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A Rare Case of Multiple Hereditary Exostosis: Making The Correct Diagnosis with Triple Diagnosis

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Abstract

Background: *A rare genetic disorder characterized by the development of multiple benign bone tumors called osteochondromas. This condition is primarily hereditary and follows an autosomal dominant pattern of inheritance, with mutations in the EXT1 and EXT2 genes being the most common genetic.* ***Case report:*** *This case report describes an 12-year-old boy with lumps in all four extremities accompanied by intermittent pain. Femur x-rays concluded MHE of the femur, tibia, and bilateral fibula. Histopathological examination shows that the cartilage tissue contains chondrocyte cells that form the cartilage cap. There is a transition of cartilage to bone trabeculae through endochondral ossification and bone marrow between the bone trabeculae.* ***Discussion and Conclusion:*** *MHE is a rare condition, with an incidence of approximately 1 in 50,000 to 100,000 live births. MHE is closely related to genetic mutations that occur in the EXT1, EXT2, and EXT3 genes. These genes code for enzymes involved in the biosynthesis of heparan sulfate, which is necessary for normal bone growth. Mutations in any of these genes disrupt the regulation of bone growth and lead to osteochondroma formation. Symptoms of MHE can range from mild to severe, and they tend to appear in childhood or adolescence. The main clinical manifestations include the formation of a hard lump on the bone, which can cause deformity, pain, and limitation of movement. Osteochondroma can also compress nerves or blood vessels, causing complications such as circulatory disorders or paralysis. We report a rare case emphasizing the typical morphology of multiple hereditary exostosis of the long bones to establish the final diagnosis without immunohistochemistry and molecular examination. In low-resource settings where molecular analysis is not available, histopathological examination are key tools to establish a correct diagnosis.*

Keywords— *Multiple Hereditary Exostosis, femur, osteochondroma*

I. INTRODUCTION

Multiple Hereditary Exostosis (MHE), also known as Multiple Osteochondromatosis, is a rare genetic disorder characterized by the development of multiple benign bone tumors called osteochondromas. These tumors typically arise near the growth plates of long bones during childhood and adolescence, leading to skeletal deformities, joint abnormalities, and other associated complications.[1,2] MHE is primarily caused by mutations in genes encoding components of the heparan sulfate proteoglycan (HSPG) biosynthetic pathway, particularly the EXT1 and EXT2 genes. These mutations disrupt the normal process of bone growth and development, resulting in the formation of osteochondromas.[3,4]

The clinical manifestations of MHE can vary widely among affected individuals, ranging from mild skeletal abnormalities to more severe complications. Common features of MHE include multiple bony protrusions (osteochondromas), limb length discrepancies, joint contractures, and nerve compression syndromes. Skeletal deformities and functional limitations may impact mobility, daily activities, and overall quality of life.[5,6] Diagnosis of MHE is typically based on clinical evaluation, radiological imaging (such as X-rays, CT scans, and MRI), and genetic testing to identify mutations in EXT1 and EXT2 genes. Characteristic radiographic findings include the presence of multiple osteochondromas arising from the bone surface, often near the metaphyses of long bones.[7]

Management of MHE involves a multidisciplinary approach aimed at addressing the diverse clinical manifestations and potential complications associated with the condition. Treatment modalities may include surgical excision of symptomatic osteochondromas, physical therapy, orthotic devices, and surveillance for complications such as skeletal deformities, nerve compression, and malignant transformation.[3] While MHE is a chronic condition that typically persists throughout life, the prognosis is generally favorable with appropriate management and surveillance. Most individuals with MHE lead productive lives and can achieve satisfactory functional outcomes with tailored treatment strategies.[8,9]

Here we report a case of a 10-year-old boy who presented with the main complaint of lumps in all four extremities accompanied by intermittent pain, which was later diagnosed as MHE by radiological and histopathological evaluation. In this article we discuss the imaging characteristics, histopathological findings, and differential diagnosis, and emphasize the importance of an integrated diagnostic approach.

II. CASE REPORT

This case report is based on the clinical, radiological, and histopathological evaluation of an 12-year-old boy with the chief complaint of lumps in all four extremities accompanied by intermittent pain. History of current illness, lumps in all four extremities accompanied by pain that comes and goes. The lump had appeared since the patient was 3 years old. Initially a small lump appeared on the left ankle and left thigh. As age progresses, lumps in other parts of the body begin to appear and enlarge. The lump feels painful and comes and goes and interferes with activities. There is a family history of suffering from the same disease, namely the patient's mother, the patient's sister, and the patient's grandfather who died during surgery for the tumor. Physical examination revealed the left extremity had slight motor weakness, no edema was found. Extremity X-ray examination in the proximal region of the femur (metaphysis), distal femur, proximal tibia and fibula as well as the distal right and left tibia show of bone protrusion towards the external/away from the bone axis and

there is no periosteal reaction, the density is the same as the original bone. The result is MHE of bilateral femur, tibia, fibula (Fig.1)

