of perinatal asphyxia (AS 8/7/8, pH umbilical cord 7,29 and lactate 0,9 mmol/L). The childs' respiratory status briefly improved allowing a reduction of oxygen to 21%. Unfortunately, over the first 12 hours of life the condition deteriorated with severe hypotension treated with dopamine and dobutamine, hypercapnia and later increased oxygen requirement. She was intubated and placed under high frequency oscillatory ventilation. The child received a dose of surfactant without clear improvement and inhaled nitric oxide was added for suspected pulmonary hypertension. X-ray of the lungs did not show signs of infiltration or other pathological findings. Cardiac echography did not reveal any anatomical problems or signs of significant pulmonary hypertension.

Abdominal distention was noted, and no meconium was emitted in the first 48 hours of life. Meconium was only eliminated following a lavage.

Progress was slow with persistently high ventilatory and oxygen requirements. There was no response to a second dose of surfactant on the 3rd day. Due to this unusual clinical course, blood was tested for metabolic and endocrinological pathology. On the 5th day, a very low free T4 with a low TSH was found suggesting central hypothyroidism. Cortisol was checked and also appeared very low. Treatment with thyroxine and hydrocortisone supplements was started the same day. The child showed rapid clinical improvement. She was extubated, the blood pressure medication was stopped and she started to have spontaneous evacuation of stools.

MRI showed a pathological aspect of the turcic saddle (flattened, empty and filled with liquid) and a normal aspect of the pituitary stalk with a normal position. On the level of the distal, lower end of the pituitary stalk, there was a small round nodular structure which may correspond to a remnant of a very hypoplastic pituitary gland.

A glucagon stimulation test, performed on day 22, confirmed virtually non existant levels of growth hormone therefore growth hormone injections were started.

Results

In this case, the first steps of treating and diagnosing the respiratory insufficiency did not succeed prompting a search for rarer conditions that may cause respiratory distress. This allowed for a rapid diagnosis of hypothyroidism (due to hypopituitarism). Rapid diagnosis and treatment is important to prevent long term complications of hypothyroidism.

The hypothesis for respiratory problems in congenital hypothyroidism is that the thyroid hormone influences the epithelial cell differentiation during foetal lung development. In hypothyroid lambs, poor alveolar differentiation and abnormal surfactant production is seen. Similarly, in rat models with hypothyroidism there is an association with abnormal intrauterine pulmonary development including hypoplasia.

In our case, the hypothyroidism was due to a congenital hypopituitarism with low cortisol explaining the severe hypotension and the hypoglycaemia.

Congenital hypopituitarism results from genetic defects that alter the normal development of the pituitary gland. Defects in any of the multiple sequentially expressed pituitary developmental transcription factors may cause deficiency of one or more anterior pituitary hormones. Most common mutations are found in PROP1 (5q), POU1F1 (3p11), HESX1 (3p21.2-p21.1), LHX3 (9q34.3) and LHX4 (1q25). Those genes are necessary for the differentiation of anterior pituitary cells to specific cell types that are precursors to somatotroph, lactotroph, thyrotroph, and gonadotroph cells.

Conclusions

If the most common causes of respiratory distress are ruled out, it is important to consider congenital hypothyroidism with or without hypopituitarism. Rapid diagnosis and treatment is vital to improve the clinical course and prevent long term complications.

N 17

Newborn infection caused by Bacillus Cereus: a germ on the rise, causing devastating brain lesions.

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Introduction

We present a case of neonatal sepsis caused by bacillus cereus, an ubiquitous germ described as a pathogen in immune compromised patients. Recent years it has been reported more frequently on neonatal intensive care units as a causative to severe invasive infections.

Aim

Case report

Methods

Case Presentation
Our patient is a male, first member of a DCDA twin, born at a gestational age of 28 weeks through caesarean section because of maternal chorio-amnionitis. He had a difficult start with persistent pulmonary hypertension requiring high inflation pressures, high frequency oscillatory ventilation and iNO. Respiratory function was further complicated by a bilateral pneumothorax, resulting into emphysema of the left lung. Intracranial haemorrhage occurred during the first days of life, but remained stable (grade II haemorrhage).
At day 13 he developed a sceptic shock needing haemodynamic supportive measures. A blood culture revealed presence of bacillus cereus. Treatment with vancomycin and cefotaxim was started intravenously.
Routine weekly brain ultrasound scanning showed several cystic lesions, different from a classical periventricular cystic leukomalacia (PVLc). MRI brain imaging confirmed a predominant subcortical location of multiple cystic lesions, with intra-luminal debris. The assumption of brain abscesses following bacillus cereus infection was made. Treatment was changed to Meropenem according to the antibiogram and Sulfamethoxazol/Trimethoprim was added to improve penetration through the blood-brain barrier. Due to intracranial involvement antibiotic treatment was continued for 6 weeks. Neurological follow-up at discharge and at the corrected age of 6 and 12 months showed a normal motor and social development.

Results

Whilst our patient had multiple reasons to develop PVLc (e.g. poor start as well as septic shock), the cystic lesions on his routine brain ultrasound did differ from a classical PVLc as they were asymmetrical and subcortically located. Previous ultrasounds also lacked an aspected periventricular increased echogenicity or 'flaring'. Brain MRI additionally showed a hypo-intensive enclosure in one of the lesions, which could not be appointed to hemosiderine, and all cysts were rather well bordered. They had the characteristics of brain abscesses (hyperintensive on T2, hypointensive on T1). Although they lacked classical diffusion restriction, this could be explained by the use of antibiotics whom cleared the pus. No gadolinium was used intravenously.
These lesions have been described earlier as a result of the liquefactive necrosis provoked by the bacillus cereus infection (Lequin, AJNR, 2005,26:2137-2143). Our patient unexpectedly showed normal motor development, which could be explained because lesions where predominantly located posterior from the central sulcus.
Bacillus cereus is an ubiquitous germ, regularly seen as a concomitant. However in immune compromised patients it has been prescribed as a pathogen resulting in high

morbidity and mortality. Several outbreaks of bacillus cereus infections have been published describing the ubiquitous origin of this germ. It can present in ventilator equipment, deep lines as well as in linen and diapers. In one case report the dust produced during construction works was identified as the origin of bacillus cereus.

Conclusions

We present a case of neonatal sepsis caused by bacillus cereus, a germ reported more frequently on neonatal intensive care units. The patient showed peculiar brain cysts, noticed on routine brain ultrasound scanning. MRI scan revealed the characteristics of brain abscesses. We emphasise the importance of routine ultrasound scanning and the distinction between PVLc and cysts originated out of an invasive infection with Bacillus Cereus since it has great impact on morbidity and mortality as well as on the duration of antibiotic use.

N 18

« Spina Bifida and maternal obesity »

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Introduction

Background
Spina Bifida (SB) was a common malformation the past centuries. Nowadays, thanks to the prophylactic administration of folic acid, incidence could be reduced till 70% and is now about 1 to 2 per 1,000. Antenatal diagnosis is essential to provide a good management.
We will expose one case of postnatal SB Diagnosis to remind us actual recommendations.

Aim

Clinical features
Baby boy born at term and with a great post-natal adaptation; pediatrician was called in the first minutes of life because of a lumbar lesion. Clinical feature showed a lumbar red crater without any signs of CSF leak or myelomeningocele; no other clinical abnormality except an absence of anal reflex and a heart murmur.
The mother had been regularly followed up and the ultrasounds never showed any foetal abnormalities. She did take a prophylactic treatment by folic acid and pregnancy vitamins. She suffered from gestational diabetes, obesity (BMI 40) and Polycystic Ovary Syndrome.
Initial management was to clean and protect the lesion.
Work-up with cardiac, EEG, abdominal and cranial ultrasound and cerebral MRI revealed an Arnold Chiari type 2 disease, confirmed myelomeningocele and a tethered cord; no other major abnormalities.
At day one of life; a myelomeningocele with protrusion and CSF leak appeared. The child was then transferred to reference center to proceed surgery.
Two weeks after surgery, his neurologic assessment showed no anal reflex and an amyotrophy with a weakness of the gluteus maximus and of the hamstring muscles.
The follow up included a cranial sonography control weekly, daily physiotherapy and a neuropediatric assessment monthly.

Methods

Discussion

Results

In this case, although the mother had a regular follow up by her gynecologist, ultrasounds were quite difficult due to maternal obesity.
Previous studies showed that maternal obesity is a risk factor of neural tube defect. These women have also higher risk of folate deficiency but there is no consensus on daily dose recommended.
Initially, the lesion should be cleaned and cover. Until the surgery, he patient should received prophylactic antibiotherapy and should be put in prone position to avoid pressure on the lesion. A complete neurological assessment has to be done at birth and should include cerebral ultrasound and RMN.
After the repair, there is a huge risk of hydrocephaly. An active surveillance of the head circumference and of the ventricular dilatation should be done.
SB is often related to other abnormalities such as Arnold Chiari II, renal abnormalities, heart defect or hip's dysplasia which we should look for.
Furthermore, SB has many complications, including ventricular dilatation, intracranial hypertension, orthopedic issues, seizures, fecal incontinence and bladder dysfunction.

Therefore, we should provide a multidisciplinary approach (neuropediatric, physiotherapy, orthopedist, nursing) and care for any neurologic sign (weakness, strabismus, worsening incontinence, ...). Also, fecal incontinence and urinary tract disabilities should be a priority to provide a great quality of life.

Conclusions

Conclusion
SB is now rare thanks to prophylactic folic acid intake and improvement of foetal diagnosis. Initial management including cleaning, cover up and antibiotics is crucial to avoid infection and has clearly improved the outcome. As well, a complete work-up should be performed to exclude other malformations. Surgery should be discussed with neurosurgeon. Babies should have a regular and multidisciplinary follow up.
Although relation between neural tube defects and maternal obesity and folate deficiency is clearly demonstrated, there is no consensus on folic acid dose adaptation according to mother's weight.
Unfortunately, the prognosis for those children is still uncertain; although 75% are ambulating in the childhood, only 50% will be in the early adulthood; around 75% of children with myelomeningocele have an IQ higher than 80.
In a few cases, children have associated malformations such urinary tract malformation, abnormalities of the spine which can be part of syndromic disease.

U 01

Value of renal and bladder ultrasound in diagnosing vesicoureteral reflux

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Introduction

Continuous antibiotic prophylaxis reduces the incidence of recurrent pyelonephritis in children with vesicouretral reflux (VUR). However, there is an ongoing debate on which children should be screened for VUR after a first episode of pyelonephritis. More concrete, the value of renal and bladder ultrasound (RBUS) in diagnosing VUR has been challenged.

Aim

In this abstract, we present our preliminary findings of a database study in children younger than 4 years of age.

Methods

Retrospective analysis of patients younger than 4 years who were followed-up at our department, after a first episode of pyelonephritis, between 2009-2015. Patients were included if clinical information concerning index pyelonephritis, and paired RBUS and voiding cystourethrogram (VCUG) were available. Patients were excluded if a VCUG had been performed preceding index pyelonephritis. Descriptive statistics and logistic regression models were used for examining risk factors for VUR, SPSS version 22 was used for performing all analyses.

Results

Data of 312 children were available for analysis. Escherichia coli was cultured in 291 cases (93.3%). Hydroureters and duplex ureters were found in 25 renal units (3.1%), any grade of VUR in 126 units (20.2%), dilating VUR in 54 units (8.6%). In our first logistic regression analysis, age over 12 months was the only statistical significant predictor for any grade of VUR. Hydronephrosis on RBUS and non-E. Coli predicted VUR, but were not statistically significant. In general, ultrasound parameters were not significantly predictive for VUR. In VUR cases that were missed by RBUS (77), the bladder was empty at RBUS in 60 children (77.9%).

Conclusions

RBUS is of limited value in diagnosing VUR. The strongest predictor of missing VUR was an empty bladder. In contrast to earlier studies, non- E. Coli UTI's and female gender were not significantly associated with high-grade reflux.

U 02

The influence of socioeconomic status in enuresis

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Introduction

Multiple studies have been conducted on the correlation between a socioeconomic status and overall health. Existing literature indicates that a low socioeconomic status causes a higher prevalence of enuresis. Moreover, it has been proven that a lower socioeconomic status has a negative impact on the vision on enuresis, on the degree of which the parents take this disease for serious, on the therapy compliance and on the effectiveness of treatment. Vice versa, enuresis has a strong negative impact on the patient's socioeconomic status. Mainly due to higher direct and indirect costs and cost related to a lower quality of life. Furthermore, enuresis negatively impacts a patient's relationship with family and friends. Moreover, a correlation between enuresis, socioeconomic status, toilet training, sleeping problems, school problems and behavioral problems have been shown.

Aim

This study investigates on the specific relation between a socioeconomic status and enuresis, which has, to our knowledge, not been investigated before.

Methods

For the literature study, databases "Pubmed", "Web of Science" and "Google Scholar" have been examined. In order to find other possible explanations that are not presented in the literature, the expertise of various specialists in the field of pediatric nephrology and pediatric psychology was called upon.

Results

To indicate how a low socioeconomic status impacts enuresis, a hypothetical model has been established. It is proven that a lower socioeconomic status leads to obesity, smoking, obstructive sleep apnea syndrome and teenage pregnancy, which all increase the risk for enuresis. Besides, etiological aspects such as the influence of an irregular lifestyle, a higher consumption of cheap food containing more salt and proteins, a higher consumption of soft drinks and other drinks containing high concentrations of caffeine and carbon acid gas and the mechanisms behind these and enuresis have been studied. Moreover, existing research indicates that a lower consumption of fibers and fluids leads to constipation which on its turn negatively impacts the treatment. In addition, parents who do not consider enuresis as pathology postpone treatments and use more punishment methods, which has a negative impact on the outcome of the therapy. Finally, lower financial strength leads to a therapy selection based on costs, instead of selecting the best therapy for the patient. Furthermore, a basic cost estimation has been made for the potential costs related to enuresis, which indicates the current lack of validated financial numbers in this area of research.

