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Hereditary Multiple Exostoses: A Case Report

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Abstract **Case Report**

Background: Hereditary Multiple Exostoses (HME) is a rare bone disease, usually associated with deformity and pressure symptoms. It is an autosomal dominant disorder characterized by the development of benign tumors growing outward from the metaphyses of long bones and can lead to considerable psychosocial problems. Thus, We report a rare case of HME with some peculiar features, in a 16- year-old Moroccan pupil, manifested with a six year history of multiple swellings on the trunk, the pelvic and scapular belt, and both upper and lower limbs, with no sign of malignancy or pressure symptoms. The patient had also a family history of similar swellings. Radiological findings showed the presence of multiple exostoses in these localisations. Biopsy of one of the lesions confirmed the presence of osteochondroma on histopathology. Though rare, HME do occur in our environment. The treatment is individualized, with small asymptomatic or minimally symptomatic lesions followed up and only supportive care provided. Larger symptomatic lesions may cause major physical handicap and may be resected.

Keywords: Hereditary, Exostoses, Deformity.

INTRODUCTION

Hereditary Multiple Exostoses (HME) is a rare autosomal dominant disorder affecting the endochondral skeleton during growth [1]. 10-20% can arise spontaneously. It is a cartilage capped bony projection found primarily at the jexta-epiphyseal regions of the most rapidly growing ends of bone [2]. The long bones of the legs, arms, fingers, toes and shoulders blades are commonly affected. Face and skull are severally unaffected. Exostoses grow as the child grows. It is the most common bone tumor seen in children [3, 4]. It is considered a harmatoma and as such stops growing at the end of the growth of affected bones.

It's estimated to occur in about 1 in 50000 people. It causes asymmetrical retardation of longitudinal bone growth with subsequent deformity and discrepancy in limb-length (very common). Significant inequality of more than or equal to 2 cm has been reported. Malignant transformation is in order of 5% of all cases. The femur is twice affected as the tibia [5, 6].

Mutation In three genes (EXT1, EXT2, and EXT3) have been implicated in the etio-pathogenesis.

These lesions have the tendency to cause mechanical interference with normal function of the soft tissues passing over them.

The pressure of the exostoses causes irritation and occasional damage to nerves, arteries and muscles, hence, the presence of pain. A second clinical setting, presents as multiple lumps, pain or deformity, while the third setting will present with multiple lumps, pain, and deformities. Management will depend on the stage of presentation.

In the absence of pain and deformities, masterly inactivity is the rule. However, surgical intervention is paramount in the presence of deforming complications. We here by present a 16 year old man with clinical and radiological features of hereditary Multiple Exostoses (HME) seen in our hospital.

CASE REPORT

M.C a 16 year old pupil, child of consanguineous marriages, presented at the surgical out- patient department of Avicenne Military Hospital in Marrakech: with a six year history of multiple swellings on the trunk, the pelvic and scapular belt, and both upper and lower limbs (Figure 1).

The Swellings were noticed by the parents. They were multiple and on the back and both lower limbs, associated with a conservative general state. Initially, they were small sized (1 cmx1cm) but progressively increased in size over time leading him to the consultation especially since he has a family history of similar swellings in his father, brother and two sisters.

No sign of malignancy was objectified, in particular localized pain or change in skin colour or ulceration. No pressure symptoms have been noticed. No history of trauma. No history of weight loss, headaches, anorexia, bone pain, jaundice, cough or breathlessness, abdominal swelling or any other constitutional symptom.

