Aggressive Tibial Lesion in a 70-year-old Man

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History and Physical Examination

A 70-year-old man presented for evaluation of a lesion in the right proximal tibia, which his primary-care physician initially identified on radiographs that were obtained after minor trauma. The patient had swelling and pain in the anterior aspect of his right knee, particularly with weight-bearing. Before his minor injury, he claimed not to notice any lump or to experience pain in his right knee. He

has mild developmental delay, which may have delayed diagnosis slightly, however he could clearly articulate his symptoms once they became more pronounced, so it is unlikely that they were present for an extended time before presentation. He did not report any other constitutional symptoms, neurologic deficits, or masses.

Physical examination of his right knee showed a visible anterior bony prominence that was tender to palpation. There were no overlying skin changes and no obvious changes to his limb alignment. The right knee had full ROM with minimal discomfort even at full flexion. The knee was stable. There was no axillary, epitrochlear, inguinal, or popliteal lymphadenopathy, and the patient's neurovascular examination was unremarkable. His laboratory workup was noncontributory. Plain radiographs (Fig. 1), MRI (Fig. 2), and CT-guided needle biopsy were obtained.

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

Imaging Interpretation

Plain films showed an expansile, multilobulated, radiolucent lesion centered in the proximal tibial metaphysis without clear evidence of a cartilaginous matrix (Fig. 1). On the MR images, the lesion measured 11.6 cm × 8.3 cm × 6 cm and extended from the diaphysis to the tibial plateau articular surface. The mass was hypointense to muscle on T1-weighted imaging and showed hyperintensity on T2-weighted images. There was no surrounding bone marrow edema or joint effusion. The mass thinned and partially destroyed the cortex anteriorly with extension into the soft tissues (Fig. 2).

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

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Fig. 1A–B (A) AP and (B) lateral radiographs of the patient's right lower leg show an expansile lytic lesion with lobulation and a septated appearance centered in the metaphysis and extending to the proximal articular surface and into the diaphysis.

Differential Diagnosis

Metastatic carcinoma
 Chondrosarcoma
 Giant cell tumor of bone
 Aneurysmal bone cyst
 Plasmacytoma
 Chondromyxoid fibroma-like osteosarcoma

A CT-guided core needle biopsy was obtained and reviewed by two independent bone pathologists (BO, AR).

Based on the history, physical examination, laboratory studies, imaging studies, and histologic picture, what is the diagnosis and how should the patient be treated?

Fig. 2A–C (A) Coronal T2-weighted fat-suppressed, (B) sagittal T2-weighted fat-suppressed, and (C) sagittal T1-weighted MR images show a large lobulated expansile mass measuring 11.6 cm × 8.3 cm × 6 cm that has hyperintensity on T2-weighted images, typical of cartilage. The mass involves the diaphysis and extends proximally to the subchondral articular surface. There is evidence of cortical breakthrough with extension into the soft tissue, as indicated by the arrows.

Histology Interpretation

Gross histologic examination of specimens showed areas of bluish-gray and white coloration. The tumor had a lobular architecture and was composed of oval, spindle, and stellate cells in chondroid, myxoid, and fibrous stroma. No evidence of osteoid was present anywhere in the specimen.

Fig. 3A–D (A) A low-magnification photomicrograph shows the lobular architecture of the chondromyxoid fibroma (Stain, hematoxylin & eosin; original magnification, $\times 2$). (B) The lobules of chondromyxoid and more fibrous components are shown with increased cellularity at the periphery of the lobule (Stain, hematoxylin & eosin; original magnification, $\times 4$). (C) A chondromyxoid lobule with scattered multinucleated giant cells at the periphery is shown (Stain, hematoxylin & eosin; original magnification, $\times 10$). (D) A higher-magnification image of the tumor nodule shows a hypercellular peripheral area adjacent to a less cellular area with scattered giant cells (Stain, hematoxylin & eosin; original magnification, $\times 20$).

The neoplastic cells were cytologically bland and mitotic activity was low. Scattered multinucleated giant cells were located predominantly along the periphery of the lobules

(Fig. 3). Evidence of cortical erosion and reactive bone formation were present. The entire resection specimen was processed to be sure that there was no sampling error from the needle biopsy, which showed identical features.

