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Painful Distal Femur Lesion in a 13-year-old Girl

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History and Physical Examination

A 13-year-old apparently healthy girl presented with mild dull pain in her right knee area of 1-month duration. There was no night pain and no history of fevers, night sweats, weight loss, or trauma to the area. The patient was not taking any pain medication. Physical examination revealed a very firm mass protruding along the lateral distal aspect of her right distal femur just proximal to her knee. There was no overlying erythema or warmth. The child had full range of motion throughout both upper and lower extremities and had a normal gait. Laboratory tests (complete blood count with differential, chemistries) were normal.

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Each author certifies that his or her institution has approved the reporting of this case report, that all investigations were conducted in conformity with ethical principles of research.

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Imaging studies, including anteroposterior and lateral radiographs (Fig. 1), CT scan (Fig. 2), MRI (Fig. 3), and whole-body bone scan (Fig. 4), were performed.

Based on the history, physical examination, laboratory tests, and imaging studies, what is the differential diagnosis?

Imaging Interpretation

Anteroposterior (Fig. 1A) and lateral (Fig. 1B) radiographs of the right knee showed a well-defined lytic lesion in the lateral femoral metaphysis with question of extension into the epiphysis. The lesion had nonsclerotic borders with the adjacent medullary bone and expanded the bone laterally with suggestion of a thin shell of overlying cortical bone in areas. There was no significant surrounding sclerosis or periosteal reaction.

Coronal (Fig. 2A) and sagittal (Fig. 2B) CT reconstructions delineated the nonsclerotic, but well-defined borders of the lesion, with discontinuity of the femoral cortex posterolaterally. There was destruction of the lateral cortex, with suggestion of extension into the surrounding soft tissues. The lesion measured approximately 3.7 × 3.0 cm with nonsclerotic borders. There was no periosteal reaction.

On MRI, the mass was homogeneously isointense to muscle on T1-weighted images (Fig. 3A) and hyperintense on T2-weighted images (Fig. 3B). The lateral physis was invaded, without obvious extension of tumor into the epiphysis. There was a moderate amount of marrow edema in the metaphysis and adjacent epiphysis.

An anterior image from a whole-body bone scan (Fig. 4) showed increased uptake of the radiopharmaceutical in the area of tumor involvement. No other abnormal foci of uptake were noted.

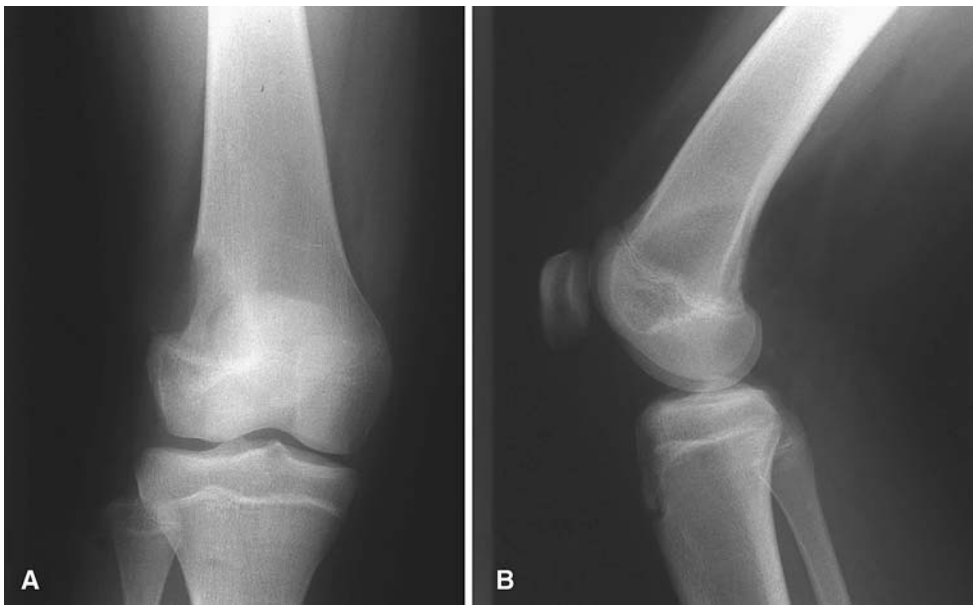

Fig. 1A–B (**A**) Anteroposterior and (**B**) lateral radiographs of the knee show a well-defined lytic lesion in the lateral femoral metaphysis with question of extension into the epiphysis. The lesion has nonsclerotic borders with the adjacent medullary bone and expands the bone laterally with suggestion of a thin shell of overlying cortical bone in areas. There is no significant surrounding sclerosis or periosteal reaction.

