Clinical Case Report

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Daughter and mother diagnosed with hereditary multiple exostoses

A case report and a review of the literature

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Abstract

Introduction: Hereditary multiple exostoses (HME) or osteochondromatosis is a rare autosomal dominant disease characterized by multiple osteochondromas and skeletal deformities.

Patient Concerns & Diagnoses: We present the case of a 5 years and 9 month-old patient who presented with inferior limb pain for approximately 6 months, associating also deformity of the right index finger for a month. Hand X-ray revealed a radiologic abnormality of the right radius, therefore the child was referred to our clinic for further investigations. The X-rays revealed multiple osteochondromas of the radius, metacarpal bones, hand phalangeal bones, femur, tibia, fibula, metatarsal bones, and foot phalangeal bones. We mention that the same radiological aspect was identified in the case of the patient's mother, undiagnosed until that moment.

Outcomes: The particularity of this case consists in identification of a rare genetic pathology, HME in a 5-year-old patient, without any known familial history, after the occurrence of a nontraumatic joint dislocation of the right index finger.

Conclusion: HME is a rare genetic condition, without a curative treatment, burdened by multiple complications, and whose diagnosis is usually established during childhood.

Abbreviation: HME = hereditary multiple exostoses.

Keywords: autosomal dominant transmission, genetic disorder, hereditary multiple exostoses

1. Introduction

Osteochondromatosis, also known as hereditary multiple exostoses (HME), is a rare autosomal dominant genetic disorder characterized by multiple osteochondromas and skeletal deformities, such as scoliosis, forearm deformities, genu valgum deformity of inferior limbs, and even length differences between limbs.[1–3] Osteochondroma is a benign tumor that affects growth cartilages, with the origin in the metaphysis of the long bones or the surface of flat bones. The incidence of osteochondromatosis among general population is of approximately 1 in 50,000 individuals.[4,5] The clinical picture of the patients afflicted by this pathology usually includes local pain due to compression and irritation of osteochondroma on the surrounding tissues, but also deformities or even nontraumatic joint dislocation and fractures.

The diagnosis of osteochondromatosis is mainly clinical and radiological. Genetic testing is not usually needed due to the clear radiologic aspect of osteochondromas, only in cases when the diagnosis is not known or it cannot be established in either of the parents. HME complications are mainly orthopedic, being represented in most cases by skeletal deformities, joint dislocations, and fractures.[5] Nevertheless, there are also more rare cases in which osteochondroma develops malignancy characteristics transforming into a chondrosarcoma.[5] Due to the fact that HME is a genetic disorder, no curative treatment is available for the patients diagnosed with this disorder. Therefore, they will benefit only from treatment of its complications, such as the orthopedic correction of skeletal deformities or joint dislocations, and fracture treatment. Radiological follow-up is probably one of the most important aspects involved in the management of patients diagnosed with HME due to the risk of these bone tumors to become malignant.[1,5]

We present this case report of HME, a rare autosomal dominant genetic disorder in a 5-year-old female patient, without positive familial history in either of the parents, with the aim of underlining the fact that diagnosis can be established during both childhood and adulthood, the patient's mother being diagnosed by us at the age of 33 years old.

Informed consent was obtained from the patient's mother (legal guardian) for the publication of this case report.

2. Case report

2.1. Presenting concerns

We present the case of a 5 years and 9-month-old female patient, who was admitted in our clinic for inferior limb pain and painful edema of the right index finger. The anamnesis revealed that the patient's mother had complained of joint pain during childhood, and she was diagnosed with acute articular rheumatism. The patient's personal history underlined that she had complained of

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inferior limb pain for approximately 1 year, but in the last month she associated painful edema of the right index finger, therefore she was referred to a pediatric surgeon, who suspected a proximal interphalangeal subjoint dislocation and requested a hand X-ray. The X-ray showed 2 opaque lesions in the right radial metaphysis, therefore she was admitted in our clinic for further investigations.

2.2. Clinical findings

The clinical exam performed at the moment of admission revealed the following pathological elements: weight and height deficit, W: 17.6 kg (−0.88 SD), H: 109.5 cm (−1.02 SD), BMI: 14.7 (−0.78 SD), deformity of the proximal interphalangeal joint of the right index finger (Fig. 1), abnormal position of the inferior limbs (genu valgum), and bilateral flat feet.