Diagnosis

Chondromyxoid fibroma

Discussion and Treatment

Chondromyxoid fibroma initially was not considered in the differential diagnosis, primarily because of its extreme rarity in our patient's age group, coupled with the aggressive nature of the lesion. However, in retrospect, the clinical features of the patient's presentation and workup were consistent with this diagnosis, which ultimately was confirmed histologically. Chondromyxoid fibromas frequently present with intermittent, nondebilitating pain that may be present for months to years before diagnosis [2, 8, 17]. Patients also may present with a tender palpable mass or swelling. Both of these features were seen in our patient. Tumors arising in certain locations, such as the ribs or ilium, may be completely asymptomatic [8, 17]. Compared with a chondroblastoma, a chondromyxoid fibroma typically is less painful and patients rarely present with limited ROM, limping, or pathologic fracture [2, 17].

Radiographically, a chondromyxoid fibroma appears as a well-defined radiolucent lesion with a scalloped margin and remodeled cortex imparting the appearance of bone expansion [2, 8, 16, 17]. On MR images, a chondromyxoid fibroma has a heterogenous appearance with hyperintense signal on T2-weighted images and isointense or hypointense to muscle on T1-weighted images. Lesions in long bones often are located eccentrically in the metaphysis [2, 15], and rarely, all three segments of bone can be involved [15–17]. These features all were consistent with the initial imaging in our patient. Radiographic evidence of calcification is infrequent compared with other cartilaginous tumors and ranges from 2.4% to 16% [2, 15].

Despite being a benign tumor, a chondromyxoid fibroma can have an aggressive radiographic appearance. As seen in our patient, 32% of tumors will be locally destructive with extension into the surrounding soft tissues or articular surface [15, 16]. It is reported to be best observed with cross-sectional imaging [2, 6, 8, 15, 16]. Despite its sometimes-aggressive appearance, chondromyxoid fibromas behave as benign tumors with no potential to metastasize [3, 6, 8, 16, 17]. Although not initially suspected, given the patient's mild to moderate pain and presence of a palpable bony mass in a characteristic

location, with imaging features suggestive of an aggressive chondroid tumor and histologic evidence of a benign myxoid, fibrous, and cartilage tumor, the most appropriate diagnosis is a chondromyxoid fibroma.

Histologically, a chondromyxoid fibroma is characterized by stellate and spindle-shaped cells with chondroid, myxoid, and fibrous elements [2, 4, 16, 17]. Giant cells are seen predominantly at the periphery of lobules in approximately 50% of patients [1, 2, 6, 16]. All these features were evident in our patient's resection specimen.

The patient's advanced age in combination with the destructive and aggressive radiologic features of the lesion suggest several possible diagnoses. Metastatic carcinoma must be considered the primary differential diagnosis in this patient. Metastatic disease is the most common diagnosis in a patient older than 40 years with a radiolucent destructive bone lesion [14]. On staging studies including the chest, abdomen, CT scan of the pelvis, and a whole body Tc99 bone scan, which can identify a primary malignancy in 85% of patients with metastatic bone lesions [11], this patient did not show any evidence of systemic or other skeletal disease.

Among the primary tumors of bone, chondrosarcoma was the leading possible diagnosis. A chondrosarcoma can have similar radiographic features as those in our patient; particularly, lobulated architecture, hyperintensity on T2-weighted MR images, cortical destruction, endosteal scalloping, soft tissue expansion, and location in the tibia. However, on histopathologic examination, chondrosarcomas have plump chondrocytes and frequent binucleated cells [7], often with marked cellular atypia and mitotic figures with a cartilaginous matrix, which were not present in our patient's lesion.

A giant cell tumor of bone also may present with similar plain radiographic features, in particular the proximity to the articular surface and destructive appearance. On MR imaging, a giant cell tumor can have hyperintensity on T2-weighted images, but usually does not have a lobulated architecture. Histologically, a giant cell tumor is characterized by the presence of mononuclear stromal cells, in a background of large, uniformly distributed multinucleated giant cells, without any cartilaginous differentiation [10]. Elements of a chondroid stroma were clearly evident in our patient.

