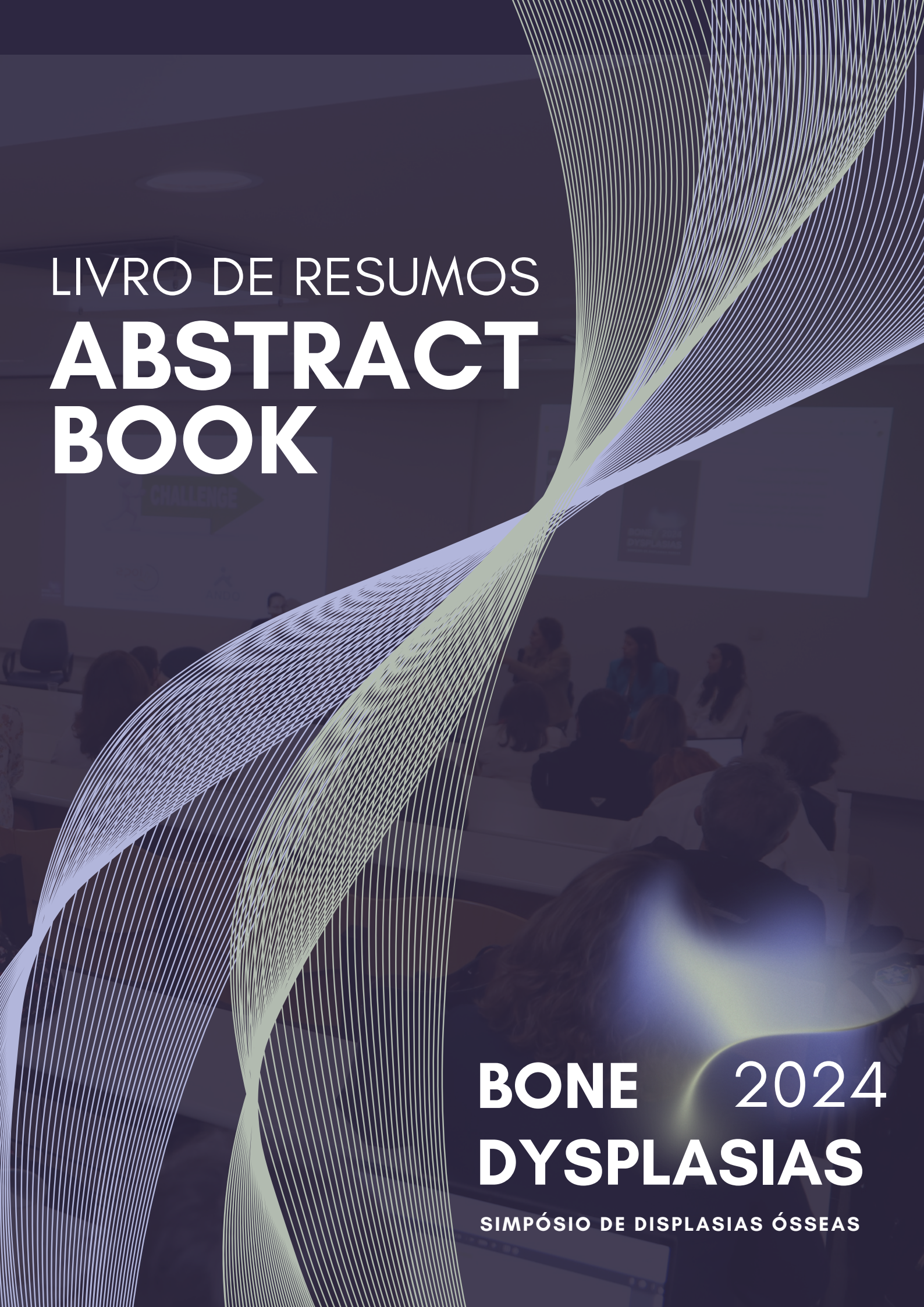

LIVRO DE RESUMOS
ABSTRACT BOOK

BONE DYSPLASIAS 2024

SIMPÓSIO DE DISPLASIAS ÓSSEAS

AS DISPLASIAS ÓSSEAS | *BONE DYSPLASIAS*

De origem genética, as **Displasias Ósseas** correspondem a um conjunto muito heterogéneo de doenças raras que afetam, maioritariamente, o desenvolvimento, a estrutura e constituição dos ossos, da cartilagem e da dentina, refletindo-se em baixa estatura, fragilidade ou deformações ósseas e frequentemente comprometendo a vida e mobilidade das pessoas afetadas.

Estas patologias representam uma área extremamente importante no âmbito das doenças do osso, mas tem sido pouco desenvolvida e reconhecida levando a falta de apoio e de implementação de medidas adequadas, particularmente significativa nos doentes adultos.

Nesse sentido, a **Associação Portuguesa de Osteogénese Imperfeita**, a **Equipa Multidisciplinar de Displasia Esquelética da ULS de Santa Maria**, membro da **Rede Europeia de Referência sobre Doenças Ósseas Raras (ERN-BOND)**, e os seus Centros Afiliados (ULS S. José, ULS Almada e Seixal e Hospital CUF Descobertas) unem esforços para implementar mais uma edição do projeto Aliança Inquebrável.

Click the Link!

Of genetic origin, Bone Dysplasias correspond to a very heterogeneous set of rare diseases that mostly affect the development, structure and constitution of bones, cartilage and dentin, resulting in short stature, fragility or bone deformations and often compromising the lives and mobility of those affected.

These pathologies represent an extremely important area within the scope of bone diseases, but have been poorly developed and recognized, leading to a lack of support and implementation of appropriate measures, particularly significant in adult patients.

*In this sense, the **Portuguese Association of Osteogenesis Imperfecta**, the **Multidisciplinary Skeletal Dysplasia Team of ULS de Santa Maria**, member of the **European Reference Network on Rare Bone Diseases (ERN-BOND)**, and its Affiliated Centers (ULS S. José, ULS Almada e Seixal and Hospital CUF Descobertas) join forces to implement another edition of the **Unbreakable Alliance project**.*

Click the Link!

BONE DYSPLASIAS 2024

O Simpósio "BONE Dysplasias 2024" surge na sequência de um projeto de continuidade organizado pela **Associação Portuguesa de Osteogénese Imperfeita – APOI,** denominado **"Aliança INquebrável"**, onde se estabelece uma parceria com múltiplos parceiros para estimular a cooperação entre doentes e seus familiares, profissionais de saúde e muitos outros *stakeholders* envolvidos de forma direta ou indireta na melhoria da qualidade de vida das pessoas com osteogénese imperfeita e outras doenças ósseas raras.

Click the Link!

Para envolver toda a comunidade e estabelecer uma verdadeira Aliança global de doenças esqueléticas raras sob a égide da **Aliança INquebrável**, muitos outros parceiros foram convidados a juntar-se a nós para este projeto, que promoveu um espaço de oportunidades para especialistas e doentes se encontrarem, discutirem, trabalharem em conjunto, compartilharem experiências e desenvolverem estratégias-chave para implementar os novos avanços.

*The "BONE Dysplasias 2024" Symposium follows an on-going project organized by the **Portuguese Association of Imperfect Osteogenesis – APOI**, called "**UNbreakable Alliance**", in which a partnership is established with multiple partners in order to stimulate cooperation between patients and their families, health professionals and many other stakeholders directly or indirectly involved in improving the quality of life of people with osteogenesis imperfecta and other rare bone diseases.*

Click the Link!

*To garantee engagement from the entire community and establish a truly global Rare Skeletal Disease Alliance under the umbrella of the **UNBreakable Alliance**, many other partners were invited to join us for this project. Therefore, the Symposium fostered a space of opportunities for experts and patients to meet, discuss, work together, share experiences and develop key strategies to implement new advances.*

PARCERIAS E APOIOS | *PARTNERS AND SPONSORS*

Este é um Projeto Solidário que pretende envolver toda a comunidade e estabelecer uma verdadeira Aliança global de doenças esqueléticas raras.
A nossa política é assegurar a participação de todos os interessados, nomeadamente Doentes, famílias, estudantes e profissionais de todas as áreas da saúde. Para isso ser possível, agradecemos a toda a comunidade, muito em particular a indústria e empresas da sociedade civil, que se juntaram a nós contribuindo com bens, serviços ou apoios financeiros.

This is a Solidarity Project that intends to involve the whole community and establish a truly global Alliance for rare bone diseases.
Our policy is to ensure the participation of everyone that might be interested, namely patients, families, students and health professionals of all kinds. For that to be possible we thank the whole community, in particular the industry and companies from the civil society that joined us by contribuiting with goods, services and financial support.

PARCEIROS | *PARTNERS*

ALIANÇA INQUEBRÁVEL

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ANDO ASSOCIAÇÃO NACIONAL DISPLASIAS ÓSSEAS

PARCEIROS CIENTÍFICOS

spot
SOCIEDADE PORTUGUESA DE ORTOPEDIA E TRAUMATOLOGIA

SOCIEDADE PORTUGUESA DE REUMATOLOGIA PEDIÁTRICA

SPEDP

SPMFR

ORDEM DOS MÉDICOS
Região do Sul

SPOP

SPGH
Sociedade Portuguesa de Genética Humana

SPO DOM

SPNP

APOIOS E MECENATO

Platinium

BIOMARIN

Silver

KYOWA KIRIN

Bronze

SYNLAB

ultragenyx

Outros

El Corte Inglés

Pastéis de Belém
desde 1837

Vila Galé
HOTÉIS

FLORINEVE
PORTUGAL

Jerónimo Martins

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barral
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Fátima Godinho
Joana Ruivo Rodrigues
Manuel Cassiano
Margarida Custódio dos Santos
Marta Rodrigues
Tiago Mendes
Susana Alberto

PROGRAMA | *PROGRAMME*

Quinta-feira, 16 de maio de 2024

14:00-14:15	Abertura | *Welcome* **Moderador**: Ana Berta Sousa **Palestrante**: André Travessa
14:15-14:45	Equipa de Displasias Ósseas da ULS Santa Maria e ERN-BOND: displasias ósseas no contexto europeu, nacional, regional e institucional | *ULS Santa Maria's Bone Dysplasias Team: bone dysplasias in the European, national, regional and institutional contexts* **Moderador**: Ana Berta Sousa **Palestrante**: André Travessa
14:45-15:45	Acondroplasia: o "novo presente" e a experiência nacional e internacional | *Achondroplasia: the "new present" and national and international experiencies* **Moderadores**: Sérgio Sousa e Lurdes Sampaio **Palestrante**: Klane White
16:00-17:00	Comunicações orais - Casuísticas e Casos Clínicos I | *Oral communications - case series and clinical cases I* **Moderadores**: Patrícia Costa Reis e Diana Antunes
17:00-17:20	Biobanco-IMM e perspectivas futuras na área das displasias ósseas | *Biobanco-IMM and future perspectives in the field of bone dysplasias* **Moderador**: Karen Heath **Palestrante**: Sérgio Dias
17:20-17:40	Iniciativas do Consórcio de Manejo de Displasias Ósseas e recomendacões para doentes com colagenopatias tipo II | *Skeletal Dysplasia Management Consortium initiatives and recommendations for patients with collagen type II disorders* **Moderador**: Karen Heath **Palestrante**: Klane White
17:40-18:10	Imagiologia nas displasias ósseas | *Radiology in bone dysplasias* **Moderador**: Joana Ruivo • Conceitos básicos de Imagiologia em displasias ósseas | *Basic concepts of Radiology in bone dysplasias* **Palestrante**: Pedro Alves • Conceitos básicos de Imagiologia em displasias ósseas | *Basic concepts of Radiology in bone dysplasias* **Palestrantes**: João Serras e Cláudia Martins

