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EXT1-related osteochondromas and neurodevelopmental features

Osteocondromas associados a EXT1 *e alterações do neurodesenvolvimento*

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Keypoints

What is known

– Hereditary multiple osteochondromas is an autosomal dominant skeletal disorder most commonly associated with pathogenic variants in EXT1 or EXT2.

What is added

– This case illustrates the incidental diagnosis of hereditary multiple osteochondromas following the detection of a familial 8q24 deletion by genomic testing, highlighting the importance of recognizing clinically relevant secondary findings uncovered through genomic investigation.

Osteochondromas are the most common benign bone tumours and can result from hereditary multiple osteochondromas (HMO), an autosomal dominant disorder most commonly caused by pathogenic variants involving the *EXT1* or *EXT2* genes. Radiographs typically demonstrate metaphyseal bony outgrowths with cortical and medullary continuity with the parent bone, which are characteristic of the condition.[1–3]

We report a 14-year-old adolescent with a history of foetal growth restriction, persistent short stature (< P3), mild intellectual disability, and language impairment. Physical examination disclosed a narrow forehead, low hairline, dysplastic eyebrows, and a broad nasal root. Genetic diagnostics by array CGH identified a heterozygous 9.739 Mb interstitial deletion at 8q24.11-q24.21 (GRCh38: 118019900–127759326), encompassing *EXT1* and multiple adjacent genes. This finding prompted a skeletal survey that showed multiple osteochondromas involving the proximal tibiae, fibulae, hands, and distal femora (Fig. 1). Her father had a history of learning disabilities, as well as multiple osteochondromas, the latter of which was not previously assessed in a clinical setting. He also tested positive for a heterozygous familial 8q24 deletion. HMO is primarily a skeletal disorder that entails musculoskeletal management. Neurodevelopmental manifestations have occasionally been reported in patients with deletions.[4,5] Although this deletion encompasses multiple adjacent genes in addition to *EXT1*, with both family members presenting with mild intellectual disability, a direct association cannot be clearly established. Most importantly, the secondary diagnosis of multiple osteochondromas allowed proper clinical management and genetic counselling.

This image highlights the characteristic radiographic appearance of HMO and underscores the importance of performing a thorough physical examination and

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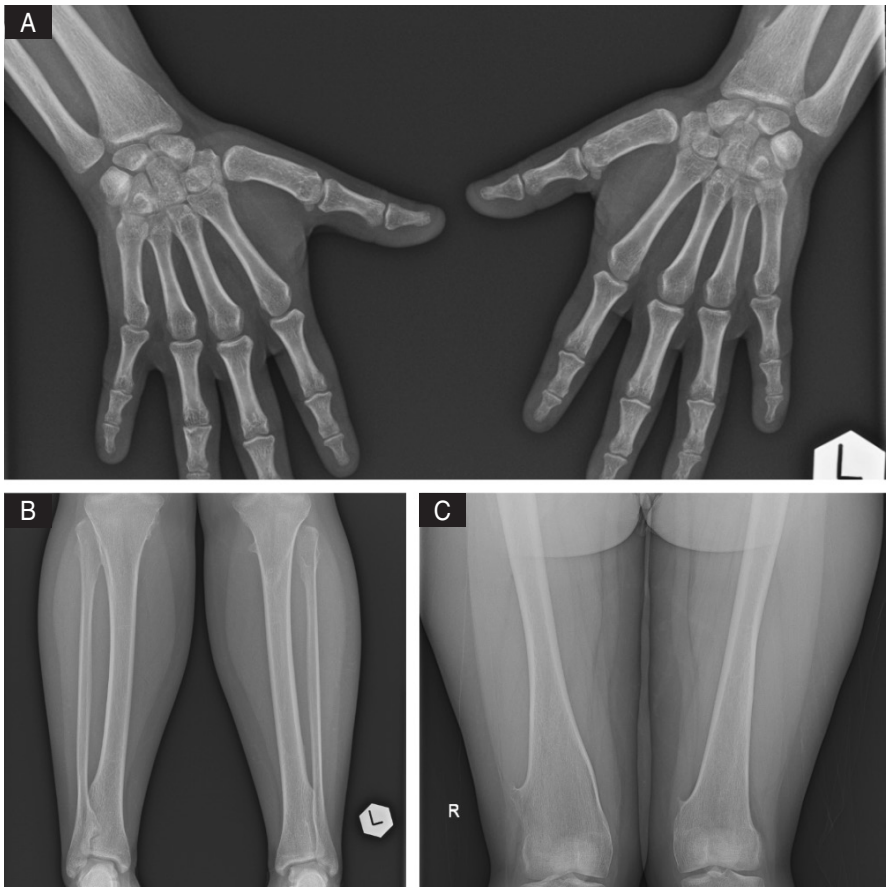

Figure 1. Skeletal survey showing multiple osteochondromas in an EXT1-related disorder. **A:** wrist and distal radius; **B:** lower limbs; **C:** distal femora.

considering the possibility of secondary findings through genomic testing.

Author contributions

O. Yahello: writing – original draft; writing – review and editing; M. Lima: writing – original draft; writing – review and editing; C. Reis: writing – review and editing; supervision; A. Pinheiro: writing – review and editing; supervision.

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Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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