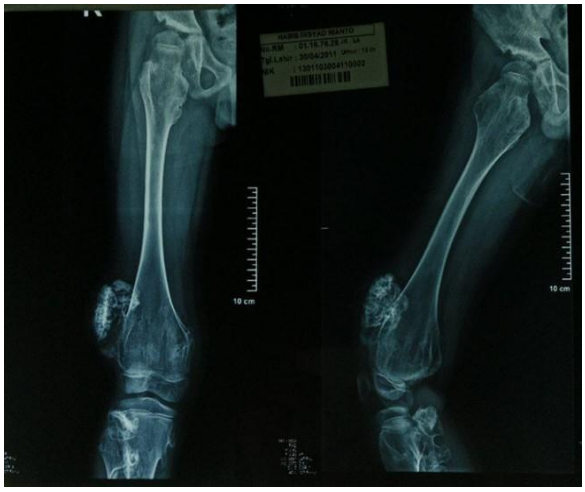
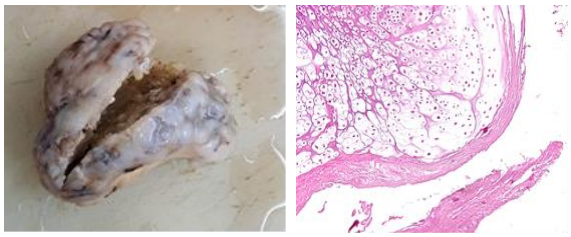


FIGURE 1. EXTREMITY X-RAY EXAMINATION

The patient underwent tumor removal surgery. Macroscopically, a piece of brownish white, hard tissue (bone) measuring 8x7x4 cm, brownish white in cross section was received. Microscopically show pieces of tissue consisting of connective tissue stroma, cartilage tissue and compact bone tissue. The fibrous perichondrium capsule appears on the outside. Below it cartilage tissue containing chondrocyte cells that form the cartilage cap. There is a transition of cartilage to bone trabeculae through endochondral ossification. Between the bone trabeculae, bone marrow can be seen consisting of fat and bleeding. This microscopic picture is suitable for Multiple Hereditary Exostosis.



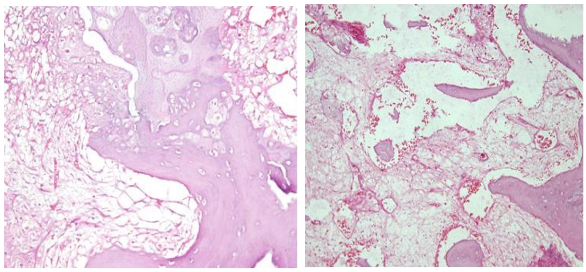


FIGURE 2 (A) MACROSCOPIC APPEARANCE, (B) CARTILAGE TISSUE CONTAINING CHONDROCYTE CELLS THAT FORM THE CARTILAGE, (C) ENDOCHONDRAL OSSIFICATION, (D) BONE MARROW.

III. DISCUSSION

MHE is a rare condition, with an incidence of approximately 1 in 50,000 to 100,000 live births. MHE is closely related to genetic mutations that occur in the EXT1, EXT2, and EXT3 genes. These genes code for enzymes involved in the biosynthesis of heparan sulfate, which is necessary for normal bone growth. Mutations in any of these genes disrupt the regulation of bone growth and lead to osteochondroma formation. Symptoms of MHE can range from mild to severe, and they tend to appear in childhood or adolescence.[1] In this patient, MHE was found in an 12-year-old boy. Of the number of MHE cases that have been reported, males are more numerous than females, namely with a ratio of 2:1. Most cases occur in the first 2 decades of life. Based on study, the most common site location in the metaphysis of long bones femur, humerus and tibia, involvement of flat bones (ilium and scapula) may occur. Involvement of small bones of the hands and feet, ribs and vertebrae is rare.[10,11]

Clinical manifestations include the formation of a hard lump on the bone, which can cause deformity, pain, and limitation of movement. Osteochondroma can also compress nerves or blood vessels, causing complications such as circulatory disorders or paralysis. We report a rare case emphasizing the typical morphology of multiple hereditary exostosis of the long bones to establish the final diagnosis without immunohistochemistry and molecular examination. In low-resource

settings where molecular analysis is not available, histopathological examination are key tools to establish a correct diagnosis.[12,13]

Microscopic examination of osteochondromas plays a critical role in confirming the diagnosis of MHE, distinguishing these benign lesions from other bone tumors, and guiding treatment decisions. Histological analysis can provide valuable information about the growth pattern, cellular composition, and architectural features of osteochondromas, aiding in the characterization and management of individuals with MHE.[14]

The anatomical pathology diagnosis obtained in this patient was a picture of osteochondroma (multiple) microscopic images show pieces of tissue consisting of connective tissue stroma, cartilage tissue and compact bone tissue. On the outside, the fibrous perichondrium capsule appears containing capillaries. Below it is visible cartilage tissue containing chondrocyte cells that form the cartilage cap. There is a transition of cartilage to bone trabeculae through endochondral ossification. Between the bone trabeculae, bone marrow can be seen consisting of fat and bleeding. Anatomical pathology diagnosis, namely this microscopic picture is suitable for Multiple Hereditary Exostosis.[15,16]

Radiological examination in the region of the proximal femur (metaphysis), distal femur, proximal tibia and fibula as well as the distal right and left tibia, there is a picture of bone protrusion towards the external/away from the bone axis and there is no periosteal reaction, the density is the same as the original bone. Impression: MHE of bilateral femur, tibia, fibula.[17,18]

IV. CONCLUSION

We report a rare case emphasizing the typical morphology of multiple hereditary exostosis of the long bones to establish the final diagnosis without immunohistochemistry and molecular examination. In low-resource settings where molecular analysis is not available, histopathological examination are key tools to establish a correct diagnosis.

Most individuals with MHE lead productive lives and can achieve satisfactory functional outcomes with tailored treatment strategies. Early diagnosis, multidisciplinary care, and proactive management of complications are essential for optimizing long-term outcomes and quality of life in individuals with MHE. Continued research into the pathogenesis and treatment of MHE holds promise for improving clinical outcomes and enhancing the overall prognosis for affected individuals.[18]

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