Sexta-feira, 17 de maio de 2024

09:00-09:45	Comunicações orais - Casuística e Casos Clínicos II | Oral communications - case series and clinical cases II **Moderadores**: Renata Oliveira e Mafalda Pires
09:45-10:05	Estudo "Vivência da transição para o mundo do adulto em jovens e jovens adultos com displasias ósseas" | *Study "Experience of transition to the adult world in young adults with bone dysplasias"* **Moderador**: Tiago Mendes **Palestrante**: Margarida Custódio dos Santos
10:05-10:50	Transição nas displasias ósseas | *Transition in bone dysplasias* **Moderadores**: Céu Barreiros e Inês Alves **Painel**: Filipa Ramos; João Campagnolo; Anabela Bandeira; Alice Mirante; Rute Sousa Martins; Joana Correia Rodrigues
11:10-11:40	As associações de doentes no apoio à comunidade (científica e de doentes) | *Patient associations supporting the community (scientific and of patients)* **Moderador:** Luís Quaresma **Palestrantes:** Fátima Godinho e Inês Alves
11:40-12:40	Ortopedia nas Displasias Ósseas | *Orthopaedic surgery for bone dysplasias* **Moderador**: Manuel Cassiano Neves • Abordagem ortopédica da Osteogénese Imperfeita | *Orthopaedic management of Osteogenesis Imperfecta* **Palestrante**: Zagorka Pejin • Ortopedia noutras Displasias Ósseas | *Orthopaedic management of other bone dysplasias* **Palestrantes**: Klane White
12:40-13:10	Key4OI e "Recommendations for Lung Function Guidance in Osteogenesis Imperfecta" | *Key4OI and "Recommendations for lung function guidance in Osteogenesis Imperfecta"* **Moderador**: Susana Moreira, Céu Barreiros **Palestrante**: Tim Kroesbergen e Dagmar Mekking
14:30-15:15	O que há de novo na terapêutica médica na Osteogénese Imperfeita | *What is new in the medical treatment of Osteogenesis Imperfecta* **Moderador**: Fátima Godinho **Palestrante**: Marie Eve Robinson

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15:15-15:45	Síndrome de Ellis-Van Creveld | *Ellis-Van Creveld syndrome* **Moderadores**: Maria Abreu **Palestrante**: Jorge Diogo da Silva
15:45-16:30	Comunicações orais - Casuísticas e Casos Clínicos III | Oral communications - case series and clinical cases III **Moderadores**: Lurdes Sampaio e José Poupino
16:50-17:20	Hipofosfatemia ligada ao X: da adolescência à idade adulta | *X-linked hypophosphatemia: from adolescence to adulthood* **Moderador**: Ana Paula Barbosa **Palestrante**: Marta Pereira
17:20-17:50	Fibrodisplasia ossificante progressiva | *Fibrodysplasia ossificans progressive* **Moderador**: Filipa Ramos • Tratamento atual | *Current treatment* **Palestrante**: Zagorka Pejin • Novos tratamentos no horizonte | *New treatments on the horizon* **Palestrantes**: André Travessa
17:50-18:10	Sessão de prémios e encerramento | *Award session and final remarks* **Intervenientes**: Heloísa Santos; Fátima Godinho; André Travessa; Manuel Cassiano Neves

Sábado, 18 de maio de 2024

09:15-09:30	Acolhimento e boas vindas **Intervenientes**: Fátima Godinho, André Travessa e Beatriz Fernandes
09:30-10:30	O que há de novo no tratamento da OI: • Terapêutica médica e novos Estudos Clínicos **Palestrante**: Fátima Godinho • Terapêutica cirúrgica **Palestrantes**: Manuel Cassiano Neves
11:00-12:15	Transição para o mundo do adulto: Estudo "Vivência da transição para o mundo do adulto em jovens e jovens adultos com displasias ósseas": • Autonomia; • Bem-estar físico e emocional; • Experiência emocianal e social; • Sexualidade; • Transição para os serviços de saúde. **Palestrante**: Margarida Custódio dos Santos **Painel**: Tânia Esteves, Mário Vilas Boas, Miguel Ganhão e Daniela Santos
14:00-15:30	Workshop prático "Lidar com Fraturas" - Primeiros-socorros **Palestrantes**: Carlos Gonçalves e Céu Barreiros
16:00-17:00	Cuidados pós-cirúrgicos, gessos e imobilizações. Voltar à vida Ativa. **Palestrante:** Miguel Rodriguez Molina

Click the Link!

PALESTRANTES | *SPEAKERS*

Para mais informações, clique na fotografia de cada palestrante. | *For more information click on each speaker's photo.*

ALICE MIRANTE

Endocrinologia Pediátrica | *Pediatric Endocrinology.*

ULS Coimbra - Hospital pediátrico.

ANABELA OLIVEIRA BANDEIRA

Pediatria/Doenças Metabólicas | Paediatric/Metabolic Diseases.

ULS Sto António - Centro Materno-Infantil do Norte Albino Aroso

ANA BERTA SOUSA

Genética | *Genetics.*

ULS Sta Maria - Hospital Sta Maria.

ANA PAULA BARBOSA

Endocrinologia | *Endocrinology.*

ULS Sta Maria - Hospital Sta Maria.

ANDRÉ TRAVESSA

Genética | *Genetics.*

ULS Sta Maria - Hospital Sta Maria.

CARLOS GONÇALVES

Cardiopneumologia | *Cardiopneumology.*
Docente na | Lecturer at ESTeSL

Hospital do SAMS; ESTeSL.

CÉU BARREIROS

Cardiopneumologia | *Cardiopneumology*.
Representante de Associação de doentes | *Patient Organization representative*.

ULS Sta Maria - Hospital Sta Maria.; APOI

CLÁUDIA MARTINS

TSDT Radiologia | *Radiology Technitian*.

ULS Sta Maria - Hospital Sta Maria.

DAGMAR MEKKING

Representante de Associação de doentes | Patient Organization representative.

Care4BrittleBones Foundation.

DANIELA PEEIRA SANTOS

Representante de Associação de doentes | Patient Organization representative.

APOI.

DIANA ANTUNES

Genética | *Genetics*.

ULS S. José - Hospital de Santa Marta.

FÁTIMA GODINHO

Reumatologia | *Rheumatology*.
Representante de Associação de doentes | Patient Organization representative.

ULS Almada e Seixal - Hospital Garcia de Horta; APOI.

FILIPA RAMOS

Reumatologia Pediátrica | *Pediatric Reumatology*.

ULS Sta Maria - Hospital Sta Maria.

HELOÍSA G. SANTOS

Genética | *Genetics.*

ULS Sta Maria - Hospital Sta Maria.

INÊS ALVES

Representante de Associação de doentes | Patient Organization representative.

ANDO; ePag ERN-BOND

JOANA RUIVO RODRIGUES

Imagiologia | *Radiology.*
Representante de Associação de doentes | Patient Organization representative.

Hospital CUF Viseu; APOI

JOANA CORREIA RODRIGUES

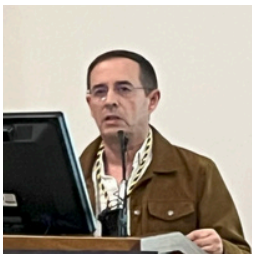
Ortopedia | *Orthopedics.*

Hospital de Ponta Delgada.

JOÃO CAMPAGNOLO

Ortopedia Pediátrica | *Pediatric Orthopedics.*

ULS São José - Hospital de Dona Estefânia.



JOÃO SERRAS

TSDT Radiologia | *Radiology Technitian.*

ULS Sta Maria - Hospital Sta Maria.

JORGE DIOGO DA SILVA

Genética | *Genetics.*

ULS Sto António - Hospital Geral Santo António.

JOSÉ POUPINO

Medicina Física e Reabilitação | *Physical Medicine and Rehabilitation.*

ULS Sta Maria - Hospital Sta Maria.

KAREN E. HEATH

Genética | *Genetics.*

Instituto de Investigación Universitario La Paz.

KLANE K. WHITE

Ortopedia | Orthopedics.

Children's Hospital Colorado.

LUIS QUARESMA

Representante de Associação de doentes | Patient Organization representative.

FEDRA.

LURDES SAMPAIO

Endocrinologia | Endocrinology.

ULS Sta Maria - Hospital Sta Maria.

MAFALDA PIRES

Medicina Física e Reabilitação | Physical Medicine and Rehabilitation.

ULS Sta Maria - Hospital Sta Maria.

MANUEL CASSIANO NEVES

Ortopedia | *Orthopedics.*

Hospital CUF Descobertas.

MARGARIDA CUSTÓDIO DOS SANTOS

Psicologia | *Psychology.*

ESTeSL.

MARIA ABREU

Genética | *Genetics.*

ULS Sto António - Hospital Geral Santo António.

MARIE-EVE ROBINSON

Endocrinologia Pediátrica | *Pediatric Endocrinology.*

Hospital Infantil de Eastern Ontario.

MÁRIO VILAS BOAS

Representante de Jovens de Associação de Doentes | *Representative for the Youth Group of a Patient Organization.*

APOI.

MARTA CONDE

Reumatologia | *Rheumatology.*

ULS S. José - Hospital D. Estefânia.

MARTA PEREIRA

Nefrologia | *Nephrology.*

ULS Sta Maria - Hospital Sta Maria.

MIGUEL GANHÃO

Membro de Associação de Doentes | *Member of a patient Organization.*

APOI.

MIGUEL RODRIGUEZ MOLINA

Fisioterapia | *Physiotherapy.*

AHUCE; Fundation AHUCE.

PATRÍCIA COSTA REIS

Pediatria | *Pediatrics*

ULS Sta Maria - Hospital Sta Maria.

PEDRO ALVES

Ortopedia | *Orthopedics.*

Hospital CUF Descobertas.

RENATA D'OLIVEIRA

Genética | *Genetics.*

ULS S. João - Centro Hospitalar Universitário S. João.

RUTE SOUSA MARTINS

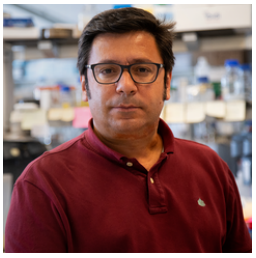
Medicina Interna | *Internal Medicine.*

ULS Sto António - Hospital Geral Santo António.

