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MULTIPLE HEREDITARY EXOSTOSES – A CASE REPORT

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ABSTRACT

Multiple Hereditary Exostoses is a rare genetic bone disorder having occurrence by 1 in 50,000 births. As such this prevalence is reported in other populations whereas in Indian population it is very rare case to occur. Hence the case study report of Multiple hereditary exostoses affected proband showing 16 exostoses all over the body wherein an exostosis of about 6cm in length and 5cm in width has been observed in the postero-medial aspect of distal femur. This exostosis was painful for the patient and hence was excised. The patient also reported that the exostoses was grown in a period of not more than 5 months, hence the excised tumor sample was analyzed for malignancy. The biopsy report revealed no evidence of malignancy in the exostoses.

KEY WORDS Multiple Hereditary Exostoses (MHE); Malignant; Biopsy; Distal Femur

INTRODUCTION

Multiple Hereditary Exostoses (MHE) is a rare medical condition in which multiple bony spurs or lumps (also known as exostoses, or Osteochondromas) develop on the bones of affected patient. The synonyms used for the disorder are Multiple Osteochondromas (MO) MIM 133700, Heredity Multiple Exostoses (HME) and Multiple Heredity Exostoses (MHE). Multiple Osteochondromas (MO) / Multiple Heredity Exostoses (MHE) is an autosomal dominantly inherited disorder in which there are numerous cartilage capped excrescences in areas of actively growing bones. MHE is a heterogeneous skeletal disorder in which the penetrance is from 96% to 100%. It is characterized by multiple outgrowing bony tumors capped by cartilage, mostly affecting the metaphyses, but also the juxta-metaphyses of the long bones of the upper and lower limbs. The Exostoses grow during the childhood and may cause symptoms as a result of compression of local tissues, deformities and discrepancies of length. A serious complication of MHE is the malignant transformation of an exostosis to chondrosarcoma and rarely to malignancies. The prevalence of MHE is estimated at 1:50,000 persons within the general population and seems to be higher in males (males to females' ratio 1.5:1). The responsible gene for MHE phenotype had been identified at EXT1 and EXT2, namely exostosin 1 and 2 (EXT1, EXT2) and they belong to a family of predicted tumor suppressor genes while gene at EXT3 has not yet been identified. MHE is genetically heterogeneous as three EXT loci have been identified so far. EXT1 (MIM 133700) has been mapped to chromosome 8q23-24, 5 EXT2 (MIM 133701) to chromosome 11p11-p12, 6 and EXT3 (MIM 600209) to chromosome 19p.

Exostosin-1 comprises 746 amino acids and is involved in heparan sulfate synthesis. It is a type II transmembrane glycoprotein that localizes to the endoplasmic reticulum. Exostosin-1 and exostosin-2 form a heterooligomeric complex that accumulates in the Golgi apparatus and has substantially higher glycosyltransferase activity than exostosin-1 or exostosin-2 alone. EXT2 contains 14 exons plus two alternative exons spanning 110 kb. Single-base polymorphisms that do not result in amino acid substitutions have been described and at least four non synonymous changes appear to be rare polymorphisms. The protein comprises 718 amino acids. Like exostosin-1, exostosin-2 is a type II transmembrane glycoprotein that localizes to the endoplasmic reticulum and is involved in heparan sulfate synthesis. Exostosin-1 and exostosin-2 form a hetero-oligomeric complex that accumulates in the Golgi apparatus and has substantially higher glycosyltransferase activity than exostosin-1 or exostosin-2 alone. Mutations in these genes typically lead to the synthesis of a truncated EXT protein which does not function normally. It is known that EXT proteins are important enzymes in the synthesis of heparan sulfate, however the exact mechanism by which altered synthesis of heparan sulfate that could lead to the abnormal bone growth associated with HME is unclear. When there is a mutation in exostosin-1 or exostosin-2, heparan sulfate cannot be processed correctly and is non-functional. Although heparan sulfate is involved in many bodily processes, it is unclear how the lack of this protein contributes to the signs and symptoms of hereditary multiple exostoses. Multiple exostoses can disrupt bone growth and can cause growth disturbances of the arms, hands, and legs, leading to short stature. Often these bone growth disturbances do not affect the right and left limb equally, resulting in uneven limb lengths (limb length discrepancy). Multiple exostoses may also result in pain, limited range of joint movement, and pressure on nerves, blood vessels, the spinal cord, and tissues surrounding the exostoses.

Here in the study report the subject was 26 year old male showing 16 exostoses all over the body. The most significant about the case is that the osteochondroma has been grown at a faster rate but still wasn't found to be malignant. Hence this would help in counseling of patients undergoing surgeries for osteochondromas.

MATERIAL AND METHODS

A consent form is filled up by the patient as per the format and guidelines given by Medical Council of India. An ethical approval for the study was given by the Institutional Ethics Committee. An evaluation Performa recording the following parameters was evaluated. Patient's age, also age of first clinical manifestation, details of any surgeries (indication, the number and location of previous surgeries) and family history. Clinical examination including registration of all palpable exostoses, measurements of the ROM (Range of Motion) in different joints (shoulder, elbow, wrist, hip, and knee), length of the upper and lower arm as well as of the upper and lower leg (clinical evaluation using a measuring tape). Digital X-rays were analyzed to detect the further palpable exostoses. Also multiplanar MRI of the right thigh was done on 1.5 Telsa machine, performed in the sagittal, coronal and transverse planes using T1 weighted spin echo, T2 and proton-density weighted fast spin echo, fast STIR and T2 weighted gradient echo sequences. Based on the details obtained, the exostoses at the postero-medial region of the distal femur was operated and removed. The tumor bone excised sample was further analyzed for malignancy.