Conclusions

This literature study concludes that socioeconomic status and enuresis are correlated in both directions. This study is a good starting point. However, to gain a deeper understanding on the influence of lifestyle and food patterns on enuresis, as well as the financial impact of enuresis, the impact on the daily life of the parents and the child and to map further relations and the weight of these relations, more extensive

research is recommended.

U 03

WORLD KIDNEY DAY : Women and CKD

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Introduction

The BPN, including pediatric nephrologists of all Belgium universities wants to promote education and screening in children with kidney diseases, in line with the IPNA initiative.. Kidney Day is a wonderful opportunity to achieve this goal. The topic concentrates in 2018 on women and CKD
The aim of this year initiative to ask for gender specific differences for mother and child
- Mothers of diseased children are more likely to stop their career and to donate an organ than fathers, what has psychological, social and financial repercussion, and especially in single parent situation
- There are gender specific diseases, like lupus nephritis, but the associated genital abnormalities in severe CAKUT patients are often not taken in account
- Girls with chronic disease and especially CKD, should receive appropriate counseling about pubertal maturation, risks of pregnancy . CKD is also considered a risk factor for adverse pregnancy outcome and reduced fertility. Females who have CKD are at increased risk for negative outcomes for the mother and the baby; pregnancies in women with advanced CKD are most challenging with high rates of hypertensive disorders and preterm births..
- Gender specific differences in drug therapy are often not taken in account in the labeling studies, but might be significant.
- Psychological items, and especially the lack of self-esteem in the pubertal girls (obesity, scars) but also often poorly developed relational skills should have major consideration

U 04

Nephrocalcinosis : an intriguing disease

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Introduction

Nephrocalcinosis is defined by a generalized deposition of calcium in the kidney, most often located in the renal medulla. This calcium deposition can be interstitial, intratubular or both. Cortical nephrocalcinosis also exists and is described in patients with more severe renal disorders. The depositions are made of calcium oxalate or calcium phosphate.
The exact prevalence of nephrocalcinosis is still unknown and many causes are involved. Therefore, it is difficult to define a common underlying pattern.
Nephrocalcinosis is associated with metabolic and genetic disorders, which are potential causes.
The presentation is, in most cases, asymptomatic and unfortunately often discovered among patients with serious diseases after a medical imaging. Renal colic, polyuria and polydipsia have been related.
Nephrocalcinosis is classified in three stages by degree of severity: stage 1- molecular, usually reversible; stage 2- microscopic, deposits identified on light microscopy; stage 3- macroscopic calcifications recognized on medical imaging. The illness is identified at stage three. Ultrasound with high frequency has become the gold standard.
The prognosis depends on the underlying cause. Most of patients do not progress to end-stage renal disease.

Three case reports:
Mathis, a ten-year-old boy, had an assessment for stunting in his early childhood. An abdominal ultrasound was performed revealing bilateral kidney calcifications. A genetic analysis detected a SLC34A3 mutation, disturbing Na/Pi cotransporter, a protein located in the proximal convoluted tubule. However the renal function was preserved.
Loan, an eight-month-old boy, was suspected to present an antenatal nephrocalcinosis at the ultrasonography screening in the 32nd week of pregnancy. At birth, dystrophy features were observed, including his right limb. No specific mutation has been yet identified by genetic analysis. However, the renal function is preserved and explorations are still in progress.
Owen, a three-month-old boy, was admitted at the pediatric department with retarded development in height and weight. The abdominal ultrasound showcased signs of nephrocalcinosis. Renal disorders were found in his family history, including pyelonephritis, lithiasis and urocystis. The renal function is preserved but hypercalcemia with hypercalciuria is on exploration.

Discussion: What to do with a nephrocalcinosis diagnosis?
Trying to understand the underlying cause is the most important part of the medical management.
To do so, you first need to discuss the pregnancy, birth details and family history to identify low-birth-weight, preterm infants, inherited defects and others. You also have to report drugs administration (Furosemide, Vitamin D and nephrotoxic), child s growth parameters, and dietary intake.
If you do not have any answer, you have to research metabolic abnormalities with blood and urine tests: electrolytes, bicarbonate, pH, calcium, phosphorus, magnesium, PTH and vitamin D metabolites. Hypercalciuria is the most important cause. The illness can also be associated with increased urinary phosphate and oxalate excretion or decreased urinary citrate and magnesium excretion. However, hydro-electrolytic disturbances cannot explain the complexity of mechanisms leading to renal calcification.

In all cases, ultrasonographic data are very important and ultrasound must be performed regulary.
Finally, you must consider potential genetic disorders. Mutations of specific transporters, channels and receptors involved in calcium and phosphate tubular reabsorption or excretion have been recently reported in illnesses associated with nephrocalcinosis. Bartter syndrome, Dent s disease, X-linked hereditary disorders and many other entities have been identified.
The treatment is not well defined. Currently, hyperhydration, calcium diet and citrate supplements are the most important medical recommendations. Thiazide diuretic may exert a protective action on the calcifications.

Conclusions

As illustrated in these three cases, most of nephrocalcinosis diagnoses are incidental echographic imaging findings. In general, the diagnosis is performed late in the childhood and therefore explains more advanced and severe diseases.
The specific pathogenic mechanisms are still unclear. However, the disturbance of the calcium homeostasis seems to be playing a key role.
To date, there is no study showcasing the outcome of the illness on the renal function. The future will give us new insights into this new disease.

U 05

Familial Nephrotic Syndrome due to MCD with diffuse mesangial hypercellularity in Twin Girls.

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Introduction

We report on a 4-year old African female patient who presented with steroid dependent nephrotic syndrome in whom renal biopsy showed the rare entity of "Minimal change disease (MCD) with diffuse mesangial hypercellularity (DMH)".

Aim

Her renal history starts in 2014, when she was admitted to a PICU service with pneumonia, hypertension and fluid overload. Her lab tests showed renal failure (eGFR 91.5 ml/min/1.73m² Schwartz Paediatric GFR), severe hypoalbuminemia (8g/L), proteinuria (4+) and hematuria (3+). A post-infectious glomerulonephritis was suspected. Additional lab values showed mildly elevated CRP, cholesterol (288 mg/dl) and normal C3, C4 values. Renal biopsy showed diffuse mesangioproliferative changes and minimal endocapillary proliferation. IF was negative for IgA, IgM, C3 and C1Q. IgG trace positive. EM showed no deposits but confirmed diffuse foot process effacement. The patient was treated with diuretics, human albumin and steroids (60 mg/m² QD for 6 weeks, 40 mg/m² alternate day for 4 weeks, followed by taper) and went into complete clinical and biochemical remission. During steroid taper she developed a relapse of severe nephrotic syndrome with ascites.

Methods

The patient was now treated with high dose steroids + cyclosporin, which resulted in complete remission for >1 year. After that she has developed two additional relapses (gastro-enteritis episode).
2 years later her twin sister similarly presented with steroid sensitive nephrotic syndrome (age 5y12 m). Kidney biopsy showed an identical picture (ie. immunofluorescence negative diffuse mesangial hypercellularity). She was treated steroids (60 mg/m² QD for 6 weeks, 40 mg/m² alternate day for 4 weeks, followed by taper) and since then remains in complete clinical and biochemical remission.

Results

Lab values were normal/negative for CRP, C3 (2/3 samples, 1/3: decrease), C4, IgA, M protein, CIC, cryo's, ANF, ANCA, a-PLAP2-R, HCV, HIV, Hep. A, Mycoplasma (PCR, nasopharyngeal aspirate), and mycobacterium tuberculosis (PCR).
a1-antitrypsine was low (69 mg/dl - genetic testing still running). C3d was mildly elevated. Mycoplasma IgM was positive. A (second) renal biopsy was performed which again showed prominent mesangioproliferative glomerulonephritis with trace endocapillary proliferation. IF was again negative (trace IgM).

Conclusions

In Classic MCD, LM shows no glomerular lesions or at most very mild focal mesangial proliferation (not exceeding three or four cells per mesangial area). Presence of more than four mesangial cells per mesangial region affecting at least 80% of the glomeruli defines the rare diffuse mesangial hypercellularity variant of MCD (3% of all MCD). Clinically, unlike children with classic MCD, these patients will often present with hematuria and hypertension and this rare variant is known to be more often steroid

resistant. Immunofluorescence is usually negative but low-intensity mesangial IgM (sometimes accompanied by C3 or C1q) staining can sometimes be found. The differential diagnosis also includes the rarely occurring combination of MCD and IgA nephropathy where MCD is accompanied by glomerular IgA deposits.

U 06

Renal Tubular Dysgenesis in a Premature Newborn.

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Introduction

Inherited renal tubular dysgenesis (RTD) is a rare disease of fetal kidney differentiation, caused by mutations in the genes encoding the components of the renin-angiotensin system (RAS).

Aim

The RTD phenotype has also been described as a complication of several conditions which result in hypoperfusion of the fetal kidneys such as twin-to twin transfusion syndrome in mono-chorionic twin gestation (in which the donor fetus may develop RTD), major cardiac malformations and severe liver disease (like haemochromatosis). Renal tubular dysgenesis is also described as part of the diabetic embryopathy spectrum. Finally, a few case reports were described where RTD is associated with massive perivillous fibrin deposition in the placenta.

Methods

We report a new case of RTD in a premature boy, born at 32 3/7 weeks of gestational age from a G1P0P0 30 year-old-healthy non-consanguineous Moroccan woman through emergency cesarean section for reason of foetal distress and IUGR. Prenatal ultrasound in the 30th gestational week had revealed oligohydramnios progressing to anhydramnios by week 31-32, in the presence of two normally sized kidneys and an empty urinary bladder. No ACE-inhibitors or ATII-receptor inhibitors had been taken before or during pregnancy. Clinical examination at delivery noted multiple dysmorphic features: a large anterior fontanel with broad open sutures, a hypoplastic nasal bridge, low set ears, and bilateral clubfeet. Two hours after delivery severe thrombocytopenia (18. 10 E 9/L) and clotting problems (APTT: 232 sec; fibrinogen:0.40 g/L), occurred. The patient developed severe metabolic acidosis (BE:-11.9 mmol/L), renal failure (creatinine:2.98 mg/dl),ferritin 125 μg/L(18-464 μg/L) in the absence of septicaemia and/or Ultrasound of the abdomen demonstrated a normal liver with a broad portosystemic shunt between the vena porta and the vena cava inferior. Both kidneys measured 3.6 cm and showed normal corticomedullar differention and somewhat hyperechogenic cortex. The urinary bladder was empty.During hospitalisation there was persistent anuria with severe metabolic acidosis and persistent severe hypotension (inotropics, plasma,physiologic serum, steroids,packed cells).The child died of muli-organ failure on day 3.

Results

A liver and kidney biopsy was done shortly postmortem. The liver biopsy showed little tissue, without noticeable defects. The renal biopsy was representative and showed few and poorly differentiated tubular structures. The tubules expressed EMA (marker of distal tubular differentiation), but not CD10 (marker of proximal tubular differentiation). Glomeruli were normal. These findings make the histopathologic diagnosis of RTD. The accompanying placenta showed no abnormalities. Genetic Analysis is ungoing.

Conclusions

We conclude that this premature boy has an inherited autosomal recessive RTD. It is

essential to consider this severe disease in anuric foetuses with structurally normal kidneys at sonography in order to allow a kidney biopsy and mutation analysis of RAS genes. Genetic counselling and early prenatal diagnosis is warranted for future pregnancies.

U 07

Coexistence of nephrotic syndrome and type 1 diabetes mellitus: coincidence?

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Introduction

A 10-year old boy, known with insulin dependent diabetes mellitus (IDDM) since the age of 2, presented with weight gain and generalized swelling for 1 week. On examination, our patient was hemodynamically stable with generalized oedema. Blood pressure was within normal ranges.

Nephrotic syndrome (NS) was suspected and confirmed by addition testing. Investigation showed normal blood count, creatinine 0.46 mg/dL, blood urea 31 mg/dL, total protein 3.4 g/dL, albumin 0.9 g/dL, total cholesterol 391 mg/dL and normal C3 level 115 mg/dL. Urinary protein/creatinine ratio was 6.2:1. Twenty-four-hour urinary protein was 2.54 g/24h without haematuria. Urinary electrolytes were in normal range. Our patient was started on diuretics, oral prednisolone and ACE-inhibition.

During prednisolone start up glycemia control was difficult to achieve with regaining from diabetes control under higher doses of subcutaneous insulin. HbA1c was 7.9% on last out-patient control one month before admission.

It is known that there is a negative correlation between serum albumin and thyroid hormone levels. In our patient TSH on admission was 9.13 mU/L with low free T3 4.2 pmol/L and normal free T4. L-thyroxin substitution was started for his subclinical hypothyroidism. This hypothyroid state is suspected to improve with remission of NS.

We considered that the association of NS and IDDM may depend on a common auto-immune substrate. As the initial clinical course was protracted before remission with relapse after 1 month a kidney biopsy was performed which was compatible with minimal change nephrotic syndrome.

Aim

Review of literate for association of NS and IDDM and possible common substrate.

Methods

MEDLINE was searched with various combination of "proteinuria", "nephrotic syndrome", "type 1 diabetes", "IDDM" and "paediatrics".

Results

Mostly proteinuria in diabetes is a consequence of diabetic nephropathy. This is characterised by progressive loss of renal function, proteinuria and associated systemic disturbances like hypertension. The association of NS and IDDM is rarely reported in literature. To our knowledge only 11 case reports of in total 20 paediatric patients have been reported of the combination NS-IDDM.

Both NS and IDDM have an immunological basis, but the aetiology for a common substrate between the two is unknown. However, a coincidental association seems unlikely as Goldman et al. (2002) have shown that the co-existence of NS and IDDM exceeds the combined estimated prevalence rates for each disease. Most attention is directed at HLA-typing for a possible common substrate.

