Bilateral scapulothoracic osteochondromas in a patient with hereditary multiple exostosis: a case report and review of the literature

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Abstract

Hereditary multiple exostosis (HME) is an autosomal dominant disorder characterized by two or more benign growing, cartilage capped tumors of long bones called osteochondromas. If abnormal growth and clinical symptoms of osteochondromas newly appear in adults, malignant transformation of the usually benign growing tumors should be suspected and diagnostic testing should be initiated. Against the background of hypothesized higher malignant transformation of osteochondromas into chondrosarcoma in individuals with shoulder exostoses, we report a case of bilateral scapulothoracic osteochondromas in a patient suffering from HME. A 60-year-old female with HME complained of chest pain while being hospitalized for bilateral femoral fractures. A computed tomography scan of the chest was performed to rule out pulmonary embolism. However, bilateral osteochondromas in the scapulothoracic spaces were detected. Due to absence of radiographic evidences for malignant transformation in the patient, invasive diagnostic procedures such as biopsy and histological examination were recommended in order to exclude malignant transformation of both osteochondromas. Physicians should be aware that patients with HME who present with shoulder pain should be examined for osteochondromas in the scapulothoracic space. Due to possible sarcomatous transformation, regular follow-ups are necessary for adolescents and adults.

Introduction

Hereditary multiple exostosis (HME) is a rare disease. Since Boyer first described a family suffering from HME in 1814, epidemiological studies generate the prevalence of the orphan disorder affecting at least one in 50,000 people.[1-4] Most often located in the proximal humerus, distal femur and proximal tibia, cartilaginary exostoses arise from metapyhsal regions of enchondral growing bones.[2,5,6] Osteochondromas increase in size throughout childhood and stop growing when skeletal maturity is reached. Number and size of osteochondromas differ widely in individuals and families with known history of HME. While mean numbers of locations in individuals suffering from HME differ between 6 to 18, osteochondromas usually occur either pedunculated or are broad based around areas of active bone growth.[2,6] Although osteochondromas are often clinically asymptomatic, symptoms like pain and orthopedic deformities *i.e.* differences in bone length, forearm deformities and varus-valgus malposition of the knee usually lead to the diagnosis of HME in the first decade of life.[7] If growth and clinical symptoms of osteochondromas newly appear in adults, malignant transformation of the usually benign growing tumors should be suspected. In up to 8% the malignant degeneration to chondrosarcoma is described.[8] Thus, regular monitoring and, if malignant tumor growth is diagnosed, surgical treatment of patients suffering from HME is necessary.[8,9] Against the background of hypothesis that severely affected patients with HME are associated with palpable shoulder exostoses, we report for the first time a coincidentally found bilateral formation of osteochondromas in the scapulothoracic spaces in a patient suffering from HME.[10] Hitherto, no case of bilateral osteochondromas arising from the scapula forming a scapulothoracic neojoint is described in the literature.

Case Report

A 60-year-old woman suffering from hereditary multiple exostosis was referred to our clinic with bilateral femoral shaft fractures after falling on ground out of a wheelchair. Due to an osteochondroma in the cervical spinal canal resulting in paraplegia of the lower extremities, the patient was already bound to the wheelchair for more than 20 years. Thus, sedentary osteoporosis of the 60-year-old lady most likely resulted in the bilateral femoral fracture after inadequate trauma in home environment. Besides suffering from a cervical spine osteochondroma resulting in paraplegia of the lower extremities, cartilaginary exostosis around both knees and the left proximal humerus were also reported. In 1976 a resection of the humeral cartilaginary exostosis was performed due to malignant transfor-

mation. This resulted in the movement impairment of both, elevation and anteversion of the left upper extremity up to 90 degrees. The patient also had a positive family history sharing HME with her father and daughter.

After open reduction and internal plate fixation of both femoral fractures the patient was mobilized in our surgical ward. Weight bearing restrictions were imposed for 12 weeks postoperatively. To prevent thrombosis the current standard-of-care therapy with enoxaparine 40 mg per day was administered to the patient. During the postoperative treatment the patient showed typical symptoms of pulmonary embolism as described by Hunt and Bull.[11]

