Radiology Case Reports

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Exophytic giant-cell tumor of the tibial tubercle

Erika Cowman Schetter; Felix S. Chew, MD; and Benjamin Hoch, MD

A 23-year-old pregnant woman presented to the orthopedic tumor clinic with gradual onset of left anteriomedial tibial pain for one month and a lytic lesion of the proximal tibia on radiography. MRI showed an exophytic mass of the left tibial tubercle with fluid-fluid levels. The patient underwent surgical excision, and pathology was consistent with giant-cell tumor. This lesion is notable for its exophytic growth pattern and its location at the tibial tubercle. Giant-cell tumors are almost always epiphyseal in location in skeletally mature patients. Although the tibial tubercle is sometimes thought of as metaphyseal, it is an epiphyseal equivalent for bone tumor growth. The role of the patient's pregnancy in the pathophysiology of her tumor is unclear.

Case report

A 23-year-old G2P1 woman in her 27th week of pregnancy presented with gradual onset of left anteromedial tibial pain and swelling for one month. She was evaluated by an orthopedist after she left her car out of gear and attempted to stop the car with her left leg. On radiographs, no fractures were present, but a lytic lesion of the left proximal tibia was noted. She was referred to the sarcoma clinic for further evaluation. On interview, she complained of fatigue, weakness, fevers, and night sweats for the past two weeks. Past medical history and review of systems were noncontributory. On examination, the patient was found to have an exquisitely tender 1-cm to 1.5-cm warm, nonerythematous mass overlying the left proximal anteromedial tibia. Range of motion, strength, and sensation of the lower extremity were intact. The remainder of the physical exam was normal.

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Ms .Schetter is a medical student at the University of Washington. Dr. Chew is a Professor in the Departmen of Radiology, and Dr. Hoch is an Associate Professor in the Department of Pathology, University of Washington, Seattle WA. Contact Ms. Schetter at ecowman@uw.edu.

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Imaging was reviewed. AP and lateral radiographs of the tibia and fibula revealed an ill-defined, oval, lucent lesion in the anterior tibial tubercle measuring 2.2 x 1.1 x 1.0 cm (Fig. 1). MRI of the knee (axial T2 FS, sagittal proton density with contrast, and sagittal T2 FS views) showed a lesion in the medial aspect of the anterior tibial tubercle. The intraosseous portion showed multilocular fluid-fluid levels. A 10-mm defect in the overlying anteromedial cortex appeared with an exophytic component of tumor extending into the soft tissue, measuring 1.7 cm in greatest dimension. There was no periosteal or endosteal reactive bone. A small amount of secondary marrow and soft-tissue edema was present (Fig. 2A-C).

Aggressive features of the lesion requiring tissue diagnosis to exclude malignancy included destruction with cortical breakthrough, soft-tissue mass, and lack of reactive bone formation. The lesion's location, unifocality, size, defined anterior border with soft-tissue displacement rather than infiltration, and lack of periosteal reaction were all important factors in narrowing the radiographic differential diagnosis. Based on the lesion's radiographic appearance, a revised differential diagnosis included giant-cell tumor (GCT), aneurysmal bone cyst, chondrosarcoma, chondromyxoid fibroma, periosteal sarcoma, and lytic metastasis.

The patient underwent surgical removal of the mass with curettage, sparing of the infrapatellar nerve, and reconstruction with bone grafting. Frozen sections of the lesion revealed a giant-cell-rich tumor with a fairly diffuse distribution of giant cells favoring GCT or possibly aneurysmal bone cyst. On formalin-fixed permanent sections, the tumor was remarkable for sheets and lobules of giant cells admixed with mononuclear histiocytic- and fibroblastic-appearing cells (Fig. 3). In some areas, giant-cell reparative