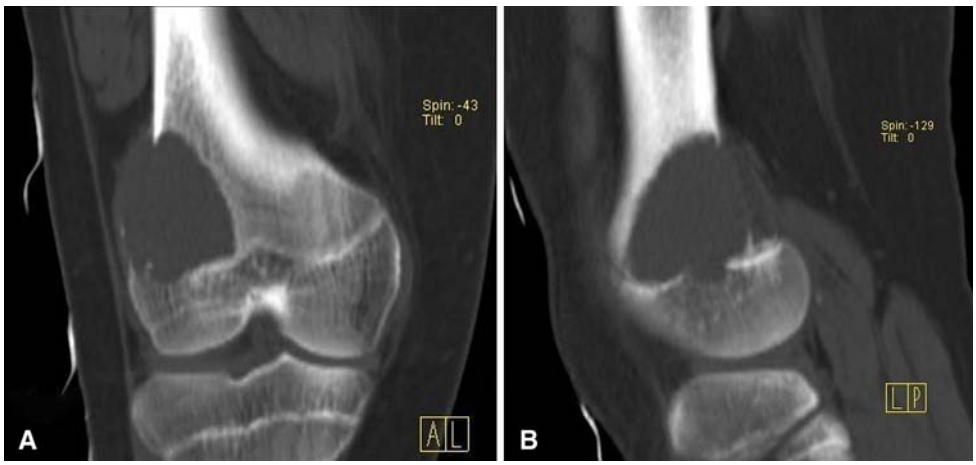

Fig. 2A–B (**A**) Coronal and (**B**) sagittal CT reconstructions show the lytic lesion with nonsclerotic, but well-defined borders. There is discontinuity of the femoral cortex posterolaterally with extension of tumor into the adjacent soft tissues.

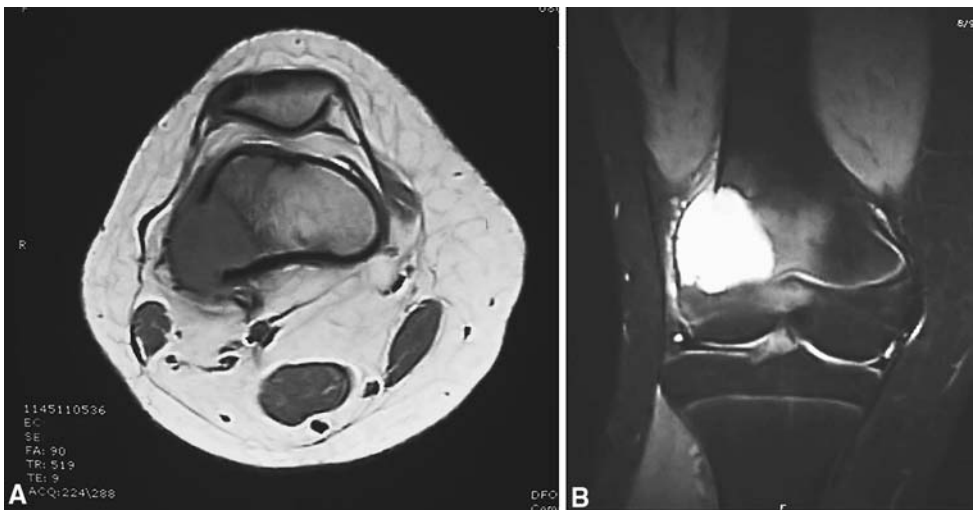

Fig. 3A–B On MRI, the lesion has a signal isointense to muscle on (**A**) the axial T1-weighted image and hyperintense on (**B**) the coronal inversion recovery weighted image. Involvement of the lateral physis and marrow edema in the metaphysis and epiphysis can be seen.

