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Case Report

HEREDITARY MULTIPLE EXOSTOSES: CASE REPORT

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ABSTRACT

Objective: Hereditary Multiple Exostoses (HME) is a genetically transmitted bone dysplasia that is inherited in an autosomal dominant manner. It usually presents after the age of two years as multiple bony growths on the appendicular skeleton. As a rare condition (incidence of 0.9-2/100,000), it is not commonly seen in our environment. This paper presents the clinical and radiological features of two patients seen in our hospital within a period of six months.

Method: The case records of two patients with hereditary multiple exostoses are presented to highlight the clinical presentation and management options of the condition.

Results: A boy and a girl who respectively manifested the features of hereditary multiple exostoses at the age of two and six years are presented. The main presenting features were painless progressively increasing bony swellings in both upper and lower limbs, with forearm deformity and ulnar deviation of the wrist. One of them had pressure symptoms which necessitated surgical excision of the symptomatic exostosis. Fine needle aspiration cytology confirmed the diagnosis of osteochondroma.

Conclusion: Hereditary multiple exostoses though rare, do occur in our environment and the management is essentially by masterly inactivity except when the bony swellings exhibit any complications or there is concomitant deformity.

Key Words: Hereditary, Multiple, Exostoses, Deformity. *(Accepted 9 June 2009)*

INTRODUCTION

Exostosis is a cartilage capped bony projection found primarily at the juxta-epiphyseal regions of the most rapidly growing ends of long bones [1]. It is the most common bone tumour seen in children[2-4]. The true prevalence is not known since many patients with asymptomatic lesions are never diagnosed. It is considered a harmatoma; as such it stopped growing at the end of the growth of the affected bones. In the clinical setting, exostosis presents most commonly as a solitary lesion while multiple exostoses affecting many bones are much rarely encountered. Patients with HME have multiple cartilage-capped exostoses that may be sessile or pedunculated.

Hereditary multiple exostoses is an autosomal dominant skeletal dysplasia affecting bones formed by endochondral ossification. It causes asymmetrical retardation of longitudinal bone growth with subsequent deformity, limb-length inequality and increased risk to secondary malignant transformation. Limb-length discrepancy is common. A clinically significant inequality of 2cm or greater has been reported with a prevalence ranging from 10-50% [4]. Shortening can occur in the femur and/or the tibia; the femur is affected approximately twice as commonly as the tibia [5]. As these lesions grow in the juxta-epiphyseal regions they have the tendency to cause mechanical interference with the normal function of those soft tissues passing over them. Tendons, muscles, nerves and arteries may all be displaced and irritated by the pressure of the exostosis. The consequence of this is bursitis, hyperaesthesia, pseudo-aneurysm or compression; some or all of which may be the pathogenesis of pain in this condition.

The implication of the progressive pathology of the condition is that the clinical presentation may be in three stages. In the first stage, patients will present with multiple lumps at the end of the long bones without any significant pain or deformity. The second stage will feature multiple lumps with pain or deformity while the third stage will consist of multiple lumps, pain and multiple deformities. Management therefore depends on the presentation. In the presence of uncomplicated exostoses, management is essentially by masterly inactivity as these patients have a normal life expectancy. However, surgical intervention (corrective osteotomy, epiphyseodesis, excision, limb lengthening) is indicated when the exostoses exhibit pressure symptoms, cause deformity or undergo malignant transformation. We hereby present the clinical and radiological features of two patients seen in our hospital within a period of six months.

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CASE REPORTS

(1) A.R., a 13 year old secondary school girl who presented at our outpatient clinic at NOHIL on October 2006 with a 7-year history of progressive swellings on both upper limbs, deformity of left forearm and bilateral knee swellings; (figures 1a and 1b). The patient noticed multiple swellings on both shoulders, forearms, and knees with associated ulnar deviation of the left wrist. The swellings appeared about the same time. The swellings were initially small in size but they had gradually increased over time. There was no preceding history of trauma and no fever, cough, weight loss or any other constitutional symptoms. No history of similar swellings in any of her siblings or the parents. There was associated pain especially over the medial aspect of both knees and the upper part of the right arm. The pain was described as a constant dull ache which was worse at night. There was no change in the skin colour over the swellings or any ulceration. She was initially treated by a traditional bone-setter before self-referral to our centre when there was no improvement. Essential findings in the musculoskeletal system revealed a tender bony hard swelling on the anteromedial surface of the proximal third of the right arm measuring 4x6cm. There were also non-tender bony hard swellings on the anterolateral surface of the proximal third of the left arm measuring 3x3cm and distal third of the left forearm measuring 4x4cm with ulnar deviation of the wrist.

