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Editorial

Hereditary Multiple Exostosis: A Pediatrician's Perspective

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EDITORIAL

Many orthopedics complaints come to the attention of the primary care doctor. While there are common conditions that are seen and managed by the primary care doctor, an astute physician will discover the rare conditions. With a good history and physical exam, the physician can diagnose the patient and refer appropriately. In this article, our focus will be on the rare disorder of Hereditary Multiple Exostosis (multiple osteochondromatosis).

Hereditary Multiple Exostosis was first described by Boer in 1814. It was later described by Guys in 1825 but it was Jaffe who finally gave it its unique characteristics (1). It is a rare disorder with prevalence of about 1:50000 (1). It has been genetically linked to 8q23-q24 (EXT1) and 11p11-p12(EXT2) (2). These genes are known to be tumor suppressor genes. EXT1 encodes 748 amino acids and EXT2 encodes 718 amino acids (3). There is also an association that has been mapped to chromosome 19p (EXT3). EXT 1 gene is expressed in many tissues but appears to cause an abnormality isolated to the bone tissue when mutated. This condition is inherited as autosomal dominant with both females and males affected. However, up to 10-20% of cases can be due to spontaneous mutations. It appears that the clinical manifestations of the disease are depending on the genetic mutation (1). Females tend to have an incomplete penetrance leading to a milder presentation. Mutations in these genes lead to abnormality in heparin sulfate polymerization with resultant formation of cartilage capped benign tumors (4,5). Tumors can be sessile or pedunculated. These tumors tend to occur along the metaphysic of long bones although other bones such as the spine, pelvis and ribs can be affected. The distal femur, proximal tibia and fibula, and humerus are common sites for development of exostosis. It was found that patients with EXT1 mutation tend to have more disease burden than other mutations (6). One study demonstrated less bone deformity with pedunculated tumors compared to sessile tumors (1).

Clinical presentation is variable with some patients presenting early in life and other in adulthood. 96% of patients are diagnosed at the latest in their second decade of life (7). The first sign of the disorder may be found in the newborn period as part of the differential diagnosis for a newborn with an enlarged digit (8). More common presentations are boney prominences noted by the patient or parent that are imaged. Diagnosis is made when at least two osteochondromas are found with a positive family history and /or and identified mutation (4). Prenatal diagnosis is available if the exact mutation in the parent is known (9).

Hereditary Multiple exostosis can cause boney abnormalities that can pose both a functional and aesthetic problem (6) These exostosis can also cause malalignment, deformity, and short limbs Shortened limbs have been reported with studies showing decreased overall adult height in patients with Hereditary Multpile Exostosis, (6) Boney growth in the shoulder, knee and elbow can cause pain and limitation of movement of these joints. Males were found to have more shoulder exostosis than females (11). These patients were also found to more likely carry the EXT1 mutation (11). It was found that patients generally have a poor quality of life as related to physical function, social function, bodily pain, vitality and emotional esteem (12). Females appeared to have a lower quality of life compared to males in regards to emotional function. Children consistently rated bodily pain and emotional self esteem as a common problem (12).

Besides the pain, limitation of movement and cosmetic problems related to Hereditary Multiple Exostosis, one must not ignore the rare but serious complications associated with these boney growths.

There is a risk varying between 0.9%-25% of malignant change in existing osteochondromas (13). Osteochondromas of the pelvis and shoulder girdle have the highest rate of malignant change estimated to be approximately .2%-5% (11).

Mandibular coronoid process osteochondromas can lead to formation of a pseudo joint and ankylosis. This causes limitation in mouth opening (14).

Claudication pain can arise when osteochondromas cause compression of the popliteal artery (15). Pseudo aneurysms of the popliteal artery have also been reported in children as well as adults requiring surgical intervention (16,17). Rib exostosis can present as chest pain with development of spontaneous hemothorax (18,19).

Spine exostosis can cause spine compression and neurological sequele. Cervical spine exostosis can occur in 7% of patients with Hereditary Multiple Exostosis. (20). In one study, as much as 27% of their patients had spine involvement with compression. Some were asymptomatic at the time of imaging (21). These patients

may require an MRI to evaluate the extent of compression of the spine (21). There are reported cases of patients who are not previously diagnosed with Hereditary Multiple Exostosis who developed cervical myelopathy. Diagnosis was made when the patient developed progressive gait abnormalities and imaging was done (22). The neurological defects were not revised by surgery (22). Management of patients with Hereditary Multiple Exostosis can be challenging. In children thought has to be taken regarding the growing skeleton. Surgical correction of deformity and limb lengthening procedures done on an immature skeleton should be done with attention to the risk of reoccurrence and long term complications. Many patients tend to have multiple surgeries to alleviate pain, improve range of motion and to relieve nerve compression. Focus should be placed on decreasing pain and maintaining function.

There is no identified management protocol for pain management. Using over the counter remedies and opiates has been the common modalities of pain control. A study has been done to evaluate the use of biphosphonates to provide pain relief in those patients in which pain control has been poor and interfering with regular daily activities (8). Biphosphonates are a synthetic medication that hinders osteoclastic activity and therefore bone resorption. It is used in other conditions such as metabolic bones disease, osteoporosis, resistant hypercalcemia, and metastatic bone disease (8). It does not have an indication for use in benign bone tumors. This study reported decrease pain and over the counter medication use with biphosphonate infusions (8). Side effects and complications are being monitored.

Primary care physicians are commonly called upon to identify uncommon conditions. They are the first medical person that a patient sees when a problem arises. Being aware of rare yet potentially debilitating chronic conditions can aid in early diagnosis and management of patients. Identifying the genetic abnormality early can provide time for genetic counseling prior to future pregnancies.

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