

# Multiple Skeletal Deformities in a Middle-Aged Man

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**A 54-year-old man was seen in our endocrinology clinic with evidence of a limited range of motion in his left foot. He had a history of diabetes mellitus type 2 and atrial fibrillation. His family history included evidence of skeletal deformities in some of his relatives. This could imply the potential existence of a hereditary condition. It is worth noting that spontaneous mutations have been reported in some cases. A pertinent physical examination revealed a surgical scar on the patient's left knee, a hallux valgus deformity on his left foot with compromised joint function, and painless bony prominences on that same foot. The skeletal survey findings were consistent with multiple hereditary exostoses. Multiple osteochondromatosis (MO) is a rare genetic disorder associated with serious complications that may significantly affect the health-related quality of life of anyone having the disorder. To prevent further complications, these patients require long-term follow-up with regular clinical and radiological examinations. [P R Health Sci J 2015;34:228-230]**

*Key words: Multiple Osteochondromatosis (MO), Hereditary Multiple Exostoses (HME), Chondrosarcoma, Exostosin Genes*

**M**ultiple osteochondromatosis (MO), also known as hereditary multiple exostoses (HME), is a rare genetic disorder with an estimated prevalence of 1/50,000 among US adults (1). It seems to be more prevalent in males than in females (male-to-female ratio of 1.5:1) (2). It is an autosomal dominant condition caused by mutations of 2 exostosin genes: EXT 1 and EXT 2. EXT1 and EXT2, located, respectively, at 8q24 and 11p11-p12, have been implicated as the cause of MO (2). An additional linkage to chromosome 19p has been found, suggesting the existence of an EXT3 gene. The EXT genes encode glycosyltransferases, catalyzing heparan sulfate polymerization (2). Mutations in EXT1 or EXT2 result in multiple benign cartilaginous capped lesions growing in the juxtaphyseal region (1). They are either pedunculated or sessile (broad based) and can vary widely in size.

Although 90% of all individuals with HME have an affected parent, 10% have a de novo mutation (2). The diagnosis of MO is based on clinical and/or radiographic findings of multiple exostoses in 1 or more members of the family (3). Sequence and deletion analysis of the entire coding region of these genes may provide a prenatal diagnosis for those fetuses that are at increased risk and provide, as well, an opportunity for genetic counseling. Although exostoses are benign lesions, they are often associated with characteristic progressive skeletal deformities and may cause clinical symptoms with serious complications.

## Case History

A 54-year-old man seen at the endocrinology clinic with evidence of multiple skeletal deformities. The patient had a past medical history of diabetes mellitus type II, diagnosed 18 years prior, dyslipidemia, arterial hypertension, atrial fibrillation, and osteoarthritis. There was a family history of diabetes mellitus type II (his mother) and lung cancer (his father), as well as skeletal prominences (his great uncle and that uncle's son). At age 17 the patient underwent a surgical procedure of his left knee because of a limb-length discrepancy. A physical examination yielded the following data: height, 72 inches, weight, 115 kg, and evidence of a slight limp. His left foot had a hallux valgus deformity with compromised joint motion due to non-tender prominent bony masses but without erythema, swelling, increased skin temperature, or regional lymphadenopathy (Figure 1). The

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**Table 1.** Differential diagnosis of bone tumors

Bone Tumor	Age	Common Location	Treatment
Periosteal chondroma	Children and Adults M>F 2:1	Proximal humerus, proximal and distal femur, and the phalanges of the hands and feet.	Complete excision by curettage is curative.
Osteochondroma/MHE	Apparent within the first 12 years of life. M>F 1.5:1	Distal femur, proximal tibia, pelvis, and metaphyseal ends of the bones near the joint.	Surgical removal of troublesome lesions or lesions which appear to possess malignant potential is associated with a good outcome.
Non-ossifying fibroma	Children 75% occur in the second decade. M>F	Juxtaepiphyseal region of the long bones.	Lesions normally regress. Treat only if pathologic fractures are present.
Paget's disease	5-80 years old	Sites of malignant transformation are the femur, pelvis, humerus and craniofacial bones.	Can vary from wide resection and chemotherapy to palliative radiation for pain control.
Solitary enchondroma	Third decade M = F	Diaphysis of the long bones of the hands and feet, proximal femur, and humerus.	Painless enchondromas may be observed.

**Figure 1.** Left foot showing hallus valgus deformity with bony prominences

patient has had these skeletal prominences since childhood. No evidence of any hemangiomas or neurofibromas was apparent. Cutaneous sensation was assessed with a monofilament; this assessment revealed the presence of diabetic neuropathy with intact pulses. The patient reported having no history of fractures, pain, nerve-related symptoms, or increases in the size of his current bony prominences. His physical function and quality of life were generally well preserved. Because Charcot joint or Paget's disease was suspected, laboratories and a skeletal survey were ordered. Blood cell count, alkaline phosphatase, 25-OH vitamin D3, ionized calcium, and phosphorus were within normal limits. A skeletal survey showed multiple broad-based cortical protuberances on the left foot and ankle, with extensive osseous deformity consistent with sessile exostoses. Similar findings were present on the left hand, first digit, and on the medial aspect of the left distal femur and on the medial tibial plateau. No evidence of malignant transformation or nerve impingement was observed. Meniscal chondrocalcinosis and bowing of the left fibula were also noted (Figure 2). A whole-body scan revealed focal skeletal abnormalities and an increased concentration of radiotracer in the left sternoclavicular region, left medial femoral condyle, left ankle, and left foot, which increased concentration is consistent with the diagnosis of multiple metabolically active exostoses.