As further diagnostics a computed tomography (CT) (Siemens Somatom Definition System, Siemens Medical Solutions, Forchheim, Germany) was performed. CT parameters were as follows: detector collimation 40×0.6 mm, pitch 1.3, rotation time 0.5 s, slice thickness 2 mm and tube voltage 120 kV. Online tube current modulation was employed to reduce patient dose. Despite of no evidence for pulmonary embolism, bilateral osteochondromas arising from both shoulder blades forming a neojoint in the scapulothoracic space were detected (Figures 1 and 2). Interestingly the patient also showed no signs of malignant growth. In addi-

tion, neither cortical destruction, moth-eaten and permeative osteolysis, nor endosteal scalloping was detected. After recognition of this rare finding, the upper extremity of the patient was examined in detail. Compared to normal anatomy a bilateral prominence was marginally visible, which was well palpable on both sides above the scapula body. Range of motion of the right shoulder was not impaired, whereas the movement of the left shoulder was impaired for more than 30 years as described above. Pressure pain or movement pain along with motor and sensible deficits were absent during physical examination. While hospitalized due to bilateral femoral fractures pain management and patient positioning were optimized thereby resulting in relief of the symptoms. In context with the detected bilateral scapulothoracic osteochondromas a magnet resonance imaging (MRI) scan was initiated, but could not be performed due to patient's claustrophobia. Further diagnostics such as biopsy of the bilateral tumors was recommended but refused by the patient as well.

Discussion

The existence of a variety of synonyms, in relation to the primarily benign tumor forming disease, indicates a diverse research interest. Multiple hereditary osteochondromas, multiple osteochondromatosis, multiple cartilaginous exostosis, multiple osteochondromatosis, familial exostosis and Bessel-Hagen disease are the most common.[2,7] Although 200 years have elapsed since its first description as hereditary disease, the origin of HME was not discovered until the 1990s. Studies could show a lack of *EXT1* and *EXT2* genes causes HME.[12-15] Later loss of function of the *EXT3* gene was also identified to be associated with multiple osteochondromatosis.[16] Different kinds of *EXT1* and *EXT2* gene mutations were identified resulting in impaired heparan sulphate synthesis by lack of exostosin 1 and 2 proteins.[13,17] Heparan sulphate proteoglycans (HSPG) are important mediators for growth factor binding to chondrocytes. Thus, biosyn-

thesis of HSPGs is in turn a regulatory process for signal cascades influencing differentiation and apoptosis of chondrocytes.[18,19] Because development of HME mainly occurs due to lack of *EXT1*, *EXT2* or *EXT3* genes, *EXT* genes are designated as tumor suppressor genes.[20] However, up to 10-25% HME cases manifests in families without known history of HME caused by new mutations (*de novo* mutation). Moreover, manifestation of HME seems to be higher in males (male to female ratio: 1.5:1). Despite limited information to support *EXT* gene penetrance in female subjects, no difference in penetrance due to sex is described as well.[1,2,7,20-22] While individuals with a mutation in the *EXT1* gene are reported to be more severely affected by HME, the manifestation of shoulder exostoses also seems to be more likely in these patients. In addition, malignant sarcomatous change seems to be most likely in patients suffering from palpable shoulder exostoses relative to any other anatomic site.[10] Hence, beside its importance as diagnostic tool, clinical examination even has a prognos-
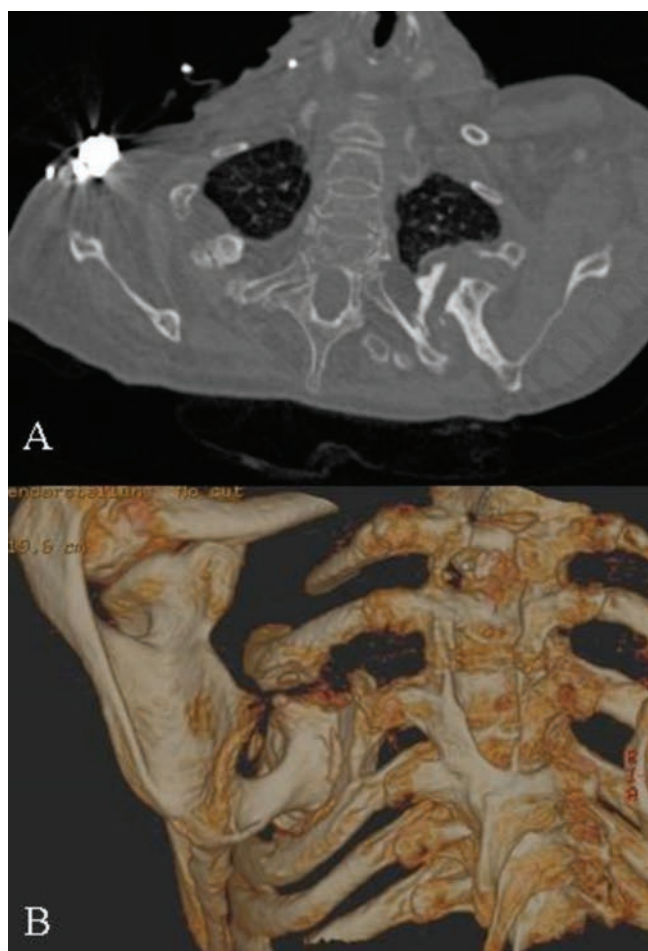

Figure 1. Axial (A) and 3D reconstructed (B) computed tomography scan. A and B show an osteochondroma rising from the left ventral scapula body forming a scapulothoracic neojoint.