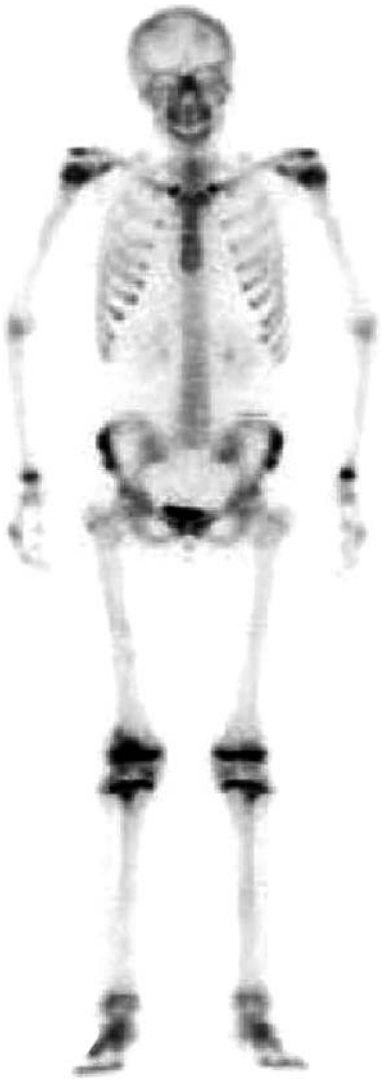

Fig. 4 An anterior image from a whole-body bone scan shows increased uptake of radiotracer in the area of the lesion.

Differential Diagnosis

Giant cell tumor of bone
Osteoblastoma
Aneurysmal bone cyst/solid variant
Chondroblastoma
Chondromyxoid fibroma

A CT-guided biopsy of the patient's right distal metaphysis of the femur subsequently was performed and the histology was studied (Fig. 5).

Based on the history, physical examination, imaging studies, and histology, what is the diagnosis and how should this lesion be treated?

Histology Interpretation

Samples from the CT-guided biopsy revealed multiple irregular fragments of white-tan, hemorrhagic, soft to rubbery tissue admixed with blood clots measuring in aggregate 1.5 × 1 × 0.3 cm. Microscopically, samples had mononuclear histiocytoid cells with prominent eosinophilic cytoplasm and osteoclastic giant cells (Fig. 5A). The multinucleated giant cells were homogeneous (Fig. 5B) and there was no evidence of bone or collagen formation.

Diagnosis

Giant cell tumor of bone

Discussion and Treatment

Giant cell tumor (GCT) is an uncommon, benign, but sometimes locally aggressive tumor that accounts for approximately 5% of primary bone tumors in adults [4, 11, 21, 32, 33, 35]. This lesion first was described by Cooper and Travers in 1818 and its benign nature recognized by Bloodgood in 1912 [4, 11, 16, 33]. Young adults are affected most often, with 80% of tumors occurring between the third and fifth decades of life [11, 21]. Reports of GCT in skeletally immature patients are rare and account for 1%

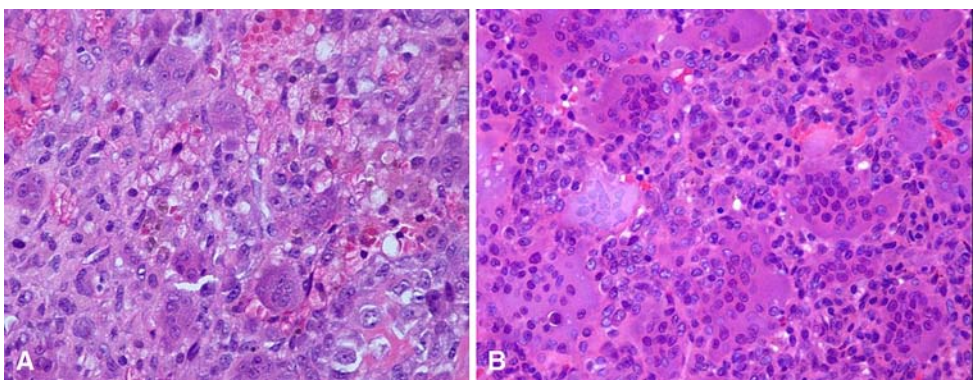

Fig. 5A–B (**A**) A low-power view (Stain, hematoxylin and eosin; original magnification, ×20) shows typical mononuclear histiocytoid cells with prominent eosinophilic cytoplasm and osteoclastic giant cells characteristic for GCT. (**B**) A higher-power view (Stain, hematoxylin and eosin; original magnification, ×40) shows a typical case of GCT.

to 3% of cases [11]. This tumor has a higher incidence in Southeast Asian patients, accounting for approximately 20% of all primary bone tumors in this population [11, 33, 35]. GCT has a predilection for the ends of long bones. Campanacci et al. [5] reported on 280 patients treated between 1913 and 1983, with presentation most often in the distal femur (36%), proximal tibia (33%), distal radius (11%), and other (20%).

