Rare Extraskeletal Osteosarcoma in the Anterolateral Right Leg of a 37-Year-Old Man

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To our knowledge, the case described in this article is the first reported case of extraskeletal osteosarcoma localized to the anterolateral compartment of the leg. Although the location of the tumor in our case is unique, the clinical presentation, diagnosis, pathology, and treatment are consistent with prior reported cases. Here we highlight the unique radiographic and pathologic findings and the support for aggressive neoadjuvant therapy of this aggressive neoplasm. It is our hope that this case report provides a crucial review of the typical reported features of extraskeletal osteosarcoma and its management and raises important questions for future study of this rare neoplasm. The authors have obtained the patient's written informed consent for print and electronic publication of his case report.

"...as metastasis is the main factor in survivability, early diagnosis is imperative."

Case Report

A 37-year-old man with a 9-month history of a large mass in the anterolateral distal compartment of the right leg was referred to us by his primary care doctor. The patient denied any traumatic event and reported that his pain had been steadily increasing and that he had been treating it with over-the-counter nonsteroidal anti-inflammatory drugs. He said that the mass had doubled in size over the past 6 weeks. Initial radiographs showed no evidence of a soft-tissue mass, osseous involvement, or osteoid production (Figure 1). Magnetic resonance imaging (MRI), however, showed a soft-tissue mass (Figures 2A, 2B). The initial impression was a diffusely enhancing soft-tissue mass involving the lateral leg appearing to involve or at least encircle the extensor digitorum longus tendon. The differential diagnosis at this point included soft-tissue sarcoma, angioma, or hemangiopericytoma.

The patient was offered either an open incisional biopsy or a biopsy with a disposable needle (Tru-Cut; Travenol Laboratories, Deerfield, Ill). He opted for the disposable needle biopsy, which we performed in the office during the initial evaluation. The specimen was reported as a giant cell–rich spindle-cell sarcoma consistent with malignant fibrous histiocytoma (MFH). Computed tomography (CT) scan of the chest, abdomen, and pelvis then showed a solitary, noncalcified pulmonary nodule in the right lung base; the 8.5-mm nodule was thought to be a benign granuloma, and repeat CT at 3 months was recommended. Neoadjuvant chemotherapy was discussed with the patient's medical oncologist, who recommended treatment with gemcitabine and docetaxel. After 2 cycles of this treatment, the tumor showed little decrease in size, but the

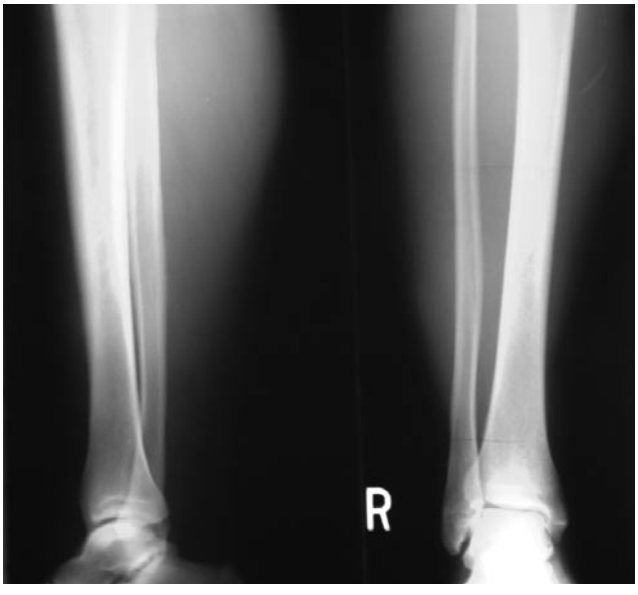

Figure 1. Initial radiographs show no soft-tissue mass, osteoid production, or osseous involvement.

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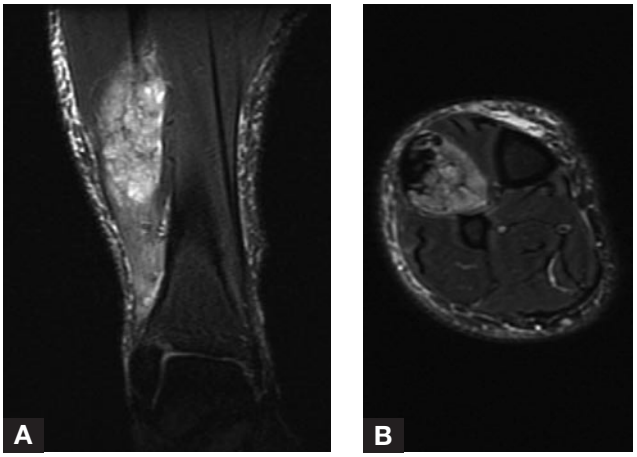

Figure 2. **(A)** Coronal and **(B)** axial magnetic resonance imaging of mass in right leg of 37-year-old man.

