A Familial Disease: Hereditary Multiple Osteochondromatosis.

Hira Masood Ghuman, Khalid Mehmood, Waqas Ali

ABSTRACT

Hereditary multiple osteochondromatosis (HMO) is a rare familial bony disease largely diagnosed in early childhood. It is characterized by multiple bony outgrowths at the juxtaepiphyseal regions of long bones, or the surfaces of flat bones. Mutations in EXT 1 and EXT 2 genes are understood to be responsible for the pathogenesis of HMO. To highlight the importance of genetic counseling for affected individuals, we describe the case of a 21 years old female, who presented for the first time with clinically apparent multiple osteochondromas at various sites. The largest one found was at the back of the left knee. This particular osteochondroma caused discomfort and a degree of functional impairment, and was consequently surgically excised. Unusual to this case is that her two younger siblings, a brother and sister, were also discovered on examination to have multiple asymptomatic osteochondromas. All three children have osteochondromas around both knee joints in common. Genetic counseling is a vital platform for educating patients on the disease itself and its pattern of inheritance, so to reduce the risk of transmission of the defective trait to future generations.

Key Words: Autosomal dominant, exostosis, genetic counseling, Hereditary multiple osteochondroma, osteosarcoma.

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INTRODUCTION

Hereditary Multiple Osteochondromatosis (HMO) was first described by John Hunter in 1839.[1] It is a rare genetic disorder, inherited in an autosomal dominant fashion, characterized by multiple cartilage capped benign tumors at juxta-epiphyseal regions of long bones.[2] HMO most commonly involves the ends of long bones especially around the knee, or flat bones like the pelvis and shoulder blade.[3]

Previous studies have shown that the majority of patients are diagnosed by 12 years of age.[3] A diagnosis is made with the clinical findings of multiple hard painless masses mostly near bone ends with possible accompanied complications of restriction of movement, unequal limb length, short stature (40% cases) and compression of surrounding neurovascular bundles.[3] Management involves either careful follow-up or surgical removal. Surgical excision is Only warranted when an osteochondroma causes such complications. While malignant transformation of an osteochondroma towards a secondary chondrosarcoma has an estimated 0.5 to 5% risk, there is no evidence or specific guidelines to suggest that surveillance must be carried out following clinical diagnosis.[2,3]

Here we present the case report of a 21 years old female, with no prior diagnosis, who we formally diagnosed in early adulthood with HMO. Her two siblings have also been found to be affected by HMO.

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CASE REPORT

A 21 years old girl presented to our clinic, at Medcare International Hospital Gujranwala, with limitations in movement due to a hard mass on the back of the left knee. Specifically, describing difficulty in sitting on the floor. On clinical examination, she was short in stature, and had osteochondromas around both knee joints, with the largest one being at the back of the left knee (Figure 1). She also had clinically apparent osteochondromas over her right proximal humerus, right scapula and left radius and ulna. Accompanying

the patient was her mother, who revealed that she had been noting these masses over the years. However, our consultation was the first instance of the patient visiting a medical professional with these findings. While we are aware that the mother does not have HMO, it is unknown if the father, who has now passed away, was affected. Further history taking revealed that the patient's two siblings, a brother and a sister, also have multiple boney masses.

Figure 1: Photographs shows the gross appearance of a clincally visible and palpable mass behind the left knee.

Radiological imaging was performed to further evaluate the patient's most distinctive mass behind the left knee. Pre-operative X- ray imaging demonstrates a sessile boney growth in close proximity to the popliteal trifurcation (Figure 2). Due to the discomfort caused by this mass, the patient was operated for excision of this exostosis. The excision itself went uneventful and she recovered well. Histopathological report correlated with clinical and radiological findings.

Figure 2: A plain X-Ray showing a sessile boney growth behind the left knee

Following this patient visit to clinic, her two siblings were then reviewed. They both showed to have the same bony lesions in different locations. Her sister has osteochondromas over right radius and ulna causing radiocarpal subluxation (figure 3). Similarly, her sister also has multiple small lesions around both knees. Furthermore, the patient's sister recently underwent excision for an osteochondroma in the first web space of her right foot. The brother has osteochondromas over both ankles, left forearm and around both knees (Figure 4). His knee lesions are larger in size than the rest.