SÉRGIO B. SOUSA

Genética | *Genetics.*

ULS Coimbra - Hospital Pediátrico.



SÉRGIO DIAS

Biologia (Investigador) | *Biology (Researcher).*

IMM-CAML Biobanco.

SUSANA MOREIRA

Pneumologia | *Pulmonology*.

ULS Sta Maria - Hospital de Sta Maria.

TÂNIA ESTEVES

Representante de Associação de doentes | *Patient Organization representative*.

APOI.

TIAGO MENDES

Representante de Associação de doentes | *Patient Organization representative*.

APOI.

TIM KROESBERGEN

Representante de Associação de doentes | *Patient Organization representative*.

Care4Brittle Bones Foundation.

ZAGORKA PEJIN

Ortopedia |*Orthopedics*.

Hospital Necker Enfants Malades.

BONE 2024
DYSPLASIAS
SIMPÓSIO DE DISPLASIAS ÓSSEAS

ABSTRACTS

BONE DYSPLASIAS 2024

MARTINS, CLÁUDIA

Inovação na Imagiologia com aplicação ao doente com displasia óssea

Martins Cláudia [1]; Serras, João [1]

[1] TSDT da área de Radiologia; ULS Sta Maria

Keywords: Risco radiológico, inovação

Introdução

O estudo radiológico do esqueleto, em pediatria, integra várias incidências sendo importante todos os procedimentos estarem devidamente otimizados tendo em conta a proteção radiológica das crianças, a qual deve ser entendida um processo multi-etápico: antes, durante e após a aquisição radiográfica.
Para além da Radiologia Convencional também a Ressonância Magnética pode contribuir para o diagnóstico e seguimento do doente com displasia óssea.

Objetivos

- Identificar as medidas mais recentes de proteção radiológica com aplicação direta no estudos radiográficos do esqueleto;
- Quantificar o risco radiológico do exame radiográfico do esqueleto em pediatria;
- Identificar as inovações tecnológicas em Ressonância Magnética aplicáveis ao doente com displasia.

Metodologia

Neste trabalho foi realizada uma recolha de dados sobre os valores de exposição radiológica (produto dose área, dose efetiva) dos estudos radiográficos do esqueleto em pediatria durante o ano de 2023 na ULS Santa Maria. Foi também realizada uma revisão de literatura que pretende enquadrar as recomendações mais recentes acerca da proteção radiológica em crianças, bem como os métodos diagnósticos alternativos.

Resultados

No ano de 2023 foram realizados 25 estudos de esqueleto pediátrico em crianças sendo o produto dose-área médio de 236,2 cGycm2.
O Serviço de Imagiologia da ULS Santa Maria adotou a recomendação do não uso de proteções de contacto nos doentes.
A inovação em Ressonância Magnética tem permitido otimizar os estudos pediátricos recorrendo a sequência mais rápidas, com melhor resolução temporal e espacial e menos artefactos.

Conclusões

O Serviço de Imagiologia da ULS Santa Maria tem tentado acompanhar e aplicar, sempre que possível, as recomendações mais recentes para os estudos imagiológicos pediátricos, nas suas várias valências.

BONE 2024
DYSPLASIAS
SIMPÓSIO DE DISPLASIAS ÓSSEAS

COMUNICAÇÕES ORAIS

BONE DYSPLASIAS 2024

A. PATRÍCIO, MARGARIDA

Spondyloepiphyseal dysplasia with metatarsal shortening, COL2A1-related: a familial Portuguese case

A. Patrício, Margarida [1] ; Modamio-Høybjør, Silvia [2, 3] ; Machado, Catarina [4, 5]; Poupino, José [6]; E. Heath, Karen [2, 3, 7]; M. Travessa, André [1, 8].

[1] Department of Medical Genetics and ERN BOND, Hospital de Santa Maria, ULS Santa Maria, Lisbon, Portugal
[2] Institute of Medical & Molecular Genetics (INGEMM), IdiPAZ, Hospital Universitario la Paz, UMA, Madrid, Spain
[3] Skeletal dysplasia multidisciplinary Unit (UMDE) and ERN BOND, Hospital Universitario la Paz, Madrid, Spain.
[4] Consultation of Medical Genetics, Hospital CUF Tejo, Lisbon, Portugal
[5] Consultation of Medical Genetics, Hospital Prof. Doutor Fernando Fonseca, ULS Amadora-Sintra, Lisbon, Portugal
[6] Department of Physical Medicine & Rehabilitation, Hospital de Santa Maria, ULS Santa Maria, Lisbon, Portugal
[7] CIBERER, ISCIII, Madrid, Spain
[8] Faculty of Medicine, University of Lisbon, Lisbon, Portugal

KeyWords: Spondyloepiphyseal dysplasia with metatarsal shortening

Spondyloepiphyseal dysplasia with metatarsal shortening, COL2A1-related (SEDMS), also known as Czech dysplasia (MIM# 609162, NOS 02-0080), is a very rare type 2 collagen disorder clinically characterized by early-onset progressive pseudorheumatoid arthritis, platyspondyly, and shortened third and fourth metatarsals, in the absence of ophthalmological abnormalities and short stature. Molecularly, it is caused by a specific missense variant, c.823C>T p.(Arg75Cys), within the triple helical domain of the COL2A1 gene and has autosomal dominant inheritance. Here, we report on a new familial case of SEDMS, highlighting its clinical, radiological, and molecular findings, and compare it with the existing literature on this disorder.

We report the case of two sibs, a 24-year-old boy and a 21-year-old girl, who were referred to our Medical Genetics Department due to suspected skeletal dysplasia. Family history was remarkable for father with similar phenotype. On personal history, both had history of recurrent joint pain since the infancy (affecting the elbows, hips, knees, ankles, and spine in the boy and the pelvis, knee, and elbow in the girls) and gait abnormalities, with no surgeries. The boy also had mild hearing loss. On physical examination, both had short trunk and gait abnormalities. The girl also had mild scoliosis, bilateral genu valgum, bilateral cubitus valgus with elbow laxity, and brachydactyly of the 4th toes. X-rays showed platyspondyly, epiphyseal dysplasia with irregular vertebral endplates irregular femoral head, and narrow intervertebral spaces. In the girl, an NGS skeletal dysplasia panel was performed, and identified a c.823C>T p.(Arg75Cys) pathogenic variant in heterozygous state in the COL2A1 gene, which was subsequently identified in the affected brother, confirming the diagnosis of SEDMS in both.

This familial case confirms that, contrarily to other type II collagen disorders, SEDMS is not associated with short stature, ophthalmological problems, and palate changes. In these sibs, the establishment of the diagnosis allowed an adequate genetic counselling and helped to define an adequate follow-up, namely in consultations of physical medicine & rehabilitation, otorhinolaryngology, and orthopaedics. The description of the clinical, radiological, and molecular findings of this very rare skeletal dysplasia highlights its characteristics and helps its recognition.

ARCÂNGELO, JOANA

A planificação pré-operatória como base do sucesso no tratamento das deformidades complexas do fémur na Osteogénese Imperfeita - a propósito de um caso clinico

Arcângelo, Joana [1]; Silva, Eduardo [2]; Wircker, Patricia [1]; Norte, Susana [1]; Cassiano Neves, Manuel [1]

[1] *Hospital CUF Descobertas*
[2] *Hospital do Outão*

KeyWords: Osteogénese Imperfeita, cirurgia

Apresentamos o caso clínico de uma doente de 31 anos de idade portadora de OI tipo IV, tendo iniciado a marcha aos 12 meses, com historial de mais de 50 fraturas envolvendo todos os ossos longos e coluna, a primeira aos 14 meses.

Iniciou terapêutica médica com bifosfonatos EV que manteve até aos 13 anos.
Submetida a encavilhamento profilático dos fémures e tíbias entre os 5 e os 6 anos, em Paris.
Aos 26 anos (2018) nova queda, da qual resultou fratura diafisária do fémur direito tratada conservadoramente, tendo perdido a marcha.

Observada nesta instituição há 4 anos por dores limitativas para a marcha e deformidade acentuada do fémur. Da análise das radiografias era de salientar a estabilização dos 4 segmentos dos membros inferiores com cavilhas mas com deformidades axiais residuais. No fémur direito apresentava uma deformidade acentuada no plano coronal em varo medial / valgo distal e no plano sagital um flexo acentuado.

Procedeu-se á analise pré-operatória utilizando um software *autoCAD* que permitiu uma análise da deformidade e ajudou no estabelecimento de um plano pré-operatório de forma a corrigir os eixos anatómicos. A doente foi submetida á correção da deformidade através da realização de osteotomias múltiplas e osteossíntese intramedular de acordo com o planeado tendo-se obtido uma reprodução completa do plano no pós operatório, com excelente resultado clinico.
Ao fim de 2,5 anos a doente tem marcha independente.

Conclusão:
o tratamento das deformidades complexas dos membros inferiores em doentes portadores de OI, é um desafio cirúrgico importante, com riscos acrescidos, mas que quando bem planeado pode ser gratificante para o doente. A utilização de software adequado para o planeamento cirúrgico é uma ajuda importante na preparação da mesma, diminuindo os riscos cirúrgicos, o tempo operatório e as perdas sanguíneas, contribuindo de forma significativa para o sucesso da mesma, conforme demostrado neste caso.

BARBOSA, ANA PAULA

Osteoporotic fractures in a premenopausal women hiding an Osteogenesis Imperfecta mosaicism

Barbosa, Ana Paula [1, 2]; Travessa, André [2, 3]; Macedo, Catarina [3] ; Rocha, José Vicente [1], Costa, Francisca [1], Alves, Eva [1, 2]; Modamio-Høybjør, Silvia [4, 5]; E. Heath, Karen [4, 5, 6]; Sampaio, Francisco [1, 2].

[1] *Multidisciplinary Fracturary Osteoporosis Outpatient Clinic. Hospital Santa Maria, ULSSM, Lisboa*
[2] *Lisboa Faculty of Medicine*
[3] *Medical Genetics Department. Hospital Santa Maria, ULSSM, Lisboa*
[4] *Institute of Medical and Molecular Genetics (INGEMM), Hospital Universitario La Paz, IdiPaz, Madrid*
[5] *Skeletal dysplasia multidisciplinary unit (UMDE) and ERN BOND, Hospital Universitario La Paz, Madrid*
[6] *CIBERER, ISCIII, Madrid, Spain*

KeyWords: Osteoporose; osteogenesis imperfecta

Introduction

The individual susceptibility to osteoporosis and fragility fractures results from a combination of environmental, lifestyle and genetic factors. Among the monogenic disorders associated to low bone mass and fractures, Osteogenesis Imperfecta is the most common one and results from abnormalities of the bone mineralization. The occcurence of osteoporotic fractures under the age of 50 requires a search for secondary causes of osteoporosis, in order to establish an etiological therapy.