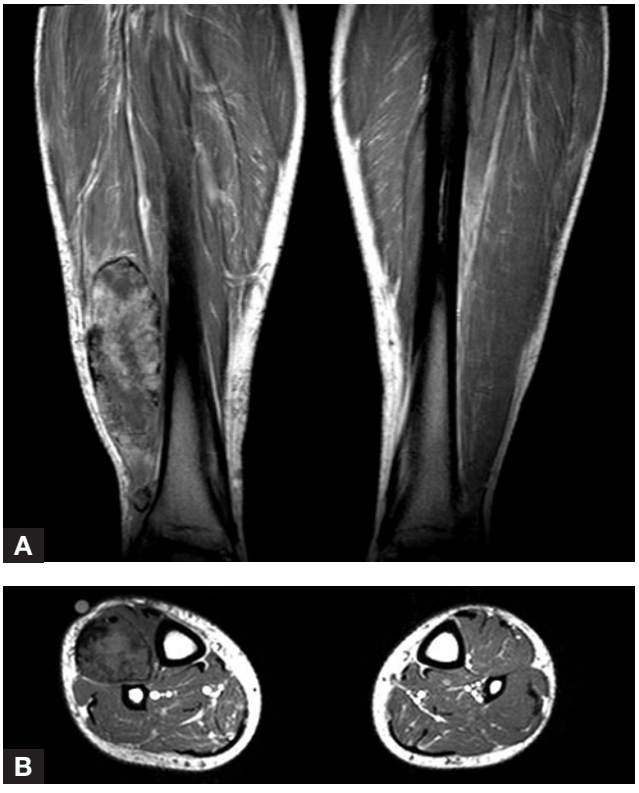

Figure 3. **(A)** Coronal and **(B)** axial magnetic resonance imaging (MRI) 4 months after index MRI and 2 cycles of chemotherapy. Formation of good "rind" facilitated resection; then, diagnosis was reclassified extraskeletal osteosarcoma.

patient had less pain, and MRI repeated after chemotherapy showed a good rind forming around the tumor (Figures 3A, 3B). Repeat chest CT now showed a stable, solitary, 8.5-mm noncalcified pulmonary nodule. Radical resection of the anterolateral distal leg mass was performed 2 months after the initial office visit. We attempted to preserve distal leg function by tenodesing the extensor digitorum longus and extensor hallucis longus with the anterior tibialis, and titanium clips were placed at the resected margins to help

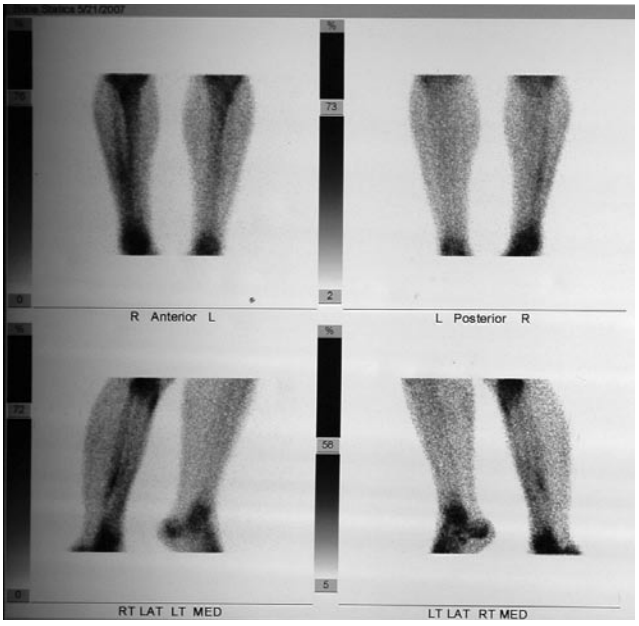

Figure 4. Four months after initial presentation, bone scan performed after 1 cycle of doxorubicin and cisplatin chemotherapy shows no distant metastatic disease.

with localization of radiation therapy. A soft-tissue mass measuring 11.5×4.7×3.6 cm was removed.

