Multiple exostosis disease

Multiple exostosis disease is a rare condition. It is characterized by the proliferation and the development of numerous bone swellings in the metaphysis of long bones with a possible abnormality in their shape and length. It preferentially affects the knees, shoulders, ankles and wrists. These lesions remain clinically asymptomatic, but the pain is the main complaint of patients. The phenotype of this disease varies greatly between patients. All bones that develop through endochondral ossification can be affected like long bones. Some localizations are rare but potentially serious such as the ribs, the spine or the pelvis due to the proximity to important structures. The most feared, although rare, complication is the transformation into chondrosarcoma, which required a close monitoring. The treatment can be conservative or surgical. The treatment and excisional surgery may be indicated in the event of functional disorders or deformities. The greater knowledge of the pathophysiology of the disease makes it possible to consider potential therapeutic targets. We report a rare case with iliac bone localization, discovered in adolescence rather than childhood.

Keywords: multiple cartilaginous exostoses ● skeletal dysplasia ● ulna lengthening ● osteochondromas

Introduction

Multiple exostosis disease, also known as familial osteochondromatosis or diaphyseal aclasis, is a rare genetic disease with an autosomal dominant disorder, characterized by the presence of multiple osteochondromas (exostoses) [1]. It is mainly caused by loss of function mutations in two genes: exostosin-1 (EXT1) and exostosin-2 (EXT2) and does not appear to have a sexual predominance. This benign tumor affects 1 in 50,000 births. Osteochondromas appears in the first decade of life and stops growing at puberty. In the majority of cases, they are asymptomatic [1,2]. The most common location is at the lateral side of the most active growth plate of a long bone. Clinical problems include pain and functional impairment. Additionally, growth deformities of bones and short stature are considerably present. Malignant degeneration of osteochondroma is a rare but important complication [3]. Sacrum localization is not usual. We report a case of a 20-year-old female patient who has an unusual localization in iliac bone, discovered in adolescence age.

Case Report

A 20-year-old female patient and the patient is the youngest of five siblings. There was no family history of bone disorder, nor consanguineous marriage or a similar case in the family. In her past medical history, she reports slip full on the pelvis at the age of fourteen causing a transient pain. Since three years a painful and progressive swelling in right buttock were of a dull and painful nature exacerbated when she walks. The patient also reports the presence of other not annoying or painful swelling since childhood in the right forefoot and the upper limbs not annoying or painful. Her main complaint for which she consulted was the painful right pelvic swelling.

Clinical exam

Clinical exam found the patient with short body type; the height was at 151 cm, and weight 58 kg. Ulnar shortening with deformity of the upper limb focusing on bayonet hand or pseudo-Madelung deformities (Figure 1A). Significant swelling of the right buttocks, measuring 10 cm in length, hard and fixed to the deep plane (Figure 1B), painful on pressure: the pain returned at 7/10. The clinical exam also identifies other swelling having the same characteristics but of variable sizes, in anterior face of the two ankles, bilateral first
metatarsophalangeal and the interphalangeal of the two first toes (Figure 1C).

Radiographic examination

Radiographic examination revealed several pedunculated or sessile metaphyseal bone growths involving the humerus, the radius, the distal tibias bone, the forefeet and the first toes, of varying size, which the biggest is located at the level of the posterior edge of the iliac bank of the right sacroiliac joint, measuring 64/63 mm. The CT-scan of the pelvis with the reconstruction images confirms the bone growth (Figure 2), involving the two iliac bones and the pelvis as well as the sacrum, with a wide implantation base and whose cortex continues with

Figure 1. Bone swellings located on the two forearms:pseudo-Madelung deformities (A- red arrows), on the right iliac bank (B- yellow arrow), on the anterior two ankles, first metatarsophalangeal and the interphalangeal of the first toes (C-blue arrow).

Figure 2. X-ray of the pelvis (A), CT-scan of the pelvis (B) with reconstruction images (C); Highlighting of several bony growths involving the two iliac bones and the pelvis as well as the sacrum, with a wide implantation base and whose cortex continues with that of the supporting bone. In the posterior edge of the right iliac bank, a voluminous bony outgrowth sits with a peripheral cartilaginous component, budding contours and protruding into the ipsilateral gluteal muscles, measuring 64/63 mm and is extended over 65 mm (white arrows). It is associated with other bone formations at the femoral necks which are enlarged (Black arrow).
that of the supporting bone. In the posterior edge of the right iliac bank, there is a voluminous bony outgrowth sits with a peripheral cartilaginous component, budding contours and protruding into the ipsilateral gluteal muscles, measuring 64/63 mm and is extended over 65 mm. It is associated with other bone formations at the femoral necks which are enlarged.