Case Report

A 51 years-old women was refered to the Multidisciplinary Fracturary Osteoporosis Outpatient Clinic because of osteoporotic fractures since 20 years-old, first left shoulder, then left ankle, foot and knees, and last bilateral distal radius at the age of 46. She had also several tendon ruptures, but never tooth problems. She was also diagnosed with erythema nodosum, carpal tunnel syndrome, fibromyalgia and gastroesophageal reflux. She had no toxiphilic habits. Her family had no consanguinity nor osteoporotic fractures. Physical examination showed grey sclera, but no dysmorphic features. DXA analysis showed low bone mineral density, while calcium, phosphorus and vitamin D were in the reference range and the laboratory tests to exclude secondary osteoporosis namely thyroid diseases and celiac disease were all negative. A NGS panel was performed and showed a complete deletion of the COL1A1 gene in mosaic state, which was confirmed by MLPA. Treatment was done with zoledronic acid, calcium and cholecalciferol.

Discussion and Conclusions

Osteogenesis Imperfecta, namely when caused by mosaicism, can present with variable and very mild features, sometimes lacking the typical extra-skeletal findings, as was our case and, because of that, her diagnosis was done in the adulthood. Heterozygous deletions of COL1A1/2 in mosaic state are very rare and can be difficult to detect by NGS panel. This clinical case highlights the importance of fully investigate the causes of secondary osteoporosis namely the genetic ones, when a young patient presents with osteoporotic fractures. The etiological diagnosis in this case allows adequate surveillance and genetic counselling.

BELEZA, INÊS

KBG Syndrome: a two-case report

Beleza, Inês [1] ; Modamio-Høybjør, Silvia [2]; E. Heath, Karen [2] ; Pereda, Arrate [3] ; Manero-Azua, África [3]; d'Oliveira, Renata [1].

[1] Serviço de Genética Médica, Hospital Universitário de São João-Porto (ULS S. João)
[2] INGEMM, Hospital Universitario de La Paz
[3] Molecular (Epi)Genetics Laboratory, Araba University Hospital

KeyWords: KBG Syndrome; ANKRD11; KBGS

KBG Syndrome (KBGS) is the ultra-rare autosomal dominant multisystemic genetic disorder caused by an altered ankyrin repeat domain 11 protein, encoded by ANKRD11 and co-factor of p160 nuclear receptor coactivator, responsible for inhibition of ligand-dependent transcriptional activation. KBGS phenotypically presents with short stature, macrodontia, characteristic craniofacial dysmorphisms and skeletal anomalies. We report two patients, in whom genotype-phenotype correlation was relevant for the establishment of KBGS diagnosis.

The first patient is a 7-year-old girl first observed during her neonatal hospitalization with congenital chylothorax, shortened neck and craniofacial dysmorphisms, anthropometry adequate for gestational age, that later had complete resolution of the congenital chylothorax. This child later presented with non-disproportionate short stature (although with shortened proximal segments of the limbs), delayed bone age, relative macrocephaly and wide anterior fontanelle with delayed closure (at around 3-years-old). At 5-years-old, she had numerous dental cavities (exodontia of 12 teeth) and global developmental delay with mild intellectual disability (behavioural issues; poor free drawing - rudimentary human figures). The early genetic diagnostic pathway, including karyotype, Noonan Syndrome NGS panel and array-CGH, was negative; a subsequent Skeletal Dysplasia NGS panel established the diagnosis, identifying a de novo heterozygous likely pathogenic nonsense variant in ANKRD11 [NM_013275.5:c.5794G>T p.(Glu1932*)].
The second patient was a 53-year-old woman first referred to Oncogenetics due to a unilateral Lobular Breast Carcinoma, maintaining a follow-up by Medical Genetics for clinical presentation of mild intellectual disability, short stature, craniofacial dysmorphisms, and brachydactyly of hands and feet. Although an acrodysostosis syndrome was the initial diagnostic suspicion, genetic testing through Acrodysostosis NGS panel established the diagnosis of KBGS, detecting an apparently de novo heterozygous likely pathogenic frameshift variant in ANKRD11 [NM _013275.6:c.6790_6791insA p.(Pro2264Hisfs*9)]. This woman currently presents with debilitating hip dysplasia (affecting her quality of life) macrodontia and other dental abnormalities.

These two patients showcase the importance of diagnosing KBGS, allowing for a precise medical follow-up, especially regarding KBGS' associated risks in adulthood, which are still fairly unknown.

CATANHO, JOANA ADELAIDE

Xp22.3 deletion Syndrome - A Case Report

Catanho, Joana Adelaide [1] ; Correia, Hildeberto [2] ; Antunes, Diana [1].

[1] Serviço de Genética Médica, Hospital Dona Estefânia, ULS São José, Lisboa, Portugal
[2] Unidade de Citogenética, Departamento de Genética Humana, Instituto Nacional de Saúde Doutor Ricardo Jorge, Lisboa, Portugal

KeyWords: Xp22.3 microdeletions, short stature

Introduction

Microdeletions in Xp22.3 can result in contiguous gene syndromes showing variable clinical manifestations such as Leri-Weill dyschondrosteosis, chondrodysplasia punctata, intellectual developmental disorder. Other phenotypes may include ichthyosis, hypogonadotropic hypogonadism, anosmia and ocular albinism.

Case Report

We describe a 7-years-old boy, first child of non-consanguineous parents. Pregnancy was marked by maternal hypertension and second trimester sonography revealed short femur. He was born at 38 weeks of gestation, with Apgar index 10/10; birth weight 3425g(P40); length 45cm(P3); head circumference (HC) 34,5cm(P27). Cardiac murmur was detected and cardiac ultrasound revealed pulmonary stenosis. Developmentally, he sat at 9-months-old, first steps and words were at 13-months; at 28-months, he walked in tiptoes and had no language. Otorhino evaluation diagnosed unilateral hypoacusis. At 7-years-old, he is nonverbal and has intellectual disability. At first observation, he presented with plagiocephaly, prominent forehead, large nasal bridge, synophrys, long eyelashes, large thumbs, feet brachidactily, weight and HC at 50th centile; length at 5th centile. Brain CT scan showed no alterations other than plagiocephaly. Skeletal radiology study at 5-years-old was normal. Microarray analysis identified 7Mb heterozygous deletion involving Xp22.33p22.31 chromosome region, classified as pathogenic. Maternal karyotype and FISH studies revealed a balanced reciprocal translocation 46,X,add(X)(p22.3)ish t(X;15)(p22.3-;p22.3+,q22+,q26+).

Discussion

Contiguous gene syndromes, including Xp22.3 microdeletions are associated with variable clinical expression. In our case, short stature was the main skeletal alteration identified.

We emphasize that punctate calcifications in the cartilage are more commonly seen from birth to 2-4 years of life. After this age, few x-ray alterations are detected and these include distal phalangeal hypoplasia; Madelung deformities may appear later in life.

Genetic counselling is of utmost importance due to maternal findings. Individuals with balanced chromosomal rearrangements are generally phenotypically normal but are at a higher risk for spontaneous abortion or birth defects due to cytogenetically unbalanced pregnancies.

Dysmorphic features in the presented case resembling a chromatin remodeling neurodevelompmental disorder prompted us to continue with genetic investigation, due to dual diagnosis hypothesis.

C. SANTOS, INÊS

Autosomal Recessive Osteogenesis Imperfecta Caused by a Homozygous COL1A1 Variant

C. Santos, Inês[1]; M. Travessa, André [2, 3] ; Modamio, Silvia [4, 5, 6]; E. Heath, Karen [4, 5, 6] ; Venâncio, Margarida [1]; Antunes, Diana [1] .

[1] *Medical Genetics Department. Hospital Dona Estefânia, ULS São José, Lisbon, Portugal*
[2] *Medical Genetics Department and ERN BOND, ULS Santa Maria, Lisboa*
[3] *Faculty of Medicine, University of Lisbon, Portugal*
[4] *Institute of Medical and Molecular Genetics (INGEMM),*
[5] *Hospital Universitario La Paz, IdiPaz, Madrid Skeletal dysplasia multidisciplinary unit (UMDE)*
[6] *ERN BOND*

KeyWords: Osteogenesis Imperfecta; COL1A1

Osteogenesis imperfecta (OI) is a clinically and genetically heterogeneous skeletal dysplasia characterized by bone fragility, low bone mineral density, growth deficiency and extra-skeletal features.

Most commonly, OI arises from monoallelic mutations in one of the two genes encoding the α1 and α2 chains of type I collagen - COL1A1 and COL1A2 - and is inherited in an autosomal dominant manner. Biallelic mutations in COL1A1 and COL1A2 are an extremely rare cause of OI. To the best of our knowledge, only 6 families with OI have been reported to be homozygous for variants in COL1A2 and none for variants in COL1A1.

We report a case of a 6-year-old boy evacuated from Sao Tome and Principe due to multiple fractures since birth and a presumptive diagnosis of OI. He is the first child of non-consanguineous parents. Pregnancy, pre and perinatal history were unremarkable. He was first observed at our outpatient clinic at the age of 6 months and, at that time, he had already suffered three long bone fractures. Skeletal X-rays revealed marked osteoporosis, alteration of bone modelling with multiple bowing and deformity, platyspondyly and multiple Wormian bones. A multigene panel for OI was performed and revealed a homozygous pathogenic variant NM_000088.4:c.1012G>A p.(Gly338Ser) in exon 16 of COL1A1.

His second cousin, a 6-year-old boy, was also referred to us due to multiple low-energy fractures and was found to be homozygous for the same variant. Skeletal X-rays revealed diffuse reduction in bone mineral density, deformity of the upper limbs, flattening of the dorsal vertebral bodies, marked greenstick deformity of the femurs, fibulas, tibias, and bone calluses. Additionally, he presented with polydactyly and global developmental delay, for which whole exome sequencing was performed, however no further pathogenic variants were identified.

Their mothers, who are first cousins, were found to be heterozygous for this variant. At our observation, neither of them presented suggestive manifestations of OI. Osteodensitometry was requested for both, but it wasn´t performed.

Despite the insufficient phenotypic characterization of the heterozygous individuals, with this case we aim to expand and add further evidence regarding the possibility of autosomal recessive forms of OI associated with variants in COL1A1. Noteworthy, the possibility of highly variable phenotype and incomplete penetrance on the COL1A1/2-related autosomal dominant forms must be taken in consideration.

CORREIA RODRIGUES, JOANA

Doença de Caffey (Hiperostose Cortical Infantil)

Correia Rodrigues, Joana [1] ; Garcia, Cláudio [2] ; Cruz, João [2] ; Canas, Tiago [2] ; Santos Pereira, Rute [2] ; Soares, Renato [2]; Paz Ferreira, Virgílio [2]; Carneiro, Fernando [2] ; Rebelo, António [2].