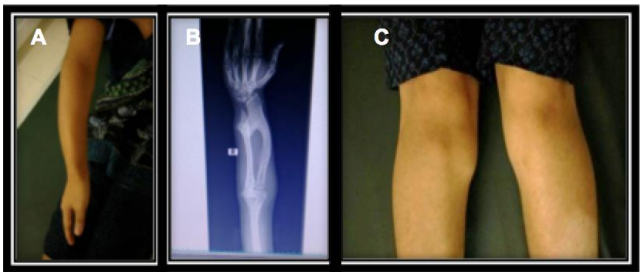

Figure 3: Patient's sister: (A) Gross appearance of osteochondroma over right radius and ulna (B) X-ray forearm showing a boney mass arising from the proximal radius and ulna (C) boney masses around right and left knees

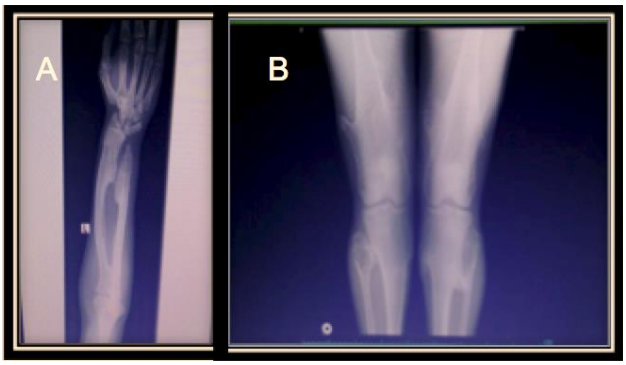

Figure 4: Patient's brother: (A) X-Ray showing a boney growth from the distal forearm (B) X-Ray of osteochondromas behind both knees.

DISCUSSION

Hereditary Multiple Osteochondroma, otherwise referred to as hereditary multiple exostosis, is a rare condition that runs in families. It is an autosomal disorder, which means that the presence of only one copy of altered allele is required to express this trait. The risk of passing this trait from affected parents to offspring for each pregnancy is 50%.[2] The defective

allele arises from a point mutation in EXT 1 and EXT 2 genes encoding exotosin 1 and 2 respectively, both proteins are involved in modifying heparin sulphate.[3] The mutated gene is highly likely to phenotypically manifest in individuals with inherited defective copies, as penetrance has been reported to be 96% in females, and 100% in males.[4] The main pathological effect of EXT 1 and 2 mutations is a resultant defect in metaphyseal osteoclast activity during bone remodeling in childhood, and as the bone matures these lesions ossify earlier predisposing to abnormal bony protuberances.[5]

Osteochondroma development is understood to be linked to bone maturation and growth, as they largely arise from the growth plates of long bones.[6] Therefore, most cases are diagnosed in the first decade of life. Nevertheless, the case presented above of a 21 years old girl newly diagnosed with HMO, is indicative that patients might only present when their boney outgrowths cause pain or limitations in movement. Although HMO has no impact on life expectancy, early diagnosis allows the patient to be educated about a condition with potential to cause physical deformities, and if the surgeon deems appropriate follow-up to assess for malignant transformation. Referral to a genetic analyst may also be necessary to further educate the patient on the nature and inheritance of HMO.

In the present case, our patient was discovered to have an osteochondroma on back of left knee causing pain and discomfort. The history failed to definitively reveal if the patient had a positive family, however, examination of the patients siblings did show that they had the condition. Radiographic assessment of our patient was consistent with HMO, showing a prominent boney outgrowth on surface of bone with a cartilage cap involving the knee. While this delayed presentation was complicated only by pain and discomfort, previous studies have shown that continued growth of boney masses after puberty along with cartilage cap >1.5cm is suggestive of malignant transformation.[4,7] CT scan and MRI is helpful in diagnosing malignant changes.[8]Other potential complications include nerve compressions (e.g. sciatic or common peroneal nerve), tendon compression, bursa formation and pseudo-aneurysm of popliteal artery.[9] The main management options for any case of HMO, including this case, are proper counseling, pain relief conservatively and surgery if it is very large and causing pain and continuous follow up might be needed to see for progression of the benign growths. Proper genetic counseling, especially in Pakistan, is of utmost importance of parents and adolescent patients is required regarding inheritance and implication of this disease so to avoid cousin marriages and to decrease transmission of this trait from one generation to the next.

CONCLUSION

Multiple hereditary osteochondroma is a rare genetic bone disease with an autosomal dominant pattern of inheritance. In some aspects the reported case is a typical case of HMO, however, it is of note as all three children of the same family are affected. There is a need for proper genetic counseling, as such traits run in families.

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Authorship and Contribution Declaration

Hira Masood Ghuman, Conception of the case report, Final approval of the case report for publication
Khalid Mehmood, Drafted the manuscript
Waqas Ali, Revised the case report critically for important intellectual content