Aneurysmal bone cysts are cystic bone tumors, which on MRI may show internal septations with fluid-filled levels [9]. Although the radiographic imaging could represent an unusual aneurysmal bone cyst, many features argue against this diagnosis, including the patient's age and the MR images, which did not show any signs of blood-filled spaces, and showed solid tissue in the lesion.

Solitary plasmacytoma of bone often present in middle-aged individuals as aggressive lytic lesions of the axial

skeleton in areas of active hematopoiesis. The MR images show isointensity to muscle on T1 and hyperintensity on T2-weighted imaging. Biopsy of the tumor consists of clonal plasma cells, which were not present in our patient.

Chondromyxoid fibroma-like osteosarcomas have many similar features as their benign counterpart and are difficult to differentiate based on needle biopsy. Both may present with an aggressive-appearing expansile lytic lesion with extension into the neighboring soft tissue. In addition to atypical cells with malignant morphologic features, the diagnostic hallmark of all subtypes of osteosarcomas is the presence of osteoid. However, no evidence of osteoid was detected in this tumor.

A chondromyxoid fibroma generally is treated with complete curettage and excision, with or without cavitary filling. The local recurrence rate is 20% to 25% [2, 4, 6, 8], with approximately 38% of recurrences developing within 1 year of treatment [17]. Lower recurrence rates can be achieved with extended curettage and allograft or polymethylmethacrylate packing [6, 10]. In the more common, younger age group on presentation, the goals for treatment are removing the tumor, while supporting and preserving the adjacent joint for the long term. Mechanically, this can be achieved with bone cement or hardware if necessary, and biologically this can be achieved with the addition of a bone grafting agent to allow for rebuilding of bone stock with time. In the elderly patient, in addition to the primary goal of removing the tumor, additional goals are for symptom control and efficient return to mobility.

A chondromyxoid fibroma is an uncommon cartilaginous tumor that accounts for less than 1% of all bone neoplasms [4, 6, 16, 17]. It most commonly arises in the metaphyseal region of long bones, especially the proximal tibia during the second and third decades of life [2, 6, 8, 16, 17]. In one reported case series, patients in the second and third decades of life had 50% of all chondromyxoid fibromas with 72% of all patients being younger than 40 years [16]. Rahimi et al. documented only one patient of 400 with a chondromyxoid fibroma, which occurred after the patient was 70 years old [8]. The histopathologic features of chondromyxoid fibromas cannot predict tumor recurrence [1, 4, 17]. Analysis of tumor biochemistry and genetics shows a heterogeneous cytogenetic profile with no specific genetic, molecular, or immunohistochemical markers that definitively identify and reliably distinguish the chondromyxoid fibroma from other neoplasms such as chondrosarcomas [1, 2, 5, 6, 12, 13].

For our patient, given the significant amount of bone destruction and his age, the goal for removal of the tumor and early return to mobility was thought to be best achievable by complete resection and reconstruction. A proximal tibial resection and modular endoprosthetic reconstruction were performed (Fig. 4). A gastrocnemius flap and split

Fig. 4A–B Postoperative (A) AP and (B) lateral radiographs show the proximal tibia resection and endoprosthesis reconstruction.

thickness skin graft were performed at the initial procedure to provide adequate coverage for the implant and provide additional support to the extensor mechanism reconstruction. The patient continues to be followed and was last seen at his 1-year followup. He currently uses a walker and is a community ambulator. He has no pain in the region and has had no evidence of recurrence.

We report the case of a patient with a rare benign bone tumor with aggressive features arising in an atypical demographic. The ability to diagnose a chondromyxoid fibroma is challenging because of its rarity and the diversity of radiographic and histopathologic findings with which it is associated. This is especially true when a patient presents with atypical features, as occurred here. It is not easily distinguished from other cartilaginous neoplastic entities; therefore caution must be exercised when evaluating entities with atypical features. A careful workup, with attention to history and physical examination, adequate imaging, and review of biopsy specimens by expert bone pathologists were critical to establishing the correct diagnosis and treatment for this patient. This methodical approach with attention to detail is appropriate for the workup and management of all bone lesions, and can assist the clinician in avoiding trouble in the treatment of patients presenting with similar problems.

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