HLA-DQ typing for type 1 diabetes in our patient was done through the Belgian Diabetes Registry and alleles DQA1*0301-DQB1*0302/DQA1*0501-DQB1-0201

(DQA3-DQB3.2/DQA4-DQB2 respectively) were detected. No additional HLA typing was performed, however trough linkage disequilibrium between the loci DQA1, DQB1 and DRB1 the most likely DR-subtype can be distracted. DQA3-DQB3.2 and DQA4-DQB2 are associated with HLA-subtype DR4 and DR3 respectively. DR3 is associated with minimal change nephrotic syndrome. So, we deem it possible that the DR3-DQA1*0501-DQB1*0201 haplotype the substrate form for the nephrotic syndrome in our patient.

Conclusions

The association of NS and IDDM is rarely reported in literature. In our patient a substrate for this association deemed possible. Further genetic testing in larger cohorts is warranted to unravel a possible substrate.

U 08

Unexplained fever and abdominal pain in an 11-year-old girl: a case of renal abscess.

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Introduction

Renal abscess with staphylococcus aureus is rare in healthy children, with a paucity of data about treatment modalities. The vast majority of pediatric renal abscess management is usually based on extrapolated results from the adult cohort. The exact incidence is unknown. The symptoms are often nonspecific: fever, asthenia, weight loss and abdominal pain. The diagnosis is confirmed by abdominal ultrasound and computed tomography. The most common isolated bacteria in kidney absecesses are Escherichia coli and Staphylococcus aureus.

Methods

We report the case of an 11-year-old girl, with no particular antecedent, presenting to the emergency department for unexplained fever for 1 month, crampiform abdominal pain, anorexia and asthenia. Urine removal in the emergency room was coca-cola color. The urinary sediment is negative with the presence of Calcium Oxalate dihydrate, the culture < 10 000 germs. The biology shows a moderate inflammatory syndrome with elevation of CRP to 143 mg/L, and normoleukocytosis to neutrophilic formula. The renal function is slightly impaired initially: serum creatinine slightly increased to 0.69 mg/dl. The blood culture remains sterile. Ultrasound, along with CT scan, was used to diagnose a 3cm - shaped, snow - crawling, renal abscess. After consultation with the pediatric surgery and nephrology team, a broad-spectrum antibiotic treatment is initiated and a percutaneous drainage guided by CT. At 3 months of follow-up, she was asymptomatic, without reflux at cystography.

Conclusions

Renal abscesses are rare in healthy children. The uncommon occurrence of this pathology can lead to delayed diagnosis and thus inadequate initial treatment. Percutaneous drainage should be considered in cases of abscess greater than 3 cm or in case of non-response to antibiotics. The smaller abscesses (<3cm) can be treated with antibiotics for 4 weeks. It is important for pediatricians to keep in mind the diagnosis of renal abscess when a child presents with the triad fever, nausea or vomiting, and abdominal pain accompanied by leukocytosis and a high rate of CRP. The anamnesis must be searched because the point of entry can occur at any part of the body.

U 09

Familal renal glucosuria: a rare case of glucosuria in children

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Introduction

A urine test positive for glucose often worries and alerts us to exclude a diagnosis of diabetes. Therefore in children, this is a cause of referral to a pediatrician for further investigation. Though if no other symptoms of diabetes are present, this can lead to another diagnosis.

Aim

We would like to present a case of a girl with isolated glucosuria who was referred to our center.

Methods

A two year old girl presented at the pediatric emergency ward. She was seen by the general practitioner because of fever and diarrhea. A route urine dip stick test was performed to screen for urinary tract infection. He referred her to the emergency ward because of a urine dip stick test positive for glucosuria.
There was no polyuria, polydipsia or weight loss. Previous medical history was negative despite a hospitalization for viral meningitis at the age of 3 months. The glucosurie was confirmed in our laboratory. Quantification of glucose in urine was 1248 mg/dL (and repeatedly above 400mg/dL). Glycemia day profile with fasting glycemia was checked, as well as Hba1c, which were both normal. Diagnosis of diabetes mellitus could be excluded. Tubular function and excretion of sodium, potassium, calcium, phosphate, uric acid and low molecular weight proteins were all within normal limits. Ultrasound of bladder and kidneys was normal. Blood pressure was always within normal ranges for age and height. There is mild nocturnal polyuria. Based on those findings we diagnosed her with a familial renal glucosuria. Genetic testing was not performed because of the additional cost and no therapeutic difference. We informed parents of the benign aspect of this glucosuria. Screening of both parents was advised. No further follow-up was needed.

Results

Familial renal glucosuria is a form of a renal tubulopathy in which isolated glucosuria is found in the absence of hyperglycemia or any other renal tubular dysfunction type renal Fanconi syndrome. The cause is a mutation in the sodium-glucose cotransporter coding gene SLC5A2. Genetics are heterogenic and inheritance can be autosomal recessive or dominant. This is a benign condition, however some patients may have volume contraction. TheyDiagnosis can only be confirmed genetically but can be formed on suspicion after excluding diabetes mellitus and other tubulopathies. There is no specific therapy needed. Correct diagnosis, as well as good patient and parents information, can avoid a lot of anxiety and unnecessary referrals.

Conclusions

In patients with glucosuria in absence of any other symptoms of diabetes, normal serum glycemia and no other tubular disfunction, familial renal glucosuria should be suspected.

U 10

Tubulointerstitial nephritis with uveitis (TINU) syndrome

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Introduction

TINU syndrome is a rare inflammatory condition who is defined by the association of an acute tubulointerstitial nephritis and uveitis. Oculo-renal manifestations usually follow varied non-specific systemic symptoms such as fever, weight loss, asthenia. The etiology of this syndrome remains, currently, still unknown.

Aim

TINU syndrome was first documented in 1975 by Dobrin, and over 250 cases have been published. The pathology affects mostly teenagers and young womens (average mean age is 15 years).

Systemic symptoms (weight loss, asthenia, anorexia, arthralgia, fever) may predominate. Concomitant involvement of the eyes and kidneys occurs in only a minority (15%) of cases. Ocular symptoms may procede (20%) or follow (65%) renal symptoms (a median of 1 month later). Furthermore, uveitis in children causes few or no symptoms, leads to the delay of the diagnosis.

A treatment by oral prednisolone starting at 1 mg/kg/day is usually prescribed to patient with progressive renal impairment and anterior uveitis is treated with topical steroids. The long-term ocular complications are rare, but uveitis tends to persist or relapse. Most patients recover a normal renal function, although some have persistent mild renal failure.

Methods

We present a 13 years-old-girl, who was admitted to hospital because of asthenia, ten days of fever and vomiting.
One week before admission, she received 3 days of Amoxicillin-Clavulanic and then 3 days of Ciproxine for fever, persistent leucocyturia and inflammatory blood test (CRP: 12,5mg/dL). Finally, the urine cultures were sterile.
The first biology at the emergency showed an important inflammation (CRP: 12,83mg/dL, VS: 90mm/h), hyperleucocytosis (12,0 G/L) and signs of renal insufficiency (serum creatinine : 1,2mg/dl).

Results

One week after admission, the patient has increased signs of acute renal failure (serum creatinin : 2mg/dl), diagnosis was still unknown.
The renal biopsy revealed acute tubulointerstitial nephritis and the slit lamp examination showed bilateral anterior uveitis without clinical signs. The patient was treated with systemic corticotherapy.

Conclusions

The TINU syndrome is a rare entity and remains a diagnosis of exclusion.
Probably underdiagnosed because a time discordance can exist between the systemic, renal and ocular symptoms ; uveitis can occur at least one year after the tubulointerstitial nephritis.
A slit lamp examination should be proceed when patient had a diagnosis of acute interstitial nephritis on renal biopsy without obvious etiology. A multi-disciplinary approach is needed for diagnosis, rapid treatment and follow-up.

B 01

Assessment of bone quality in children with CP by quantitative ultrasound of the mid-shaft tibia.

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Introduction

Children with cerebral palsy (CP) are at risk for low bone mineral density (BMD), which is influenced by multiple factors. As a consequence, fragility fractures are 20% more common in non-ambulatory individuals with CP, with important impact on their quality of life. Gold standard for assessing bone mineral density remains Dual X-ray Absorptiometry (DXA), yet this technique does not take bone geometry into account. As children with CP have smaller bones than their peers, this is a major downside. As an alternative, peripheral quantitative computed tomography (pQCT) has been tested. Because of positioning problems and movement artefacts, this is not easy to use in children with CP. Recently assessment of bone quality by ultrasound measurements has been introduced and has been found reliable. In this study we investigated the feasibility of ultrasound measurement for assessing bone quality in children with CP. We compared the bone quality in children with CP with that in typically developing (TD) peers. In addition, we investigated the differences in bone quality in children with CP with different levels of motor disability and between the different types of CP (spastic, dyskinetic, atactic). Lastly, we investigated possible factors influencing bone quality.

Methods

We performed Speed of Sound measurements at the mid-shaft tibia and calculated Z-scores in 312 children (196 boys and 116 girls; 2 to 20 years old) with variable type and severity of CP, classified according to the Gross Motor Classification Scale. Anthropometric measurements were done and a patient questionnaire was filled in.

Results

Speed of Sound was higher with increasing age. Mean Z-score was -1.68 (SD 1.49) with 37.2% Z-score below -2, which meets the definition of low BMD. The more severe the motor disability, the higher the Z-score was, with a statistically significant difference in Z-score between GMFCS 2 and GMFCS 4 and 5. Children with atactic type CP had statistically significantly lower Z-scores when compared to spastic and dyskinetic type CP. Reported swallowing problems and history of bone fractures were found to be statistically significantly correlated with Z-score. Also knee height, mid upper arm circumference and calf circumference were statistically significantly correlated with Z-score. The presence of anti-epileptic drugs, a recent fracture and pubertal development were not found to be statistically significant.

Conclusions

Assessing bone quality by means of ultrasound has proved to be feasible. Bone quality was significantly lower in children with CP compared to TD peers. More research is needed to explain the complex interaction between CP severity, CP type and bone quality.

B 02

Burr hole surgery for treatment of moyamoya disease: an illustrated overview of the best surgical techniques

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Introduction

Moyamoya disease is a cerebrovascular disease with a bimodal age distribution, with an important pediatric patient population. The disease causes progressive stenosis of the internal carotid artery and its branches. It ultimately leads to cerebral hypoperfusion, ischemia and - if left untreated - stroke or intracranial hemorrhage. Treatment of symptomatic moyamoya disease consists mainly of surgical revascularization techniques. The goal of these surgical interventions is to improve the cerebral circulation in order to prevent stroke.

Their are two main categories of surgical techniques: the direct and indirect revascularization procedures. An example of direct revascularization is superfical temporal artery to middle cerebral artery bypass or middle meningeal artery to medial cerebral artery bypass procedures. These are generally difficult to perform in pediatric patients because of the small vessel size of the donor and recipient vessels. For these patients, an indirect revascularization technique is a valid alternative, such as burr hole cranial surgery. In contrast with direct vascularization techniques, burr hole surgery is not dependent on the size of the donor or recipient artery size, and is a proven versatile, efficient, effective and relatively easy technique.

Aim

The goal of this presentation is to focus on the technical operative aspects of multiple burr hole surgery as we perform it in our center, and highlight some of the procedure's details.

Methods

We will present an overview of different details and nuances of the technique as it is performed in our hospitals and in other internationally renowned centers, and will discuss results of personal correspondence with international experts to have an overview of the best "tips and tricks" of this indirect revascularization technique.

Results

In accordance with the literature, maximal collateralization and revascularization occurs between 6 to 12 months after surgery, with significant clinical improvement of the evolution of the disease.

Conclusions

An overview of the literature and our own experience demonstrate results that confirm that - with the presented procedure, special emphasis on a meticulous technique and center expertise - a significant overall clinical improvement and prevention of the development of further cerebrovascular events can be achieved in patients with moyamoya disease.

B 03

Multiple Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)-reactions caused by two different anticonvulsants in one patient: a case presentation.

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Introduction

An 8-year-old boy presented twice with a skin eruption and systemic symptoms (fever, elevated liver enzymes, edema and lymphadenopathy). The patient is the first child of non-consanguineous parents. From birth, a psychomotor delay was present, beside slight dysmorphic signs. Later on, he developed epilepsy.

At the time of the first episode of DRESS in January 2017, his epilepsy was treated with valproate and ethosuximide. After stopping the ethosuximide the symptoms disappeared. A skin biopsy in this episode showed an interface dermatitis with striking dyskeratotic/apoptotic keratinocytes over the entire thickness of the epidermis with a beginning (basal) epidermal necrosis. This image is suitable for an erythema multiforme. Purely based on these histopathological findings, an erythema multiform is difficult to distinguish from a Stevens-Johnson syndrome or a toxic epidermal necrolysis (TEN).

After this hospitalization, he needed topiramate to control his epilepsy.

In June 2017, he presented again with similar symptoms (fever, elevated liver enzymes, edema and lymphadenopathy). A new skin biopsy showed pronounced papillary edema with detachment of the epidermis, as well is spongiosis with vesicle formation and eosinophilic infiltration of the dermis. A favorable outcome was seen after discontinuation of the topiramate.

Aim

To discuss the aspects of Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) as a reaction on anti-epileptics, relevant for referring pediatricians.

Methods

Review of literature accessible through PubMed.

Results

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) is a quite rare, potentially life-threating, drug-induced hypersensitivity reaction that includes skin eruptions, hematologic abnormalities, lymphadenopathy, and internal organ involvement. It is characterized by a long latency of onset after exposure of the offending medication. These medications are most of the time anticonvulsants (phenobarbital, carbamazepine, phenytoin, lamotrigine) but also for example allopurinol, dapsone, vancomycin and olanzapine. The exact incidence of DRESS is unknown. The frequency varies depending upon the type of drug and immune status of the patient. It ranges from 1-5/10.000 patients exposed to the anticonvulsants, carbamazepine and phenytoin. It is higher amongst patients using lamotrigine (1/100 children exposed).

A strong, drug-specific immune response is the main factor in the pathogenesis of DRESS; it can also trigger a viral reactivation (most of the time herpes group). Histopathologic examination of a skin biopsy can show a variable combination of

patterns: most often, an interface dermatitis is seen, followed by eczematous, erythema multiforme-like, and acute generalized exanthematous pustulosis (AGEP)-like pustulosis.