In the lower limbs, there were also similar bony hard swellings on the medial and lateral surfaces of the distal third of both thighs and the anteromedial surface of the proximal third of both legs. However the swelling on the right leg which measures 6x6cm was tender. There was a limb length discrepancy of 2cm with the shortening located in the right leg. There was no neurovascular deficit. The full blood count and the erythrocyte sedimentation rate were within normal limits.

X-ray findings in the shoulders revealed bony outgrowths from the proximal ends of both humeri with expansion of the proximal third of the bones and thinning of the cortices. In the left forearm, there is also expansion of the distal ends of both radius and ulna with shortening of the ulna and ulnar deviation of the wrist joint. In the knees, there are bony outgrowths in the distal femoral and proximal tibia metaphyses growing away from the physes. There are mottled opacities over the top of the outgrowths with expansion of the metaphyseal regions.

Fine Needle Aspiration and Cytology of the swellings on both tibiae revealed an aspirate consisting of fragments of osteoid, mesenchymal cells and cartilage with numerous plasma cells, lymphoid cells and giant cells. The impression was that of an exostosis with underlying chronic inflammatory process. A diagnosis of hereditary multiple exostoses with bursitis and or neural compression was made.

The patient had excisional biopsy of the painful swellings from the proximal right humerus and proximal right tibia. The findings at operation were a pedunculated bi-lobed 4x6cm bony mass in the bicipital groove of the humerus stretching the long head of biceps brachii and another bony mass 4x4cm at the proximal tibia with triple spikes. The tumours were shaved off the bone and sent for histopathology which revealed features consistent with exostosis without any malignant change. The postoperative period was uneventful and post-operative x-rays done showed that the excised lesions were no longer visible. The patient has remained pain-free since then. She is still being followed up in the outpatient clinic.

(2) O.G., a 9-year old primary school boy who presented at the Casualty Department of NOHIL on the 3rd of July 2006 with a 7-year history of multiple bony swellings of both wrists and knees and a 7-day history of swelling and blisters in the right hand; (figures 2a and 2b). The father noticed multiple swellings on both wrists and knees about 7 years prior to presentation. The swellings appeared at about the same time and had progressively increased in size. There was no associated pain or limitation of joint movements. There was no preceding history of trauma, fever, cough or weight loss and no history of similar swellings in any other member of the family. Seven days prior to presentation, the father took him to a traditional bone-setter where the right wrist was manipulated and compressive splints applied and he was sent home. The following day, the hand became swollen with blisters. He was taken back to the bone-setter who applied some concoctions on it and told them not to worry. However, the swelling increased with associated severe pain which prompted the parents to bring him to this centre.

Essential findings in the musculoskeletal system revealed a non-tender bony hard swelling on the ulnar border of the left wrist with no differential warmth. The right hand was markedly swollen with desquamated blisters on the dorsum of the hand and distal forearm. The wrist was in ulnar deviation with the fingers flexed at the PIP joint and tenderness on passive extension of the fingers. There was sensory loss over the radial aspect of the thumb and the wrist but the radial pulsation was however present. There were also multiple non-tender bony hard swellings around the medial and lateral surfaces of both knees. There was no neurovascular deficit. X-rays revealed multiple bony outgrowths from both wrists and knees.

He was admitted and co-managed with the plastic

surgeons. He had elevation of the right upper limb, volar splint of the wrist in position of function, daily honey dressings, antibiotics, analgesics and physiotherapy. The wound healed and he was discharged home after twenty-five (25) days on admission to continue physiotherapy on outpatient basis.

