Ewing Sarcoma Superimposed on a Previous Osteochondroma in Multiple Osteochondromatosis

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abstract

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It has been reported that patients with hereditary multiple exostoses (called multiple osteochondromatosis by the World Health Organization) are at increased risk for malignant transformation of osteochondromas to secondary chondrosarcomas. A review of the literature found 14 cases showing transformation of osteochondromas into osteosarcomas; however, Ewing sarcoma has never been reported superimposed on an osteochondroma. This article presents the case of a boy who underwent biopsy of a previously existent osteochondroma for which the pathology report showed cytologic and immunohistochemical properties consistent with Ewing sarcoma. A 13-year-old boy with hereditary multiple exostoses (multiple osteochondromatosis) presented to an orthopedic clinic because of waxing and waning pain superficial to a previous osteochondroma on the lateral aspect of the right leg, below the knee, of 1 month’s duration. On examination, inflammation was noted over a bony mass associated with tenderness to palpation of the affected area. There was no evidence of penetrating injury or trauma, and the patient reported no constitutional symptoms, including fever. Radiographs showed marked osteolysis and signs of periosteal reaction. Magnetic resonance imaging showed evidence of cortical bone erosion and extension of the mass into soft tissue. Malignant transformation was suspected, and the patient underwent biopsy. The pathology findings were consistent with Ewing sarcoma. The highly uncommon presentation of this malignancy must serve as a red flag to other physicians who treat patients with hereditary multiple exostoses. Ewing sarcoma tends to be of higher grade and have a worse prognosis than other malignancies that are more commonly seen in these patients.
Osteochondromas are a type of benign bone tumor and are commonly seen in children and adolescents. They may be either pedunculated or sessile, with a cartilaginous cap, and are usually located at the most rapidly growing end of the long bones. Usually these are isolated lesions, but other patients may have hereditary multiple exostoses (HME), also called multiple osteochondromatosis by the World Health Organization. This autosomal dominant disorder presents with multiple osteochondromatous lesions. Three related genes have been implicated in the disorder: EXT1, EXT2, and EXT3. EXT1 and EXT2 are the most common, and EXT1 shows the most severe phenotypes. Reported complications associated with osteochondromas include nerve impingement, limb length discrepancy, limb deformity, vascular compromise, and decreased range of motion and pain caused by rubbing of soft tissues over the exostoses. However, the most dreaded complication associated with osteochondromas is malignant transformation. Fortunately, this seldom occurs. The three most frequent malignant bone tumors, in descending order of incidence, are parosteal osteosarcoma, chondrosarcoma, and Ewing sarcoma. Malignant transformation of osteochondromatous lesions into chondrosarcomas has been described to have a male-to-female ratio of 2:1, with an average age of onset of 34 years.

For solitary osteochondromas, the risk is less than 1%, and in patients with HME there is a 2% to 4% chance that chondrosarcoma will develop. Only a handful of cases have been shown to transform into osteosarcomas, and to the authors’ knowledge, Ewing sarcoma has never been reported to arise on a previous bony lesion such as an osteochondroma. This report describes the unique case of a 13-year-old boy with HME who was found to have Ewing sarcoma on biopsy of a symptomatic osteochondroma. This patient’s medical history of HME, which has been shown to increase the risk of malignant transformation, and the fact that an Ewing sarcoma has never been reported to arise on an osteochondroma make this case particularly interesting.

**CASE REPORT**

A 13-year-old boy with a medical history of multiple osteochondromatosis (Figure 1) diagnosed at 1 year presented to an orthopedic clinic after being referred by his pediatrician for a 1-month history of recurrent pain and tenderness of the right leg, localized “just below the knee” laterally, just superficial to a previous osteochondroma. The patient stated that the pain started the morning after he played a game of basketball with his friends. He noted that the game was not particularly intense, nor did the area receive any trauma or penetrating injury. He described the pain as pulsating, waxing and waning, with a pain intensity score of 7 out of 10 when the pain was the worst. The patient reported no alleviating or exacerbating factors. The pain was associated with redness, warmth, and swelling over the site. The patient reported no fever, recent weight loss, loss of appetite, general malaise or weakness, difficulty sleeping, night sweats, or suppuration over the area of pain. The patient’s father reported no use of any kind of medication except recently. The patient was taking acetaminophen for the pain and stated that it was not working.

Figure 1: Radiograph showing multiple osteochondromas around the right knee articulation and a “moth-eaten” appearance over the fibular head mass.

Figure 2: Anterior (A) and lateral (B) gross preoperative views of the right leg. On physical examination, the patient had erythema, swelling, pain, and warmth to palpation. In addition, a noticeable deformity was present over the fibular head.

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Unlike Ewing sarcoma, Technetium bone scan showed pain to radiograph showing marked osteolysis, a sunburst appearance, and Codman triangle sign.

Unlike other cases reported, this case report describes Ewing sarcoma superimposed on a previous osteochondromatous lesion. The location in which the disease manifested itself is also unusual because these malignancies tend to arise from the diaphysis, with only 5.3% occurring in the metaphysis and 0.5% occurring in the epiphysis. These malignancies are usually high grade, requiring more aggressive treatment, such as radiation therapy and chemotherapy, as well as early suspicion and diagnosis to prevent metastasis to other tissues. Unlike Ewing sarcoma, secondary chondrosarcoma, which is composed entirely of cartilaginous tissue, usually arises from pre-existing benign chondroid tumors, most typically osteochondromas. It is a low-grade malignancy and wide resection alone is usually curative. The prognosis is usually better than that for Ewing sarcoma. In this case, a high level of suspicion and proper tumor management and protocol led to this unlikely diagnosis by biopsy.

Sudden onset of pain associated with inflammation in a patient with no history of trauma or obvious cause of pain or irritation should raise a flag for malignancy, especially in the presence of multiple osteochondromatosis. These symptoms also suggest osteomyelitis, which can resemble Ewing sarcoma in presentation, including inflammation, pain, and fever.

**CONCLUSION**

It is important to maintain a high level of suspicion, especially in patients with HME, because of the increased risk of malignancy. The rare presentation of this disease raises questions about its etiology as well as a red flag. Was this case a chance phenomenon, or does HME set the environment for gene mutation leading to increased risk of a high-grade malignancy, such as Ewing sarcoma? Will having this malignancy superimposed on an osteochondroma increase the risk of recurrence in another osteochondroma in this unknown genetic environment?
patient? It is possible that there are other patients with similar presentation; therefore, an increased level of suspicion in patients with multiple osteochondromatosis is warranted to avoid complications associated with delayed diagnosis.

REFERENCES