Malignant Transformation of Giant Cell Tumor: A case study

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Abstract/Background Information:

A giant cell tumor (GCT), also known as an osteoclastoma, is a relatively common, generally benign but aggressive and destructive tumor of bone that typically affect females slightly more commonly than males within the ages of 20-40 years old, following skeletal maturity. In the United States, giant cell tumors represent “approximately 3-5% of primary bone tumors and 20% of benign bone tumors”. There are no known risk factors for giant cell tumors (1,2,3). The most common region of GCT occurrence is at the end of the long bones, especially the knee joint area. The distal femur and proximal tibia region account for more than 50% of GCT location (4). These typically benign tumors can interestingly metastasize to the lungs and is seen in up to 5% of cases (1). Even with these benign lung metastases “patients can still have a good long-term prognosis and excellent survival rate” (5). In 1-3% of giant cell tumor cases, “spontaneous transformation to a high-grade malignancy” can occur (1). Malignant transformation can be primary or secondary, but this distinction can be difficult to assess. A primary malignancy is extremely unusual in giant cell tumors however malignant transformation in secondary tumors (tumors that recur several years later in the same location as an initial benign giant cell tumor, following surgical or radiotherapy) is more common (6). The prognoses of malignant giant cell tumors are poor and are that of high grade sarcomas (4). The primary therapy of choice is surgery or curettage, depending on the local spread of the tumor (3).

This case discusses rare primary malignant transformation and metastasis of a giant cell tumor in a 28 year-old female, surgically resected in April of 2014. Her initial presentation began with sharp, knife-like pain in her right knee in September of 2012. Her x-ray at that time showed only fluid within the joint. Due to persistent pain, she was worked up further with an MRI in December, 2012 in her home town of Kuwait. At this time, curettage and cementation was performed on the lesion in her knee. The pathology from that time was consistent with a benign giant cell tumor of the bone with focal increased mitotic activity. By March of 2013 however, the pain returned in the same area and by May a focus of tumor had eroded through the skin. She underwent denosumab chemotherapy treatments, a more recent, clinically proven successful treatment option of GCT, without much improvement (7). In April 2014 she was seen at the Mayo Clinic for a second opinion. MRI at that time revealed a large, destructive mass centered at the right proximal tibia and soft tissues of the medial knee as well as multiple pulmonary nodules. Based on the extent of the tumor, the fact that the treatment had only a minimal effect on the tumor and that pulmonary nodules were identified following her initial MRI in Kuwait were all worrisome for a malignant transformation. The patient subsequently underwent an above the knee amputation and multiple lung wedge resections.

Methodology:

With the gross description as well as gross, radiologic, and microscopic photographs, the process of diagnosing this case is explained.

Discussion/Results:

The features of both benign giant cell tumors and those with malignant transformation are very similar. Grossly, the tumors are typically soft, lobulated and hemorrhagic with erosion of the adjacent bone (1). Radiographically, giant cell tumors are “aggressive osteolytic tumor(s) with cortical destruction and soft tissue
extension” (8). Histologically, there are sheets of ovoid or round mononuclear stromal cells interspersed with uniformly distributed, sparse, large, osteoclast-like giant cells with centrally located nuclei without atypia (1, 9). In malignant transformation, sarcomatous features are present within the stromal components including cells with “hyperchromatic nuclei with variably prominent nucleoli”. Mitotic activity and atypical mitoses are also often found. “Malignant spindle cells [may also] be found infiltrating the normal bone trabecula” (9). Differential diagnoses would include other sarcomas in which giant cells are found including osteosarcoma, chondroblastoma, fibrosarcoma, and undifferentiated high grade pleomorphic sarcoma (1, 9). To diagnose a malignant giant cell tumor, there must be “documentation of either a prior or coexisting benign giant cell tumor at the same location as the sarcoma” (10). Immunohistochemistry can be helpful in narrowing down some of the differential diagnoses but the stains are unfortunately very non-specific to giant cell tumors with malignant transformation. Consequently, the histologic morphology with basic hematoxylin and eosin is the most indicative diagnostic tool in determining malignant transformation of giant cell tumors of bone.

In this case study, the above the knee amputation showed a 19.0 cm solid necrotic, hemorrhagic, fungating mass arising from the proximal tibia involving the epiphysis and metaphysis and extending proximally through the soft tissue, cortical bone, medullary bone, periosteum, soft tissue, and marrow cavity, with pathologic fracture. The tumor showed histologic features consistent with high-grade malignant fibrosarcoma within the giant cell tumor. Three lung wedges were also received showing multiple nodules histologically consistent with malignant metastatic giant cell sarcoma.

Due to the extremely short time span between initial occurrence and when the tumor recurred, this was most likely a primary malignant transformation of giant cell tumor of bone that was conceivably missed on the initial curettage. It is probable that the tumor in this case study was malignant from the start, was incompletely resected and therefore not a recurrence. It is immensely important to initially correctly diagnose giant cell tumors with malignant transformation so proper treatment is administered, which likely includes a wide excision of the initial tumor. Without a wide excision with clear margins, the tumor is highly likely to recur.

Conclusion:

Giant cell tumors of bone are commonly benign but locally destructive tumors. Malignant transformation can be difficult to diagnose clinically, radiographically, and grossly due to the fact that the malignant components are interspaced within the benign components and can be easily missed on biopsy or when sections are taken at the grossing bench. Pathologists’ assistants oftentimes play a critical role in the process of a diagnosis of malignant giant cell tumor. By generously sampling these cases, especially areas that appear to have gross sarcomatoid changes, the less likely it is that malignant components are missed and therefore, most importantly, patients receive the most appropriate follow-up treatment.
Works Cited