In most patients, the reaction begins two to six weeks after starting the offending medication. Fever, malaise, lymphadenopathy and skin eruption are the most common initial symptoms. These systemic symptoms are what differentiates DRESS from any other drug eruption in anti-epileptic use. The rash stars as a morbilliform eruption which progresses to a diffuse, confluent, and infiltrated erythema with follicular accentuation. An eruption is suggestive for DRESS if it involves more than 50% of the body surface area (BSA) and/or if it includes two or more of facial edema, infiltrated lesion, scaling and purpura.

Identification and prompt withdrawal of the offending drugs is the most important treatment for patients with DRESS. Patients are treated symptomatically.

Conclusions

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) is a quite rare, potentially life-threating, drug-induced hypersensitivity reaction that includes skin eruptions, hematologic abnormalities, lymphadenopathy, and internal organ involvement. Most likely causative agents are anticonvulsants. Our patient presented with two separated DRESS reactions, both on different anticonvulsants (ethosuximide and topiramate). In literature, only one case is described with a DRESS reaction to ethosuximide, we did not find a case with a reaction to topiramate. For clinicians, it is important to consider DRESS in any drug reaction with systemic symptoms and eosinophilia.

B 04

Retrospective study of a cohort of children with posterior fossa tumor

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Introduction

The diagnosis and management of posterior fossa tumors in children remain a challenge. The difficulty lies in the multiplicity of clinical expressions, histological types and localizations.

Aim

The aim of this work is to provide a better clinical description of posterior fossa tumors in children. The treatments and sequelae are also studied in order to optimize management and follow-up of these tumors.

Methods

The medical reports of children aged between 0 and 15 years and 11 months old diagnosed between 1st January 2000 and 31st December 2014 in Cliniques Universitaires Saint-Luc were reviewed. The cohort consists of 86 patients. The different tumors are categorized according to the fourth edition of the WHO classification (Louis et al., Acta Neuropathol., 2007, 114: 97-109). Clinical and radiological presentations, oncology diagnosis, patient care, survival and sequelae have been studied. The Fisher and Chi-squared statistic tests and the Kaplan-Meier curves have been carried out.

Results

65 of the 86 patients were divided into 4 categories: medulloblastoma (31), pilocytic astrocytoma (19), infiltrating brain stem tumor (10) and atypical teratoid/rhabdoid tumor (5). The main symptoms of all tumors involved are vomiting (67% of the patients) and headaches (59%). The gait ataxia is also frequent (54%). For all the patients, except those with infiltrating brain stem tumor, surgical removal was the first step. Apart from the cases of the pilocytic astrocytoma, chemotherapy and radiotherapy were also provided. However, the latest wasn't applied to children under three years old. The one-year survival rate for medulloblastomas is estimated at 90%, three- and five-year survival rates at 78% and ten-year survival rate at 55%. For the infiltrating brain stem tumors, the one-year survival rate is 50% and the three- and ten-year survival rates are 15%. Regarding the atypical teratoid/rhabdoid tumors, the 1.2-year survival rate is 0%. There was no objectified death among the pilocytic astrocytomas. Among these 65 patients, those diagnosed under the age of three presented a 7.2-year survival rate of 0% whereas those diagnosed over the age of three showed a ten-year survival rate of 66% ($p<0.05$). The main long-term sequelae common to patients suffering from medulloblastoma or pilocytic astrocytoma are visual disorders, dysmetria, walking ability disorders and balance disorders. Endocrine disorders ($p=0,0002$), spine deformations ($p<0,01$) and hearing loss ($p<0,05$) are more frequent in cases of medulloblastoma than in cases of pilocytic astrocytoma.

Conclusions

Given the non-specificity of the main symptoms, the diagnostic phase is often difficult. Patient care usually causes long-term sequelae requiring oriented monitoring based on the received treatments. The majority of deaths occur in the first three years following diagnosis except for medulloblastomas where deaths are still observed between five and ten years following diagnosis. The diagnostic age is a major

prognostic factor given the high death rate for children diagnosed under the age of three.

B 05

Hypokalemic periodic paralysis: focus on an unknown pathology.

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Introduction

The loss of strength is a complaint with which pediatricians are rarely confronted. As a result, few of them feel comfortable with the approach of this symptomatology. We report the story of a 13-year-old boy who consults for sudden appearance, upon waking, of a loss of muscular strength located to the 4 members, without complaint affecting the oculomotor muscles, the sphincter continence or the sensory system. He also presented two vomitings. His cardio-respiratory parameters are normal, he is afebrile. When questioning the patient about his medical history he explains having felt the same kind of sensation of weakness, but much less intense, during the preceding month while he was participating in a training session of tennis. On clinical examination, the only anomaly is muscle strength, measured using the Medical Research Council (MRC) scale, at 3/5 at both lower limbs, 3/5 at the left upper limb and 2/5 at the right upper limb (where the loss of strength seems a little fluctuating). This loss of strength is more proximal than distal. The rotulien reflex is symmetric and a quite brisk, the plantar reflex is indifferent bilaterally. A biology revealed a natremia at 138 mmol / L (N: 135-145), a hypokalemia at 1.9 mmol / L (N: 3.5-5.5), creatine kinase at 116 U / L (N: 24-204), TSH at 1.313 mIU / L (N: 0.35-4.94) and free T4 at 14 pmol / L (N: 10.7-18.6). Uremia is at 23 mg / dL (N: 15-55) and serum creatinine at 0.8 mg / dL (N: 0.55-0.87). A urinary spot shows a urine creatinine at 3.36 g / L (N: 0.24 - 3.92), a protein-to-creatinine ratio at 0.11 g / g (N <0.5), a natriuresis at 23 mEq / L and kaliuresis at 27.7 mEq / L.

Aim

To feel more comfortable with the management of the complaint of loss of strength and to better undersand the hypokalemic periodic paralysis which is the most frequent periodic paralysis.

Methods

Review of the literature concerning the loss of strength without disturbance of sensibility.

Results

In front of an objective generalized loss of force, more proximal than distal, several etiologies must be considered: myasthenia, metabolic myopathies and periodic paralysis. Anamnesis and biology reveal, for our patient, a high probability of hypokalemic periodic paralysis. A biological control confirming the hypokalemia (2.1 mmol / L), the patient benefits, in his perfusion of Hartmann with 5% glucose, complements KCl 60 mEq / L. In spite of the improvement of the symptoms the next morning, a control of the kalemia shows the persistence of a hypokalemia at 2 mmol / L, probably due to the glucose in the perfusion, reinforcing our initial hypothesis of hypokalemic periodic paralysis. The stop of this perfusion and the oral potassium complementation (Chloropotassuril) is then proposed. A control performed 8 hours later shows a clear normalization of the kalemia to 4.8 mmol / L. Given the normal renal function and urinary spot, allowing excluding a secondary hypokalemia, a genetic analysis looking for a mutation of genes SNC4A and CACLN1A3 is launched (results still not known). The patient is discharged from the hospital with a treatment in the form of prolonged-release KCl, a low-salt diet as well as the recommendation to practise a regular physical activity.

Conclusions

Once the confirmation of the loss of strength reported by the patient, a differential diagnosis based on the location of this one, the anamnesis and additional examinations can be built. The hypokalemic periodic paralysis is the most frequent periodic paralysis and the first crisis occurs between the age of 2 and 30 years with for average age 14 years. So, this is an entity who must be particularly well remembered at all paediatricians.

B 06

Symmetric thalami hypodensity on T2-weighted images: a pathognomonic sign of GM1 gangliosidosis

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Introduction

GM1 gangliosidosis is a lysosomal storage disorder due to Beta-galactosidase deficiency. The diagnosis of GM1 gangliosidosis is confirmed by the GLB1 gene molecular testing. However, before this final step, an extensive workup is needed. Pathognomonic signs on neuroimaging can lead quickly to the diagnosis and must be searched. We report here the case of a young boy with a typical MRI presentation of type 1 GM1 gangliosidosis.

Aim

To highlight that MRI can give the answer facing a differential diagnosis of storage disorders.
To describe our imaging findings as few cases with these typical signs are reported in the literature.

Methods

We report here the case of a young boy of 1 year of age. He was born at 36 weeks 6/7 of gestational age. Oligoamnios occurred at the end of pregnancy. At 3months old, his pediatrician started to worry about persistent hypotonia and eye contact absence. He was referred to a neuropediatrician. At 7 months, clinical evaluation demonstrated mongoloid spots on his back, hypotonia, no visual eye contact, facial dysmorphism, gingival hypertrophy and hepatomegaly. Metabolic disorder was suspected and an extensive workup was started. Ophthalmologic examination showed cherry red macular spots. MRI neuroimaging was performed. Symmetric thalami hyperintensity on T1-weighted and hypointensity on T2-weighted images were observed. Caudate nuclei and putamina presented hyperintensity. Decreased myelination was observed globally in white matter. Those findings where highly suggestive of GM1 gangliosidosis. Spectroscopic analysis also showed decreased NAA in the thalami. Four months later, type 1 GM1 diagnosis was confirmed by decreased beta-D-galactosidase activity (0,08 nmol/mg/min, range 0,3-7,4) and genetic confirmation. Two mutations were detected in the GLB1 gene, including one known to be pathogenic.

Results

Metabolic disorders are part of the differential diagnoses of infantile hypotonia. Ophthalmologic examination showing cherry red macular spots are compatibles with storage disorders such as Nieman-Pick disease, sialidosis and GM1 and GM2 gangliosidosis. Neuroimaging can lead to the diagnosis as GM1 gangliosidosis present typical alterations. However, few cases with typical MRI presentations were reported.
Neuroimaging pathognomonic features for GM1 gangliosidosis were described for the first time in 1994. T2-weighted images showed thalami hypointensity combined with hypointensity in basal ganglia. Hyperintensity was observed on T1-weighted images. This alteration is suspected to be caused by diffuse dysmyelination leading to a symmetric thalami signal change: hyperintense on T1-weighted and hypointense on T2-weighted images. Decreased T2 signal is a sign of lysosomal storage disorders or more rarely of ceruloplasmin deficiency with hemosiderosis. However, symmetric alteration is pathognomonic of GM1 gangliosidosis. Caudate and lenticular nuclei

anomalies seen in our patient have also been reported in another case report. Reduction of NAA in the thalami was also reported once and is thought to be related to damage or even loss of neuroaxonal tissue.
If these images are present, diagnosis of GM1 gangliosidosis is confirmed.
The incidence of GM1 gangliosidosis is about 1/100000 - 1/200000. There are three clinical phenotypes according the severity and the age of presentation. Type 1 manifests during the first months of life, type 2 in early childhood and type 3 concerns adult's population. The severity is linked to the residual beta-D-galactosidase activity. Type 1 life expectancy is limited about 2 or 3 years of age. Major hypotonia develops with impaired breath capacity. Patients are at high risk of severe pulmonary tract infection and food inhalation. Death usually occurred by bronchopneumonia within the 2 or 3 first years of life. The diagnosis is based on the residual activity of the beta-D-galactosidase and on the GLB1 gene mutations. These evaluations can be done only with high suspicion of GM1 gangliosidosis. Presence of these pathognomonic alterations on MRI are then highly valuable.

Conclusions

Neuroimaging is part of neurologic evaluation for patients with hypotonia. However, it is rarely the key to the diagnosis. We report here the case of a young boy with GM1 gangliosidosis for whom the diagnosis was greatly helped by the MRI findings. Typical T2 symmetric thalami hypointensity and T1 hyperintensity must be evaluated by trained radiologist. This is a pathognomonic sign of GM1 gangliosidosis. Also, altered signal in putamina and caudal nuclei should make consider this diagnosis. We think these findings could help in the differential diagnoses of lysosomal disorders.

B 07

Melkersson-Rosenthal Syndrome - Unusual cause of recurrent peripheral facial palsy: a case report.

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Introduction

Melkersson-Rosenthal Syndrome (MRS) is a rare neuro-cutaneous disorder usually seen in adults but can rarely occurs during childhood. Patients with MRS classically presents with persistent or recurrent orofacial edema, relapsing facial palsy and fissured tongue. Classical triad is rarer than incomplete forms: clinical presentations are more commonly monosymptomatic or oligosymptomatic, making this unusual diagnosis even more difficult.

Aim

The purpose of this case report is to present Melkersson-Rosenthal Syndrome in children.

Methods

Here we report the case of a child with recurrent facial palsy who was finally diagnosed with MRS.

Results

Case report:

A 9-year-old girl presented in our department with recurrent peripheral facial palsy since she was 7. Each episode was unilateral but could occur on both side separately. She had no significant personal or family medical history.
On the fourth episode, physical examination showed a left orofacial edema, an incomplete left eye closure, a nasolabial fold deviation with mouth asymmetry and a mild macroglossia without fissured tongue.
Serological testing were negatives for HSV and borrelia burgdorferi. Acute phase reactants were negatives. No IgE elevation. Sarcoidosis was excluded.
Viral and bacterial cultures were negatives in cerebrospinal fluid as was PCR for HSV1 and HSV2. Cerebral magnetic resonance imaging (MRI) was normal. She was treated with methylprednisolone, quickly tapered associated with artificial tears and physiotherapist. She recovers slowly and unfortunately only partly.
In front of a recurring facial palsy associated with normal clinical workup, we finally decided to perform a lower lip biopsy. A Miescher granulomatous macrocheilitis confirmed then the diagnosis of Melkersson-Rosenthal Syndrome (MRS).