2.3. Diagnostic focus and assessment

The laboratory test performed during admission, namely CBC count, transaminases, immunity status (IgA, IgM, and IgG) tests, peripheral smear, but also thyroid hormones, rheumatoid factor, antistreptolysin O titer, anticitrulinated protein antibodies, antinuclear antibodies, circulating immune complexes, parathormone, and serum phosphorus, were all within normal limits. The X-ray of inferior limbs revealed multiple metaphyseal osteochondromas of the distal femur, proximal tibia, and fibula of the 3rd right metatarsal bone, and proximal and medial phalanges of the 2nd, 3rd. and 4th right toes (Fig. 2, 3 and 4).

We also performed a thorax and a spinal column X-ray, but no pathological aspects were identified. We referred the patient to an endocrinologist, but both clinical and ultrasound exams of the thyroid gland were normal. We also requested a genetic consultation, and the genetics specialist suggested a radiological investigation of parents and also periodic radiological assessment of bone lesions with pediatric monitoring.

Based on all these clinical and radiologic findings, we established the diagnosis of multiple osteochondromas.

2.4. Therapeutic focus and assessment

We assessed both parents radiologically in order to identify a possible hereditary transmission of these bone tumors. The mother X-rays revealed multiple osteochondromas of the left radius, bilateral femur, tibia, and peroneus, and also bilateral metatarsals.

Therefore, the final diagnosis was of HME.

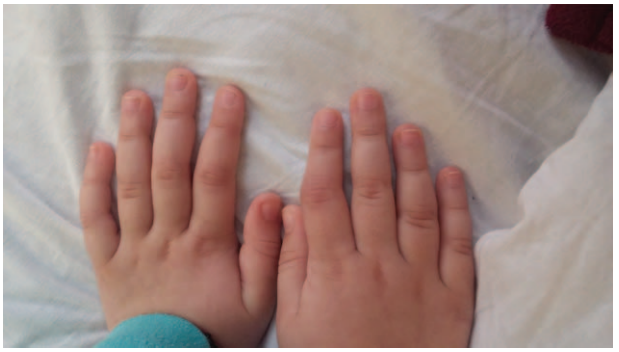

Figure 1. Aspect of the proximal interphalangeal joint right index.

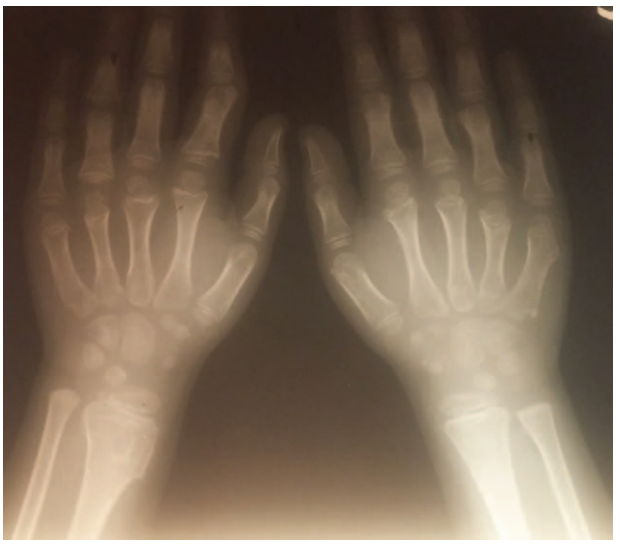

Figure 2. Multiple osteochondromas of the hands – radiological aspect.

2.5. Follow-up and outcome

We discharged the patient with the recommendation of radiological monitoring at least once a year or if any clinical sign of complications appears, taking under consideration the risk of malignant transformation.[6] The radiological aspect at 6 month follow-up did not reveal any additional modifications.

3. Discussions

Multiple hereditary exostoses is a rare pathology, whose prevalence in the Western countries is 1:50,000 individuals, with a higher frequency in males in comparison to females.[4,5] Nevertheless, in the case presented above, this condition was diagnosed in 2 female persons, mother and daughter. Approximately 90% of the patients with hereditary exostoses present mutations in the following genes: exostin-1 (EXT1) localized on chromosome 8q23-q24 or exostin-2 (EXT2) localized on chromosome 11p11-p12 of the germinal line that encode glycosyltransferases involved in the synthesis of heparin sulfate, but the substrate of this condition is a heterogeneous one.[7,8]