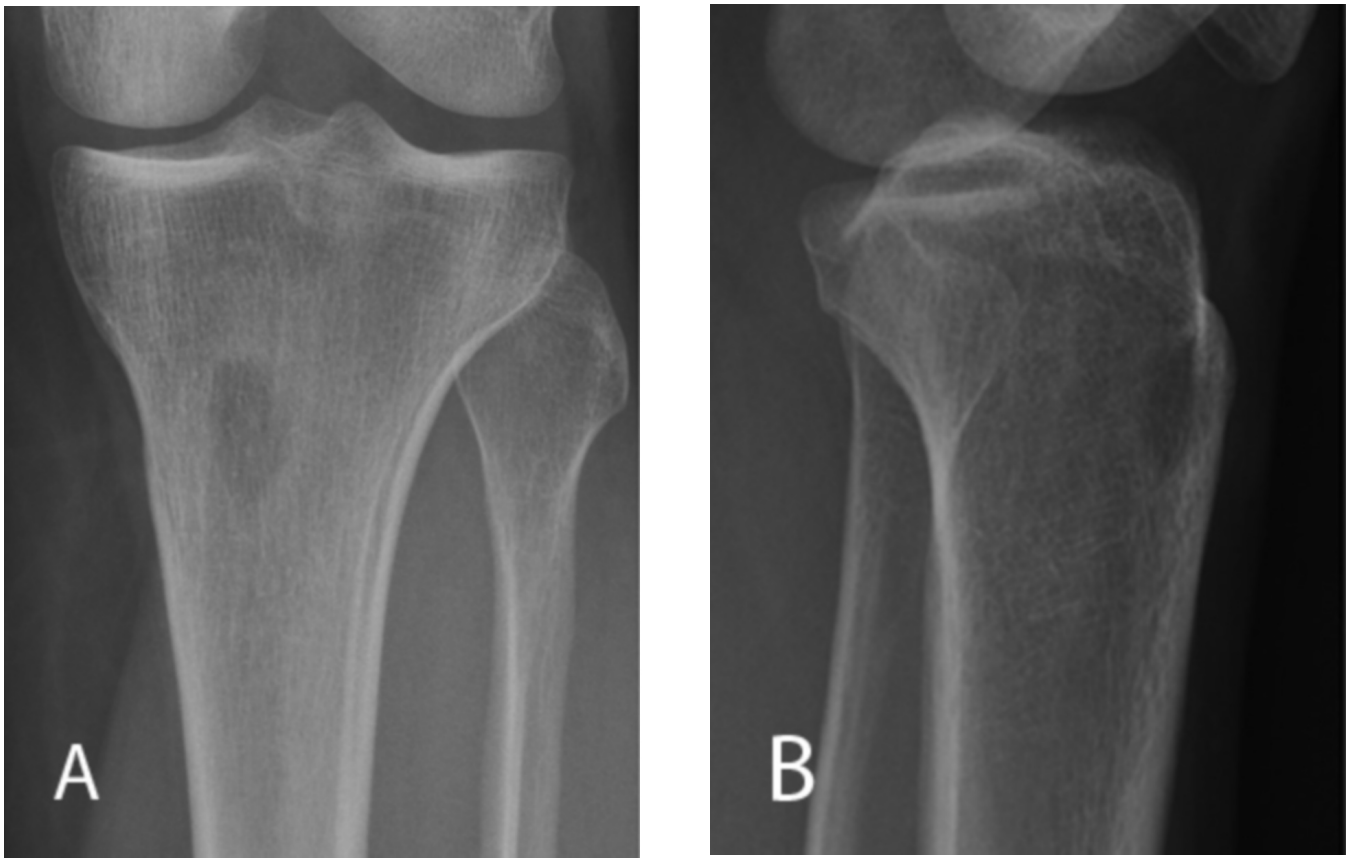

Figure 1. 23-year-old woman with giant-cell tumor. **A**. AP radiograph shows an ill-defined, oval, lucent lesion in the proximal tibial metaphysis. **B**. Lateral radiograph shows that the lesion is located in the anterior tibial tubercle.