Figure 1:

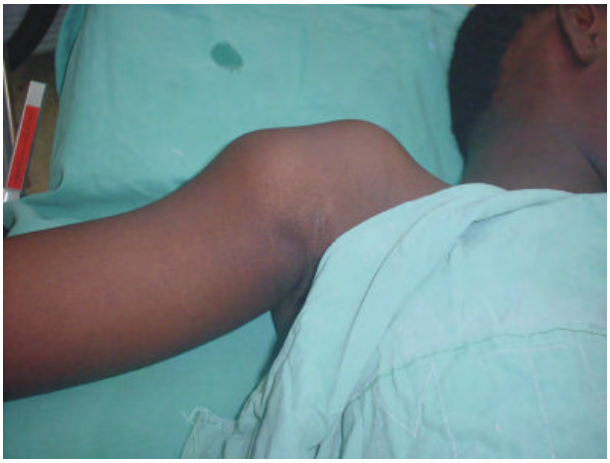


Figure 1b:

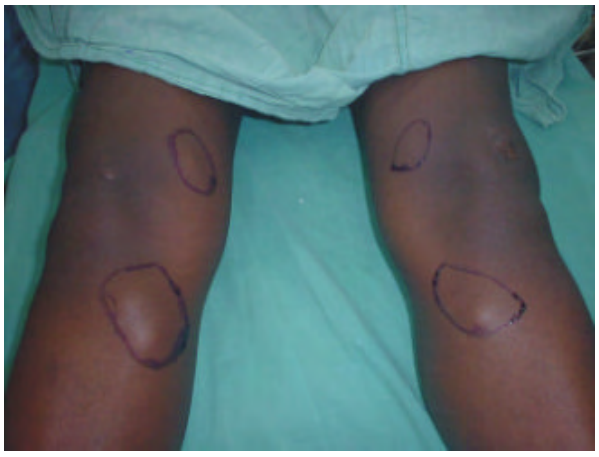


Figure 2

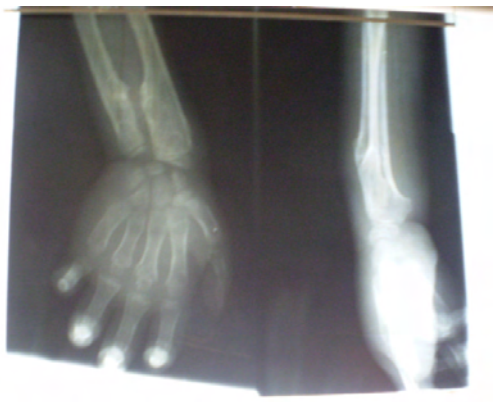
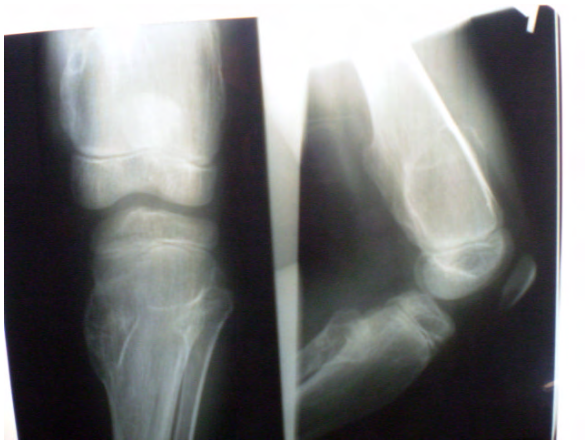


Figure 2b:



DISCUSSION

Hereditary Multiple Exostoses (HME) is an autosomal dominant skeletal dysplasia which affects 0.9 to 2 individuals per 100,000 [2,4,6-8]. It is a genetically heterogeneous disorder that has been associated with mutations in at least 3 different genes termed *EXT* genes. The three *EXT* loci have recently been mapped: *EXT1* is in chromosomal regions 8q23-q24, *EXT2* is on 11p11-p12, and *EXT3* is on chromosome arm 19p. Epidemiologic analysis of linkage and mutation data indicate that mutations of *EXT1* and *EXT2* are likely to be responsible respectively for one half and one third of all cases of multiple hereditary exostoses whereas *EXT3*, which has not been fully isolated and characterized, is probably less frequently involved [4,6].

Although previously thought to have a male predominance [9], HME now appears to affect both sexes equally [4,10]. Exostoses are initially recognized and diagnosed in the first decade of life in over 80% of individuals with HME and are most commonly first discovered on the tibia or scapula as these are often the most conspicuous locations [5]. Penetrance of this condition is said to be 100% but expressivity is variable. Therefore in a family with a negative history, the patient may be the first person to demonstrate the clinical expression of the trait. It is therefore not surprising that our two patients have a negative family history which may be due to this phenotypic variability or to the sporadic mutation reported in a number of patients with Hereditary Multiple Exostoses.