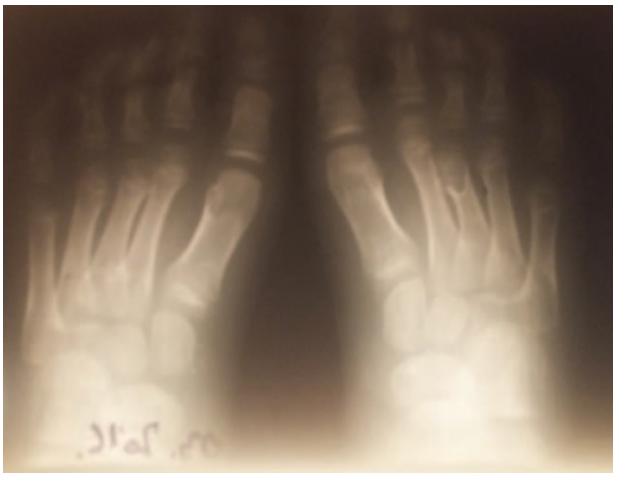

Figure 3. Multiple osteochondromas of the legs – radiological aspect.

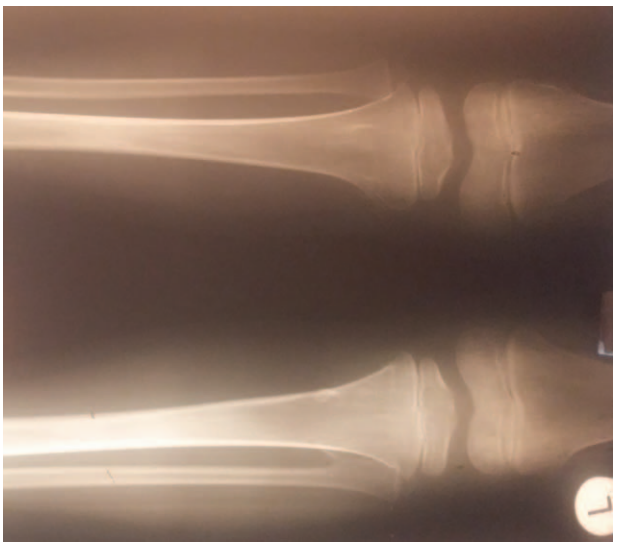

Figure 4. Multiple osteochondromas of the lower legs – radiological aspect.

Osteochondromas develop in the 1st decade of life, as in the case of our patient, diagnosed at the age of 5 years, and they stop once the growth process is completed due to their connection with the growth cartilages. Long bones are almost always affected, but cases were reported where osteochondromas developed in the scapula, ribs, or pelvis.[9] Radiologic assessment of the hip is also needed in children with HME, and if hip osteochondromas are identified, radiologic follow-up is needed in order to detect hip subluxation.[10] In the case presented above, the thoracic radiography did not reveal osteochondromas of the ribs or scapula. Also, the pelvic and hip lesions were excluded by the inferior limbs X-ray. Most of the patients afflicted by this condition complain of limb pain, similarly to our case. Osteochondomatosis can lead to growth impairment with short stature, limb length inequality, joint, and limb deformities.[1–3] Our patient also presented vicious position of inferior limbs (valgum), deformity of the right index, and short stature (-1,02 DS). HME are usually diagnosed radiologically by identification of 2 or multiple benign lesions in the long bones.[11] In the case presented above, multiple osteochondromas were identified in both daughter and mother, at the level of radius, femur, tibia, fibula, metatarsal bones, and phalanges. The most important complication of this pathology remains the malignant transformation of osteochondroma with development of a rare form of bone cancer called chondrosarcoma, with an incidence of approximately 0.5% to 5%.[5,12] Thus, periodic radiological monitoring of patients diagnosed with HME is one of the most important aspects in the management of these patients. The increase in size of osteochondroma in case of adult patients represents a characteristic of malignant transformation, while in children the development of new osteochondromas or even increase in size of preexisting ones represent elements of normal evolution in case of HME.[13] The radiological follow-up of our patient at 6 months after diagnosis did not reveal any additional modifications in comparison to the initially performed X-rays. Nevertheless, the literature reports cases with spontaneous disappearance of osteochondromas during childhood or puberty.[14,15] Surgical treatment of these lesions must be taken into consideration only in case of complications development, such as infection, synovial cysts, vascular, or nervous impairment, but also malignant transformation.[16] Callus distraction of the ulna with angular correction of the radius and ulna is used in patients suffering from multiple hereditary osteochondromas to improve forearm function.[17] Nerve compression, another complication encountered in patients with HME, can lead to nerve damage. Nerve decompression by resection of the offending exostosis should be considered for these patients.[18]

4. Conclusions

HME is a rare genetic condition, without a curative treatment, burdened by multiple complications, whose diagnosis is usually established during childhood. Nevertheless, this condition can also be diagnosed during adulthood in the lack of complications.

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