Figure 2. Axial (A) and 3D reconstructed (B) computed tomography scan showing an osteochondroma in the right scapulothoracic space.

Table 1. Studies reporting rare complications caused by chest wall osteochondromas.

Study	Year	N. patients	Age	Location	Symptom/complication
Twersky et al.[33]	1975	3	12 - 13 - 11	Vertebral - Costal	Spinal cord compression
Harrison et al.[34]	1994	1	36	Costal	Hematothorax
Simansky et al.[35]	1997	1	17	Costal	Diaphragm laceration
O Brien et al.[36]	2011	1	12	Costal	Thoracic outlet syndrome
Imai et al.[37]	2014	1	16	Costal	Pneumothorax
Chen et al.[38]	2014	1	7	Costal	Pleural effusion, chest pain
Rodrigues et al.[39]	2015	1	18	Costal	ACS, coronary artery compression

ACS, acute coronary syndrome

tic relevance. Against this background it is not unexpected that the patient described above has a malignant sarcomatous transformation in her medical history.

Furthermore, the presented case shows the topographic occurrence of osteochondromas in patients suffering from HME. Cartilaginary exostoses are most likely located around the knee. The probability of involvement of the knee in affected individuals is described with 94%.[2] Besides location of osteochondromas close to the knee the cartilage caped bone tumors are most likely located in the proximal humerus (50%), proximal forearm (radius 38%, ulna 37%) and distal ulna (80%).[5,23,24] The risk that a patient with HME has a spinal lesion is described with 27%.[25] Numerous case presentations of vertebral osteochondromas in children and adults suffering from HME result in cervical myelopathy thereby showing its clinical relevance.[26-31] Therefore a routinely performed spinal image screening of HME patients is recommended.[26,32] Concerning shoulder exostoses, which are most likely associated with *EXT1* gene mutation, and thus predisposed for sarcomatous change are of special clinical interest, the reported prevalence ranges from 14 to 45%.[2,5,10] Among the rare but severe complications caused by chest wall osteochondromas as described in the literature such as spontaneous hemothorax, pneumothorax, extrinsic coronary compression and spinal cord compression (Table 1),[33-39] malignant transformation is the most feared situation for patients suffering from HME. According to the possible fateful diagnosis, a standardized clinical evaluation criteria should be met as it is usual for bone tumors in general.[40,41] A standardized screening of patients suffering from HME is recommended. Besides taking patient's history and performing a detailed physical examination plain radiographs of areas that cannot be manually examined, *i.e.* the chest, pelvis and scapula, should be performed. If differences are seen in the regularly performed examinations, further imaging diagnostics like conventional radiographs should be carried out, followed by cross-sectional imaging techniques, such as CT and MRI. If the diagnosed tumor seems to be aggressive in growth in any case, a MRI should be done to detect the dimension of the lesion before performing a biopsy by an orthopedic or surgical specialist. Often growth of the cartilage cap of an osteochondroma indicates malignant transformation. A millimeter thick cartilage normally caps the projecting bone. Although a strict cut-off in terms of thickness of the cartilaginous cap being pathognomonic of malignancy does not exist, a rare transformation of the normally benign tumor into an epiexostotic chrondrosarcoma should be suspected, if the cartilage cap is wider than 2 cm and has grown after adolescence.[42-47] In case of confirmed malignancy, surgical resection of the tumor is necessary as far as possible. Following which confirmation of tumor free margins of the resected tissue has to be done by an experienced pathologist. En-bloc resection and confirmed complete margin-free resection show an excellent long-term clinical result.[9,48] As a result of surgical resection due to sarcomatous change, pain, functional problems due to nerve and vessel compression, deformities or even early degenerative arthritis may require further orthopedic surgical therapy. For conservative treatment, in addition to the standardized pain management, use of bisphosphonates is considered to be helpful in management of refractory pain in patients suffering from HME.[49,50] If conservative treatment is exhausted, depending on the anatomical site different operative strategies are discussed.[23,51,52] In regard to shoulder exostoses different kinds of surgical techniques, open as well as endoscopic minimally invasive procedures, are described.[46,53-55] Due to possible malignant transformation and limited non surgical treatment options in chondrosarcoma, endoscopic minimally invasive procedures should be regarded with a critical eye.

Conclusions

In summary, patients suffering from HME along with shoulder pain should remind examiners of osteochondromas for being the responsible cause for motion induced pain. The possibility of sarcomatous change should be the reason for regular examinations of patients suffering from HME by specialists. Hitherto, surgical treatment is the appropriate measure in case of malignant degeneration and if necessary for refractory pain and functional impairment.

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