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Left Hip Pain in a 62-year-old Man

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History and Physical Examination

A 62-year-old man was referred for dull pain of the anterolateral side of his left hip with limited motion for 2 months duration. The pain radiated to the left knee, became worse after long periods of walking or standing, and was not relieved with common analgesics. The pain gradually worsened, and began awakening him at night. He had no history of previous trauma or hip disease. During these 2 months, his body weight decreased by approximately 10 kg. He had no fever, chill, or night sweats.

On physical examination, the patient had deep tenderness in the left groin and over the greater trochanter and pain in the left hip when striking the left heel in the straight leg position. There was no swelling, deformity, varicosity, or redness. Sensation was normal, and skin temperature was a bit higher than that of the right hip. The range of motion was decreased: flexion-extension, 75° to -5°; internal-external rotation, 15° to -20°; abduction-adduction, 15° to -25°; however, motion of the left knee and ankle was 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, and that informed consent for participation in the study was obtained.

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Laboratory studies, including complete blood count, erythrocyte sedimentation rate, serum chemistries, and carcinoma markers were unremarkable. Plain radiographs (Fig. 1) and computed tomography (CT) scans of the left hip and pelvis (Fig. 2) were obtained.

Based on the history, physical findings, and imaging studies, what is the differential diagnosis?

Imaging Interpretation

Anteroposterior plain radiographs of the pelvis showed irregularly expansive, loculated lytic bone destruction, especially the medial cortex, with surrounding sclerosis and internal septation and scattered internal calcification in the metaphysis of the left femur and femoral head (Fig. 1), but no periosteal reaction or soft tissue extension was present. CT scans showed a large osteolytic lesion with calcifications and mixed density in the femoral head and intertrochanteric region with erosion of its medial cortex with marked thinning and destruction of the cortex posteromedially and thickening anteriorly. Some swelling of the soft tissue also was seen (Fig. 2). CT scans of the chest did not show any obvious metastasis. Technetium⁹⁹ bone scintigraphy showed the lesion was localized in the proximal part of the left femur.

Differential Diagnosis

Fibrous dysplasia with sarcomatous degeneration
Paget's disease with sarcomatous degeneration
Liposclerosing myxoid fibrous tumor (LSMFT) with
sarcomatous degeneration

Fig. 1 An anteroposterior view of pelvis shows irregularly expansive lytic bone destruction with surrounding sclerosis and endosteal scalloping in the metaphysis of the left femur and femoral head.

Osteosarcoma
Angiosarcoma

We performed curettage and biopsy (Fig. 3).

Based on the history, physical findings, imaging studies, and histologic picture, what is the diagnosis and how should this lesion be treated?

Histology Interpretation

Grossly, the lesion consisted of grayish-white, soft, rubbery, hypervascular soft tissue and solid, whitish multinodular masses with some hard foci of bone, measuring 11 cm at its greatest diameter. Necrotic and cystic areas were interspersed in the lesion. The medial cortex was eroded and breached by the tumor. An intraoperative

frozen section showed hyperplasia of a large amount of fibrous tissue intermixing with some bony tissue.

Permanent sections from formalin-fixed paraffin-embedded tissue were stained with hematoxylin and eosin and antibodies specific for vimentin, CD31, CD34, CD68, and epithelial membrane antigen. Hematoxylin and eosin staining of the tumor showed a large amount of necrotic tissue, fibrous hyperplasia could be seen between trabeculae, with pieces of a heterogeneous cell population in some parts of the tissue, and significant vessel structures also were seen. The tumor consisted of solid nests or large sheets of spindle or epithelioid cells interspersed between and around preexisting vessels with flat endothelium (Fig. 3A). The tumor cells were large and pleomorphic and showed a moderately abundant eosinophilic cytoplasm and a round-to-oval nucleus with one or two prominent nucleoli. Mitotic figures were numerous and frequently abnormal. Mitotic counts frequently exceeded three to four per high power field (Fig. 3B). Necrosis and apoptosis were readily seen throughout the tumor.

Immunohistochemistry showed strong staining of tumor cells for vimentin and CD31 (Fig. 3C). The immunostaining for CD34 was partially positive (Fig. 3D) and staining for epithelial membrane antigen and CD68 was negative.

Diagnosis

Angiosarcoma of the proximal part of the left femur

Discussion and Treatment

A lytic lesion in the intertrochanteric region of the femur might have many differential diagnoses, including fibrous

Fig. 2A–D An (A) axial scan of the pelvis shows erosion of the medial cortex with marked thinning and destruction of the cortex posteromedially and thickening anteriorly of the left femur. (B) A coronal reconstruction CT scan of the bony window shows a large osteolytic lesion with spotty calcifications and mixed density in the metaphysis of the left femur and femoral head with erosion of its medial cortex. These coronal reconstruction CT scans of the soft tissue window show (C) some swelling of the soft tissue and (D) an obvious breach of the medial cortex of the left femur.