RESULTS AND DISCUSSION

The notable characteristics of the patient recorded were as accordingly. Age- 26, Weight 55kg, Height 163cms; the BMI of the patient was found to be 20.7, hence the patient was considered healthy weight since his BMI index falls under the range 18.5 to 24.9 BMI index. The complaint of the patient was limbing caused because of the enlargement of the exostoses located at the distal end of the femur. Hence for diagnosis, digital X-rays of the anteroposterior and lateral sides of the femur were done. The X-rays revealed the prominent enlargement of the exostoses. The patient also had reported that the growth of the exostoses was observed in 4-5 months span of time, hence for further diagnosis MRI scan of the right thigh region was also done to see further complications in muscles or tissues. Multiplanar MRI of the right thigh was done without contrast on 1.5 Telsa machine in sagittal, coronal and transverse planes. The MRI was interpreted as following: there was a exostosis of about 6 cm in length and 5 cm in width seen at the postero-medial aspect of the distal femur. It was lobulated with area of altered signal intensity within. It compressed the adjacent muscles. No abnormal associated soft tissues were seen. Small exostosis was also seen in the lateral aspect of the distal femur wherein no focal altered marrow signal intensity was seen. Rest of the femur shows a normal morphology and signal intensity. There was no focal area of the altered signal intensity observed in the muscles and soft tissues of the thigh region. Neurovascular bundles were also normal. The exostosis observed at the distal end of the femur was pedunculated with marrow edema in the bones. Since the adjacent muscles near the pedunculated exostosis were compressed, it caused pain to the patient and hence the pedunculated exostosis about 6cm in length and 5 cm in width were removed using surgery (Ooctectomy). Since the patient reported the growth of the exostoses in very short span of time the wide excision surgery was done to remove the tissues surrounding the bone. The Bone sample removed was further analyzed for malignancy. The cut surface of the specimen of tumor from distal femur, right side measuring 5.5 x 4 x 3 cm did not show any areas of necrosis or hemorrhage and hence no evidence of malignancy.

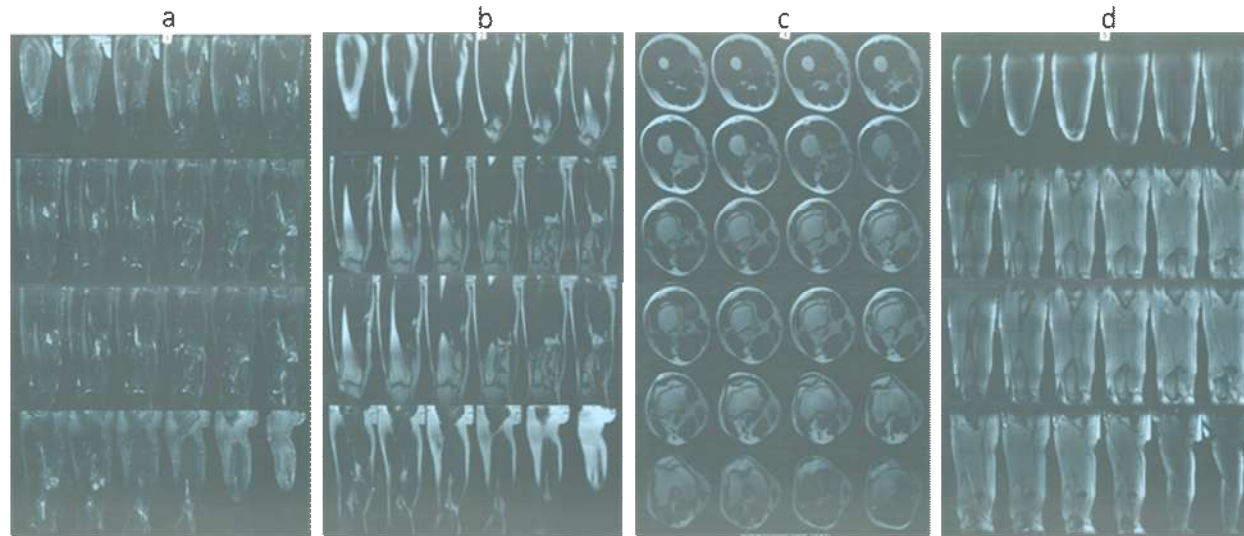


Figure 1- Multiplanar MRI Images (a, b, c, d) of the right thigh done on 1.5 Telsa machine, performed in the sagittal, coronal and transverse planes using T1 weighted spin echo, T2 and proton- density weighted fast spin echo, fast STIR and T2 weighted gradient echo sequences.



Figure 2- Digital X-ray of R-Femur – AP/LAT



Figure 3- Image of the exostoses exposed during surgery.



Figure 4- Exostoses about 2”/3” removed and was sent for biopsy

CONCLUSION

It is hereby concluded from the study that osteochondromas can at any times grows at a faster rate but does not be malignant. In such a case the patient’s normal functions are altered and affect significantly in all respect.

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