Laboratory investigations

Laboratory investigations results showed normal routine serum chemistry; serum calcium at 91 mg/l, serum phosphorus at 33 mg/l, serum alkaline phosphatase at 108 UI/l, creatinin 12 mg/l, urine calcium 315 mg/24hr, urin phosphorus 1208 mg/24 hr, parathormon 57 pg/ml, 25 (OH)vitamin D insufficiency 22,30 ng/ml. C-reactive protein and sedimentation rate at 1 mg/l and 5 mm/1th hour, respectively. The biopsy of the pelvic voluminous bony outgrowth confirmed itsosteeochondromas origin.

A diagnosis of hereditary multiple exostosis was made according to the clinical, radiological and histological findings. In this case, there were no signs of bone weakness or signs of malignant transformation. The analgesic treatment has been instituted, and a surgical approach of the pelvic bone growth is planned.

Discussion

Multiple exostosis disease or hereditary multiple exostosis also known as familial osteochondromatosis or diaphyseal aclasis is a rare genetic disease characterized by the presence of multiple benign exostoses [1]. It’s an autosomal dominant disorder caused by loss of function mutations in two genes: exostosin-1 and exostosin-2 that are linked to heparan sulfate synthesis. The specific molecular mechanism of the disruption of the cartilage structure and exostosesformation is still not known [2]. This condition affects 1 in 50,000 births, such values are probably underestimated because the asymptomatic lesions. In approximately 50% of individuals, multiple ostechondromas are initially diagnosed before 3,5 years of age. In more than 80%, it is diagnosed before the end of the first decade [2]. Otherwise, some studies found a significant correlation between male sex and severe clinical presentations, like pain and sensitivomotor deficits, even deformities of the limbs which can be explain by hormonal differences between genders, or genetic cause [3].

Most patients present most than 6 exostosis which they can be clearly visible and palpable. The habitual location includes the distal femur (90%), proximal tibia (84%), fibula (76%), and humerus (72%) but they are often first discovered on the ribs and the proximal tibia. They are rarely located in carpal and tarsal bones, and never in the facial bones because they are developed by intramembranous ossification [3]. Knees, shoulders, ankles and wrists are the most involved joints during diagnosis.

Exostoses can cause disturbances in the growing diaphysis occasioning deformities and functional limitations. A clinical classification system determine the burden and life limitations secondary to the disease classifying the patients on three groups according to the number of involved segments [4]. The typical deformity on the upper member is ulnar shortening and deformity focusing on bayonet hand or pseudo-Madelung deformities; and in the lower limbs the “Erlenmeyer flask”. The hip joint of the patients could be a “coxalvalga” and the knee joint with genu valgum with early knee arthritis and patella subluxation. Spinal exostoses could lead to severe and acute neurological syndromes. The lesion can become bigger and causes more problems [5]. The most serious complication is the transformation into secondary peripheral chondrosarcoma, which occurs in 0.5 to 5% of cases [6].

Conventional radiographs are able to focus ostechondromas in the appendicular skeleton. Computerized tomography can be considered for regions that are difficult to visualize (thorax, spine, pelvis). Magnetic resonance imaging can determine the cartilage thickness and the effect of the lesion on surrounding soft tissue structures, detecting the malignant transformation. The positron emission tomography and cintigraphy can be used such as alternative [5,7,8]. In the absence of genetic proof, the diagnostics are based on clinical and radiological data. Like the case of our patients.

There is no specific treatment which is symptomatic and surgical. The excisional surgery may be indicated in the event of functional disorders or deformities. The conservative treatment is indicating if there are no clinical problems to avoid. The spontaneous regression of the lesions has been documented in single cases during childhood and adolescence [9]. Excision is associated with low morbidity. A role for adjuvant radiotherapy and chemotherapy has not been proved in secondary chondrosarcomas. The prognosis of secondary chondrosarcomas is good, since these tumours rarely metastasise: the 5-year survival is estimated to be 90% [10].

Conclusion

Multiple Exostoses Disease is a chronic and rare disorder that requires a careful follow-up to avoid many possible complications. It is considered a difficult disease to
manage and has variable presentation between each patient. This case highlighted the importance of monitoring of patients with HME and how changes in bone structure can lead to deformities and pain. The originality of this case report is the pelvic localization, age of diagnosis and the rarity of the disease.

Conflicts of interest
The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or nonfinancial interest.

Authors’ contributions
Kawtar Nassar compiled this case report and performed the necessary literature review with the redaction and continues to follow this patient.

Saadia Janani revised then approved this case report.

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