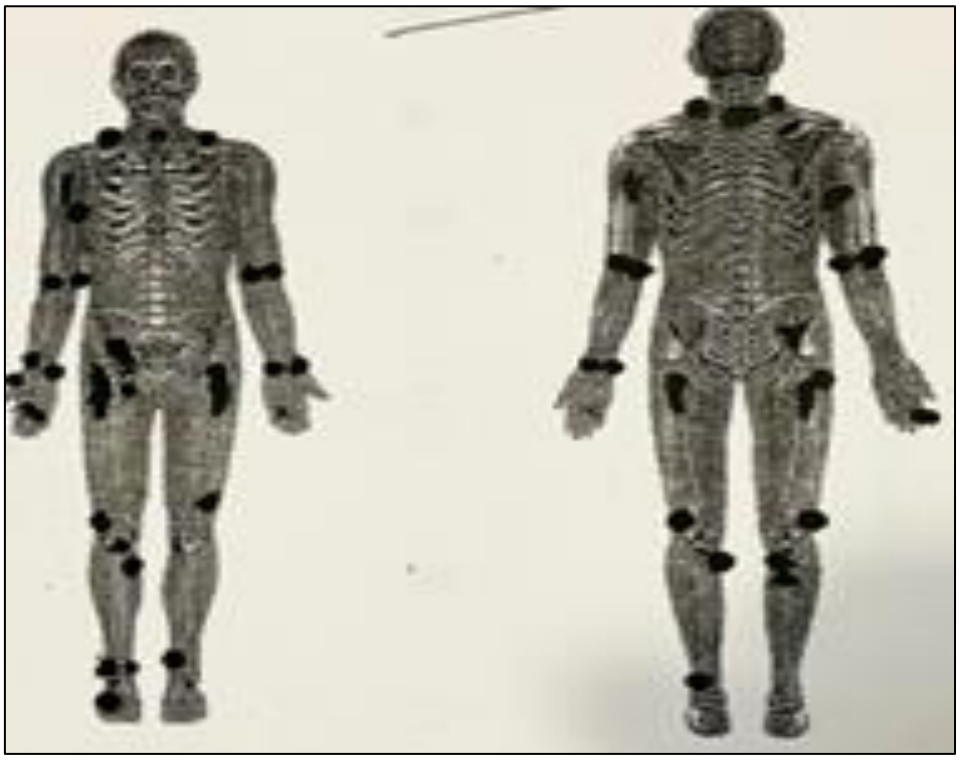

Figure 1: Diagram showing the location of exostoses

On clinical examination the patient was cooperative, well oriented with respect to higher functions and especially intellectual functions he is in good hemodynamic and nutritional condition he weighs 42 kg for a height of 148 cm (BMI: 19kg/m2)

Indeed, we note that the patient presents a nanism with a dorso-lumbar scoliosis. Also, the upper limbs are shortened in half-pronation with deviation of the right middle finger and a megadactyly.

In addition to these anomalies, there are irregular rigid bone tuberosities that are insensitive and adherent to the deep plane of the girdles and the upper limb, compatible with exostoses (Figure 2) with a sensitive warm multicentric mass on the inner side of the right thigh measuring 10 -5 cm, multiple locations are noted and schematized herewith, the largest was 3 – 6cm, the smallest 1-2cm in widest diameters.

There were also multiple hard non-painful swellings on the shoulder girdle and proximal third of both arms. There were similar swellings on the distal third of both forearms.

On both lower limbs, there were similar bony hard swellings on the medial and lateral surfaces of the distal third of both thighs and medial side of the proximal third of both legs. However, the lesions on the right lower limb are bigger. There were no limb length discrepancies.

There was no change in color of overlying or surrounding skin. No differential warmth or lymphadenopathy. No loss of distal neurovascular function. A diagnosis of hereditary multiple exostoses was made.

