



Reporte de caso

METACHONDROMATOSIS: CLINICAL AND RADIOLOGICAL DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Palabras clave: Encondromatosis; Metacondromatosis; Exostosis; Osteocondroma; *PTPN11* gene.

Keywords: Enchondromatosis; Metachondromatosis; Exostosis; Osteochondroma; *PTPN11* gene.

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SUMMARY

The clinical case of a 9-year-old patient derived from an Orthopedics service to the Institute of Genetics at Universidad Nacional de Colombia due to a longstanding medical history of multiple bony outgrowths that required surgical management without etiologic diagnosis is presented in this paper. A possible diagnosis of metachondromatosis is suggested based on the clinical course, the family history, and the findings of the biopsy and regular growth parameters. On the other hand, differential diagnoses were compared taking into account the most common enchondromatosis type, based on data obtained during physical examination, radiological signs and other variables. This comparison was grounded on the review of existing literature on this type of entities.

INTRODUCTION

Metachondromatosis is a very rare entity pertaining to the large group of enchondromatosis, which was described in 1971 by Pierre Maroteaux (1). It is an autosomal dominant hereditary disorder characterized by the appear-

ance of irregular cartilaginous and, occasionally, bone exostosis mainly in hands and feet, which is associated with iliac crests and femoral neck irregularity, and spine integrity (1-3).

Until very recently, it was found that the loss of function in the *PTPN11* gene (tumor suppressor gene) was directly related to the occurrence of this entity (4, 5) that has a benign course during which some injuries may spontaneously return, causing deformities that require surgical intervention (2, 3).

CASE PRESENTATION

Nine-year-old, female patient attending consultation in the Institute of Genetics at Universidad Nacional de Colombia, who was referred by the orthopedic service of a hospital in Ibagué; the child developed the condition at age seven, with a mass in the right ankle associated with abnormal gait. In the place of origin, an X-ray of the foot was taken to initiate the study, and it clearly showed an exostosis of the talus, reason why the patient was subsequently taken to surgery for resec-



Fig 1. X-ray taken in 2011. It shows a round lesion over the talus with bone density compatible with an exostosis. Source: Own elaboration based on the data obtained in the study.

tion (see Figure 1). After continuing with the study, a second exostosis in the left anterior tibial spine was observed (see Figure 2) and a surgical treatment, as in the previous case, was necessary (see Figure 3). The histopathology of both surgical specimens was reported as benign osteochondroma.

Approximately one year later, the child's mother notices a new mass in the left collarbone and takes the patient back to the orthopedic oncology clinic, which refers her to genetics along with a shoulder X-ray (see Figure 4), to obtain a comprehensive assessment under the diagnosis of multiple osteochondromatosis.

The mother reported a refractive error managed with correction, chronic constipation, back

pain and frequent costalgia during the review of systems. According to the mother, the patient was adopted from an institution which fostered her together with her siblings; one of them had a similar medical profile and, apparently, the father had an unidentified bone condition (see Figure 5). The patient also presented atopic dermatitis and underwent umbilical hernia repair at age eight, with no other record of importance. She is currently attending school with good performance.

Physical examination showed a female child with proper weight and height for her age, normocephalic and with positive signs of apparent ocular hypertelorism, posteriorly rotated ears, dental enamel hypoplasia and apparent webbed neck (see Figure 6);



Fig 2. Radiography that shows a bone mass dependent on the anterior tibial spine and slightly sclerotic smooth edges.

Source: Own elaboration based on the data obtained in the study.



Fig 3. Radiography taken after surgical resection, in which lytic lesions and sclerotic edges in the left tibial diaphysis are seen.
Source: Own elaboration based on the data obtained in the study.