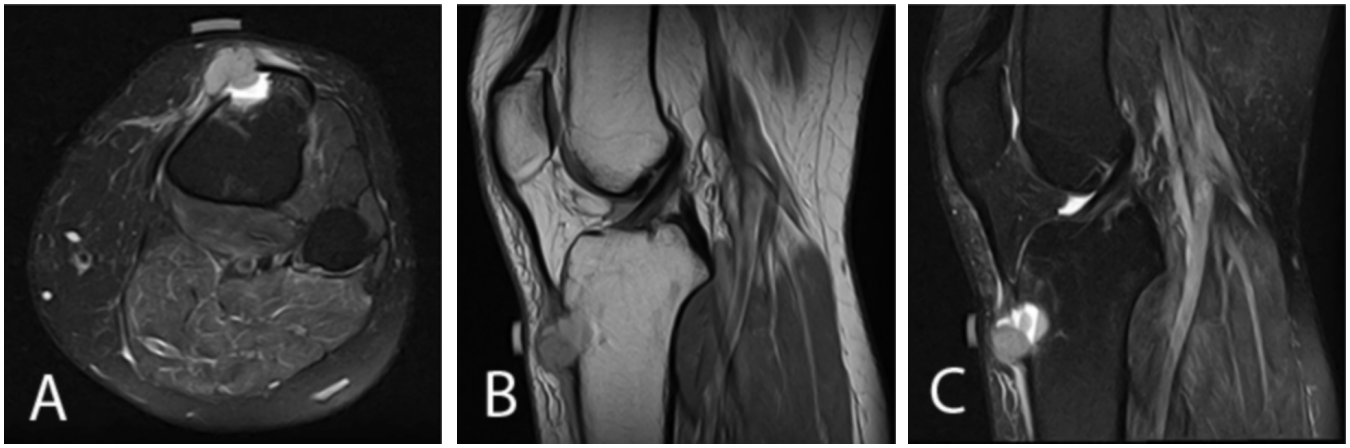

Figure 2. 23-year-old woman with giant-cell tumor. **A**. Axial T2 FS shows a lesion in the medial aspect of the anterior tibial tubercle. The intraosseous portion shows multilocular fluid-fluid levels. There is a 10-mm hole in the overlying anteromedial cortex with an exophytic component of tumor extending into the soft tissues, measuring 1.7 cm in greatest dimension. There is no periosteal or endosteal reactive bone. A small amount of surrounding marrow and soft-tissue edema is present. **B**. Sagittal SE TE:24 TR:2300 + contrast MRI. **C**. Sagittal T2 FS MRI.

granuloma-like features appeared, including a prominent fibroblastic population and more lobulated architecture. In other regions, a more polygonal- to histiocytic-appearing mononuclear population appeared among sheets of giant cells with similar-appearing nuclei and a syncytial distribution—such that the giant cells and mononuclear cells were difficult to distinguish from each other. The latter areas were diagnostic of GCT of bone. Hemorrhage and focal cystic changes were also noted, corresponding to the fluid-fluid levels seen on imaging. Reparative granuloma-like features were seen as a secondary phenomenon in benign bone tumors, including GCT. Although the radiologic findings in this patient were not classic for GCT of bone, the histopathological findings supported classification as GCT.

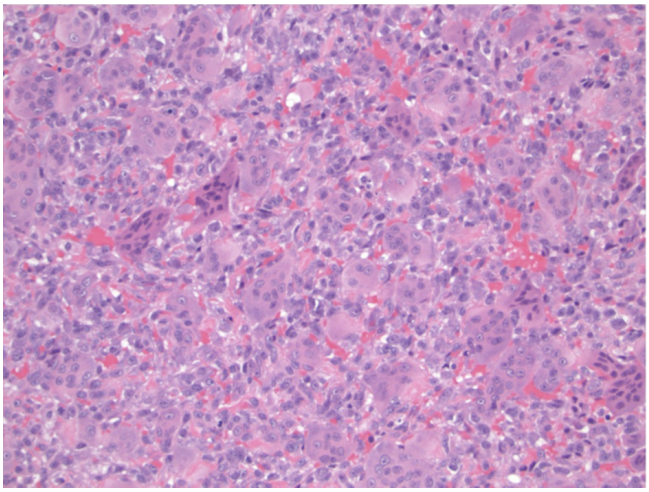

Figure 3. 23-year-old woman with giant-cell tumor. Light microscopy of formalin-fixed permanent section reveals a polygonal- to histiocytic-appearing mononuclear population among sheets of giant cells with similar appearing nuclei and a syncytial distribution, such that the giant cells and mononuclear cells are difficult to distinguish from each other.