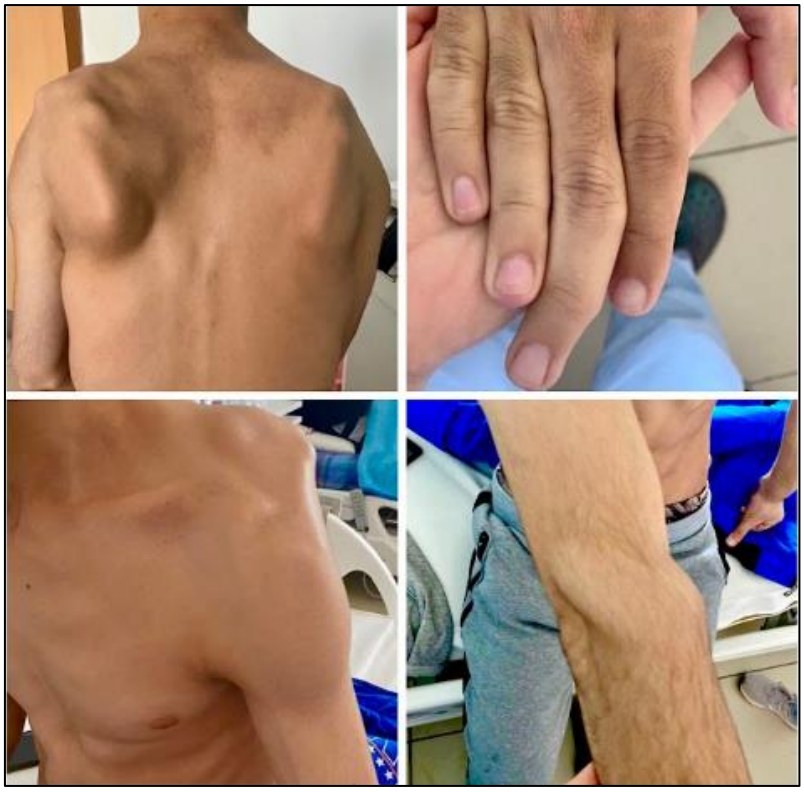

Figure 2: Patient's clinical images

The complete blood count and complete inflammatory markers were within normal limits.

Radiological findings (X-rays, CT body scan, MRI) individualized multiple exostoses deforming the bone structures, responsible for blowing of the cortices in sight scattered at the level of the axial and extra-axial skeleton of which some are the seat of osteolysis and calcification in popcorn, with a collection of the posteromedial face of the right thigh extended from the root to the middle 1/3, spontaneously hypodense and a bilateral tibiofibular synostosis (Figure 3, 4 & 5). These radiological aspects show the presence of areas of obvious fragility with a high risk of fracture. No bone abnormalities were noted on cranioencephalic and facial CT.

Biopsy of one of the lesions showed Osteochondroma on histopathology.