[1] Serviço de Ortopedia do Hospital do Divino Espírito Santo de Ponta Delgada
[2] Hospital do Divino Espírito Santo de Ponta Delgada

KeyWords: Doença de Caffey, Hiperostose Cortical Infantil, Gene COL1A1

A Hiperostose Cortical Infantil, ou Doença de Caffey, é uma doença genética autossómica dominante, rara, que se manifesta habitualmente antes dos 5 meses de idade. Caracteriza-se por irritabilidade, hiperostose subperiosteal maciça e inflamação dos tecidos moles adjacentes. O envolvimento ósseo é frequentemente assimétrico, afetando as diáfises dos ossos longos, mandíbula, clavícula, costelas e omoplata. Outros sintomas associados são febre, recusa alimentar e pseudoparalisia secundários à dor. Geralmente, a doença é autolimitada, verificando-se resolução até aos 2 anos de idade.

Caso clínico
recém-nascido com 6 dias de vida, sexo feminino, trazido ao Serviço de Urgência por irritabilidade, dor, rubor e tumefação da perna esquerda sem história traumática. Não tinha antecedentes familiares de relevo, gestação de termo vigiada e parto distócico sem intercorrências. Objetivamente, apirética e com diminuição da mobilidade dos membros inferiores (menor à esquerda). Realizou radiografia da perna esquerda onde se identificou aparente calo ósseo na tíbia com reação periosteal exuberante, ainda que sem evidência de traço de fratura. Analiticamente, sem leucocitose, neutrofilia ou elevação da Proteína C Reativa ou Velocidade de Sedimentação. Teve alta orientada para a consulta externa para estudo e reavaliações periódicas, verificando-se melhoria clínica, apesar de manter as alterações radiográficas. O caso foi discutido com centro de referência, tendo sido proposto o diagnóstico de Doença de Caffey, confirmado em estudo genético. Realizou radiografias da face e dos membros superiores, que não demonstraram alterações. Atualmente, com 2 anos, mantém-se assintomática, com melhoria radiográfica da hiperostose, apresentando, no entanto, antecurvatum da tíbia. Mantém seguimento na consulta de Pediatria e Ortopedia para vigilância.

Com este caso clínico pretendemos dar a conhecer/recordar esta entidade rara, que apesar da sua aparente benignidade coloca desafios em termos de diagnóstico diferencial, nomeadamente síndrome da criança batida, doença tumoral, metabólica e infeciosa. Simultaneamente, torna-se fundamental uma abordagem multidisciplinar na orientação destes casos.

DIOGO, RUI

Osteogénese Imperfeita - Experiência de um Centro Pediátrico

Diogo, Rui [1]; Rua, Inês Barros [2]; Salgado, Joana [3]; Modamio-Høybør, Silvia [4]; Heath, Karen E. [4]; Sousa, Sérgio [3]; Diogo, Luísa [1]; Ferreira, Sara [1].

[1] Centro de Referência de Doenças Hereditárias do Metabolismo, membro MetabERN e ERN BOND, Hospital Pediátrico, ULSCoimbra
[2] Unidade de Endocrinologia, Diabetes e Crescimento, Serviço de Pediatria Ambulatória, Equipa Multidisciplinar de Displasias Ósseas, membro ERN BOND, Hospital Pediátrico, ULS Coimbra
[3] Serviço de Genética Médica, Equipa Multidisciplinar de Displasias Ósseas, membro ERN BOND, Hospital Pediátrico, ULS Coimbra
[4] Institute of Medical and Molecular Genetics (INGEMM), IdiPAZ and Skeletal dysplasia multdisciplinary unit (UMDE-ERN BOND), Hospital Universitário La Paz, UAM, Madrid, Spain

KeyWords: Osteogénese imperfeita, Osteopenia, Fraturas, Bifosfonatos

Introdução
A osteogénese imperfeita (OI) é uma doença hereditária do metabolismo caracterizada por fragilidade óssea e osteopenia. O seguimento implica uma abordagem multidisciplinar, com tratamento médico e cirúrgico.

Objetivos
Descrever os doentes com OI seguidos no nosso Centro e avaliar o tratamento realizado e a evolução clínica e da densidade mineral óssea (DMO).

Métodos
Estudo observacional e retrospetivo de crianças com OI seguidas no nosso Centro e nascidas nos últimos 20 anos. Os dados obtidos foram registados em Excel® 2019 e tratados com o IBM® SPSS® Statistics 29.0. Adotou-se um nível de significância de 5%.

Resultados
Foram incluídas 21 crianças com OI, 67% do sexo masculino. O diagnóstico foi suspeitado em mediana aos 2,2 anos, com duração mediana de seguimento de 7 anos. Em 52% havia antecedentes familiares de OI. Os genes envolvidos nos 20 doentes com confirmação genética foram: COL1A1(65%); COL1A2(10%) e IFITM5, FKBP10, TMEM38B e WNT1. A maioria (62%) foi classificada como tipo 1, seguida do tipo 3 (14%). Na primeira consulta, 29% apresentava baixa estatura e 14%, obesidade. A primeira fratura foi em mediana aos 1,2 anos, 33% no período neonatal e 86% antes dos 3 anos. O número médio de fraturas/doente/ano foi de 0,9, com predomínio dos membros inferiores (50,4%). Durante o seguimento, 52% desenvolveu deformidades osteoarticulares e 5% apresentou hipoacusia. Todos foram acompanhados pela Ortopedia Pediátrica, 48% pela ORL e 33% fez fisioterapia. 95% foi suplementado com cálcio e/ou vitamina D e 81% foi tratado com bifosfonatos intravenosos (7-pamidronato, 5-zoledronato e 5-pamidronato seguido de zoledronato), com média de 5 ciclos/doente. Houve febre no 1º ciclo de pamidronato-20% e zoledronato-18%, sem outros efeitos secundários. Sob bifosfonatos, o z-score médio da DMO da coluna lombar passou de -3,1 (n=11) para -1,7 ($p<0,001$) e o nº médio de fraturas/doente/ano (n=17) , de 2,5 para 0,6 ($p=0,02$).

Conclusão
A OI apresenta grande variabilidade genética e fenotípica. Estão em curso diversos ensaios clínicos, mas não existe ainda tratamento eficaz. Os bifosfonatos melhoraram a densidade mineral óssea e reduziram o número de fraturas de forma significativa nos nossos doentes, com poucos efeitos secundários, de acordo com a experiência de outros centros. O zoledronato, iniciado em 2019, permite a redução do tempo de administração de 3 para 1 dia/ciclo, com grande vantagem para os doentes e famílias.

HOMEM, EMANUEL

Achondroplasia: the magnetic way to grow.

Homem, Emanuel [1]; Modesto, Gonçalo [1]; Monjardino, Maria Pia [1]; Carvalho, Marcos [1]; Cabral, João [1]; Traquini, Oliana [1]; Sousa, Sérgio [2]; Cardoso, Pedro [1]; Balacó, Inês [1]; Ling, Tah Pu [1]; Alves, Cristina [1].

[1] Serviço de Ortopedia Pediátrica do Hospital Pediátrico de Coimbra, ULS de Coimbra
[2] Serviço de Genética Médica, Hospital Pediátrico, ULS Coimbra (ERN-BOND Member).

KeyWords: Achondroplasia, Lengthening, Short stature, Magnetic nail

Objective
Short stature is defined as height less than 3rd percentile for chronological age and it is a critical topic in achondroplasia. Often parents and patients demand lengthening procedures due to the social bias and psychosocial pressure, despite the need for multiple surgeries and related complications. The aim of this study was to review the results of lower limb lengthening with PRECICE nails in pediatric achondroplastic patients.

Methods
This is a retrospective study of pediatric achondroplastic patients who underwent intramedullary lengthening with PRECICE nails from 2017-2023. We report on the accuracy and reliability of the nail, distraction rate, healing rate, time to full load after completion of lengthening and the presence of problems, obstacles, and complications. Functional results were assessed by the ASAMI bone and functional score.

Results
12 magnetic limb-lengthening procedures (6 femoral, 6 tibial) were performed on 3 achondroplastic patients (2 female : 1 male). 2 patients with FCFR3 c.1138 G>A(p.G38R) mutation and 1 patient with FCFR3 p.G380R(G-A) mutation. 2 patients underwent bilateral femur and tibia lengthening in a sequential manner (femur first) to treat short stature and 1 only tibial lengthening. 2 anterograde femoral, 1 retrograde femoral 3 tibial PRECICE® nails were used. The median age at the time of lengthening was 15(13-18)years. The median predicted heigh at end of growth was 124,9cm (116,3-130,0) - Multipler®Achon. The median lengthening achieved was 142mm(61-145). The accuracy of the nails was 93% and their reliability 100%. The median distraction rate was 0.97(0.81-1.15)mm/day. The healing rate was 23(9-45)days/cm. The ASAMI bone and functional score was: Excellent (2 patients) and Good (1 patients). There was 1 deep infection and 1 hardware failure without need to exchange nail.

Conclusion
Intramedullary magnetic lengthening of the lower limbs can be performed safely in pediatric patients, with good clinical and functional results. Magnetic intramedullary nail is an important surgical resource in limb lengthening in achondroplasia. However, should be faced as a major undertaking potentially associated with significant complications whose success depends on detailed planning, careful follow-up, proper education, and shared responsibility.

HOMEM, EMANUEL

Bone dysplasia: the orthopedic surgeon's masterpiece, but also his worst nightmare.

Homem, Emanuel [1] ; Jordão, António [1]; Cabra, João [1]; Sousa, Sérgio [2]; Mirante, Alice [3]; Balacó, Inês [1] ; Pagaimo, Filipe [4] ; Alves, Cristina [1] .

[1] Serviço de Ortopedia Pediátrica do Hospital Pediátrico de Coimbra, ULS de Coimbra;
[2] Serviço de Genética Médica, Hospital Pediátrico, ULS Coimbra (ERN-BOND Member);
[3] Unidade de Endocrinologia Pediátrica, Serviço de Pediatria Ambulatória, ULS Coimbra (ERN-BOND Member);
[4] Pagaimo Medical

KeyWords: Metabolic bone disorder, Orthopedics, Severe deformity

Introduction/Objective
Genetically skeletal disorders are a heterogeneous group of over 700 diseases classically divided into dysplasias, disostosis and metabolic disorders, that can lead to skeletal deformities. They require a multidisciplinary approach to aid in precise diagnosis, optimize management, genetic counseling and identify those at risk for complications. Long-term orthopedic management is often necessary. We present a clinical case of a patient with complex knee deformity in context of bone dysplasia.

