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A Rare Presentation and Management of Hereditary Multiple Exostoses

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ABSTRACT

Hereditary multiple exostoses (HME) is an inherited genetic condition characterized by the presence of multiple exostoses (osteochondromas). We report here the management of a rare case of a 29-year-old woman presented with multiple painless bony lumps that had developed insidiously over the past 10 years. The sites of involvement were the knees and the distal thirds of the fore arms and femurs. Radiographs showed well-defined sessile bone-density spurs arising from the metaphyses, with no alterations in the surrounding soft tissues. After surgical resection, histological examination of the operative specimens established the diagnosis of hereditary multiple exostosis.

Introduction

Hereditary multiple exostoses (HME) is an inherited genetic condition characterized by the presence of multiple exostoses (osteochondromas). MHE is a relatively rare autosomal dominant disorder, mainly caused by loss of function mutations in two genes: exostosin-1 (EXT1) and exostosin-2 (EXT2). We report here the management of a rare case of a patient with HME.

Case Report

A 29-year-old woman presented with multiple painless bony lumps that had developed insidiously over the past 10 years. The sites of involvement were the knees and the distal thirds of the fore arms and femurs. Laboratory tests were normal. Radiographs showed well-defined sessile bone-density spurs arising from the metaphyses, with no alterations in the surrounding soft tissues. After surgical resection, histological examination of the operative specimens established the diagnosis of hereditary multiple exostosis (fig 1 – 2).

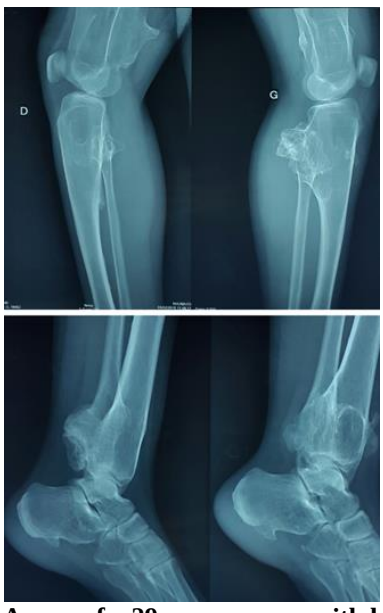

Figure 1. A case of a 29-year woman with hereditary multiple exostoses.

Physiopathology

HME is an autosomal dominant disorder caused by loss of function mutations in two genes: exostosin-1 (EXT1) and exostosin-2 (EXT2). The first gene was located on chromosome 8 (locus 8q24.1) and the second was identified on chromosome 11 (locus 11p11-13) [1]. Recently, 429 mutations in EXT1 and 223 in EXT2 have been described; most of them are sporadic [2]. EXT1 and EXT2 are very similar genes; their protein sequence showed structural similarities (both 80kD). Independent studies in 1998 linked EXT1 and EXT2 to heparan sulfate synthesis [3, 4]. In HME, EXT genes may have mutations leading to structural changes in EXT glycosyltransferases Those changes lead to disturb enzymatic activity with a consequent lower production of HS which the main cause of the formation of exostoses [5].

Diagnosis

Early diagnosis can only made by genetic screening because most of the patients are asymptomatic at birth. When symptoms become evident diagnosis result simple. Conventional radiographs are able to focus osteochondromas in the skeleton. Magnetic resonance imaging (MRI) allows measurement of cartilage cap thickness and the effect of HME on surrounding soft tissue structures. Kok et al. in 2013 claimed that a thickness of more than one centimeter claimed that a thickness of more than two centimeters have sensitivity and specificity greater than 95% for the detection of secondary chondrosarcomas [6].

Differential Diagnosis

Hardly exostoses may be confused with HME. They are intra-osseous tumours of hyaline cartilage. Enchondromas are the second most common benign cartilaginous tumour after osteochondromas. While Ollier disease is characterized by multiple enchondromas. Finally, Maffucci syndrome is characterized by multiple enchondromas and soft tissue hemangioma. Moreover, malignant degeneration in chondrosarcoma can be observed in both these disease. Another condition where exostoses can be found is Langer-Giedion syndrome, a very rare congenital disease caused by deletion of chromosome 8 [7].