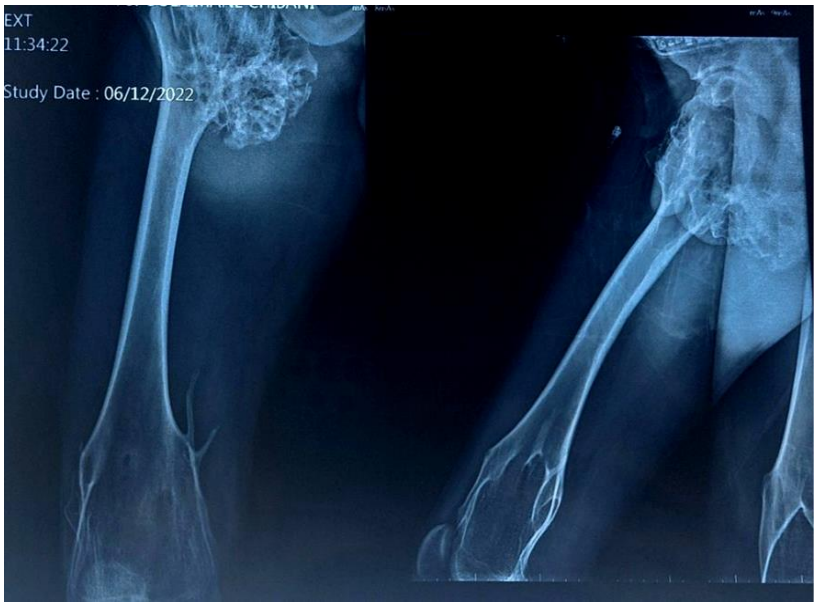

Figure 3: Standard X-ray of the thigh taking the patient's hip

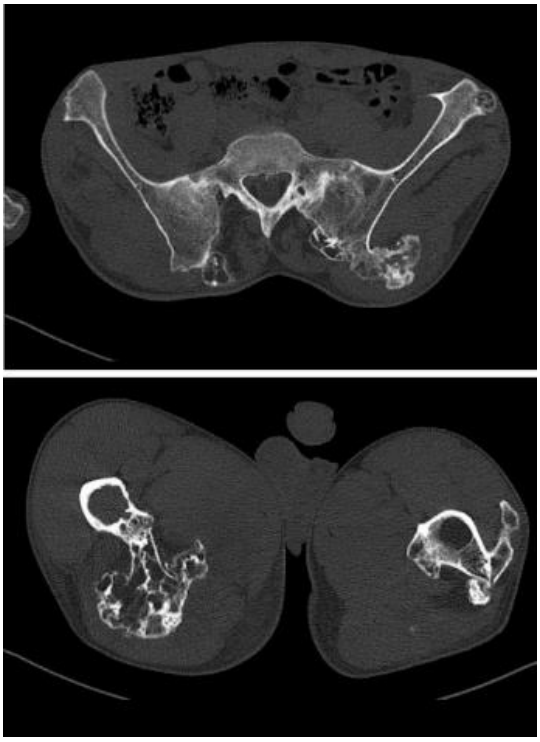

Figure 4: Cross-sectional CT images of the pelvic girdle

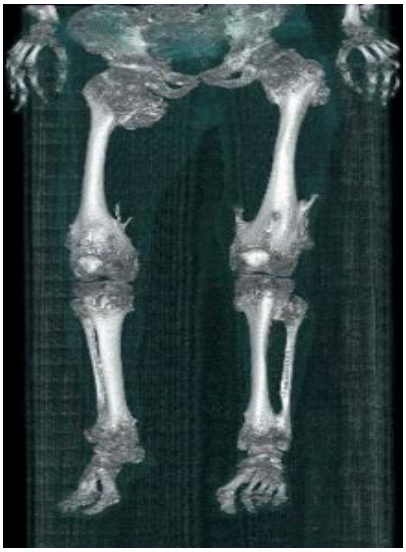

Figure 5: CT images of the lower limbs in 3D reconstruction

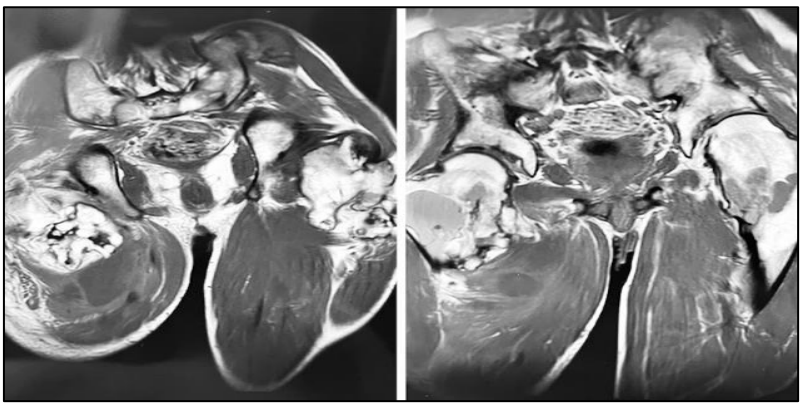

Figure 6: MRI of the patient's thighs

Clinical and radiological monitoring was recommended, and education of the patient by making him aware of the risks involved in practicing violent or less violent sports.

A genetic investigation and counseling is undertaken. Also a specialized genetic consultation is in progress.