Case report (Methods/Results)
An 11-year-old girl was referred for bone dysplasia suspicion. The patient presented at the age of 3 years with progressive bilateral genu valgum and underwent unsuccessful hemiepiphysiodesis of the femurs at 8-year-old and later varus osteotomy of the right knee (10 years). Multidisciplinary evaluation in our center was performed pointing to a metabolic disorder based on radiographic (metaphyseal dysplasia) and biochemical findings: persistent low phosphate, normal calcium levels, slightly elevated PTH, low vitamin D, and Fractional Tubular Reabsorption of Phosphate 87,2%. Extensive genetic studies, including a 430 gene NGS skeletal genetic disorders panel, failed to identify etiology and was discussed with international experts. Trio-WES is ongoing. Hypophosphatemic rickets diagnosis was proposed and medicated with oral phosphorus supplementation and calcitriol. Physical findings included progressive short stature (-0.24SD at 11yrs; -2.14SD at 13yrs, and -2.3SD at 18yrs), windswept knees and right-sided habitual patellar dislocation. Radiographically: right genu valgum (LDFA 98.6º, MPTA 83.6º) and left genu varum (LDFA 93.4º, MPTA 91.7º). Over the course of 6 years, various procedures to correct the right knee deformity were unsuccessful - a complex right knee deformity and permanent dislocation of the patella persisted. The solution was a 3D printed cutting guide for acute supracondylar correction of the femur fixed with a plate, complemented by Langenskiöld procedure for patellar stabilization. At 19 years, the patient has a good outcome with improvement in lower limb alignment and no patellar dislocations. She is a student nurse with no limitations in her daily activities and has a patient-reported Lysholm score of 93.

Conclusions
The management of limb deformities in bone dysplasia is challenging, unpredictable and often associated with secondary complex deformities, posing a real threat to even the most experienced orthopedic surgeon.

MACEDO, CATARINA; SOARES, MARTA

Clinical and molecular features of 5 cases of Tar Syndrome

Macedo, Catarina [1]; Soares, Marta [1] ; Machado, C. [1] ; Soeiro e Sá, M. [1] , Dias, P. [1] ; Santos, R. [1] ; Custódio, S. [1]; Rodrigues, R.[1] ; Rolo, E. [1]; Moldovan, O.[1] ; Sousa, A.C.[1] ; Travessa, A.[1] ; Sousa, A.B [1].

[1] Serviço de Genética Médica, Departamento de Pediatria, Unidade Local de Saúde Santa Maria

KeyWords: RBM8A, skeletal dysplasias, TAR syndrome

Introduction

Thrombocytopenia-absent radius (TAR) syndrome presents with limb anomalies predominantly affecting the upper limbs, consisting of severe radial defects ranging from absence to hypoplasia with present thumbs. Most patients exhibit thrombocytopenia from birth, which tends to ameliorate with age. Cardiac and urogenital malformations occur in about 17% and 24% of patients, respectively. TAR syndrome arises from biallelic variants in the RBM8A gene (1q21.1), typically involving a null allele alongside a hypomorphic noncoding variant. Only a few hypomorphic variants have been identified so far, with the variant c.*6C>G being common in African populations. There are some genotype-phenotype correlations, such as the association of the c.-21G>A variant with lower platelet count and the intronic c.67+32G>C variant with higher platelet count.

Methods and results

We retrospectively analysed the clinical, radiological, and molecular data from five patients with TAR syndrome, two of whom had African ancestry. One case resulted in termination of pregnancy due to severe upper limb phocomelia. All cases presented with radial defects, with only one exhibiting an additional skeletal abnormality (congenital hip displacement); no lower limb defects were observed. Bilateral radial agenesis was present in all cases except for one, which exhibited asymmetrical radial hypoplasia. Thrombocytopenia was present in three patients. In one adult patient, moderate thrombocytopenia and recurrent epistaxis persisted into adulthood and required regular follow-up. In addition, three patients were noted to have short stature, two (of African descent) had congenital heart defects (CHD), two had urogenital abnormalities, and one had a cow's milk allergy. Molecular diagnosis involved arrayCGH identifying the recurrent 1q21.1 deletion, followed by RBM8A gene sequencing which detected three hypomorphic variants.

Conclusion

Our study corroborates the high allelic frequency of the c.*6C>G variant in African populations, suggesting targeted testing for this variant in African patients suspected to have TAR syndrome. Additionally, our findings indicate a potential association between this variant and CHD, warranting further investigation. The cohort in our study confirms established genotype-phenotype correlations related to thrombocytopenia. No genotype-phenotype correlations were observed regarding the severity of limb reduction defects, reaffirming previous research findings.

MACHADO, CATARINA

PLS3 Mutation in X-linked Osteoporosis: A clinical case

Machado, Catarina[1]; Costa, Adriana[1]; Martins, Andreia[1]

[1] Hospital Amadora Sintra

Keywords: childhood-onset primary osteoporosis, PLS3 mutation

Introduction

Childhood-onset osteoporosis is a rare but clinically significant condition characterized by low mineral bone density and high risk of fractures. Studies have shown pathogenic variants in more than 20 different genes as causative for childhood-onset primary osteoporosis. The X-chromosomal PLS3, encoding Plastin-3, is one of the more recently identified genes.

Clinical description

An 11-year-old Portuguese boy, the only child of a healthy Portuguese couple, has a past history of two finger fractures after a sports injury at the age of 8 years and obesity. He was admitted to the hospital due to a 3-month progressive worsening of lumbar pain with increasing difficulty to walk due to multiple spinal fractures. There was no history of trauma. The physical examination was unremarkable. His 36-year-old father had lumbar spine osteoporosis but no fractures. The mother is healthy, has no history of bone fractures and has a normal BMD. An MRI of the spine revealed multiple vertebral body fractures (from C7 to L5, only sparing T1, T2, T10, and L1) with collapse and a height reduction of 25-50%. Full body X-ray scan revealed diffuse osteopenia but did not find any other fractures. The DXA revealed a Z-score of -5.0 in LS. Neurological, cardiological, ENT, and ophthalmological evaluations were normal. Next-generation sequencing of genomic DNA for 26 genes, including PLS3, was performed and led to the identification of a novel hemizygous deletion removing the whole PLS3 gene. Array comparative genomic hybridization, CytoScan 750 K, confirmed the presence of a 775 kb deletion on chromosome X (coordinates X:114644041-115418576) removing the entire PLS3 gene as well as AGTR2, encoding type-2 angiotensin II receptor. A heterozygous variant of unknown signifcance (VUS) in LRP5 was also identifed [NM_002335.3:c.3443C>T(p. Thr1148Ile)]. The patient inherited the PLS3 deletion from his unafected mother and the LRP5 variant from his father with spinal osteoporosis but no fractures. The patient started quarterly intravenous pamidronate cycles (1 mg/kg/day for 3 days), calcium and vitamin D. After 1 year of treatment the DXA revealed a general increase in all BMD values (Z-score+0.7 in LS) and regression of all symptoms, with no new fractures.

Discussion

Hemizygous mutations in PLS3 cause a monogenic form of X-linked osteoporosis with a few cases reported in the literature. Early diagnosis is of great importance to patient management and treatment.

PINHO, SARA

Genetic “double trouble”: one patient with two X-linked diagnoses

Pinho, Sara [1] ; Dias, Patrícia [1] .

[1] *Serviço de Genética, Departamento de Pediatria, ULS Santa Maria, Lisboa, Portugal*

KeyWords: X-linked Otopalatodigital spectrum disorder

Introduction

While clinicians usually try to find a single explanation for all the clinical manifestations of a patient, in some cases, there is more than one disease contributing to a compound phenotype. Therefore, an already established molecular diagnosis should not prevent us from continuing the diagnostic odyssey when suspicion of another pathology remains.

Case description

We report a 13-year-old boy, second child of a healthy non-consanguineous couple with unremarkable family history, presenting with elevated CK, myalgia, mild intellectual disability, ADHD, facial and skeletal dysmorphisms. Physical examination revealed prominent supraorbital ridges, hypertelorism, bilateral epicanthal folds, flat nose with anteverted nares, posteriorly rotated ears, prognathism, long fingers with camptodactyly, 5th finger clinodactyly and distal phalangeal hypoplasia of the halluces. He also exhibited limited joint extension of the elbows and knees.

Results/Discussion

Genetic testing began with chromosomal microarray (CMA), given the hypothesis of a contiguous gene deletion syndrome involving the dystrophin gene that could explain both the increased CK and dysmorphisms. CMA revealed a hemizygous deletion of at least 10 exons of DMD gene, confirming the diagnosis of Becker muscular dystrophy. Subsequent full-body skeletal x-ray showed supraorbital hyperostosis, underdeveloped frontal sinuses, coat-hanger shaped ribs, fusion of carpal bones, hands with elongation and poor modelling of phalanges and distal phalangeal hypoplasia of the great toes, characteristics typical of Otopalatodigital Spectrum Disorders (OPDSD). A multigene NGS bone dysplasia panel was performed, identifying the likely pathogenic hemizygous missense variant c.733G>A, p.(Glu245Lys), in FLNA gene (NM_001456.4), previously described in the literature linked to Frontometaphyseal dysplasia type 1. The proband’s skeletal and facial features perfectly fit this diagnosis, although he seems to have a milder phenotype, without hearing loss, urologic abnormalities, subglottic stenosis or cleft palate. Both DMD and FLNA variants were inherited from the mother, located in cis in the same X chromosome.

Conclusion

Our patient has two unrelated X-linked diagnoses. His carrier mother has a 25% risk of having another affected son with both diseases. It is important to consider testing his two healthy sisters once they start planning to have offspring, to better determine the recurrence risk and offer reproductive options if needed.

RIBEIRO, BIBIANA

MYH3-associated arthrogryposis: a small case series

Ribeiro, Bibiana [1] ; Cerqueira, Rita [2] ; Falcão Reis, Cláudia [3] ; Abreu, Maria [3].

[1] Master's Degree in Genetic Counseling, Abel Salazar Institute of Biomedical Sciences, University of Porto, Porto, Portugal
[2] CGC Genetics, Unilabs, Porto, Portugal; rita.cerqueira@unilabs.com
[3] Medical Genetics Department, Jacinto Magalhães Medical Genetics Center, Santo António Local Health Unit, Porto, Portugal

KeyWords: arthrogryposis; MYH3; skeletal dysplasia

Introduction

The MYH3 gene is associated with several skeletal and arthrogryposis phenotypes, with different forms of inheritance. Distal arthrogryposis phenotypes are usually autosomal dominant, but the more proximal contractures, pterygia, and spondylocarpotarsal fusion syndrome may be autosomal dominant with incomplete penetrance, or have recessive inheritance.

Case series

We present the cases of three patients from two families (family 1 - two female patients, sisters, family 2- one male patient) with congenital diagnosis of arthrogryposis with varying severity, and varying x-ray anomalies. All three patients presented articular and spinal involvement, and both patients 1b and 2 had significant knee contractures, with pterygia. In all three patients, a variant with an expected loss of function effect was identified, inherited from an asymptomatic parent. Autosomal dominant contractures, pterygia, and spondylocarpotarsal fusion syndrome 1A syndrome with incomplete penetrance was initially suspected, but after external discussion of a similar case, a review of exome data (and Sanger confirmation) was requested in order to search the relatively frequent variant NM_002470.4: c.-9+1G>A, which was present in compound heterozygosity in all patients, compatible with autosomal recessive inheritance.

Discussion/Conclusion

We present this small cohort in order to further expand on the phenotype of MYH3-associated disorders, and its variability. In the presence of apparent incomplete penetrance alleles in MYH3-associated disorders, it is important to consider a potentially recessive form of inheritance, which has considerable implications for genetic counseling.