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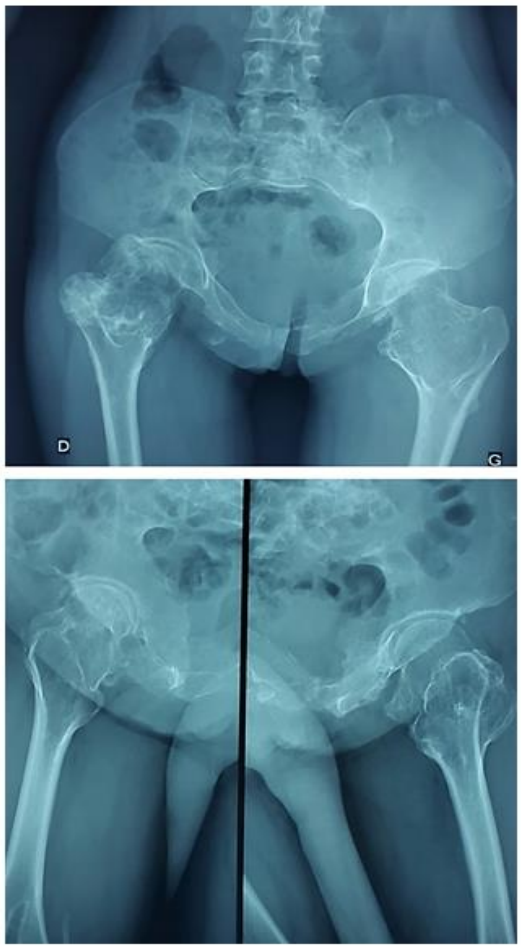

Figure 2. X-rays of pelvic region showing multiple exostoses.

Prognosis

HME is a disease that requires a regular follow-up to avoid many possible complications. The prognosis of secondary chondrosarcomas is good (the 5-year survival is estimated to be 90% [1]). However, regular clinical examination is needed for early detection of malignant transformation; this should be done every 12-24 months.

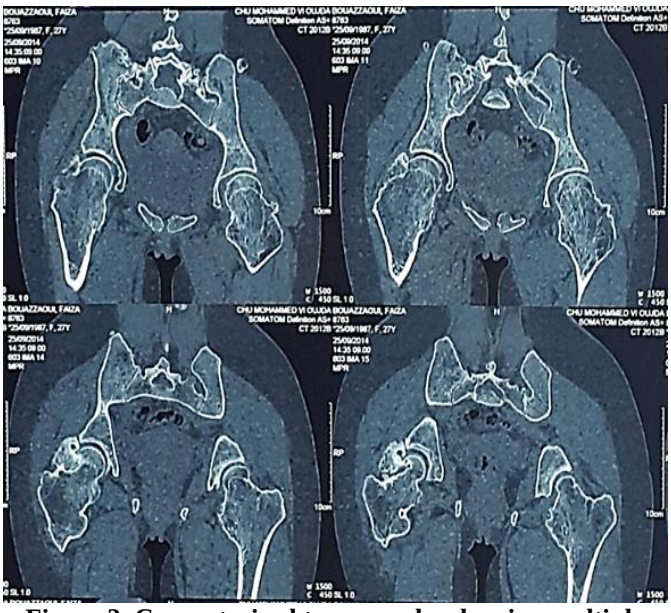

Figure 3. Computerized tomography showing multiple exostoses.

Treatment

The medical treatment for the HME is still at an experimental level. The therapeutic approach to HME is surgical. The treatment of exostoses must be conservative if there are no compression syndrome or clinical problems to avoid eventual surgical complications. However, spontaneous regression of these lesions has been noted in some single cases during childhood [8]). Surgical excision is a mostly easy procedure with low morbidity. Largest resections may require reconstructive techniques such allo-grafting and internal fixation. Local recurrence may occur for the development of a new lesion at the same location or incomplete surgical excision. In case of malignant degeneration (chondrosarcoma) surgical resection alone is usually sufficient because these tumors tend to be low-grade lesions. At last, HME is first of all a genetic disease. Research in this field is very active and recent discovers about physiopathology can individuate useful therapeutic target like the role of heparanase highlighted by Huegel et al. [9]. This protein is easily detectable in growth plates of unaffected people and has the ability to stimulate chondrogenesis. Through testing on mouse models, the researchers experimented a potent heparanase inhibitor, which inhibited chondrogenesis. These observations make heparanase as a conceivable therapeutic target for the future in HME.

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