DISCUSSION

Hereditary Multiple Exostoses (HME) is a genetically heterogeneous disorder and has been associated with mutations in at least three different genes, termed EXT genes. At least two of these genes are thought to function as tumour suppressor genes. These mutations may disrupt normal cartilage growth, resulting in the formation of an osteochondroma. The three described EXT loci have been recently mapped: EXT1 on chromosome 8q23-q24, EXT2 on 11p11-p12, and EXT3 on chromosome 19p [7-9]. According to linkage analysis, the EXT1 and EXT2 loci appear to be altered in the majority of families while, EXT3, which has not been fully isolated and characterized, is probably less frequently affected [7-9]. 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 MHE cases. Genetic studies were however not conducted for the index patient.

Mutations in this genes cause synthesis of truncated EXT protein with abnormal function. EXT protein is important in Heparan Sulfate synthesis. It is thought that normal chondrocyte proliferation and differentiation may be affected, leading to abnormal bony growth. Pre-implantation genetic testing and prenatal diagnosis are available for new couples. HME has 95% penetrance. Expressivity is variable. In a patient with a negative family history of the disease, the patient may be the first to clinically express the trait, just like in our patient. This may be due to sporadic mutation.

Hereditary Multiple Exostoses is characterized by formation of ectopic, cartilage-capped, growth plate-like exostoses next to growing long bones and other skeletal elements. The exostoses usually originate proximal to an active growth plate, may occur at or after birth and throughout puberty, and may continue to grow slowly during adulthood [7, 10, 11]. They form predominantly on the physes of long bones, pelvis, ribs, scapula, and vertebrae and begin to appear as early as 2 years of age [10-12]. Most patients are diagnosed by age 5 years, and virtually all are diagnosed by age 12 years. In families with the genetic predisposition, members who do not demonstrate lesions by age 12 years will not manifest the disease. After adolescence and skeletal maturity, osteochondromas usually exhibit no further growth [13].

Exostoses are initially recognised and diagnosed in the first decade of life in over 80% of individuals with HME. Tibia and scapula are often most noticeable locations. Clinical and radiological findings are usually diagnostic [7]. Clinical features will depend on time of presentation. Pathology will depend on site, size and extent of physeal involvement.

Multiple bony swellings of the proximal humerus and distal radius and ulnar, with swellings of the distal femur and proximal tibia are the hallmark of presentation. The scapula and pelvis can be involved [14]. Late presentations are usually accompanied by complications such as pain and deformities. Peripheral nerve compression symptoms can occur in up to 22.6% of patients [15].

In our patient, there was a late presentation at the age of sixteen. Symptoms were mainly multiple swellings on the trunk, the both upper and lower limbs, the scapular and pelvic belts.

Central exostoses involving the skull base, spine, or rib heads are seen in 1%–9% of patients with HME, and may cause cranial nerve deficits, radiculopathy, spinal stenosis, cauda equina syndrome, myelomalacia and spinal cord compression [13, 17, 18]. Interestingly, in patients with HME, spinal lesions are usually solitary. The cervical spine is most frequently affected (50% of lesions), followed by the thoracic and the lumbar spine. Lesions that protrude dorsally from the posterior vertebral elements (lamina or spinous process) are typically large and manifest at an earlier age with cosmetic deformity and palpable mass but lack neurologic symptoms [13]. In contradistinction, osteochondromas that extend into the spinal canal are often small but are associated with neurologic symptoms. It is therefore not surprising that despite the considerable size of the spinal lesions causing limitation of range of flexion and extension of the trunk and significant deformity, the index patient had no neurological deficit. The fact that the deformity was on the back, usually covered with cloths, could account for the late presentation. Osteochondromas that extend anteriorly from the vertebral body may produce symptoms of dysphagia, hoarseness, and vascular compromise. Affected individuals may also show disturbance of growth with short stature, wrist and ankle deformity and mental handicap as had been reported by other workers [10, 19], but these features are variable and were not seen in the index case.