SANTOS, INÊS

Fibrodysplasia ossificans progressiva: a rare and not so obvious diagnosis

Santos, Inês [1]; Aguiar, Francisca [2, 3]; Ganhão, Sara [2, 3]; Rodrigues, Mariana [2, 3]; Brito, Iva [2, 3].

[1] Rheumatology Unit, Centro Hospitalar Tondela-Viseu, Viseu, Portugal
[2] Pediatric and Young Adult Rheumatology Unit, Centro Hospitalar São João, Porto, Portugal;
[3] Department of Medicine, Faculty of Medicine, University of Porto, Porto, Portugal;

KeyWords: Fibrodysplasia ossificans progressiva

Clinical case

We report the case of a 27-year-old female who presented significantly limited mobility due to progressive heterotopic ossification (HO) since she was 6 years old. Initial involvement was located to the cervical and thoracic regions, followed by the shoulders, costal grid, left wrist, lumbar spine, hips, right thigh and feet. She had previously undergone multiple surgical interventions for osteochondroma of the hallux. Her family history was irrelevant. Physical examination revealed hallux hypoplasia, limited mobility of multiple joints and kyphoscoliosis, resulting in fixed lumbar flexion of 30º. Laboratory studies were normal. Radiographs showed diffuse HO. Respiratory function tests revealed a mild restrictive syndrome.
In an early stage, local biopsy of the initial lesion was suggestive of aggressive juvenile fibromatosis and chemotherapy with vinblastine and methotrexate was initiated.
The patient remained stable until the age of 13, when she started experiencing frequent painful episodes of soft tissue swelling with disease progression. The clinical and radiographic evolution suggested fibrodysplasia ossificans progressiva (FOP) and the diagnosis was later confirmed by the identification of a heterozygous c.617G > A p.(Arg206His) mutation in the ACVR1 gene. The patient was advised to avoid trauma. The acute flare-ups were managed with nonsteroidal anti-inflammatory drugs or corticosteroids. Maintenance therapy with monthly infusion of pamidronate 90 mg was continued for 4 years, resulting in chronic pain improvement and lower frequency of acute episodes.

Discussion

FOP is a genetic disorder characterized by congenital malformation of the hallux and postnatal progressive HO of connective tissue, which may be spontaneous or precipitated by trauma.
The reported prevalence is approximately 1:2,000,000 with no sex, racial, ethnic, or geographic predisposition. (1)
Early FOP lesions can be histologically identical to the fibroproliferative lesions of aggressive juvenile fibromatosis, like in our case. Awareness of this disease can avoid delayed diagnosis and unnecessary interventions, such as biopsies or surgical procedures, which could worsen clinical course. (2)

References:
1. Pignolo RJ, Shore EM, Kaplan FS. Fibrodysplasia ossificans progressiva: clinical and genetic aspects. Orphanet J Rare Dis. 2011;6:80.
2. De Brasi D, Orlando F, Gaeta V, et al. Fibrodysplasia Ossificans Progressiva: A Challenging Diagnosis. Genes (Basel). 2021;12(8):1187.

SOARES, MARTA

Clinical and molecular features of 3 patients with Acrodysostosis

Soares, Marta [1]; Macedo, Catarina [1]; Moldovan, Oana [1]; Dias, Patrícia [1]; Rodrigues, Márcia [1]; Heath, Karen E. [2]; Travessa, André [1].

[1] Serviço de Genética Médica, Departamento de Pediatria, ULS Santa Maria
[2] Instituto de Genética Médica y Molecular, Instituto de Investigación Hospital Universitario La Paz, Hospital Universitario la Paz

KeyWords: acrodysostosis, PDE4D, PRKAR1A, skeletal dysplasias

Introduction

Acrodysostosis is a peripheral dysostosis affecting the GPCR-Gsα-cAMP-protein kinase A (PKA) signalling pathway, being clinically characterized by severe brachydactyly and facial dysostosis. Two autosomal dominant forms are recognized: acrodysostosis type 1 (ACRDYS1) (OMIM#101800), resulting from PRKAR1A gain-of-function variants, and acrodysostosis type 2 (ACRDYS2) (OMIM#614613), resulting from PDE4D suspected gain-of-function variants. While both types share similar skeletal features, only ACRDYS1 is associated with PTH and TSH hormone resistance. Cognitive functioning appears to be more severely affected in ACRDYS2.

Methods and results

We report three patients of acrodysostosis (all male, diagnosed between ages 5 and 23), comprising one ACRDYS1 and two ACRDYS2 cases. All presented prenatal features (increased nuchal translucency, short limbs or intrauterine growth retardation), dysmorphic features [high forehead (2/3), frontal bossing (3/3), hypertelorism (2/3), epicanthus (2/3), flat face (3/3), malar hypoplasia (3/3), short nose (3/3), depressed nasal root (3/3), wide nasal base (2/3), anteverted nares (2/3)], and skeletal anomalies [brachydactyly (3/3), brachymetacarpia (3/3), trident hands (2/3), hypoplastic nails (1/3) and spine curvature anomalies (2/3)]. Their radiological findings encompassed cone-shaped epiphyses (3/3), shortened tubular bones of the hands and feet (3/3), absence of widening of the interpedicular distance (2/3), and spinal stenosis (1/3). Additionally, extra-skeletal features observed were pseudohypoparathyroidism (in the ACRDYS1 patient), intellectual disability (in both ACRDYS2 patients), behavioural problems (in the ACRDYS1 patient), urogenital anomalies (2/3), unspecific brain abnormalities (2/3), neurological features (1/3), sleep apnea (1/3), and deafness (1/3). Initial GNAS sequencing yielded negative results in all patients and was followed by targeted sequencing of PRKAR1 and PDE4D genes or skeletal dysplasia panel which identified one heterozygous pathogenic variant in PRKAR1 and two in PDE4D, all of which had been previously reported.

Conclusion

Our case series contributes to the characterization of the acrodysostosis phenotype, expanding its prenatal manifestations and suggesting urogenital anomalies as a previously unreported feature. Acrodysostosis, particularly ACRDYS1, should be considered in the differential diagnosis of Albright Osteodystrophy.

GUNEZLER, ALEXANDER

A criação da primeira banda desenhada de um super-herói com Osteogénese Imperfeita aplicada como meio de sensibilização para o público jovem.

Gunezler, Alexander [1, 2]

[1] *IADE;*
[2] *APOI.*

Keywords: Osteogénese, banda desenhada, jovens, super, herói.

Através da contemplação de casos de jovens que vivem com Osteogénese Imperfeita, uma das problemáticas contempladas é a falta de aceitação ou por parte de um público alheio à condição, isto é, a exclusão, a superproteção e sobretudo o Bullying, causado pela falta de conhecimento ou rejeição devido ao traço distintivo.

O objetivo é levar ao público um artigo que ajude a saber mais sobre uma pessoa com osteogénese e a informar-se sobre a doença de uma forma mais criativa e divertida.

Foi por isso que me propus criar uma banda desenhada intitulada "TOUGHNESS", um projeto de banda desenhada que conta as aventuras do primeiro super-herói com Osteogénese Imperfeita e mostra as experiências desta personagem, salientando os problemas que o público jovem pode ter. O protótipo foi elaborado tendo em conta os conhecimentos sobre a formação e a perceção dos jovens segundo vários psicólogos e fatores como a PSI (interação parassocial), em que se pretende estimular os jovens que desconhecem a doença a estarem mais abertos a interagir e a aceitar as pessoas com Osteogénese Imperfeita.

O protótipo foi mostrado a pessoas com Osteogénese para ver se tinham algum respeito pela personagem e pela história, e o resultado foi aprovado por este público, para além de ter interesse na história em si. No entanto, existe atualmente um protótipo que não foi publicado, gostaria de mostrar e aumentar o apoio a este projeto para sensibilizar as massas.

BONE 2024
DYSPLASIAS
SIMPÓSIO DE DISPLASIAS ÓSSEAS

PRÉMIO

MELHOR TRABALHO

Vencedor

Emanuel Homem Costa

"Skeletal Dysplasia: Looking at the right angle?"

Homem, Emanuel

Skeletal Dysplasia: Looking at the right angle?

Homem, Emanuel [1] ; Ricardo, Raquel [1] ; Monjardino, Maria Pia [1] ; Carvalho, Marcos [1] ; Traquini, Oliana [1]; Cabral, João [1], Sousa, Sérgio [2]; Cardoso, Pedro Sá [1] ; Balacó, Inês [1]; Ling, Tah Pu [1]; Alves, Cristina [1].

[1] Serviço de Ortopedia Pediátrica do Hospital Pediátrico de Coimbra, ULS de Coimbra
[2] Serviço de Genética Médica, Hospital Pediátrico, ULS Coimbra (ERN-BOND Member)

KeyWords: Skeletal Dysplasia, hemiepiphysiodesis, Orthopedic surgery

Introduction/Objective
Skeletal dysplasias can result in severe bone deformities due to impaired bone metabolism. Angular deformities of the lower limb can be treated either acutely with osteotomies or by gradual correction during growth (guided-growth). We present the results of temporary hemiepiphysiodesis using eight-plates in children with skeletal dysplasia with lower extremity angular deformities.

Methods
Retrospective comparative study of all patients with varus or valgus deformity submitted to hemiepiphysiodesis with 8-plates, in one institution, from 2011 to 2023, grouped by the presence (Group A) or absence (Group B) of Skeletal Dysplasia. Variables collected were epidemiological, radiographic, surgical and follow-up data. Statistical analysis as performed using SPSS.

Results
Total of 85 lower limbs, in 53 patients. The mean age at index surgery was 12(±2.4)years for both groups. All patients were followed until end of growth. The plates-8 remained in place for an average of 21 (±13.8) months. 66 knees achieved deformity correction with this technique.
GroupA: 18 patients, 28 limbs, 11:7 male:female ratio. The most common diagnosis was Hereditary Multiple Osteochondromas (7 patients). 18 knees had valgus deformity. The average axis deviation was 14.7°(±10.4)
GroupB: 35 patients, 57 limbs, 17:18 male:female ratio. Most cases were idiopatic (16). 43 knees had valgus deformity. The average axis deviation was 8.3°(±3,1)
Starting deformity was statistically higher in Skeletal Dysplasia group ($p<0,05$), as was complication rate (insufficient correction, hardware failure or deformity inversion), recorded in total of 10 patients. Residual deformity after correction was also higher in Group A ($p<0.05$).

Conclusions and Clinical Relevance
The management of limb deformities associated with Skeletal Dysplasias is challenging, unpredictable and often associated with complications. Growth modulation with an 8-plate is a relatively simple surgery, has low risk of mechanical failure or physeal damage and can be performed at very young age. Our results show that guided growth in skeletal dysplasia not so good results compared to other etiologies, nonetheless, is still a safe and effective procedure.