Discussion:

The causes of facial nerve palsy are numerous: congenital, infectious, neoplastic, traumatic, or idiopathic. The most common cause, found in approximately half of the cases, is the Bell's palsy. It is an acute facial nerve palsy of unknown cause. Serologic testing for Lyme disease is recommended for all children with acute onset facial palsy when exposure is possible. No further study is needed for patients with a typical facial palsy and a fully recover. Neuroimaging or lumbar puncture are indicated if physical signs are atypical and help to research an underlying etiology. In our case those additional investigations were realized because of the slow recovery and the recurrence. When facial paralysis is recurrent, other clinical findings should be actively

research and unusual causes should be evoked such as MRS.
Due to the low incidence of this disease and to the incomplete forms of presentations, a delay in diagnosis is frequent. MRS diagnosis is based on the association of one or two clinical features and on the presence of Miescher granulomatous cheilitis in lip biopsy. Granulomatous cheilitis can also be found in other diseases as Crohn disease, sarcoidosis, or tuberculosis so those diseases need to be ruled out.
Etiology and pathogenesis of MRS keep unclear. Various factors such as genetic predisposition, infections, immune deficiency, atopy and stress have been suggested but not clearly proved.
Thus far, treatments of MRS keep unknown and unproved. H1 and H2 antihistamines, corticosteroids, nonsteroidal anti-inflammatory drugs, anabolic drugs and antibiotics have been used. Corticosteroids remain the first-line treatment with a good response in the reduction of orofacial swelling.
Intra-lesional corticosteroid administration or surgical decompression of the facial nerve through its bony canal are other therapeutic options.

Conclusions

MRS is a rare cause of recurrent peripheral facial palsy. The diagnosis is difficult and should be evoked when palsy relapses, especially if associated with orofacial edema or fissured tongue and without clear other etiology.

B 08

Third cranial nerve palsy in children, about 3 cases.

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Introduction

Third cranial nerve palsy is rare in childhood. As a reminder, the third nerve innervates the levator muscle of the eyelid, four extraocular muscles (medial rectus, inferior rectus, superior rectus and inferior oblique) and the constriction of the pupil through its parasympathetic fibers.
Palsy of the III symptoms can be diplopia, ophtalmoplegia, ptosis, blurred near vision, mydriasis pupil. Third nerve palsy can be isolated or associated with others neurological symptoms.

Aim

Nerve dysfunction may start with the same phenotype but have different etiologies. Third nerve palsy may be the first sign of a deadly intracranial process.
Reasons for a third cranial nerve palsy car be either congenital, what is the most frequent reason (third to a half of pediatric III palsy), or be acquired after a head injury, a neoplasia, a infection, a post-viral infection, a inflammation, a migraine or an intracranial vascular disease which is rare in the pediatric population.

Methods

We would illustrate 3 pediatric patients disclosing third cranial nerve palsy, who recovered with the adequate treatment.

Results

Patient 1: 2 years-old-boy, suddenly ptosis and limitation in adduction and elevation of the left eye. Cutaneous eruption on the left knee.
- Biology: Leucocytes: 7.51 G/L - CRP 0.63mg/L - VS 12mm/h
- Lumbar punction : 8 leucocytes - proteins 0.20g/L - glucose 44mg/dl , persistent intrathecal secretion of oligoclonal, Borrelia burgdorferi-specific IgG
- Magnetic resonance imaging : neuritis (left nerve III, right and left nerve V)
- Diagnosis : neuroborreliosis
- Treatment : Ceftriaxone IV - 14 days
- Recovery : rapid after 48 hours of treatment

Patient 2: 4 years-old-girl, suddenly right ptosis, diplopia and ocular pain.
After 1 day, progression to hemiparesis of the upper limb and lower left limb and areflexia.
- Biology: Leucocytes: 6.97 G/L - CRP 4.1mg/L - VS 16mm/h
- Lumbar punction: 6 leucocytes - albuminocytologic dissociation
- Magnetic resonance imaging : meningo-polyradiculo-neuritis
- Slowing of conduction velocity
- Diagnosis : atypic Guillain-Barre
- Treatment : intravenous immunoglobulin 1g/kg/j - 2 days
- Recovery : slowly, after 7 days - diminution of ptosis, persistent areflexia

Patient 3: 11 years-old-boy, ophtalmic migraine at first, no recovery and then suddenly right ptosis.
- Biology : Leucocytes: 3.71 G/L - CRP 4.2mg/L
- Lumbar punction: 1 leucocyte
- Brain scanner : normal
- Magnetic resonance imaging: right schwannoma on the cisternal path of the third

nerve.
- Treatment :Medrol per os (1 month)
- Recovery: total recovery of symptoms

Conclusions

Third cranial nerve palsy is a rare condition in childhood,
A complete neurological examination is mandatory.
It is important to remember that it can be the first sign of progressive multiple cranial nerve dysfunction as shown in patient 2.
That's why an ophthalmologic assessment and neuroimaging (MRI is more sensitive) is necessary in the evaluation of third cranial nerve palsy. The prognosis and the treatment depends on the etiology. The development of amblyopia is the major complication of the ptosis and requires early treatment with patching at first.

B 09

Peri-cerebral effusion in infant: diagnosis and management

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Introduction

Introduction:

In paediatrics, growth curve about weight, height and head circumference is one of the most important aspect of the follow-up.
Macrocephaly is defined as a head circumference above 97 percentile according the age of the patient. However, the paediatrician should be worried as soon as the head circumference crosses the curve of the percentile.
The macrocephaly may be one of the first sign of peri-cerebral effusions. The differential diagnosis of aetiology is large and we must be careful. The management varies depending on the aetiology, the method of presentation and the impact on the infant's development.

Aim

Case report:
The case is based on a 4-month old infant redirected to emergencies by his family doctor for macrocephaly.
The growth curve confirms this diagnosis and shows a trend in the head circumference curve since 2 months. The macrocephaly is isolated and weight and height curve was harmonious.
At the clinical examination, L. shows a severe axial hypotonia, an anterior fontanel under tension, and a disjunction of cranial sutures. His hemodynamic parameters are correct.
The cerebral CTscan show a bilateral hygroma, a left posterior hematoma as well as a left parietal hypodense lesion.
The cerebral IRM confirms the peri-cerebral effusions with subdural collection and of a cortical haemorrhagic contusion. The effusions nature highlighted by the IRM indicates blood degradation products.
A blood sample, haemostasis tests and a complete metabolic assessment do not explain these effusion. Eye fundus reveals two preretinal haemorrhages on the right side. A complete radiology of the skeleton does not exhibit any bone lesion.
Considering the importance of the effusions, a temporary and bilateral subdural drainage brought back a hemorrhagic fluid.
With all those elements, a traumatic aetiology is the first hypothesis.
It has to be noted that L. was hospitalized two months ago in the context of gastroenteritis and sepsis without fever. A complete check-up including a lumbar punction and a trans-fontanellar echography could not bring explanation of the sepsis status. The conclusion was viral gastroenteritis associated with an allergy to cow's milk protein.

Results

Discussion:

Macrocephaly can be fortuitoud discovery during general screening of patient or could be discovered in a context of infection, traumatism, neurological disorder.
Peri-cerebral effusions are usually caused by subdural hematomas (less frequently extra-dural) following traumatisms. Minor traumatisms in the context of external hydrocephaly might also provoke subdural hematomas. Rarely an infectious syndrome or a severe dehydration may also be responsible of those bleedings.
These can subsequently lead to disorders in the cerebrospinal fluid resorption or

sub-arachnoid effusion.

The anamnesis of neonatal history, (micro)traumatisms, and the context in which symptoms appeared is crucial. The evolving characteristic of macrocephaly and the association with a psychomotor retardation should be researched.
A familial anamnesis and the measurement of parents' head circumference is necessary to exclude the hypothesis of a familial benign macrocephaly.

The diagnosis requires brain imaging (MRI is the exam of first choice but sometimes not accessible at first step), blood sample with advanced haemostasis check, a metabolic check-up and copper dosage, eye fundus and bone radiography.

If the blood sample is completely normal, the highlight by imaging of various ages lesions, association of peri-cerebral collection and of parenchymatous lesions is a solid argument for a traumatic aetiology.
This hypothesis must be discuss with the parents. It is also important to look for history of medical consultation during which the state of the infant worried the medical team.
According to the evolution of the head circumference, the signs of intracranial hypertension and the impact on the psychomotor development, we proceed to a ponctual, temporary or definitive drainage.

Conclusions

Conclusion:

Discovery by imaging of peri-cerebral effusions in the context of progressive and secundary macrocephaly requires MRI to study the nature of the effusions and to look for parenchymal lesions.
The hypothesis of an external and benign hydrocephaly should be investigated but be excluded by signs of intracranial hypertension and impact on the psychomotor development.
In case of a traumatic effusion, the check-up should exclude coagulation disorder, metabolic disorder or any pathology which could cause bleedings. This has to be fulfilled by an eye fundus, a skeleton radiography and a oriented anamnesis. A psychosocial check-up seems meaningful.
The drainage treatment shall be decided considering the evolutive characteristic of the macrocephaly and the impact on the psychomotor development and the parenchyma.

B 10

Intracranial aneurysm in a 9 year old girl : A case report and literature review.

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Introduction

Intracranial aneurysms are extremely rare in children. They can be an isolated disease or associated with other medical conditions. We report the case of a 9 year old girl who presented with a ruptured cerebral aneurysm. We also conducted a brief literature review in the field.

Aim

Our aim is to summarize recent findings regarding the epidemiology, presentation and treatment of pediatric intracranial aneurysms.

Methods

We conducted a literature review by using the PubMed database and by searching for articles published after 2000.

Results

Summary : A 9 year old girl, with clear medical history, presented in the emergency department with sudden headache followed by a brief loss of consciousness and vomiting as well as alteration of her general condition. A computer tomography and magnetic resonance of the brain revealed a subarachnoid hemorrhage in the right parietal region and a 7 mm aneurysm of the left posterior inferior cerebral artery. The aneurysm was confirmed by cerebral angiography and an endovascular treatment with stent-assisted coiling was conducted. The patient received oral Nimodipine for 3 weeks for prevention of vasospasm sequelae and antiaggregant treatment (oral Clopidogrel and Acetylsalicylic acid). Multiple diagnostic exams were conducted so as to exclude other risk factors and comorbidities. She was discharged after two weeks with no complication during hospitalization.
Pediatric intracranial aneurysms are very rare. They account for less than 5% of the total number of patients with aneurysms. In a recent review article, a total of 573 patients are mentioned in the period between 2000 and 2015. There is a male predominance. The etiology and precise pathophysiologic mechanism remain unclear, but there are several cases of post-traumatic or infectious etiology (for example bacterial endocarditis, septicemia) and it is suggested that they should be thought of as a vessel wall disorder rather than a luminal disease. Most of the aneurysms are symptomatic with the commonest clinical presentation being subarachnoid hemorrhage, followed by mass effect neurological symptoms and unspecific symptoms, predominantly headache. Rarely, they are detected as an incidental finding during cerebral imaging in the frame of other medical conditions. Conventional angiography is the definitive procedure for the detection and characterization of cerebral aneurysms. Almost 75% of the aneurysms are located in the anterior circulation and the most common vessels are the internal carotid artery and middle cerebral artery. In the posterior circulation, the basilar artery is the most common parent vessel. The treatment is either microsurgery for aneurysm occlusion with cerebral bypass, which is the commonest option, and endovascular treatment with coiling and stent-assisted coiling. Vasospasm is reported in approximately 10% of the cases, but delayed cerebral ischemia is not frequent (less than 20% in case of vasospasm). Sometimes treatment with Nimodipine, induced arterial hypertension, and hypervolemia is applied. Comorbidities are often reported, such as polycystic kidney disease, aortic coarctation sickle cell anemia, type IV Ehlers-Danlos syndrome, collagenopathy, Takayasu's disease and Kawasaki syndrome. Favorable outcomes

are achieved in most of the pediatric cases.

Conclusions

Pediatric intracranial aneurysms are a rare disease and there are differences by the ones found in the adult population. Better understanding of their etiology and pathophysiology as well as implementation of high quality clinical studies are necessary so as to make evidence-based treatment decisions and to achieve best outcomes for the young patients.

PULMONOLOGY

Oral Presentations

P 01

A Novel Imaging Technique for Bronchopulmonary Dysplasia: Functional Respiratory Imaging.

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Introduction

Bronchopulmonary dysplasia (BPD) is a common complication of premature birth. However, little is known about the long-term consequences of this disease. Lung function testing and different imaging modalities are classically used to assess the severity of BPD. Functional Respiratory Imaging (FRI) is a relatively new technique based on High Resolution Computed Tomography (HRCT) and Computational Fluid Dynamics (CFD) that combines a structural and functional assessment of the airways and their vasculature.

Aim

The aim of this study is to assess BPD with FRI and correlate these analyses with the clinical presentation.

Methods

We included 37 patients, 22 patients with BPD and 15 without BPD. All patients were born before 31 weeks gestational age, were admitted to the NICU and needed ventilatory support immediately after birth. These patients, now aged 13 to 16 years old, were included in the present follow-up study including a detailed history (assessed through questionnaires), lung function testing and HRCT (at TLC and FRC) with FRI. The CT images were also assessed with the Aukland scoring system by a radiologist who was blinded for the outcome.

Results

BPD patients had significantly lower birth weights (p=0,04), lower gestational age (p<0,01) and more often received surfactant in the neonatal period (p=0,04) compared to matched controls. The Tiffeneau index was lower in adolescents with BPD, even after administration of a bronchodilator (p=0,02 and p=0,04 respectively). Patients with BPD also had impaired diffusion capacity (p=0,02).
The Aukland CT score was not different between both groups. Patients with frequent respiratory symptoms (e.g. wheezing, waking up at night, dyspnea, exercise intolerance, nocturnal cough) had significantly higher total CT scores (p<0,01) and

more air trapping (p=0,05). FRI and CFD showed higher lobar volumes in BPD patients, especially when measured at FRC (p<0,01). When measured at TLC, the differences were not significant. Airway resistance was also significantly higher in the BPD group, more particularly in the distal part of the lungs. Additionally, FRI indicated significantly more air trapping in BPD patients; this in contrast to findings on conventional CT images. There was no significant difference in vasculature between both groups.

Conclusions

This study is the first to use FRI in research for BPD. CFD analysis showed higher lobar volumes in BPD patients, which indicates hyperinflation and reduced inspiratory capacity. BPD patients also have more air trapping. Interestingly, FRI seems to be a more sensitive way to detect air trapping than regular CT-analysis. To our knowledge, this is also the first study that demonstrates higher resistance specifically in the peripheral airways of BPD patients. FRI is a promising new imaging technique for BPD, combining a structural and functional assessment. This combined approach might lead to a better understanding of the pathophysiology of BPD.