Complications commonly associated with these exophytic masses include cosmetic and osseous deformity, pressure symptoms, fracture, vascular compromise, neurologic sequelae, overlying bursa formation, and malignant transformation. Of these, outstanding complications in the index patient were cosmetic deformity, restricted joint movements affecting the vertebral joints, the upper and lower limbs

and pain. This is of great concern as the patient was already out of school because of these complications, possibly facing physical, psychological and social distress which has a negative impact on his quality of life.

Malignant transformation has been reported, with documented risk of 1-6% in patients with HME in adulthood, with chondrosarcoma developing more frequently than osteosarcoma [9, 10, 13, 19, 20]. Higher estimates of 10-25% have been cited but they have been a function of bias and incomplete detection of affected individuals who did not have a sarcoma but were members of a family that had exostoses [10]. Lesions that grow or cause pain after skeletal maturity should be suspected of malignant transformation which is distinctly unusual before the age of 20. The index patient should therefore be kept under regular review both clinically and radiologically to evaluate progression of deformities and development of complications. The diagnosis depends largely upon X-rays while the radiographic appearance of a lesion composed of bone demonstrating cortical and medullary continuity with the underlying parent bone is often pathognomonic [13]. Lesions that involve complex areas of anatomy (spine or pelvis) are frequently better assessed with CT or MR imaging to detect the characteristic marrow and cortical continuity [18, 21]. Bone scintigraphy has been demonstrated to be useful in the periodic surveillance of adult patients with HME [22]. A biopsy should be done in doubtful cases and to help assessing malignant degeneration [20]. Differential diagnosis include Dysplasia Epiphysealis Hemimelica (DEH) or Trevor's disease, which is described as a type of over growth at one or more epiphyses, and metachondromatosis, a rare disorder that exhibit symptoms of both multiple osteochondromas and enchondromas in children and is also inherited in autosomal dominant mode [8]. Treatment of HME is individualized and much more problematic and complex than that of patients with solitary osteochondromas. Small asymptomatic or minimally symptomatic lesions are followed up and only supportive care provided while larger symptomatic lesions may be resected. Thus, depending on the deformity, the surgical intervention may involve corrective osteotomy, epiphysiodesis, excision or limb lengthening. Surgical treatment is often directed at correcting the associated deformities rather than restricted to the exostoses alone [13]. The surgeries may be multiple thus, the psychological effect on the patient should be considered. Genetic counselling is an important aspect of the management of HME as each individual is at 50% risk of transmitting the disorder to his offspring [6, 8, 23].

CONCLUSION

Though rare, HME do occur in our environment. The treatment is individualized, with small asymptomatic or minimally symptomatic lesions followed up and only supportive care provided. Larger symptomatic lesions may cause major physical handicap and may be resected. Introduction of palliative care and health insurance coverage for rare disorders of childhood are recommended to improve outcomes.