On three-month followup, the patient had given birth to her child in the interval. She complained of mild to moderate pain in the distribution of the infrapatellar nerve but was otherwise asymptomatic. She was without evidence of locally recurrent tumor on physical exam as well as three-view radiography of the tibia and fibula. Chest radiography showed no evidence of pulmonary metastasis.

Discussion

GCT of the bone is a common benign bone tumor, accounting for 6.6% of bone tumors and 21.87% of benign bone tumors in a large Mayo Clinic series (1). Pathologically, GCT is characterized by the presence of many multinucleated giant cells evenly spread throughout a field of mononuclear stromal cells (2). GCT of bone has slightly increased incidence in women (50.7 to 57% of cases) (1, 3-5). It arises most frequently in the third through fifth decade of life (1, 4) and is relatively rare in children and adolescents prior to epiphyseal closure (1, 4, 6).

Radiographically, GCT of bone typically appears as an eccentrically located lytic lesion associated with cortical thinning and bone expansion, most commonly arising in the epimetaphyseal region of long bone. Protrusion through the cortex and extension into the adjacent soft tissues may also occur (2). MRI can further elucidate the soft-tissue findings in GCT of bone. MRI of GCT of bone typically shows solid components with low to intermediate signal intensity at T1- and T2-weighted imaging. Fluid components may also be present, with low signal at T1 and high signal at T2. Aneurysmal bone-cyst changes are commonly found within GCT lesions and may have fluid-fluid levels (1, 2). Our patient's lesion is atypical for GCT in that cortical thinning and bone expansion are not prominent; rather, penetration of the cortex appears to have occurred in the absence of cortical thinning. This exophytic morphology may be related to the lesion's uncharacteristic location at the tibial tubercle.

GCT of bone is nearly universally located at the epiphysis and is thought to arise from the metaphyseal aspect of the epiphyseal plate (2). Rare examples of metaphyseal and diaphyseal GCT have been described, with reported incidence of nonepiphyseal GCT of only 0.8% in one large case review (7). The most common location is around the knee joint, with the distal femur and proximal tibia accounting for 26% to 32% and 18% to 28% of cases, respectively (1, 3-5). GCT lesions are typically peri-articular, with subchondral location a major criterion for the diagnosis of GCT (8). However, GCT has also been shown to occur at apophyses such as the patella and the greater trochanter, which can be considered epiphyseal equivalents (1, 9).

Our patient's lesion's location at the tibial tubercle is unusual and led to misidentification as a metaphyseal lesion at initial review of the radiographs. In one case series (n = 1682), four cases of GCT involved the tibial tubercle and had been erroneously described as metaphyseal in location (7). Importantly, the tibial tubercle is a projection of the proximal tibial epiphysis with its own ossification center, which closes in adolescence (10). As such, it can be regarded as an epiphyseal equivalent for bone tumor formation.

The role of our patient's pregnancy in the pathophysiology of her GCT is unclear. There are several case reports of GCT of bone incidence or recurrence in pregnancy (11, 12, 13). Progesterone receptors have been described in GCT of bone, but a clear functional effect has not been demonstrated (14, 15). On the other hand, estrogen receptors have been identified and shown to have a slight anti-apoptotic effect in one mononuclear cell population derived from a GCT (15). The presence of increased mitotic figures in GCT in women who are pregnant or using hormonal contraception has also been anecdotally described (2). Conversely, estrogen has a well-established pro-apoptotic effect on osteoclasts (16), and an anti-osteolytic effect of estrogen

on the osteoclast-like multinucleated giant cells derived from GCT of bone has been demonstrated (17). The osteoclast-like activity of multinucleated giant cells is thought to be a mechanism of tumor growth, and a monoclonal antibody against RANKL (an osteoclast activating ligand) is a promising therapy for inoperable GCT of bone (18). Based on this evidence, estrogen could both promote and inhibit GCT tumor growth through differential action on two cell types, and further investigation on this topic is warranted. Finally, it is important to remember that the peak incidence of GCT coincides with the peak incidence of pregnancy, which may lead to coincidental occurrence.

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