Osteoblastomas are usually geographic lesions with a varying amount of peripheral sclerosis. Plain radiographs or CT scans may show mineralization in an osteoblastoma but not in a GCT. Aneurysmal bone cysts have a higher incidence in patients younger than 20 years [22, 28]. Aneurysmal bone cysts may need to be excluded after histologic evaluation but often expand the bone greater than GCTs on radiography [33]. A GCT is reportedly an underlying condition in 10% of secondary aneurysmal bone cysts. In addition, aneurysmal bone cysts usually have fluid-fluid levels on MRI. GCT should be differentiated from chondroblastoma in the pediatric population, which is much less common than the latter. Chondroblastomas are typically geographic epiphyseal lesions [33] and occasionally extend into the metaphyses [12] but have not been reported as purely metaphyseal lesions as seen in this case. Similar to osteoblastoma, chondroblastoma may have punctate mineralization. Histologically, microscopic calcifications are often prominent, showing the appearance of a chicken-wire fence [30]. Immunostaining for S-100 is positive in chondroblastomas [28] and negative in GCT. Chondroblastoma has a higher incidence in skeletally immature individuals and young adults and frequently has a sclerotic rim not typical of GCT [33]. Chondromyxoid fibroma is a benign cartilaginous tumor typically affecting individuals between the second and third decades of life [28]. Chondromyxoid fibroma is located mostly in the metaphyses of the long bones [8]. Chondromyxoid fibromas are typically eccentric geographic lesions with an extremely expansile border projecting into the soft tissues and a densely sclerotic medullary border. Internal trabeculations also may be present but also can be seen in GCTs and aneurysmal bone cysts [33]. Chondromyxoid fibromas do not typically have calcifications. The histologic features of chondromyxoid fibroma are characterized by clustered stellate chondroid cells in a myxoid background forming lobules that are separated by fibrous septae [8, 28].

The most common clinical presentation of GCT is pain in the associated region from mechanical destabilization, which may result in pathologic fracture in 10% to 12% of patients [11, 21, 33]. Campanacci et al. [5] reported hematogenous metastases to the lung in three of 280 patients (1%) with benign GCT, although this may occur in as much as 5% of patients with benign GCT of bone. Pulmonary metastases usually progress slowly and as much as 70% of patients can be prolonged survivors with repeated surgery [3, 5, 33].

The presentation of this lesion before closure of the epiphyseal growth plates is exceedingly rare [5, 14, 26, 32]. Picci et al. [26] reported a 1.8% incidence in skeletally immature individuals of the 326 patients treated for GCT, which coincides with their literature review of 1162 cases identifying this lesion in patients younger than 15 years in only 20 cases (1.7%). Kransdorf et al. [14] reported a slightly higher incidence (5.7%) in a retrospective study of 876 patients fitting the criteria of GCT by histologic appearance and open epiphyseal plates documented radiographically, but the authors acknowledged selection and misclassification bias. However, cases of multifocal occurrences each with histologic characteristics similar to solitary primary lesions have been reported to occur with greater frequency in children [5, 32].

Plain radiographs are useful for an initial assessment of the location of the lesion, pattern of bone destruction, and presence of mineralized matrix or periosteal reaction. CT may provide much of the same information with multiplanar imaging and more detailed evaluation of cortical integrity. MRI is the most sensitive modality for evaluating soft tissue extension, associated reactive changes, and in some cases, specific imaging findings, such as fluid-fluid levels. A bone scan may be valuable in detecting other sites of primary tumor formation and chest CT [11] in identifying pulmonary metastases [21, 33]. GCT is usually an eccentrically located, lytic lesion with nonsclerotic borders that may be centered in the metaphysis but commonly extends to the epiphysis in a subarticular location [7, 33]. Expansion of the bone contour and internal trabeculations, representing uneven destruction of bone and reactive thickening of trabeculae, often are present [33]. They usually do not incite surrounding sclerosis or periosteal reaction. In 10% to 15% of cases [7], these lesions may destroy the overlying cortex and extend into the surrounding soft tissues [33]. This feature is best seen on cross-sectional imaging including CT and MRI. The tumor is usually similar in density to the surrounding soft tissues on CT with no mineralized matrix and has low to isointense signal on T1-weighted images and heterogeneous high signal on T2-weighted images [15, 26, 33].

Many orthopaedists prefer to perform an open biopsy to make the diagnosis of GCT, fearing that seeding at the time of image-guided biopsy will lead to later tumor recurrence. Although there is no consensus in the literature regarding open versus percutaneous biopsy, we believe an image-guided biopsy conducted by a well-trained radiologist after consultation with the referring surgeon can be safe and accurate with decreased morbidity to the patient.