REFERENCES

1. Venuta, A., Laudizi, L., Forese, S., Bettelli, F., & Caroli, A. (1994). The multiple exostoses syndrome. 3 cases in one family. *La Pediatria Medica e Chirurgica: Medical and Surgical Pediatrics*, *16*(4), 403-404.
2. Peterson, H. A. (1989). Multiple hereditary osteochondromata. *Clinical Orthopaedics and Related Research®*, *239*, 222-230.
3. Dahlin, D. C., & Unni, K. K. (1996). Bone Tumors: General aspects and data on 11, 087 cases. 5th Ed. Philadelphia: Lippincott-Raven; P. 11-23.
4. Ga, S. (1994). Conrad 3rd EU, Raskind WH. *The natural history of hereditary multiple exostoses. J. Bone Joint Surg Br*, *76*, 986-992.
5. Pannier, S., & Legeai-Mallet, L. (2008). Hereditary multiple exostoses and enchondromatosis. *Best practice & research Clinical rheumatology*, *22*(1), 45-54.
6. Hennekam, R. C. (1991). Hereditary multiple exostoses. *Journal of medical genetics*, *28*(4), 262-266.
7. Pierz, K. A., Stieber, J. R., Kusumi, K., & Dormans, J. P. (2002). Hereditary multiple exostoses: one center's experience and review of etiology. *Clinical Orthopaedics and Related Research®*, *401*, 49-59.
8. Bovée, J. V. (2008). Multiple osteochondromas. *Orphanet journal of rare diseases*, *3*, 1-7.
9. Richardson, R. R. (2005, October). Variants of exostosis of the bone in children. In *Seminars in roentgenology* (Vol. 40, No. 4, pp. 380-390). WB Saunders.
10. Adelowo, O., & Adebayo, S. (2009). Hereditary multiple exostosis in two Nigerian siblings. *Case Reports*, *2009*, bcr0920080901.
11. Eke, G. K., Omunakwe, H. E., & Echem, R. C. (2016). Hereditary multiple exostoses in a 15-year-old boy: A case report and review of literature. *Nigerian Journal of Paediatrics*, *43*(4), 295-298.
12. Yinusa, W., Owoola, A. M., & Esin, I. A. (2010). hereditary multiple exastoses: Case report. *Nigerian Journal of Clinical Practice*, *13*(2), 218-222.
13. Murphey, M. D., Nomikos, G. C., Flemming, D. J., Gannon, F. H., Temple, H. T., & Kransdorf, M. J. (2001). Imaging of giant cell tumor and giant cell reparative granuloma of bone: radiologic-pathologic correlation. *Radiographics*, *21*(5), 1283-1309.
14. Cardelia, J. M., Dormans, J. P., Drummond, D. S., Davidson, R. S., Duhaime, C., & Sutton, L. (1995).

Proximal fibular osteochondroma with associated peroneal nerve palsy: a review of six cases. *Journal of pediatric orthopedics*, *15*(5), 574-577.
15. Shapiro, F., SIMoN, S. H. E. L. D. O. N., & Glimcher, M. J. (1979). Hereditary multiple exostoses. Anthropometric, roentgenographic, and clinical aspects. *JBJS*, *61*(6), 815-824.
16. Wicklund, C. L., Pauli, R. M., Johnston, D., & Hecht, J. T. (1995). Natural history study of hereditary multiple exostoses. *American journal of medical genetics*, *55*(1), 43-46.
17. Labram, E. K., & Mohan, J. (1996). Diaphyseal aclasis with spinal cord compression: report of two cases and review of the literature. *Journal of neurosurgery*, *84*(3), 518-521.
18. Bess, R. S., Robbin, M. R., Bohlman, H. H., & Thompson, G. H. (2005). Spinal exostoses: analysis of twelve cases and review of the literature. *Spine*, *30*(7), 774-780.
19. Welsh, G. A., & MacLeod, I. (1999). Diaphyseal aclasis affecting the temporomandibular joint. *Dentomaxillofacial Radiology*, *28*(5), 320-323.
20. Human, L. (1965). Diaphyseal aclasis: review of literature and report of an unusual case (a massive vertebral osteochondroma with complications). *South African Medical Journal*, *39*(2), 27-29.
21. Vanhoenacker, F. M., Van Hul, W., Wuyts, W., Willems, P. J., & De Schepper, A. M. (2001). Hereditary multiple exostoses: from genetics to clinical syndrome and complications. *European journal of radiology*, *40*(3), 208-217.
22. Epstein, D. A., & Levin, E. J. (1978). Bone scintigraphy in hereditary multiple exostoses. *American Journal of Roentgenology*, *130*(2), 331-333.
23. Crandall, B. F., Field, L. L., Sparkes, R. S., & Spence, M. A. (1984). Hereditary multiple exostoses. Report of a family. *Clinical orthopaedics and related research*, (190), 217-219.