The pathologically examined specimen was reclassified as an extraskeletal osteosarcoma 2 months after the initial biopsy. Microscopic examination revealed prominent lymphovascular permeation and margins free of involvement. Given the revised histology, the medical oncology group changed the chemotherapy protocol to 2 cycles of doxorubicin and cisplatin. The patient underwent cycle one 3 months after the initial biopsy and cycle two 4 months after the initial biopsy. Bone scan performed 3 days after the first cycle showed a symmetrical distribution of tracer throughout the peripheral skeleton without suggestion of definite metastatic disease (Figure 4). After the second cycle, bone scan results were reviewed with the patient; several days after this office visit, MRI of the right leg showed a nodularity measuring 3.4 cm, which suggested residual tumor or possible recurrence (Figures 5A, 5B). Radiation was considered, but, given the clinical progression, radical resection was recommended.

Five months after the initial office visit and 3 months after the diagnosis of extraskeletal osteosarcoma was made, the patient underwent radical resection of the anterolateral right leg, including 12 cm of the fibula, and the sarcomatous bed (Figure 6). The specimen was consistent with a high-grade extraskeletal osteosarcoma. Histopathology demonstrated uniform amounts of large pleomorphic cells with abundant osteoclast-like giant cells with various amounts of osteoid (Figures 7A, 7B). The resected fibula was negative for tumor. Six months after initial presentation, the patient was doing well clinically. Repeat CT scan, however, showed innumerable bilateral pulmonary nodules consistent with metastasis. CT-guided lung biopsy 2 weeks later was positive for metastatic extraskeletal osteosar-

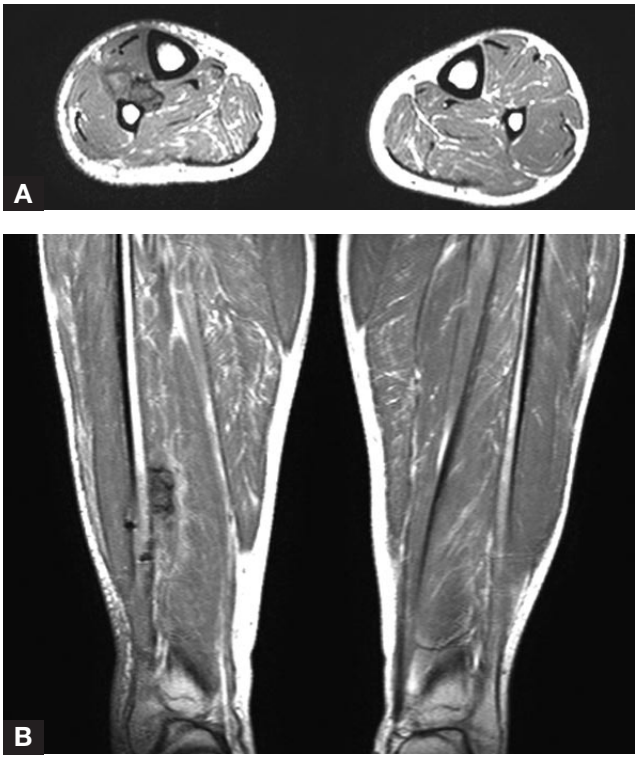

Figure 5. **(A)** Axial and **(B)** coronal magnetic resonance imaging after initial resection and 2 cycles of doxorubicin and cisplatin shows recurrence.

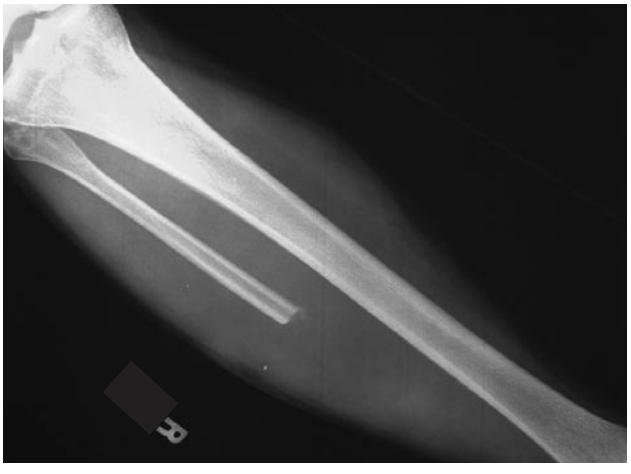

Figure 6. Radiograph after radical resection.

coma. This was the first confirmation of metastasis.