P 02

Intrapleural use of tissue plasminogen activator and dornase alfa are successful as treatment of pediatric empyema: a pilot study.

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Introduction

No consensus is present regarding the treatment of parapneumonic empyema (PPE) in children. Intrapleural fibrinolytics offer benefit over chest tube drainage while video-assisted thoracoscopic surgery (VATS) is most commonly performed. No significant differences in outcome are seen between fibrinolytics and VATS although VATS has higher costs. Adult studies reported less surgery and reduced hospital stay with intrapleural combination of tissue plasminogen activator (tPA) and dornase alfa (DNAse) as treatment for empyema.

Aim

The purpose of this study was to determine whether intrapleural treatment with tPA-DNAse is safe and successful in children with empyema.
Methods
Previous well children diagnosed with PPE >= 1/4 of hemithorax (chest X-ray) or complicated effusion entered the treatment arm. After chest tube insertion, intrapleurally tPA 0.15 mg/kg for 3 days and DNAse 2.5 mg for 2 days was given after which the chest tube was clamped for 4hours. Primary outcomes were safety and the need for additional surgery.

Results

With respect to in-and exclusion criteria, 8 consecutive children were included (3 boys; mean age of 5yrs - range 2.3 to 15.0). No adverse events were seen. One child developed urticaria but additional intervention or cessation of the trial was not needed. There was no bleeding or mortality and no additional procedures were performed. The mean hospital stay after intervention was 10±7.0 days. The mean chest tube duration was 7±4 days. Mean oxygen therapy was 5±4 days after tube insertion.

Conclusions

This pilot study investigated the efficacy and safety of tPA and DNAse as treatment of empyema in a small consecutive series of children with PPE. With this study, we can conclude that intrapleural fibrinolysis with tPA and dornase is safe and successful as demonstrated in adults. Therefore, the series will be expanded in preparation of comparative studies.

P 03

A case report of a tracheoesophageal fistula successfully managed by Chemocauterization.

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Introduction

Tracheoesophageal fistula (TEF) occurs as a common complication after primary repair of esophageal atresia. Many surgical and endoscopic techniques have been developed to reduce the risk of complication associated with thoracotomy or cervicotomy. Since 2008, a few studies described chemocauterization as an effective, simple and safe procedure for treatment of TEF. However, different methods were described and studies included small numbers of patients. Recently, the efficacy of 50% trichloroacetic acid was evaluated as minimally invasive technic for the management of TEF. This technique, little used in Belgium, is exposed here.
We describe the case of a 14 month-old Caucasian girl born at full term after normal pregnancy. She presented an esophageal atresia type C and benefited from an uncomplicated surgical correction by thoracotomy during her first day of life. She developed an esophageal stenosis at 3 months of life, successfully treated by endoscopic dilatation. During the next months, she presented a persistent respiratory congestion with two bronchitis and one bronchopneumonia treated by antibiotics. She was referred to our pediatric pulmonology department at 14 months of age. The physical exam showed an eupneic child with moderate respiratory congestion. Decision to perform a combined bronchoscopy and gastroscopy was taken. The bronchoscopy revealed the presence of a tracheal dyskinesia and a recess in the upper third of the trachea. The gastroscopy showed a suspicion of fistula which was confirmed by the blue methylene test. At the age of 19 months, the patient benefited from a rigid bronchoscopy with chemocauterization. After precise location of the TEF, the fistula was chemocauterized three times with cottons soaked in 50% trichloroacetic acid. Each cotton was applied between 30 and 60 seconds. There was no local or general complication. A bronchoscopy with blue methylene test performed one year later didn't detect any sign of recanalization. This technique was performed in four other patients who still need to be re-evaluated.
Chemocauterization with 50% trichloroacetic acid is a simple and effective technique for the management of TEF. It is a promising minimally invasive procedure which avoids the morbidity of open surgery.

P 04

Pulmonary embolism in childhood and adolescence: an often forgotten diagnosis.
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Introduction

Pulmonary embolism (PE) in the pediatric population is relatively rare compared with adults but evidence suggests it is underestimated. The diagnosis often comes late even though typical clinical features might already have appeared.

Aim

We want to raise awareness by means of a case report the medical community in the diagnostic of PE at the child. This diagnosis has to be considered for children with evocative clinical features.

Methods

We present the case of a 14 years old teenager hospitalized for dyspnoea MRC3 ans palpitations that had been evolving for 1 month and who has been taking an oral contraception for 3 months. At the time of the hospitalization, after visits to the general practitioner, she complained about unbreath dependent retrosternal thoracic pain, effort related presyncopal weaknesses and a left lower limb pain stronger in the calf that appear one week ago. The clinical examination shows a painful palpation of the left calf and the left thigh. The diameter of the left limb corresponds to 3 cm. The clinical features evoke a PE. We proceed to a full check-up to confirm this diagnosis and to find all risk factors. We realize a Wells score and a Geneva score revised to assess the clinical probability of PE. We perform a doppler pelvis ans lower left limb, a CT pulmonary angiography and a thoracic echocardiography. We also carry out a blood test and we ask for an hematologic opinion.

Results

Wells Score is rated at 3 and attests to a high clinical probability of PE. The Geneva score revised is rated at 10 and attests to an intermediate clinical probability of PE. The diagnosis is confirmed by the imaging investigations that show a bilateral PE and a deep vein thrombosis (DVT) that spreads from the left iliac vein to the left popliteal vein. Finally, besides oral contraception, the hematological check-up highlights factor V Leiden mutation. So this teenager has two risk factors for venous thromboembolism. After the diagnosis has been confirmed, we start a low molecular weight heparin (LMWH) therapy from the beginning of the hospitalization.

Conclusions

Pulmonary embolism is a rare, but potentially fatal, condition that often goes unrecognised among the pediatric population. It is important not to underestimate the likelihood of pulmonary embolism for a teenager whose clinical features are obvious

and who has one or more risk factors.
An oral contraception must be considered even among teenagers as a risk factor for venous thromboembolism.
The search for underlying risk factors and previous DVT or EP in family and personal history must be systematic when the patient has typical clinical features.

P 05

Severe paradoxical reaction during anti-tuberculosis therapy: a report of two related infants.

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Introduction

Paradoxical reaction (PR) during anti-tuberculosis therapy (ATT) is the clinical or radiological worsening of findings in a patient who initially improves. PR is an exclusion diagnosis whose incidence would be around 10-14% in the pediatric population. Some risk factors have been reported in pediatric studies in immunocompetent children, that is young age, low weight, high initial bacterial load and BCG-unvaccinated status. Gangliopulmonary form of tuberculosis (TB) is particularly affected.

Aim

We report two clinical cases to analyse others factors that may explain PR.

Methods

Retrospective, descriptive, cases study. Data were abstracted from medical records.

Results

Case 1. A 6-month old HIV-negative male infant born in Belgium from Cameroonian parents presented with a 1-month history of persistent cough. Previous medical history was uneventful, BCG vaccine was not administered. Clinical examination revealed tachypnea, subcostal retractions, pharyngitis, mild crackles and wheezes diffusely. His weight was at the 99th centile. Chest radiograph (CXR) demonstrated left upper lobe infiltrate with hilar enlargement. Tuberculin skin test (TST) showed a 23 mm induration. Gastric aspirates were smear negative but grew drug-susceptible Mycobacterium tuberculosis (M.tb.). A three-drug ATT was started. Twenty days after ATT initiation, the infant developed progressive stridor, wheezing and dysphonia. While, 2 weeks later, flexible nasopharyngolaryngoscopy (NPL) was attempted, he suffered cardiorespiratory arrest requiring intubation and mechanical ventilation. Chest computed tomography (CT) revealed right tracheal shift with voluminous mediastinal lymph nodes and left upper lobe parenchymal consolidation. Trachea narrowing was not observed due to endotracheal tube. Diagnosis of PR was suspected, and methylprednisolone 2 mg/kg/day was added to his ATT. Nine days later, he was extubated and recovered spontaneous breathing. Methylprednisolone was tapered off over 4 weeks and two-drug ATT started, as scheduled, 70 days after ATT initiation. Control chest CT showed a significant regression of the lymph nodes mass with normal airways appearance.

Case 2. Two days later, a 2-month old HIV-negative male infant born in Belgium from Cameroonian parents presented with fever and cough for 2 days. He was the cousin

of the previous case and lived in the same house. Perinatal period was uneventful, he was not BCG-vaccinated. Examination revealed tachypnea. Weight was at the 70th centile and temperature of 38,2°C. CXR revealed middle lobar opacity with hilar enlargement of lymph node. A 12 mm TST induration was measured. Gastric aspirates were smear negative, but one grew drug-susceptible M.tb.. He was started on three-drug ATT. After 60 days of well-conducted therapy, he developed cough, stridor, subcostal retractions and again tachypnea. Chest CT demonstrated large multilobulated right hilar and paratracheal lymph nodes causing significant narrowing of the distal trachea and the right primary bronchus with parenchymal consolidations in middle and right upper lobes. The patient was given empirical antibiotherapy to overcome possible bacterial superinfection. However, PR was diagnosed, and methylprednisolone was added 3 days later to his treatment. Symptomatic improvement was observed 2 days after corticotherapy was started, which was pursued for 7 days before tapering off over 3 weeks. The transition to two-drug ATT occurred 70 days after its initiation. Given the excellent clinical and biological evolution, control imaging was not considered necessary.
During both deterioration incidents, endotracheal and gastric aspirates were collected and revealed smear positive in the oldest boy, but cultures did not grow M.tb. in any cases. Besides, a transient viral nasopharyngitis coincided in the two boys with the clinical deterioration observed during ATT. M.tb. strains isolated from the two specimens revealed fully matching genotypes, confirming involvement of a single LAM10-CAM lineage strain in both diseases.

Conclusions

Investigations about both cases demonstrate the severity and the potentially lethal nature of airway compression mediated by PR complicating gangliopulmonary TB in very young children.
Involvement of the same M.tb. strain in both infants, raised the question about the existence of strain types prone to induce PR. Literature and studies over this hypothetical link are extremely poor and inconclusive. Young age, low weight, large initial bacterial load and BCG-unvaccinated status have been identified as PR risk factors. While pediatric TB is usually paucibacillary, positive cultures, in our two cases, suggest a non-negligible bacterial load at TB diagnosis which may have contributed to a hypersensitive response against massive antigens exposure following ATT.
However, large bacterial load could also reflect some level of immunodeficiency occasioned by the M.tb. strain itself and/or present constitutionally.

P 06

Diffuse alveolar hemorrhage in an infant: a case report.

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Introduction

Aim

Case report:
We report the case of 2 infants aged 3- and 7-weeks, respectively. They were previously healthy full terms newborns, who presented hemoptysis, pallor, sudden dyspnea and cough. Initial laboratory investigation showed moderate anemia and moderate metabolic acidosis. Both babies had diffuse infiltrates on chest x-ray. Computed tomography scan revealed interstitial lung disease in the first baby and consolidated opacities in the second one. For both babies' blood transfusion was deemed necessary. Flexible bronchoscopy provided visualization of areas of active bleeding. Bronchoalveolar lavage has been sent for cytologic and culture analysis. Interestingly, hemosiderin-laden macrophages were not found in both cases. However, chlamydia trachomatis was identified in the first baby. Further investigation was non-contributive. The first baby was diagnosed with a diffuse alveolar hemorrhage due to an infectious agent and received antimicrobial therapy. For the second baby, as no underlying pathology was found, the diagnosis of idiopathic pulmonary hemosiderosis was suspected and thus, corticosteroid therapy and hypoallergenic diet were started. After discharge from the hospital, the two babies are well and closely followed-up in the outpatient clinic of out department.
Methods

Results: Discussion:

Bleeding into the alveolar spaces of the lungs characterizes the syndrome of diffuse alveolar hemorrhage (DAH) and is due to disruption of the alveolar-capillary basement membrane. This disruption is the result of injury or inflammation of arterioles, venules or alveolar septum capillaries. Hemoptysis is the usual presenting symptom, but is not cosntant. A variety of diseases are associated with the development of the DAH. Current classification schemes organize the etiologies of DAH on the presence or absence of pulmonary capillaritis. Disorders associated with pulmonary capillaritis may include severe immune disorders such as systemic vasculitis (systemic lupus erythematosus, Goodpasture syndrome, Henoch-Schönlein purpura..). In addition, disorders not related to pulmonary capillaritis may be of cardiac- or non cardiac origin (Heiner syndrome, celiac disease, infections, coagulation disorders..) or be idiopathic disorders.

Conclusions

We report two cases of DAH. In children, a careful evaluation and early diagnosis of an underlying infection is critical to implement the necessary antimicrobial treatment. Additionally, idiopathic pulmonary hemosiderosis is a rare clinical entity of unknown etiology that the pediatrician should consider in DAH cases. Furthermore, it is important to remember that the latter can exist isolated, but more commonly in association with an underlying condition. New and more extensive investigations with

immune and allergic checkup will be needed for the early detection of underlying condition.

P 07

Digital clubbing in a seven-year-old boy born in Burundi.

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Introduction

Digital clubbing is an uncommon finding, but can be observed in children with chronic lung disease, associated with inflammation or hypoxemia, as well as, in children with chronic non-pulmonary pathology involving heart, liver, intestines and in certain conditions of immunodeficiency. Congenital clubbing has also been described (without underlying disease).

It is regarded to be one of the oldest signs in medicine (Hippocrates nearly 2500 years ago)

Digital clubbing is characterized by loss of the normal Lovibond angle, and mostly seen in a mild or moderate stage in children. Clinical examination with attention to the nail bed is helpful in a better understanding, as it reflects the chronic course of an underlying disease.

HIV infection continues to pose challenges in diagnosis and management and remains an infrequently encountered infection for many paediatricians in non-endemic areas. Lymphocytic interstitial pneumonia (LIP) is on the spectrum of lymphoproliferative diseases that can affect the lungs in HIV infected children. LIP occurs in slow progressors and is associated with a relatively preserved CD4 cell count. This condition is seen in older children and it is thought to be a lymphoproliferative response to HIV or Epstein-Barr virus (EBV). Anti-retroviral therapy often leads to complete healing.