The diagnosis of HME was made on the basis of clinical and radiological examinations. The clinical features of HME depends on the time of presentation, the site, the size and the extent of physeal involvement in the pathology. Early presentation is characterized by painless bilateral multiple bony lumps at the ends of the long bones. Usually, the

proximal humerus, distal radius and ulna, distal femur and proximal tibia are the favoured sites. Other sites of involvement include the apophyseal border of the scapula and pelvis [5]. When they present late pressure and obstructive symptoms, asymmetrical growth retardation and deformities may predominate. Thus pain, hyperaesthesia, limb-length discrepancy, wrist, ankle, forearm and leg deformities may be the presenting clinical features. The most common deformities seen in HME include short stature, limb-length discrepancies, valgus deformities of the knee and ankle, asymmetry of the pectoral and pelvic girdles, lateral bowing of the radius with ulnar deviation of the wrist, and subluxation of the radial head [4,5,10,11]. A few reported cases of urinary tract obstruction and spinal cord compression complicating multiple exostoses have been reported in the literature [5,11-14].

Our two patients presented late and had identical presentations. They both presented with bilateral symmetrical bony lumps in the radius and ulna, femur, tibia and fibula, along with ulnar deviation of the wrists. In addition the first patient also presented with a limb length discrepancy of 2cm located in the tibia. The anatomic proximity of the lesion to the physis is responsible for its tethering effect on one side of the physis, thus producing an asymmetrical growth of the bone. This latter effect is the basis of the limb-length discrepancy and the observed forearm varus, ulnar deviation, genu and ankle valgum in HME. The thinner of the two bones in the forearm and the leg is usually more affected and this serves as the basis for the deformities that were seen in our patients and in others with HME. Exostoses of the upper extremities frequently cause forearm deformities. The prevalence of such deformities has been reported to be as high as 40-60% [4,5,15]. Disproportionate ulnar shortening with relative radial overgrowth has been frequently described and may result in radial bowing [5]. Subluxation or dislocation of the radial head is a well-described sequelae in the context of these deformities and was seen in 8 of 37 elbows examined by Shapiro et al. [16]. Dislocation of radial head has been associated with a loss of pronation, greater ulnar variance, and functional impairment [17].

The persistent pain and the increase in size of the proximal humeral exostosis in the 13-year old patient which were due to bursitis under the long head of biceps and pressure symptoms on adjacent nerves were eliminated immediately after excision of the exostosis. Both neurological and vascular problems can arise throughout the extremities as complications of HME. Wicklund et al. reported peripheral nerve compression symptoms in 22.6% of patients patients in their series of 180 [10].

Peroneal neuropathy associated with exostoses of the proximal fibula in children is a recognized complication [18,19]. Cardelia et al. in a review of six children found peroneal nerve palsy associated with exostoses of the proximal fibula in all his cases [13]. Ulnar neuropathy secondary to compression by an exostosis of the elbow has also been described [20]. Malignant transformation of a benign osteochondroma to a chondrosarcoma or other sarcoma is another complication of HME. Fortunately, most chondrosarcomas in this setting are low grade and can be treated with wide excision. Patients with such lesions usually present with a painful mass. Rarely, nerve compression can be the presenting complaint [21]. The reported incidence of malignant degeneration is highly variable, ranging from 0.5-25% [8,22]. The first patient presented with a painful lesion but histology showed no evidence of malignant change.

The treatment of non-complicated cases of HME is masterly inactivity as it is inadvisable to operate before skeletal maturity for fear of damage to the physis. However, surgical excision is indicated only when the lesion causes pain, deformity, disability and when in close relationship with a neurovascular bundle. The aim of surgery is complete excision of the cartilaginous cap. Recurrence rate of about 2% is associated with incomplete excision. The management of secondary deformities depends on the severity and the age at presentation and may entail corrective osteotomy, timely epiphyseodesis and limb lengthening. One of our patients had excision of exostosis to relieve pressure symptoms while the other, in seeking treatment from a traditional bone-setter, suffered from complications of tight splintage and scarification which we treated with antibiotics and elevation of the affected upper limb.