Seven months after initial presentation, the patient was seen by medical oncology, and repeat CT scan of the chest, abdomen, and pelvis demonstrated progression of the lung nodules as well as a 3.2×2.4-cm pelvic mass with pathologic fracture of the pelvis. The patient received 1 cycle of an experimental trial chemotherapy with isophosphoramide mustard. However, follow-up several weeks later demonstrated continued progression of the disease. Participation in the clinical trial was discontinued, and the patient was given 1 cycle of palliative chemotherapy with ifosfamide and etoposide. The patient's clinical condition continued to

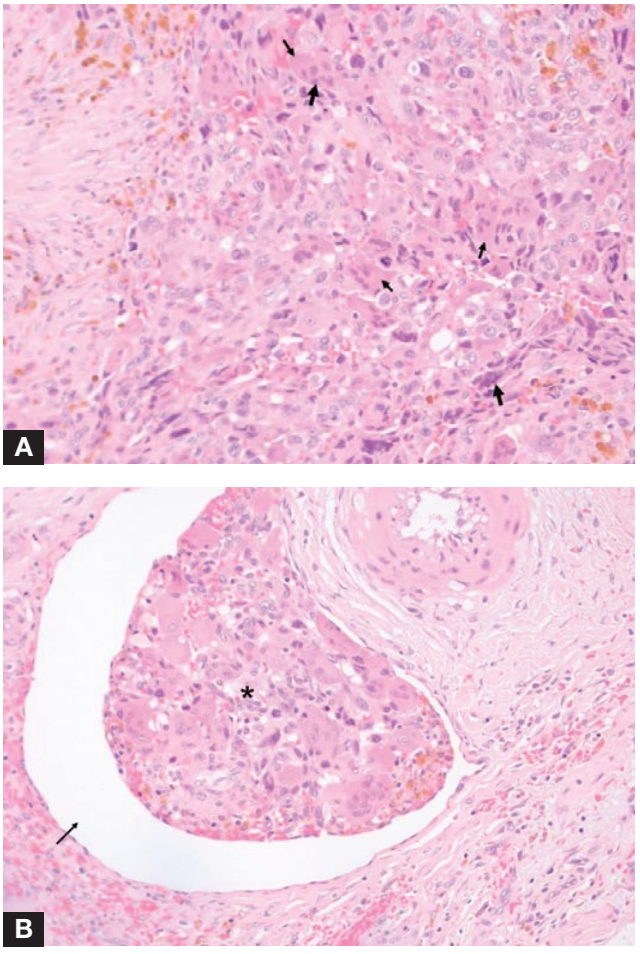

Figure 7. **(A)** Histopathology after radical resection (see Figure 5) showed uniform amounts of large pleomorphic cells with abundant osteoclast-like giant cells (large arrow heads) and various amounts of osteoid (small arrow heads). **(B)** Vascular involvement with tumor (asterisk) within vessel (arrow), a poor prognostic sign.

deteriorate, and he expired 9 months after initially presenting to the office.

Epidemiology/Presentation

Extraskeletal osteosarcoma is a rare malignant mesenchymal neoplasm that accounts for approximately 1.2% of all soft-tissue sarcomas. Unlike conventional osteosarcoma, which has a bimodal distribution, extraskeletal osteosarcoma affects patients most commonly in the fifth decade of life. As of 2005, there were fewer than 300 reported cases of extraskeletal osteosarcoma in the literature.[1] By definition, an extraskeletal osteosarcoma must arise in the soft tissue and not be attached to bone or periosteum; have a uniform sarcomatous pattern (to exclude a mixed malignant mesenchymal neoplasm); and produce osteoid matrix with or without cartilage.[1-5] Although extraskeletal osteosarcoma in the thigh, upper extremity, trunk, and retroperitoneum has been well described, we found no literature reports of cases that involved the anterolateral compartment of the leg, and extraskeletal osteosarcoma is rare in patients younger than 40.[1-16] In addition, our

patient's case illuminates a relationship with malignant fibrous histocytoma. This is important because treatment is unique to both.