Aim

We report about 7-year-old boy born in Burundi who presented with important digital clubbing and worsening dyspnea over a period of 8 months.

Methods

Good clinical examination was a key point in the diagnosis. Additional tests as chest CT scan, tuberculin skin test, bronchoscopy, serological tests, pulmonary function tests, immune evaluation and lung biopsy were performed.

Results

The boy 7-year-old was born in Burundi. At the age of 8 months, he was administered a blood transfusion in the context of severe malaria infection. He immigrated to Belgium at the age of 9 months and got all recommended vaccinations including BCG vaccine. He remained healthy until the age of 4 when he developed repetitious respiratory infections. Pneumococcal pneumonia with sepsis was documented at the age of 6. Further examination by chest CT scan revealed bronchiectasis and disseminated pulmonary micronoduli, for which he was referred for a bronchoscopy.

Clinical examination showed beside tachypnea and crackles over both lungs an

important digital clubbing, however with normal blood gasses and a normal oxygenation. Bronchoscopy showed mucosal inflammation, uncolored secretions and negative cultures. Tuberculin skin test was negative. Chronic lung disease of unknown origin was believed to be the cause of digital clubbing as other features such as cystic fibrosis, primary ciliary dyskinesia, cardiac disease, liver disease...) were ruled out. Immunophenotyping on peripheral blood was normal, except for a decreased CD4/CD8 (0.44) with normal CD4 T-cell count (725 cells/uL) and percentage (22.5%). HIV work-up was not part of the initial screening. Serologic response against tetanus and pneumococcus was also suboptimal.
A few months later, the boy presented a new respiratory distress with drop of forced expiratory volume (FEV1) from 60% to 30%predicted, again due to a pneumococcal pneumonia.
Additional work-up revealed a positive HIV-1 serology. CD4 T-cell count was still within normal range (589 /mm3) but with persistent decrease in CD4/CD8 ratio. HIV-1 plasma viral load was determined at 93.400 copies/ml.
Based on a preserved CD4 T-cell count, an AIDS defining diagnosis was less likely. PCR for Epstein-Barr-virus was also positive. The radiologic findings together with digital clubbing and documented HIV infection led to the suspicion of a lymphocytic interstitial pneumonia (LIP). The latter was confirmed by lung biopsy.

Conclusions

Careful physical examination remains an essential key finding the diagnose. Digital clubbing might be the only clinical sign of a severe underlying chronic disease and requires further work-up.
The described case is a typical feature of HIV-related lung pathology (LIP) in the child, where digital clubbing played an important role in the diagnostic work-up.

P 08

Bronchiolitis with an atypical course: which differential diagnoses to consider
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Introduction

Bronchiolitis is a common and mostly self-limiting disease. However, it may be the first presentation of underlying disease.

Aim
This abstract aims to raise awareness that an atypical course or inconsistent oxygen requirement, as subtle it may be, must be the trigger for further examinations.

Methods
We present the clinical, biochemical and radiographic data of 3 infants with (atypical) bronchiolitis.

Results
Three infants with classical signs of bronchiolitis (rhinitis, cough and dyspnea) presented at the emergency department. Ages were respectively 4, 5 and 9 months. Because of need of supplemental oxygen, all were admitted at the department of pediatrics. The 4-month-old boy had a history of previous bronchiolitis with need of additional oxygen but with adequate recovery. However, this second episode was complicated by the need of invasive ventilation and the development of atelectasis after which respiratory distress and hypoxemia persisted. The second case, a 5-month-old girl with no medical history, showed mild symptoms of disease however oxygen requirements were discrepant with hypoxemia persisting up to day 12. The last boy, had a history of recurrent chest infections with persistent nasal secretions since the start of daycare, but also persistent ausculatory findings such as crackles and wheeze. All children underwent work up including chest CT that showed 3 different findings: case 1 showed normal CT findings, case 2 showed mosaic perfusion, vascular attenuation and central bronchiectasis, case 3 had marked bronchiectasis and atelectasis of the right upper lobe. Additional work up existed of sweat test, immunological work up, pH-metry and cardiac ultrasound. The latter 2 were normal in all children. Sweat test proved to be borderline in the third case and IgG proved to be low in the first case on 2 different occasions. Therefore, the diagnosis of hypogammaglobulinemia was established in case 1, bronchiolitis obliterans in case 2 and cystic fibrosis (genetically confirmed) in case 3.
We speak of prolonged or abnormal oxygen requirement when the oxygen requirement doesn't correlate with the initially established diagnosis. Prolonged oxygen requirement is not so rare, but making the right diagnosis can be challenging as there is a broad differential diagnosis. Causes of prolonged or abnormal oxygen requirement based on the pathophysiology are: hypoventilation (e.g. neuromuscular disease), ventilation / perfusion mismatch (e.g. interstitial disease), right-to-left shunt (e.g. pulmonary hypertension), diffusion defects (e.g. lung fibrosis), circulatory problems (e.g. anemia, hypotension),...
Based on the history, clinical course and the most probably diagnosis we can consider following additional examinations to establish the diagnosis: a blood gas, Rx thorax,

CT thorax, bronchoscopy, sweat chloride test, immunological screening, lung function, cardiac ultrasound, polysomnography, consult of ENT specialist,...
Conclusions
Bronchiolitis in infants is common, with almost 100% of children experiencing at least 1 episode before the age of 2. The disease is mostly self-limiting but the clinician must be aware of an atypical course and inconsistent or prolonged oxygen requirements. Underlying disease may be serious and requiring additional therapy other than the normal supportive treatment. Based on the clinical course and history additional examinations need to be performed to establish the diagnosis as soon as possible. This can prevent progression of the underlying disease.

P 09

The prevalence of lower airway anomalies in children with Down syndrome.

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Introduction

Children with Down syndrome (DS) often present with a wide variety of respiratory symptoms that may impose a significant morbidity. Several congenital airway anomalies have been described in association with DS, but reports presenting overall prevalence are scarce.

Aim

To present the endoscopic lower airway findings and associated clinical presentation in a cohort of children with DS.

Methods

We performed a retrospective chart review of all endoscopic procedures performed under general anaesthesia (flexible bronchoscopy and/or flexible and rigid laryngoscopy) in patients with DS between 2011 and 2017. Respiratory symptoms and data on endoscopic findings were collected. We also looked at (cardiac) comorbidities and treatment following endoscopy. These findings were compared to a cohort of children without significant underlying disorder undergoing endoscopy for similar indications.

Results

Endoscopic data were available for 55 children with DS. Age ranged between 2 months and 17 years of age with a median of 3 years. Sixty-three percent were boys. Most common clinical presentation was recurrent lower respiratory infections (40%). Other reasons for endoscopic evaluation were chronic cough and/or noisy breathing (21%), stridor (20%), persistent radiographic abnormalities (11%) and respiratory failure (7%). Endoscopy was normal in 31 % of patients. The largest group of patients (44%) had some form of airway malacia (tracheomalacia, laryngomalacia and bronchomalacia respectively). Tracheal bronchus was an isolated finding in 3.64% of patients. Eighteen percent presented with a combination of airway anomalies. The proportion of airway anomalies in our cohort of DS children is significantly higher than in our control group. We also find a high incidence of cardiac comorbidities.

Conclusions

Congenital airway anomalies (isolated or in combination) were encountered in 69% of patients with DS presenting with chronic respiratory symptoms. A complete lower airway endoscopic assessment is strongly recommended in these patients as it may influence therapeutic decision making.

P 10

Idiopathic acute eosinophilic pneumonia in a teenage girl: a case report

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Introduction

We report the case of a 13-years-old girl presenting to the emergency department for fever and dyspnea.

Aim

A 13-years-old girl was admitted with a one-day history of fever and dyspnea. Her past medical history was unremarkable. She had no history of smoking and took no medication. Interestingly, she explained us having fifty birds at home.

Methods

On physical examination, she was febrile at 38,8°C with a heart rate at 142 per minute and blood pressure at 129/86 mmHg. She presented moderate respiratory distress signs with a respiratory rate of 42/min and an oxygen saturation at 89%. Chest auscultation revealed bilateral diminished breath sounds and diffuse crackles. The rest of the physical examination was normal.
Blood test showed an inflammatory syndrome with an increased C-reactive protein level at 128 mg/l and a white blood cell count at 29300 cells/mm3 with 77.5% neutrophils (22708 cells/mm3) and 8.9% eosinophils (2610 cells/mm3).
Chest radiograph showed signs of interstitial lung disease.
She was admitted to the ward where oxygen therapy by face mask and an empirical antibiotic treatment were started. Despite oxygen administration, her dyspnea worsened. Her respiratory rate increased at 60/min with heart beats at 166/min, justifying a transfer to the pediatric intensive care.
As the patient clinical status worsened, more investigations were needed. Bronchoalveolar lavage (BAL) fluid demonstrated increased cellular elements at 400.000/ml, including 47% eosinophils and 20% neutrophils. Thoracic CT-scan revealed diffuse ground glass opacities, air-space consolidations, thickened lung fissures and septa, and bilateral pleural effusions.
Idiopathic acute eosinophilic pneumonia (IAEP) was proposed as diagnosis.
Despite her initial medication, she developed a critical respiratory failure requiring invasive ventilation for 3 days. An intravenous corticosteroid therapy was initiated with shift towards the oral route for a total length of 28 days, resulting in a rapid clinical improvement. She was weaned off any respiratory support 6 days after admission.
The patient was discharged after 13 days. Chest radiograph showed no more infiltrates. Six weeks later, her lung function tests were normal for the age. To date, the patient continues to be asymptomatic.
Results
IAEP is a very rare cause of interstitial lung disease. Pathophysiological mechanisms and etiology remain poorly understood. An association between a recent onset of cigarette smoking and the disease has been previously reported. Some authors describe association between IAEP and recent exposure to inhaled agents or dusts.

The diagnosis is based on clinical, biological and radiological criteria:
1) Acute onset of febrile respiratory manifestations (< one month, and especially < one week duration before medical examination)
2) Bilateral diffuse pulmonary opacities on chest radiograph
3) PaO2 on room air < 60 mmHg or PaO2/FiO2 < 300 mmHg or pulse oxygen saturation on room air < 90 percent
4) Pulmonary eosinophilia with > 25 percent eosinophils on BAL differential cell count
5) Absence of known causes of eosinophilic pneumonia (including infection or exposure to drugs).
The treatment consists of a respiratory support, an empirical antibiotic treatment and a systemic corticosteroid therapy.

Conclusions

IAEP is an extremely rare disease in children, where diagnosis remains a challenge. It should be considered in patients presenting with an history of fever and progressive dyspnea. A ventilatory support is very often required. A BAL must be performed in any case of radiographic pulmonary opacities. This analysis and the exclusion of other causes of pulmonary eosinophilia allow to confirm the diagnosis. Early treatment with systemic glucocorticoids results in a rapid and often dramatic clinical improvement, without relapse.

P 11

Paradoxical response and hepatic dysfunction during anti-tuberculosis treatment.

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Introduction

Therapy against Mycobacterium tuberculosis (MT) disease in a child can lead to many complications. Among them, we report an infant who developed paradoxical reaction with hepatic dysfunction during her anti-tuberculosis treatment (ATT).

Aim

A Congolese 6-month-child was presented at consultation for fever since 10 days without any other symptom. She was born at term in Belgium with no relevant medical history. Calmette-Guérin bacillus (CGB) vaccination was not administered. Physical examination showed normal pulmonary auscultation. Chest radiography demonstrated a right para-cardiac infiltration. Tuberculin skin test (30mm erythema, 13mm induration) and QuantiFERON-TB dosage (antigen TB 15.52UI/mL, mitogène 13.82UI/mL) were positive. Examination by smear microscopy from gastric aspirates and bronchiolo-alveolar lavage was negative. PCR Xpert did not detect MT. Cultures did not grow. Serological tests for HIV were also negative. An index case, a native uncle from Congo, was found. He stayed during one month in the family with contagious pulmonary tuberculosis. Drug susceptibility of his MT was not available. Cousins, brothers and sisters of our patient were also infected, with a multi-sensitive MT culture. A diagnostic of high probability of pulmonary tuberculosis was made for our patient. Because of smear-negative pulmonary tuberculosis with parenchymal involvement, quadritherapy with Isoniazid (12.5mg/kg/j), Rifampin (15mg/kg/j), Pyrazinamide (30mg/kg/j) and Ethambutol (20mg/kg/j) was begun. Fever stopped after four days.

After taking correctly this treatment during one month, the child was presented with progressive inspiratory respiratory distress with wheezing, dysphagia and weightloss (6% of the weight since the onset of the disease). Thoracic and cervical CT-scan showed mediastinal adenopathies compressing bronchi and oesophagus. At this time, Rifampin-sensitive MT was detected by Xpert in nasopharyngeal aspiration. PCR on gastric aspirates remained inconclusive and MT cultures did not grow. Lumbar puncture was negative. Corticotherapy (Solumedrol 2mg/kg/j) and overfeeding by nasogastric tube were added to the treatment. A diagnostic of probable paradoxical reaction (PR) to ATT was made.

At the same time, she also developed drug toxicity with increased liver enzymes (ALT/GPT 203U/L; nv <45, AST/GOT 313U/L; nv <40, GGT 198U/L; nv 8-61, direct bilirubin 0.7mg/dL; nv <0.3). No hepatic lesion or periportal lymphadenopathy was found on abdominal echography. Antituberculosis therapy was then changed for Amikacine (15mg/kg/d iv during 5days out of 7), Levofloxacine (15mg/kg/d po) and Ethambutol. Biologic markers of cytolysis normalized in ten days and cholestasis in 30 days allowing to switch to a tritherapy with Isoniazid, Rifampin and Ethambutol. Dyspnoea gradually improved and disappeared 18 days after. She regained her weight curve in a month. She had nonoxygeno-dependent viral bronchitis one month

after her paradoxical reaction. Chest radiography showed partial regression of pulmonary focus after 7 month. Steroids were stopped after 37 days. After two month of intensive treatment, ATT was continued with Izoniazid and Rifampin. Because of persistent pulmonary focus, treatment was prolonged to one year.