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PRÉMIO

BONE DYSPLASIAS 2024

Menção Honrosa

Isabel Serra Nunes

"A shrouded case of autosomal recessive osteopetrosis requiring emergent care"

SERRA NUNES, ISABEL

A shrouded case of autosomal recessive osteopetrosis requiring emergent care

Serra Nunes, Isabel[1, 2, 3]; da Silva, Jorge Diogo[1, 2, 3, 4, 5] ;Bandeira, Anabela[6] ; Costa, Emília [7]; Guerra, Isabel [7] ; Alonso, Isabel[5] ; Soares, Ana Rita[1, 2, 5]; Tkachenko, Natália [1, 2]

[1] Serviço de Genética Médica, Clínica de Genética e Patologia, ULS Santo António, Porto, Portugal.
[2] Unit for Multidisciplinary Research in Biomedicine, Abel Salazar Biomedical Sciences Institute, Porto University, Porto, Portugal, and ITR-Laboratory for Integrative and Translational Research in Population Health, Porto, Portugal.
[3] Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal
[4] ICVS/3B's – PT Government Associate Laboratory, Braga/Guimarães, Portugal.
[5] Genetyca-ICM, Atrys, Porto, Portugal.
[6] Unidade de Doenças Hereditárias do Metabolismo, Clínica de Pediatria, ULS Santo António, Porto, Portugal.
[7] Unidade de Hematologia Pediátrica, Clínica de Pediatria, ULS Santo António, Porto, Portugal.

KeyWords: osteopetrosis, TCIRG1, ARO

Introduction

Autosomal recessive osteopetrosis (ARO) is an ultra-rare skeletal dysplasia caused by a defect in the osteoclasts responsible for bone destruction. Clinically, it is characterized by bone fragility and increased density, bone marrow fibrosis, extramedullary haematopoiesis and cranial nerve compression. Although the clinical presentation is very typical, there is a moderate degree of genetic heterogeneity, with genotype-phenotype correlations having a significant impact as ARO may be curable with hematopoietic stem cell transplant (HSCT) depending on the affected gene.

Case report

Six-month-old male infant, with no relevant family history or consanguinity, was referred for Metabolics consultation with the suspicion of hypophosphatemic rickets due to cranial bone dysplasia with hyperparathyroidism. Blood tests revealed pancytopenia and leukoerythroblastosis, and the patient was referred for Pediatric Hematology and Clinical Genetics. At this time, clinical assessment was remarkable for failure to thrive, cranial dysmorphic features with macrocephaly, divergent strabismus with fixed mydriasis, and hepatosplenomegaly. Skeletal survey revealed diffuse sclerosis, and bone marrow biopsy detected hypocellularity and a mos 47,XYY[??] / 46,XY[??] karyotype (confirmed in a constitutional analysis). A targeted WES-based NGS panel revealed pathogenic heterozygous compound variants c.979_982del, p.(Arg327Thrfs*18) and c.1370_1384del, p.(Thr457_Tyr461del) in the TCIRG1 gene, compatible with ARO type 1. The patient was referred and is currently waiting for HSCT.

Conclusion

This case illustrates the need for increased awareness for ultra-rare disorders which require urgent treatment that can be curative, such as ARO. Only with knowledge and awareness on these conditions, and with the collaboration of a multidisciplinary team, will timely diagnosis be possible.

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PRÉMIO

BONE DYSPLASIAS 2024

Menção Honrosa

Inês Barros Rua

"IHH-related short stature: clinical and molecular characterization of six Portuguese families"

RUA, INÊS BARROS

IHH-related short stature: clinical and molecular characterization of six Portuguese families

Rua, Inês Barros [1] ; Ramos, Fabiana [2]; Rosas, Catarina [2] ; Santos, Mafalda [2] ; Heath, Karen E. [3, 4] ; Mirante, Alice [1] ; Sousa, Sérgio B [2, 5, 6] .

[1] Paediatric Endocrinology Department, Bone dysplasia multidisciplinar team (ERN BOND), Hospital Pediátrico de Coimbra, ULS Coimbra, Portugal
[2] Medical Genetics Department, Bone dysplasia multidisciplinar team (ERN BOND), Hospital Pediátrico de Coimbra, ULS Coimbra, Portugal
[3] Institute of Medical and Molecular Genetics (INGEMM), IdiPAZ and Skeletal dysplasia multdisciplinary unit (UMDE-ERN BOND), Hospital Universitário La Paz, UAM, Madrid, Spain
[4] CIBERER, ISCIII, Madrid, Spain
[5] University Clinic of Genetics, Faculty of Medicine, Universidade de Coimbra, Portugal
[6] Clinical Academic Center of Coimbra, Hospital Pediátrico de Coimbra, Unidade Local de Saúde de Coimbra, Coimbra, Portugal

KeyWords: IHH, bone dysplasia, short stature

Introduction
Heterozygous variants in the Indian hedgehog gene (IHH) have been reported to cause brachydactyly type A1 and, more recently, short stature associated with mild hand and feet skeletal anomalies. Biallelic IHH variants cause a more severe phenotype known as acrocapitofemoral dysplasia. Our goal is to describe families in which IHH heterozygous variants were identified.

Methods
Clinical and molecular characterization was performed through retrospective analysis of medical records.

Results
We report on six Portuguese families with IHH heterozygous variants, in a total of 10 patients, 7 adults and 4 children. In adults, height was often disproportionate with variables degrees of limb-shortening and/or brachydactyly. In adult females, it varied from 1.41m and 1.56m. The only adult male was 1.48m tall. Concerning the genotype, three known variants were identified in 5 families: p.(Arg149His) [n=3]; p.(Arg128Gln) [n=1]; and p.(Arg446His) [n=1]. One variant of unknown significance was identified in the remaining family p.(Ser189Pro).

Conclusion
With widespread use of genetic testing, IHH turned out to be a crucial gene to include in short stature evaluation. In three of the reported five families, diagnosis was reached in the context of an ongoing pregnancy with mother with short stature and/or foetus with short limbs, highlighting the importance of multidisciplinary evaluation. Growth hormone treatment was shown to be effective in several cases in the literature.

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COMUNIDADE DE DOENTES NO APOIO

À CIÊNCIA E INVESTIGAÇÃO

Osteogenesis Imperfecta Federation Europe

Osteogenesis Imperfecta Federation Europe (OIFE) is an umbrella association for organizations dealing with the rare genetic bone condition osteogenesis imperfecta (OI).

We are happy to support and endorse the important Simposium **Bone Dysplasias 2024**.
OIFE was first established in 1993 in the Netherlands. From 2022 we have been registered as a non profit in Belgium. Our mission is to connect and empower organizations, professionals and individuals to improve lives of people with OI.
Our ordinary member organizations are European, and our main activities are based in Europe. The Portugese OI-organization APOI is one of our valuable national member organizations. In addition to having members in Europe, we collaborate with OI-organizations around the world with the intention to exchange ideas, information and best practices. The OI-organization in Brazil (ANOI) is one of our associate member organizations, and OIFE has supported representatives from ANOI to attend this conference. We hope it will inspire new collaborations across the Atlantic!

At the moment, OIFE include 41 member organizations (20 European national organizations; 16 partner organizations - national OI-organizations outside Europe; and 5 supporting organizations).

OIFE is a member of EURORDIS - the umbrella for rare disease organizations in Europe, the European Rare Bone Forum and we recently became an affiliated member of the European Society of Endocrinology (ESE).
Our vision is children and adults with OI living active and independent lives - with access to competent healthcare and necessary social support.
Our most important projects at the moment include dissemination of results from the IMPACT survey, the Pain and OI project, patient involvement in research and development and advocating for access to better care, services and treatments for people with OI.

You can find more information about OIFE at www.oife.org

INVESTIGATOR MEETING

NOVEMBER 15TH, 2024 (ON ZOOM)
2 PM - 7 PM Central European Time
8 AM - 1 PM Eastern Standard Time

THE EVENT IS FREE
CME - the event is NOT CME accredited

GOALS OF THE EVENT

- Highlight new OI research
- Facilitate collaboration between clinical and basic researchers
- Provide a collaboration space for OI researchers in Europe and beyond
- Attract new people to OI research
- To support the younger generation of OI researchers

TARGET GROUPS

- The target group is primarily researchers and clinicians working with OI in Europe and other countries.
- Patient representatives from OI-organizations can attend if they have a special interest in research and development.
- Industry representatives are also welcome.

ABSTRACT SUBMISSION
DEADLINE 4 OCTOBER 2024

We invite your abstracts on any aspect of OI research, whether basic, translational or clinical. **A limited number of oral slots are available on the programme and priority will be given to abstracts describing novel research and hot topics related to OI.**

This is an opportunity for you to present and discuss your OI-related work with an international group of fellow OI-researchers in a relatively informal setting and without the costs and time involved in travelling to in-person meetings. The aim is to facilitate collaboration and development of research in OI.

ABSTRACT SUBMISSION FORM OPENS IN JUNE 2024

For more info:
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apoi associação portuguesa de osteogenese imperfeita

A **Associação Portuguesa de Osteogénese Imperfeita – APOI**, representa uma doença rara que provoca grande fragilidade óssea, levando a fraturas frequentes e deformações ósseas progressivas.

Sobre a organização

A nossa associação é uma organização nacional, voluntária e não lucrativa, reconhecida como IPSS em 2012, e inscrita como ONGPD pelo INR.IP desde 2015.

Sobre a Missão

A nossa **MISSÃO** consiste em melhorar por todos os meios possíveis a qualidade de vida dos portadores de Osteogénese Imperfeita (OI). Para isso, tentamos focar as nossas atividades no estímulo ao melhor conhecimento médico e à investigação, no ensino aos doentes e suas famílias como uma forma de os tornar parte ativa na promoção da sua própria saúde e na sensibilização da comunidade civil como uma forma de minimizar o estigma e melhorar a integração social.

Sobre a Osteogénese Imperfeita

A **Osteogénese Imperfeita (OI)**, tal como a maior partes das doenças ósseas raras, traz grandes e graves consequências para o dia-a-dia destes doentes, "arrancando-os" subitamente do seu contexto social e isolando-os por períodos de tempo prolongados, pelo que as consequências da doença vão muito além de simples fraturas e estendem-se no ponto de vista psicológico, familiar, escolar e de integração social.

uma instituição vocacionada para a *ciência* e *investigação* em prol do conhecimento médico e dos seus doentes

Apesar dos seus poucos recursos, a APOI tem promovido todos os esforços para estimular o interesse público e profissional pela OI, e tem-se afirmado como uma instituição de referência nas suas relações com a comunidade científica e com a indústria, muito em particular através do seu **Conselho Científico** e do seu **Gabinete de Apoio à Investigação**.

JUNTE-SE A NÓS

Junte-se à **Associação Portuguesa de Osteogénese Imperfeita** e beneficie de atualizações científicas em primeira mão, ficar ligado a uma rede de especialistas nacional e internacional e obter descontos e serviços nas nossas atividades e nas dos nossos parceiros.

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associação portuguesa de osteogenese imperfeita

JUNTE-SE A NÓS

VISITE APOI.PT

BONE 2024
DYSPLASIAS
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ALIANÇA INQUEBRÁVEL