CT-guided percutaneous core needle biopsy was performed on our patient, as opposed to an open biopsy. The

benefits of this minimally invasive approach include minimal contamination of surrounding soft tissues, hopefully minimizing the risk of tumor recurrence after removal. There also is less risk of infection, hematoma, and postoperative fracture [1, 13, 18, 19, 31]. The main limitation pertains to the amount of tissue that can be obtained compared with an open biopsy, which may not yield an accurate diagnosis [9, 10, 13, 35].

On gross pathologic examination, GCTs present as well-demarcated, soft, friable, fleshy lesions with reddish-brown yellowish areas [11, 33]. Often there is gross evidence of hemorrhage and cyst formation [11, 33]. Histologically, the basic pattern of GCT is that of moderately vascularized stroma with oval to plump, spindle-shaped mononuclear cells uniformly interspersed with multinucleated giant cells [11]. The mitotic rate of mononuclear stromal cells can be quite high, but atypical mitoses are not present [33]. There is no mitotic activity in multinucleated giant cells [33]. Microscopic foci of an aneurysmal bone cyst frequently can be documented if appropriate samples are available [33].

Many factors must be considered when developing the appropriate therapeutic strategy for treatment of GCT. Location and aggressiveness of the tumor may indicate a wide en bloc resection, especially with recurrent cases or when the integrity of the bone or joint cannot be maintained with other approaches [3, 11, 21, 33]. Difficult locations, such as the pelvis, sacrum, and spine, might require preoperative bland transcatheter embolization to decrease bleeding and reduce blood supply to the tumor [2, 16, 33]. Radiotherapy has been used to treat inoperable lesions in these difficult locations, but its success in decreasing local reoccurrence comes with increased risk of malignant GCT and secondary sarcomatous changes [11, 33].

The most widely used treatment for GCT of bone is intralesional curettage [3, 16, 17, 21, 33]. En bloc resection is associated with the lowest local recurrence rates although it often requires sacrifice of an entire bone and joint [21, 24, 33]. Curettage alone has a high recurrence rate of 25% to 50% but allows for preservation of the bone and adjacent joint in the most cases [9, 17, 33]. A high-speed burr often is used to shave the walls of the tumor cavity after hand curetting all gross tumor to extend the curettage [3, 16, 33]. Adjuvants, such as liquid nitrogen [16, 20, 33], bone cement [2, 6, 25, 29, 33], zinc chloride [33, 36], phenol [6, 17, 23, 26, 27, 33], and argon beam cauterization [33], have been used after curettage to destroy microscopic tumor cells and reduce the local recurrence rate.

Cryosurgery has been reported to reduce the rate of local recurrence to less than 3% [16, 20]. The direct-pour application of liquid nitrogen is thought to extend the margin of resection by inducing a circular area of necrosis up to 2 cm by causing thermal shock, electrolyte changes, intracellular ice crystal formation protein instability, and microvascular failure [16, 20, 33]. After intralesional curettage, methylmethacrylate cement on bone graft has been advocated to fill the defect [3, 16, 33]. The lowest rates of postoperative fracture have been associated with composite fixation that emphasizes a combination of methylmethacrylate and metallic hardware to fill and stabilize the defect [16]. In a series of 73 cavities fixed with a combination of cement and metallic internal fixation, there were no postoperative fractures [16]. Cement permits immediate stabilization and mobilization of the adjacent joint and also potentially permits earlier radiographic detection of local recurrences [16]. Our preferred method for treatment of GCT of bone, whenever feasible, consists of intralesional curettage using a high-speed burr followed by cryosurgery of the tumor cavity.

Our patient was treated in this manner. The tumor cavity was filled with allograft bone instead of cement because of the excellent healing capacity of children and because the cortical defect was believed to be relatively small (⅙ the circumference of the bone), placing the child at low risk of postoperative fracture with proper postoperative external immobilization. The child was immobilized with a fracture brace postoperatively for 14 weeks. The bone graft appeared consolidated on plain radiographs at this time. At 2 years postoperatively, there has been no local recurrence. The growth plate was open at 1 year after the surgery but closed between the first and second years postoperatively, indicating the growth plate probably closed normally and not secondary to the tumor or surgery. The growth plate probably was close to closing at the time of the surgery as evidenced by the tumor crossing a small area at the time of presentation. Thus, there was no development of an angular deformity or leg-length discrepancy at the last followup at 2 years.

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