It is generally accepted that the diagnosis of extraskeletal osteosarcoma carries a poor prognosis. Reported 5-year survival rates have ranged from 37% to 50%.[5,17] However, it is difficult to characterize survivability for this rare sarcoma because it has considerable histologic variability that is yet unclassified.[2,3,5,17] The most common site of involvement is the lower extremities.[1-5] Up to 30% of the cases reported occur after a history of trauma; however, the significance of this has not been elucidated.[1,5] Extraskeletal osteosarcoma can be difficult to distinguish from MFH, fibrosarcoma, and malignant schwannoma.[1,3,5,9,14,16,18]

By definition, extraskeletal osteosarcoma arises from soft tissues without osseous or periosteal involvement. The lesion is composed of malignant cells that produce osteoid with or without a cartilage matrix.[1-18] In our patient, the initial biopsy revealed pleomorphic cells with a small amount of osteoid-like material.

In the vast majority of published cases, extraskeletal osteosarcoma is a high-grade aggressive tumor.[1-3,5,14,16,17] Many authors have attempted to classify prognosis by tumor size. Bane and colleagues[2] reported only 1 death in 7 patients with tumors smaller than 5 cm, suggesting that small size may imply increased survivability and large size a comparably poorer prognosis. However, Lee and colleagues[5] found no association between size and survivability. Therefore, a classification system that guides treatment on the basis of prognostic factors is as yet undefined. Nevertheless, as metastasis is the main factor in survivability, early diagnosis is imperative. Given the proclivity of extraskeletal osteosarcoma for early metastatic disease, adjuvant chemotherapy theoretically directed at microscopic metastatic disease presumed to be present but as yet undetectable appears to be warranted.[2,3,5,14,16,17]

Treatment

Recommended treatment has primarily been surgical. The surgical treatment reported in the literature has involved intralesional excision, marginal excision, wide excision, and radical resection as an initial operation with or without adjuvant radiation depending on the overall size of the lesion.[5] Furthermore, it appears that local recurrence is indicative of an aggressive cancer, and repeated recurrence is possible.[5] Radical resection seems to result in a decrease in recurrence but has a questionable impact on distant metastases, supporting the need for an aggressive multimodal approach early in the disease process.[3,5] Lee and colleagues[5] reported that radical resection decreased the likelihood of recurrence but did not affect distant metastases. Recurrence usually occurs within the first year after excision and has not been reported to occur after 3 years.[5] Metastasis occurs more often than recurrence, and distant metastasis has usually been equated with death from the disease.[2,3,5,14,16] Lung metastasis is by far the most common site for the neoplasm (reported in >80% of the cases), but other sites, including liver, lymph nodes, skin, and bones, can be involved.[1,5] McCarter and colleagues[17] suggested that, though the number of patients they studied was small, type of adjuvant therapy seemed not to influence survival.[17]

Discussion

In our patient's case, the diagnosis of extraskeletal osteosarcoma was initially considered, but the osteoid material was thought to be most likely a focal osseous metaplasia consistent with a much more common MFH. Our patient was much younger than other patients (mean age, 50.8 years[5]), making the diagnosis much more difficult and the possibility of a fibrosarcoma more likely. Therefore, the differential diagnosis of the pathology in this case is consistent with previous cases describing similar behavior of extraskeletal osteosarcoma and MFH of the soft tissue.[3] Current research suggests a relationship between MFH and extraskeletal osteosarcoma on a genetic level.[18]

Despite continued publication of case reports of extraskeletal osteosarcoma, many controversies exist. Although other authors have suggested that chemotherapy for advanced disease is palliative,[5] the hope is that preoperative radiotherapy with adjuvant multichemotherapy will improve survival by obviating cancer metastasis.[3,5]

However, accurate diagnosis and improved classification of the subtle variations in the nature of extraskeletal osteosarcoma may improve prognosis by better directing treatment. Because of the rare nature of this tumor and the lack of consistency in classification, it is difficult to guide treatment recommendations that will provide consistent encouraging results. Therefore, further study could be directed at increasing the number of case studies available for review prospectively studying treatment outcomes on the basis of selective classification of the histologic grade of extraskeletal osteosarcoma.

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The authors report no actual or potential conflict of interest in relation to this article.

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This paper will be judged for the Resident Writer's Award.