In conclusion, we have been able to use our two patients to illustrate the clinical and radiological features and indications for surgery in HME. The pathogenesis of most of the pathologies in HME has been highlighted while the differential diagnosis and surgical options were mentioned.

REFERENCES

1. **Peterson HA.** Multiple hereditary osteochondromata. *Clin Orthop 1989;* 239:222-230.

2. **Black B, Dooley J, Pyper A, Reed M.** Multiple hereditary exostoses: an epidemiologic study of an isolated community in Manitoba. *Clin Orthop 1993;* 287:212-217.

3. **Dahlin DC, Unni KK.** Bone Tumors: general aspects and data on 11,087 Cases 5th ed. Philadelphia, Lippincott-Raven; 1996: pp 11-23.

4. **Schmale GA, Conrad EU III, Raskind WH.** The natural history of hereditary multiple exostoses. J Bone Joint Surg(Am) 1994; 76:986-992.

5. **Stieber JR, Pierz KA, Dormans JP.** Hereditary multiple exostosis: a current understanding of clinical and genetic advances. Spring 2001; 14:39-48.

6. **Hennekam RCM.** Hereditary multiple exostoses. J Med Genet 1991; 28:262-266.

7. **Nawata K, Teshima R, Minamizaki T, Yamamoto K.** Knee deformities in multiple hereditary exostoses: a longitudinal radiographic study. Clin Orthop 1995; 313:194-199.

8. **Voutsinas S, Wynne-Davies R.** The infrequency of malignant disease in diaphyseal aclasis and neurofibromatosis. J Med Genet 1983; 2:345-349.

9. **Canella P, Gardini F, Boriani S.** Exostosis: development, evolution and relationship to malignant degeration. Italian J Orthop Traumatol 1981; 7:293-298.

10. **Wicklund CL, Pauli RM, Johnston D, Hecht JT.** Natural history study of hereditary multiple exostoses. Am J Med Genet 1995; 55:43-46.

11. **Shapiro SA, Javid T, Putty T.** Osteochondroma with cervical cord compression in hereditary multiple exostsoses. Spine 1990; 15:600-602.

12. **Ergun R, Okten AI, Beskonakli E, Akdemir G, Taskin Y.** Cervical laminar exostosis in multiple hereditary osteochondromatosis: anterior stabilization and fusion technique for preventing instability. European Spine J 1997; 6:267-269.

13. **Quirini GE, Meyer JR, Herman M, Russell EJ.** Osteochondroma of the thoracic spine: an unusual cause of spinal cord compression. Am J Neuroradiology 1996; 17:961-964.

14. **Silber JS, Mathur S, Ecker M.** A solitary osteochondroma of the pediatric thoracic spine: a case report of and review of the literature. Am J Orthop 2000; 29:711-714.

15. **Wood VE, Sauser D, Mudge D.** The treatment of hereditary multiple exostosis of the upper extremity. J Hand Surg 1985; 10-A:505-513.

16. **Shapiro F, Simon S, Glimcher MJ.** Hereditary multiple exostoses. J Bone Joint Surg(Am) 1979; 61:815-824.

17. **Stanton RP, Hansen MO.** Function of the upper extremities in hereditary multiple exostoses. J Bone Joint Surg(Am)1996; 78:568-573.

18. **Cardelia JM, Dormans JP, Drummond DS, Davidson RS, Duhaime C, Sutton L.** Proximal fibular osteochondroma with associated peroneal nerve palsy: a review of six cases. J Ped Orthop 1995; 15:574-577.

19. **Levin KH, Wilbourn AJ, Jones HR Jr.** Childhood peroneal neuropathy from bone tumors. Pediat Neurol 1991; 7:308-309.

20. **Ruth RM, Groves RJ.** Synovial osteochondromatosis of the elbow presenting with ulnar nerve neuropathy. Am J Orthop 1996; 25:843-844.

21. **Paik NJ, Han TR, Lim SJ.** Multiple peripheral nerve compressions related to malignantly transformed hereditary multiple exostoses. Muscle Nerve 2000; 23:1290-1294.

22. **Garrison RC, Unni KK, McLeod RA, Pritchard DJ, Dahlin DC.** Chondrosarcoma arising in osteochondroma. Cancer 1982; 49:1890-1897.