Methods

PR during an ATT is defined as "a clinical or radiological worsening of pre-existing tuberculosis lesions or the development of new lesions in a patient who initially improves". Diagnosis can only be established after exclusion of other etiologies of symptoms worsening under treatment (secondary acquired infections, drug resistance and poor compliance). In pediatric HIV-negative population, incidence varies from 3.3% to 14% and median duration of ATT before deterioration is reported between 39 days and 3.5 months. Enlarging mediastinal lymphadenopathies is one of the most common features related with PR in children. Symptomatic disease at diagnostic, no CGB vaccination and infant younger than 3 years are risk factors for paradoxical deterioration.

Results

This clinical history asks the link between liver injury and PR. To our knowledge, only one study in adult population showed that adverse drug reactions such as liver enzymes abnormality were more frequent in patients presenting PR.

On the other hand, hepatic tuberculosis has been described without any lesion on abdominal echography. As in our patient, cases series noticed that hepatic tuberculosis causes a disproportionate elevation of biliary canalicular enzymes. Could this anomaly of liver enzymes not be a part of PR in place of being drug toxicity?

Conclusions

Young children treated for pulmonary tuberculosis should carefully be monitored for respiratory distress and dysphagia. Special attention should also be paid to liver enzymes during the biological follow up. Indeed, PR and hepatic toxicity are two frequent and maybe linked complications of ATT in infants.

P 12

Hypertonic saline nebulisations as a treatment for bronchiolitis : a review of the recent literature

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Introduction

Bronchiolitis is the main cause for admission of children aged 0 to 24 months. Being a potentially severe disease, especially in younger or fragile patients, it requires some effective treatments. Supportive care is currently the basis of the management of children with bronchiolitis and few other options have proven their efficacy. These past few years hypertonic saline nebulisations (HSN) have become widely used to treat in and outpatients with bronchiolitis

Aim

We reviewed the recent literature in order to assess whether hypertonic saline could be generalized as a treatment for bronchiolitis.

Methods

We looked at reviews published since the last Cochrane database review in 2013. We identified three more recent reviews of HSN as a treatment for in and outpatients with bronchiolitis.

Results
The 2013 Cochrane database review had established that HSN produced a reduction of the length of hospitalisation in inpatients, supporting the repeated use of hypertonic saline in hospitals. However, the studies included had a mean length of stay of 5 to 6 days, thus the data could not be generalized to children admitted for shorter periods. In 2015, Zhang et al performed a meta-analysis including trials from the Cochrane review and more recent trials and found that the overall benefit on length of stay had become not significant. However, trials lacked power and heterogeneity between studies was great. Moreover different doses and frequency of administrations were used. Thus it is concluded that more studies are needed to confirm the efficacy of HSN in bronchiolitis, yet the authors thought that even a small effect on length of stay could be beneficial as the prevalence of the disease is so high.
Most trials involving outpatients were conducted in emergency departments and evaluated the admission rate. The 2013 Cochrane database review had found no effect of HSN on the admission rate. However recent trials included in later reviews seem to show some efficacy of HSN in this indication. Once more the dosage regimen used in these studies was not consistent. Zhang et al have pointed out more statistically significant effects of HSN when it was given at least 3 times a day, and a recent trial conducted in France by Angoulvant et al showed a lack of efficacy when 2 nebulisations of HSN were given 20 minutes apart in the emergency department. There are some limitations of these outpatient studies conducted in emergency departments as they are time-limited and thus may be too short to show an effect on the admission rate. Thus outpatient studies conducted in the ambulatory setting are needed to determine whether a more prolonged treatment can be beneficial to these patients.
Conclusions
HSN could be a potentially effective treatment for bronchiolitis in the outpatient setting and in patients admitted to hospitals. However, more trials are needed to confirm these benefits, and they should include large cohorts and standardised dosage regimen and diagnosis criteria. Given the high prevalence of bronchiolitis and the high cost of care, we believe that HSN, a low-cost and safe treatment, should be part of the management of this disease.

P 13

A premature infant with congenital lobar emphysema

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Introduction
Tachypnea is a common sign in premature infants, especially with IRDS. But if not resolving in a few days, you must think of other pathologies and evaluate. Unilateral findings must point to a congenital lung malformation.
Aim
To raise awareness for underlying diseases in neonates with persistent tachypnea.
Methods
We present the clinical, biochemical and radiographic data of a preterm infant with persistent tachypnea, due to congenital lobar emphysema.
Results
A premature infant of 30 weeks gestational age was born in our tertiary center. He was the second child from a DCDA twin, born by a caesarean section because of pre-eclampsia of the mother. Apgar scores were 2/6/7, birth weight was 1365g.

Surfactant was given twice because of an IRDS grade 3. After detubation, he had tachypnea together with apneas and bradycardias of the premature infant, for which we started caffeine and non-invasive respiratory support. During the first few weeks there was persistent tachypnea, with normal blood gases. There was no difference in tachypnea or respiratory distress with or without respiratory support. X-ray of the lung showed a hyperinflation of the left upper lobe, which wasn't obvious on the first X-ray after birth (where an IRDS was seen, but discretely more severe on the right side compared to left). CT-scan of the thorax showed hyperinflation of the left upper lobe, with atelectasis of the other lobes and a mediastinal shift to the right by mass-effect. During bronchoscopy a mild tracheobronchial malacia was seen and a bronchial malacia of the left upper lobe. There was diffuse inflammation. Antibiotics and high-flow nasal cannula were started. Cardiac pathology was excluded by echocardiography.
His respiratory condition stabilized and respiratory support was stopped at the age of two months. Conservative treatment was initially proposed because of the stable clinical condition. However, due to a progression of the overinflation accompanied by more respiratory distress, the patient developed a growth failure.
Tube feeding and nasal cannula were restarted for optimal support. Due to progressive respiratory distress, an elective lobectomy of the left upper lobe was performed at the age of five months. Pathology confirmed the diagnosis of lobar emphysema.
Congenital lobar emphysema is a rare congenital anomaly of the lung, characterized by hyperinflation of one or more pulmonary lobes. The prevalence is 1 in 20.000 to 1 in 30.000. It is more common in males. It is most frequently diagnosed in the neonatal period, but still 5% is diagnosed around the age of six months. Congenital lobar emphysema is reported with other congenital anomalies as double superior vena cava and horse shoe kidney. Mostly the left upper lobe is affected as in our case.
The cause of congenital lobar emphysema can be identified in 50% of cases. Most common causes are bronchial stenosis or agenesis, viscous bronchial mucus, congenital cartilage defects or extrinsic compression of aberrant vessels.
Clinical presentation is typical on neonatal age with tachypnea, tachycardia and costal retraction. This can be progressive with evolution towards respiratory failure.
Radiology shows hyperinflation of the affected lobe, with compression of surrounding lobes. If severe, mediastinal shifting is seen. CT/NMR is required for diagnosis, to initiate early treatment for a favorable prognosis.
In asymptomatic patients a conservative treatment is used. In patients with respiratory failure resection of the lobe segment or a lobectomy is performed.
In our case, the hyperinflation was masked on the first X-ray by the typical signs of an IRDS (ground-glass). Retrospectively there was a subtle left-right difference. Mild respiratory distress or tachypnea is often seen in premature infants, therefore the diagnosis in this case was only clear after repeating the X-ray by persistent tachypnea.
Conclusions
Tachypnea is a common sign in premature infants, especially with IRDS. But if not resolving in a few days, you must think of other pathologies and evaluate. Unilateral findings must point to a congenital lung malformation.
This case shows a premature infant with respiratory support during a few weeks, due to congenital lobar emphysema. This is a rare diagnosis, but important to recognize to give the right support and follow-up. If respiratory failure, resection is necessary.
P 14

Thoracoscopic aortopexy for severe tracheomalacia in an infant after esophageal atresia repair

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Introduction

Tracheomalacia (TM) is an intrinsic large airway abnormality characterized by a lack of rigidity of the tracheal wall resulting in antero-posterior collapse of the tracheal wall. This leads to airway occlusion during expiration. TM is common in patient with esophageal atresia and tracheo-esophageal fistula. Symptoms include expiratory stridor, wheezing, recurrent respiratory tracts infections. Tracheal weakness can be severe and Acute Life Threating Events (ALTE) can occur. Amongst several possible treatments, including tracheostomy, non invasive ventilation, airway stenting and surgical approaches, aortopexy is the favored option.

Results

We report the case of a patient with a VACTERL syndrom and esophageal atresia type 3. Atresia repair was performed the first day of life. Nissen's fundoplication was necessary despite of treatment for GER at the age of 2 months. He also benefited from esophageal pneumatic dilatations due to secondary achalasia at the age of 6, 13 and 16 months, respectively.

He was referred to our department at the age of 18 months for recurrent lower respiratory tract infections, uncontrolled asthma and perioral cyanosis during feeding or crying episodes. Several ALTE were described. A bronchofibroscopy was realized to exclude tracheao-esophageal fistula. Methylene blue test was negative but a severe TM with 90% tracheal occlusion and collapse during cough were observed. In order to exclude vascular ring or double aortic arch anomalities, CT angiography was performed with no extrinsic compression found.

Thoracoscopic aortopexy was realized without complication and intraoperative bronchofibroscopy was improved. Favorable clinical evolution was observed with moderate bronchitis and no more recurrence of ALTE or acute cyanosis episode.

Conclusions

Aortopexy is the treatment of choice for localized severe TM. Placements of extratracheal or intratracheal stents and/or splints have been described but appear to be associated with a higher failure rate and a significant morbidity and mortality compared with aortopexy. There are no evidence-based guidelines for the treatment of TM in children. The indications for surgery are: one or more events of ALTE and/or severe apnea, recurrent respiratory tracts infections. Severe TM must be confirmed by trachea-bronchoscopy with more than 90% the trachea being occluded. Other potential causes of symptoms have to be excluded including cardiovascular anomalies, external compression by anomalous vasculature or tumor. In repaired EA/TEF patients, it is important to rule out recurrent fistula, GER and oesophageal stricture before aortopexy.

P 15

Accidental Poisoning with Isoniazid in an infant

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Introduction

Isoniazid (INH) has been widely used for treatment and prophylaxis of tuberculosis. The most important side effect of isoniazid is reversible hepatic toxicity. In high doses,

acute INH intoxication manifests by seizures, metabolic acidosis, coma refractory to standard therapy and even death.
Aim
We report a case of unintentional acute isoniazid poisoning in a child, its clinical presentation and management, and provide a short literature review.
Methods
case description. Medical record has been reviewed and data extracted retrospectively.
Case Report: A 6-month-old boy born in Belgium of Syrian parents and not breastfed was admitted to our unit for work-up after close contact with smear-positive pulmonary tuberculosis presented by his father. Cough represented the main symptom and on physical examination, weight loss was noted.
Chest Xray showed right hilar enlargement. Tuberculin skin test demonstrated 18 mm induration. According to fully sensitive drug susceptibility pattern of father's mycobacterium tuberculosis (M. tb)., treatment by isoniazid and rifampicin was started. Accidentally, he received, after being fasted, isoniazid 400 mg equivalent of 50mg/kg/day (100mg by sirop and 300mg by tablets) on first day of treatment. 8 hours later, the intoxication was discovered by checking administered doses. Clinically, no symptoms and normal vital signs were observed. Continuous cardio-respiratory monitoring and fluid perfusion was started immediately.
Blood test showed normal hepatic and kidney functions, as well as normal electrolyte and creatinine kinase levels. Capillary blood gas excluded metabolic acidosis.
Isoniazid serum concentration measured 9 hours after intoxication, showed a value of 5.2µg/L.
Neurologic examination and blood tests remained normal during the following days. After 96 hours, treatment by isoniazid and rifampicin was pursued with recommended weight-adapted doses (10mg/kg/j for each drug).
Results
Isoniazid, isonicotinic acid hydrazide, is rapidly absorbed from the gastrointestinal tract and the peak serum level is reached 1-2 h after administration. INH is metabolized primarily by the genetically polymorphic N-acetyltransferase 2 (NAT2) enzyme, the rate of acetylation is constant in every individual but varies between patients. Three different phenotypic groups exist according to acetylation rate, that is, slow, intermediate, and fast acetylators.
Moreover, younger children eliminate INH faster than older children.
We measured an INH serum concentration of 5.2 µg/ml at 9 hours.
The reference value of therapeutic INH serum concentrations is above 3 µg/ml at maximum drug concentration (Cmax). In slow acetylators, a Cmax as high as 8 µg/ml without toxicity is described.
Fast acetylators have a lower Cmax and a higher clearance. Moreover, formula fed infants showed a lower Cmax.
The reported case suggests being a fast acetylator since he did not show any symptoms after being exposed to toxic doses and he was not breastfed. Additionally, he was only 6 months old, eliminating INH faster.
Toxicity occurs with doses as low as 10-30mg/kg with manifestations being nausea, vomiting, blurred vision, slurred speech. A dose over 20mg/kg may be associated with hallucination, recurrent seizures, metabolic acidosis, rhabdomyolysis, hypotension and coma. Death may occur at doses of over 50mg/kg. Accidental or intentional poisoning with Isoniazid may manifest within half to three hours as intractable seizure, acidosis

and coma
Evaluation should include a basic metabolic profile, serum lactate, creatinine kinase and a gas analysis. INH concentrations are not clinically useful as results are not immediately available,
Seizure management is accomplished by intravenous administration of both pyridoxine (to overcome functional pyridoxine deficiency) and a benzodiazepine like lorazepam, which potentiates the effects of available gamma-aminobutyric acid (GABA).
Conclusions
INH toxicity is reported for doses as low as 10mg/kg but doses over 20mg/kg are more likely associated with severe complications like seizures not responding to standard therapy.
The reported case did neither show any symptoms nor abnormal laboratory findings with doses as high as 50 mg/kg, suggesting a fast acetylator associated with less toxicity. Further investigations are needed, but clinicians should be aware of the high risk of acute toxicity.