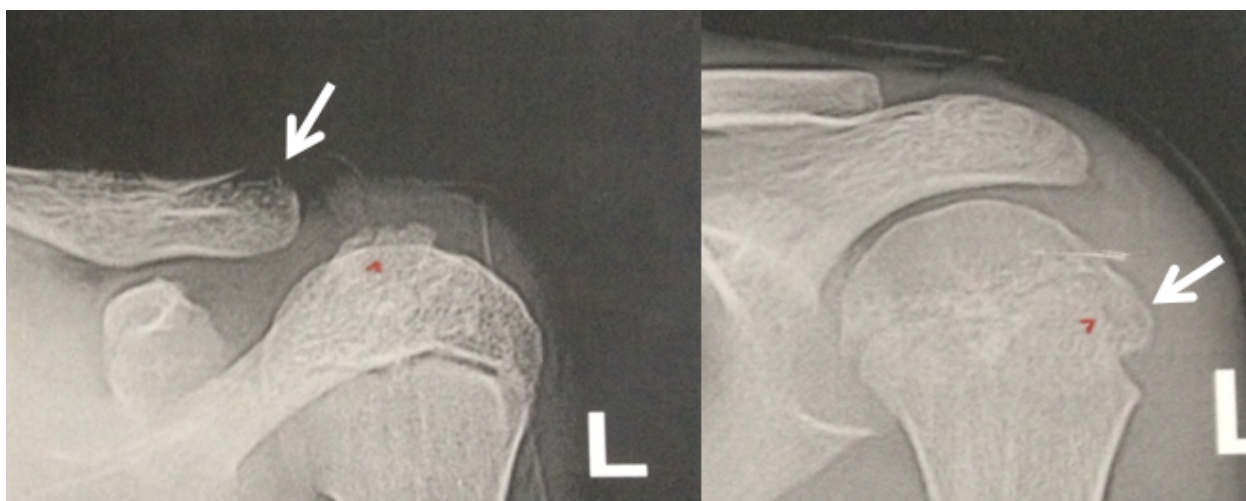


Fig 4. Left shoulder radiographs show bony outgrowths towards the posterolateral part of the collarbone, and in the outer region of the humeral head.
Source: Own elaboration based on the data obtained in the study.

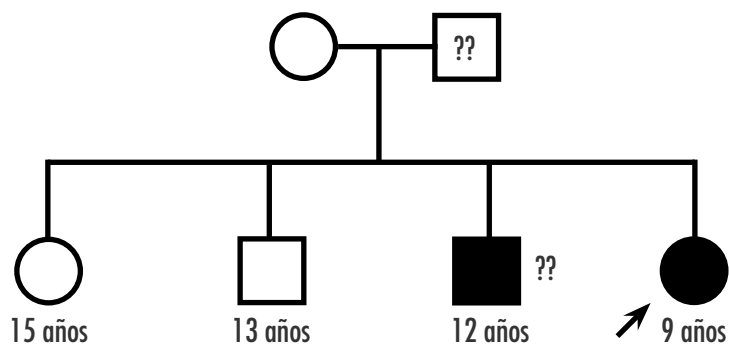


Fig 5. Genogram of the case patient.
Source: Own elaboration based on the data obtained in the study.



Fig 6. Case patient.

Fuente: Own elaboration based on the data obtained in the study.

the patient's thorax presents pectus excavatum, right nipple slightly lower than the left one and breast Tanner II; normal female external genitalia, Tanner II; spine without apparent deviation or alteration and limbs with observable and palpable small tumefaction in the outer third of the left clavicle, proximal left humerus and a deformity in the left anterior proximal tibia.

DISCUSSION Y CONCLUSIONS

Metachondromatosis is a rare bone disorder in which enchondromas and osteochondromas simultaneously appear, and whose prevalence in Colombia and Latin America is unreported. The few existing case reports describe families in which the disease seems to be associated with loss of function mutations in the PTPN11 gene (12q24) (5). Apart from the distinctive clinical presentation during the first decade of life and the location of the lesions, the diagnosis is based on the tenden-

cy to spontaneous remission of some injuries and the lack of involvement of height, on radiographic findings such as images that suggest osteochondroma in the metaphyses of short tubular bones that coexist with images reminiscent of enchondromas, and on bone biopsies that allow confirming the structure of the lesions (2).

This case presents a patient whose clinical profile fits in the differential diagnosis of hereditary multiple osteochondroma, Ollier disease and Maffucci syndrome but one in which the biopsy of lesions in the tibia allowed confirming that the injuries actually correspond to enchondromas and osteochondromas. While this particular finding suggests metachondromatosis, other criteria based on the understanding of the clinical, radiological and hereditary characteristics of various differential diagnoses, which are exposed in Table 1, should be taken into account. Additionally, metachondromatosis is transmitted through autosomal dominant inheritance.

Table 1. Differential diagnosis of enchondromatosis

Disease	Ollier disease	Mafucci Syndrome	Metachondromatosis	Spondylo enchondrodysplasia	Dispondyloenchondromatosis	Genochondromatosis
	It generally appears during the first decade of life. This disease is distinguished by the appearance of masses, usually in hands and feet, of different characteristics and asymmetrical distribution, with little involvement of the skull and vertebral bodies. It usually implies a major compromise of growth (2, 3, 7).	It manifests as multiple, asymmetric, enchondromas in metaphyseal areas of the hand, feet, femur, tibia and fibula. This is associated with multiple soft tissue hemangiomas. 25% of these cases appear during the first year of age, 45% before age six and 78% before puberty (2, 3, 9).	This condition is characterized by the appearance of osteochondromas in hands and feet and enchondromas in femur, tibia and iliac crest. It presents early onset during childhood, without significant joint or bone skeleton involvement, with particular spontaneous regression of exostosis that can occur during childhood or even in adulthood. No new lesions appear after bone maturation. (2,3,10).	It is associated with facial abnormalities, short stature, rhizomelic micromelia, changes in the curvatures of the spine (particularly lordosis), and funnel chest. It can be accompanied by angular changes of the limbs (3, 11, 12).	It is characterized by progressive kyphosis, scoliosis, asymmetric shortening of the lower limbs, of early onset (even neonatal), neonatal dwarfism, flattening of the midface with frontal bossing without involvement of hands or feet. It usually manifests "windswept deformity", a disorder characterized by varus rotation of one limb and valgus in the other (14, 15).	It has very few clinical manifestations and is usually found by chance; however, it can be presumed when: Type I: presence of a lump in the medial end of the clavicle, without involvement of hands, feet or hips. Type II: presence of symmetrical masses in hands and feet, without any clavicular involvement. It has a benign course, does not affect the growth of patients and usually regresses, leading to asymptomatic adults (16, 17).