Fig. 3A–D Photomicrographs show histologic sections of the lesion. **(A)** Solid nests or large sheets of spindle or epithelioid cells are interspersed between and around preexisting vessels with flat endothelium (Stain, hematoxylin and eosin; original magnification, $\times 40$). **(B)** Tumor cells are large and pleomorphic and show a moderately abundant eosinophilic cytoplasm and a round-to-oval nucleus with one or two prominent nucleoli. Mitotic figures were numerous and frequently abnormal (Stain, hematoxylin and eosin; original magnification, $\times 400$). **(C)** Immunohistochemical analysis revealed strong staining of tumor cells for CD31 (Original magnification, $\times 200$). **(D)** Immunostaining for CD34 was partially positive (Original magnification, $\times 200$).

dysplasia with sarcomatous degeneration, Paget's disease with sarcomatous degeneration, liposclerosing myxoid fibrous tumor (LSMFT) with sarcomatous degeneration, osteosarcoma, angiosarcoma, etc. The final diagnosis depends on the histologic and radiographic features.

Fibrous dysplasia of bone starts in early childhood but is usually mild and asymptomatic, often being discovered at the onset of symptoms by pathologic fracture. Sarcomatous degeneration of fibrous dysplasia is rare [13]. The tumors commonly seen in such degeneration are osteosarcoma (53.4%), followed by fibrosarcoma (17.8%), and chondrosarcoma (8.9%). These can be diagnosed by histologic analysis and usually show sudden transition from benign fibrous tissue to undifferentiated osteogenic sarcoma and production of malignant bone and osteoid by tumor cells, or clear transformation of the superficial dysplastic tissue into sarcoma in some areas [13]. Our patient, however, lacked those histologic characteristics.

Malignant degeneration in Pagetic bone is a well-recognized but rare complication and the majority of malignant degenerative cases are osteosarcomas [10]. Imaging typically shows an aggressive bone-forming lesion on a background of typical Paget's disease. The characteristic pattern is that of a large lytic lesion with cortical breakthrough and a soft tissue mass that may be the most prominent feature. The radiographs of our patient showed no soft tissue extension and the histologic features were distinct.

Liposclerosing myxofibrous tumor (LSMFT) is a benign fibroosseous lesion that has a marked predilection for the

intertrochanteric region of the proximal femur. It is characterized by a complex mixture of histologic elements that includes lipoma, fibroxanthoma, myxoma, myxofibroma, and so forth. The malignant transformation of LSMFT included necrotic fat with secondary calcification and reactive ossification with ischemic woven bone. It is speculated that malignant transformation arises in the reactive border of the ischemic bone marrow [8]. The radiographs showed areas of aggressive biologic behavior in a preexistent benign process, with areas of focal bone destruction and an associated soft tissue mass. The malignant transformation of LSMFT is different from angiosarcoma histologically and radiographically.

For osteosarcoma, its peak incidence is the second decade of life and it rarely is seen in patients older than 50 years. Its clinical and radiographic presentations vary in different types. Typically, periosteal reaction such as the sunburst phenomena or Codman's triangle are common in osteosarcoma; however, our patient lacked these features.

Angiosarcoma is a malignant neoplasm of mesenchymal cell origin that tends to differentiate in an angioblastic sense, leading to formation of blood vessels. Angiosarcoma of bone also is a rare vasoformative tumor and occurs exclusively in adults. Primary angiosarcoma of bone is extremely rare and accounts for less than 1% of all angiosarcomas [2, 5, 7, 15]. Dorfman and Czerniak [4] reported only 36 (1.4%) of 2627 primary bone sarcomas were classified as angiosarcomas. These tumors usually occur in long tubular bones and much less frequently in the

ribs, pelvis, and vertebrae. Angiosarcoma of bone has a predilection for the femur, a striking male predominance, and patients have a mean age of 57 years at the time of diagnosis [6, 17]. Pain, typically of a few months' duration, is the usual presenting complaint. The lesion usually is solitary and greater than 5 cm [6, 17]. Diagnosis is particularly difficult as vascular tumors of the bone often show heterogeneous differentiation [9].