**Figure 2.** X-ray of the left foot showing multiple exostoses/ x-ray of the left leg showing bowing of the left fibula

## Discussion

Osteochondromas may cause pain and a reduction in skeletal growth, bony deformity, restricted joint motion, shortened stature, premature osteoarthritis, and the compression of peripheral nerves. The median age at diagnosis is 3 years; nearly all affected individuals are diagnosed by age 12 (3). Osteochondromas form predominantly on the physes of the long bones, pelvis, ribs, scapula, and vertebrae and begin to appear as early as 2 years of age (4).

MO patients have a lower health-related quality of life than does the general population (1). MO patients suffer more pain and undergo more surgeries compared to the general population. Osteochondromas are removed only when they cause pain, when they are the source of functional complaints (the compression of nerves or vessels), or for cosmetic reasons (3).

Often, associated with relative shortening and bowing of the ulna and fibula, wrist and ankle deformities are observed. Also, distal radioulnar, tibio-fibular diastasis, tapering and tilt of the tibial epiphyses and distal radius could be present. This condition can be treated effectively by combining hemiphyseal

stapling of the distal radius and tibia with ulnar and fibular lengthening (5). Limb length discrepancies greater than 1 inch are treated with epiphysiodesis (growth plate arrest) of the longer leg; early treatment of ankle deformities may prevent further deterioration of function.

The most dreaded of all the complications is the malignant transformation to secondary chondrosarcoma, which occurs in 0.5 to 5% of all cases. The clinical signs of this malignant transformation include a sudden increase in the size of the tumor after puberty accompanied by pain. An increase in the thickness of the cartilaginous cap of more than 1 cm (visible on an x-ray) should raise the suspicion of chondrosarcoma (6). When malignancy occurs, satisfactory results are obtained by undergoing an en-bloc resection of the lesion and its pseudocapsule with tumor-free margins, best done in a bone tumor referral center. Usually this procedure renders good long-term clinical results (2).

The differential diagnosis of hereditary multiple exostoses includes the enchondromatosis, which are a heterogeneous group of syndromes that present with multiple enchondromas associated with pathological fractures, pseudarthrosis, limb shortening, malignant transformation risk, and scoliosis. Enchondromatosis, such as Ollier disease, present as asymmetric intraosseous benign cartilaginous tumors, which are usually not the result of an inherited disorder (7). Other differential diagnoses of bone tumors are mentioned in Table 1.

In patients with multiple family members with bone tumors, obtaining a careful history and doing a physical examination are crucial for suspected MO. Our patient declined genetic counseling and refused, as well, to undergo any surgery related to correcting his left ankle deformity. He presented with orthopedic deformities early in life, for which he underwent left knee surgery. He has remained stable over time, without significant complications.

A high level of suspicion is important in patients having a family history of bone tumors and osteochondroma visible in plain x-rays. These patients may benefit from genetic testing as well as from being counseled to seek medical attention; to avoid further complications if their conditions changes. Changes could be manifested as pain, and increase in size of existing lesions.

It must be noted that eventually the majority of these cases will end up undergoing reconstructive surgery and single or multiple joint replacement (knee, hip and ankle).

Early diagnosis of this condition will not only prevent the burden to society that will be caused by the many patients who will end up becoming incapacitated because of their physical

problems, but will also further prevent the need for lifelong treatments to maintain the quality of life of these patients.

Although there is good literature review published regarding cases of hereditary multiple exostoses, however, only a few cases have been reported in Puerto Rico. We believe that our case will alert the medical profession to the importance of recognizing this disorder early so as to avoid its long-term consequences.

## Resumen

Paciente masculino de 54 años de edad evaluado en las clínicas de endocrinología por limitación al movimiento del pie izquierdo. Presentaba historial de diabetes tipo 2 y fibrilación atrial. Algunos de sus parientes presentaban deformidades óseas, lo cual pudiese implicar la posibilidad de una condición hereditaria. Sin embargo se han reportado mutaciones espontaneas en algunos casos. El examen físico pertinente demostró una cicatriz quirúrgica en su rodilla izquierda, deformidad de hallux valgus y anomalías esqueléticas no dolorosas del pie izquierdo. Los hallazgos en radiografías óseas fueron consistentes con exostosis múltiple hereditaria. Esta condición es un desorden genético poco común asociado con complicaciones que pueden afectar significativamente la calidad de vida de estos pacientes. Por esta razón es recomendable ofrecer seguimiento a largo plazo con exámenes físicos y radiografías frecuentes para prevenir serias complicaciones.

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