Disease	Ollier disease	Mafucci Syndrome	Metachondromatosis	Spondylo enchondrodysplasia	Dispondyloenchondromatosis	Genochondromatosis
Radiology	Radiolucent oval or elongated lesions, with asymmetrical distribution that depart from the metaphysis and extend towards the diaphysis, usually found in long bones or in the small bones of the hands and feet. Associated pathological fractures can be observed (3, 7).	Radiolucent areas with eccentric protrusions, irregular mineralization, cortical thinning and endosteal scalloping are evident. Flebolitis and soft tissue calcifications in hemangiomas can be seen (2, 9).	Radiolucent lesions near the metaphyseal, pointing towards the joint, are seen. Bone deformity is also found in iliac crests, proximal tibia and, to a lesser extent, proximal femur. Calcification found in peritubular soft tissue (2, 3, 10).	Lytic alterations are seen in the vertebral bodies resulting in the presence of platyspondyly, with areas showing ossification alteration. It is associated with enchondroma type lesions in tubular and flat bones, which are also shortened and have irregular metaphysis and epiphysis, especially in the proximal fibula and distal ulna. Changes in the pelvis are also found because the iliac bones are usually short and wide, with horizontal acetabular roofs (3, 11, 12).	It is mainly characterized by anisospandy, leading to kyphoscoliosis. It also shows enchondroma type lesions in metaphyseal and diaphyseal of long and flat tubular bones (14, 15).	It is characterized by symmetrical enchondromas in the lower femoral, and upper tibial and humeral metaphysis (12, 13). Type I: enchondromas are also found in the medial end of the clavicle (12). Type II: enchondromas in small tubular bones are found (17).
	No hereditary component has been observed, however mutations in PTHR1 have been described (2, 3, 7).	No hereditary component has been observed, however associated mutations in PTHR1, IDH1 and IDH2 have been found (3).	Autosomal dominant associated with mutation in PTPN11 (3.10).	Heredity patterns in both autosomal dominant and autosomal recessive due to mutation in ACP5, have been suggested (3, 11, 12).	No heredity pattern because it has been associated with a missense mutation in the COL2A1 gene of collagen type 2 (14, 15).	So far, the characteristic family involvement is presumed to be autosomal dominant heredity (16, 17).

Disease	Ollier disease	Mafucci Syndrome	Metachondromatosis	Spondyloenchondrodysplasia	Dispondyloenchondromatosis	Genochondromatosis
	Malignant transformation	It varies between 5% and 50%; the most frequent is the shift to chondrosarcoma in the involvement of long or flat bones (2,8).	Malignization is found in 23% of the cases, mainly chondrosarcomas directly related to the dysplastic cartilage. (9)	No significant increase in the malignization rates of these lesions has been found (10).	There are no reports in the literature (2).	Literature has not reported any malignant transformation (2).
	Prevalence	1/100.000 (2, 7).	250 cases described in the literature (13).	25 cases reported in the literature (13).	36 cases reported in the literature (13).	12 cases reported in the literature (15).
Associated entities	Certain association to entities such as glioma tumor and juvenile granulosa cell tumor has been observed (7).	No association with vascular or cartilaginous tumors such as astrocytoma, demopituitary and juvenile granulosa cells tumor has been found (2, 9).	Nerve paralysis has been reported due to the effect of the mass associated with exostosis; avascular necrosis of the femoral head, which may lead to angular deformities, has also been reported (2, 10).	It is the only entity of Mendelian inheritance associated with autoimmunity (3, 11, 12).	Because of the associated mutation, it is postulated as a type II collagenopathy (14, 15).	No associated entities have been reported.

Source: Own elaboration based on the data obtained in the study.

It is worth noticing that the lesions of this patient have been surgically treated, so its exact course towards progression or resolution is unknown, although one fact that leads to the diagnosis of metachondromatosis is the larger tibial lesion that has apparently gone through periods of remission and the absence of alterations of the spine.

In conclusion, metachondromatosis is considered as the first probable diagnosis, and in order to be confirmed, it is necessary to validate new excrescence biopsies, a full assessment of the siblings and, eventually, of the parents, to determine if they show the same profile, along with a molecular analysis to identify a mutation, particularly the PTPN11, which is fundamental for a definitive diagnosis.

INFORMED CONSENT

Informed consent was given by the mother, who acts as legal guardian of the child, and by the patient, to publish this report.

DECLARATION OF TRANSPARENCY

The authors state that this text is an honest, accurate and transparent account of the case report presented, that no important aspect of the study has been omitted and that all limitations found have been exposed.

CONFLICT OF INTERESTS

None stated by the authors.

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