Besides clinical presentation, imaging plays an important role in the diagnosis of angiosarcoma of bone. Plain radiographs reveal lytic lesions, with or without surrounding sclerosis. CT scans show similar findings and expansion of bone and bony involvement or cortex erosion. However, one of the characteristic features of angiosarcoma is the tendency to develop multicentric disease. Multiple lesions can develop in a single bone or involve multiple bones with lesions randomly distributed throughout the skeleton or clustered in an anatomic region, such as a single extremity. The presence of multicentric lesions may be the only clue that suggests the diagnosis of a vascular tumor, whereas the solitary lesion might have numerous differential diagnoses [1]. When an angiosarcoma of bone is identified, a skeletal survey is recommended to evaluate whether the patient has multicentric disease or to show areas of increased activity. MR images may reveal the inner features and may be helpful in establishing the differential diagnosis. However, the radiographic presentation of angiosarcoma of bone is not specific. The diagnosis is established by the presence of the bulk of the tumor in the bone and characteristic histologic features. Histologically, it is composed mainly of a mass of anastomosing vascular channels. Its diagnostic feature is always the formation of new blood vessels, and typical endothelial cells should be identified. Angiosarcoma exhibits vasoformative features and angiosarcomas of bone occasionally display only weak reactivity for endothelial immunohistochemical markers [12, 16]. The absence of cytokeratin reactivity and strong reactions to antibodies for vimentin help to distinguish these tumors from spindle cell-type carcinomas [9, 11]. In poorly differentiated tumors, immunohistochemistry is mandatory for identification of an endothelial lineage. Antibodies currently used are Factor VIII-related antigen and CD31, which are specific markers for endothelial cells [2, 3]. CD31 is considered the most sensitive and specific routine marker for all types of angiosarcoma [3]. The tumor in our patient was diffusely and intensely immunoreactive for CD31. However, because CD31 positivity also is observed in carcinomas and mesotheliomas, albeit weakly [14], it is advisable to use multiple endothelial markers for the immunohistochemical diagnosis of angiosarcoma. Therefore, in our case, immunohistochemical staining of vimentin, CD34, CD68, and epithelial membrane antigen also were

performed. Among them, CD34 is another most sensitive and specific marker for angiosarcoma, whereas CD68 can help to differentiate it from malignant histiocytoma and epithelial membrane antigen can exclude epithelial carcinoma. The results showing strong staining of tumor cells for vimentin (Fig. 3C), partial positivity for CD34 (Fig. 3D), and negativity for CD68 and epithelial membrane antigen were helpful for the differential diagnosis.

An angiosarcoma is an extremely aggressive malignancy that often has spread hematogenously before it is recognized and exhibits variable malignant behavior related to its microscopic appearance and degree of vascular differentiation. The tumor is said to have a long clinical course depending on the sites involved [16]; however, it always is characterized by the rapid onset of symptoms and high frequency of local recurrence or metastasis. Angiosarcomas have a strong metastatic potential and extensive staging must be clarified at the time of diagnosis. As suggested by Bourekas et al. [2], the most effective treatment is complete surgical removal of the tumor, however obtaining adequate surgical margins often is difficult. The role of adjuvant treatment is not well defined. Radiotherapy has been given as an adjunct to surgical therapy or as palliative treatment in numerous cases of angiosarcoma.

In our patient a benign tumor was suggested by clinical presentation, radiographic examination, and CT scan; therefore, MRI was not obtained. A biopsy was performed. Because the intraoperative frozen section had a tentative diagnosis of a benign tumor, we performed curettage and inserted a dynamic hip screw as fixation (Fig. 4). However, because the lesion tissue by curettage appeared grayish

Fig. 4 A postoperative anteroposterior view shows the left hip after curettage was performed and a dynamic hip screw was inserted in the intertrochanteric region of the left femur.

white, there was hypervascular soft tissue with a large amount of bleeding, and aggressive growth with some cortical breakthrough (as observed via curettage during surgery), we doubted a completely benign nature and regarded the lesion as a borderline tumor. As a result, we used cryotherapy with liquid nitrogen, and packed non-opaque cement rather than bone graft into the cavity of the lesion to reinforce the intertrochanteric region of the left femur. We reasoned if the tumor was a sarcoma, the heat released during polymerization of methylmethacrylate might kill some residual tumor cells and reduce the recurrence rate of the tumor.

The initial treatment strategy for this patient was not appropriate for the final diagnosis of angiosarcoma. An angiosarcoma has a high risk of recurrence and metastasis, therefore, after the final pathology reading of angiosarcoma, a radical excision (half-pelvis amputation) was immediately recommended to the patient and his family, but they rejected this surgery for cultural reasons. Radiotherapy was given as an adjuvant treatment. By 6 months postoperatively the tumor had metastasized to the lung and by 7 months postoperatively to the patient's brain; he died 7 months after surgery. The case is a reminder of the possibility of misinterpreting a benign appearance by imaging and by frozen sections.

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