Unusual Form and Location of a Tumor: Multiosseous Ewing Sarcoma in the Foot

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Abstract

Ewing sarcoma, as the prototype of a small round blue cell tumor of bone, typically affects adolescents and young adults. The most commonly involved sites include the diaphyses of long bones, ribs, and flat bones, such as the pelvis and scapula.

We report a case of multifocal Ewing sarcoma involving multiple bones in the foot. Given the multifocal nature of the disease confined to the foot, the initial impression was that of osteomyelitis. We describe the histologic, radiologic, and diagnostic features of the tumor and outline treatment and prognosis. To our knowledge, this is the first report of multifocal Ewing sarcoma involving multiple bones in the foot.

Ewing sarcomas are characterized as primitive malignant round cell tumors.[1] These tumors are diagnosed by neuroectodermal differentiation and by their common histologic and immunohistochemical properties.[2] Ewing sarcoma is the second most common malignant bone tumor in adolescents and young adults. It is the fourth most common primary malignant tumor, accounting for about 9% of all malignant tumors of bone. The most common primary bone tumors are multiple myeloma, osteosarcoma, and chondrosarcoma.[3]

The diaphyses of long bones (eg, femur, tibia, humerus) and flat bones (eg, pelvis, scapula) are the most commonly involved sites. Involvement of bones in the hands and feet is uncommon (3%-5% of reported cases).[4] The foot bones most commonly involved include the calcaneus and the metatarsals, in the series by Casadei and colleagues.[5]

About 90% of Ewing sarcoma cases present before age 20 years (mean age, 13 years).[6] Typical presentation is that of localized pain at the involved site. Some patients have systemic symptoms, such as fever, malaise, weight loss, leukocytosis, and increased erythrocyte sedimentation rate (ESR) mimicking infection. Radiographically, Ewing sarcoma appears as a permeative destructive bone lesion with a moth-eaten appearance (almost 76% of cases).[7] This is usually associated with lamellated periosteal new bone formation or an "onion skin" appearance. Less commonly, a sunburst configuration with an associated soft-tissue mass can be seen. Computed tomography (CT) and magnetic resonance imaging (MRI) show the osseous extent of the tumor and the presence or absence of the soft-tissue component of the tumor. Radionuclide bone scans show increased technetium-99m methylene diphosphonate accumulation and are typically hot.[6]

Histopathologically, the tumor is composed of small, uniformly sized cells characterized by an almost clear eosinophilic cytoplasm and very little intercellular matrix. There are lobules and strands divided by prominent septa. Macroscopically, appearance can range from a soft, fleshy solid mass to an almost liquid form, as the lesion does not produce any matrix. At time of surgery, the tumor may have a liquefied component and the appearance of pus.[6] Prognostic factors are tumor site in foot and treatment according to the series by Casadei and colleagues.[5] Patients with large central tumors, especially in the pelvis, have worse outcomes than patients with distal tumors.[8]

In this article, we report a case of multifocal Ewing sarcoma involving multiple bones in the foot. Given the multifocal nature of the disease confined to the foot, the initial impression was that of osteomyelitis. We describe the histologic, radiologic, and diagnostic features of the tumor and outline treatment and prognosis. To our knowledge, this is the first report of multifocal Ewing sarcoma involving multiple bones in the foot. The patient provided written informed consent for print and electronic publication of this case report.

Case Report

A 19-year-old man visited our clinic with the chief complaints of left foot pain and swelling. The pain started 10 months earlier and was followed by swelling. Complaints started after a minor local trauma. The man sought outside medical attention 8 months after pain onset. At his first visit at another institution, an initial radiograph was reported as normal, and all laboratory measures, including complete blood cell count (CBC) differential, ESR, and C-reactive protein (CRP) level, were within normal limits. Under the erroneous diagnosis of infection, the patient was treated with cloxacillin 500 mg 4 times a day for 4 weeks.

The patient's pain had started 10 months before presentation (2 months after antibiotic therapy was initiated) (**Figure 1**). Physical examination at our institution revealed a

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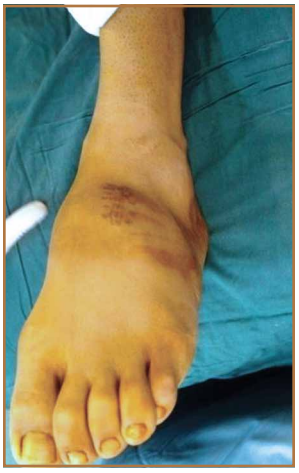
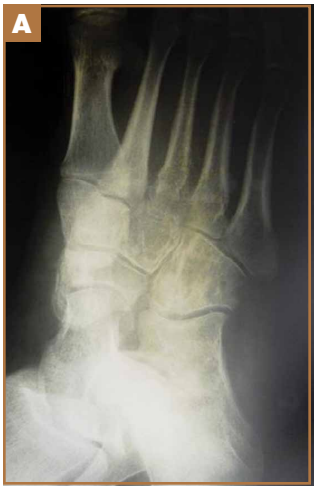


Figure 1. Patient's left foot after incisional biopsy and before surgery.



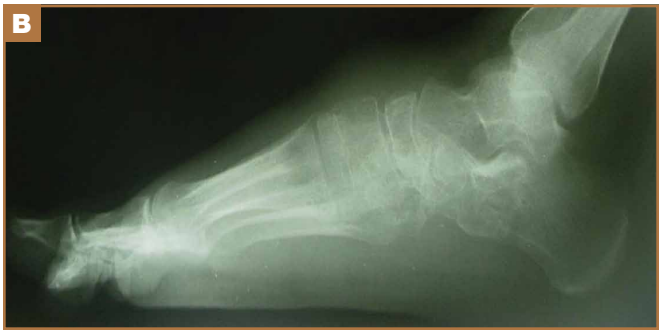
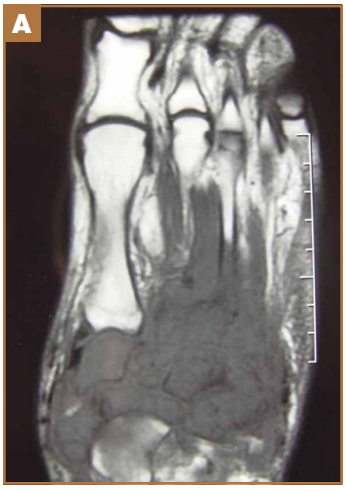


Figure 2. Ewing sarcoma. (A) Oblique and (B) lateral views of bony lesion.



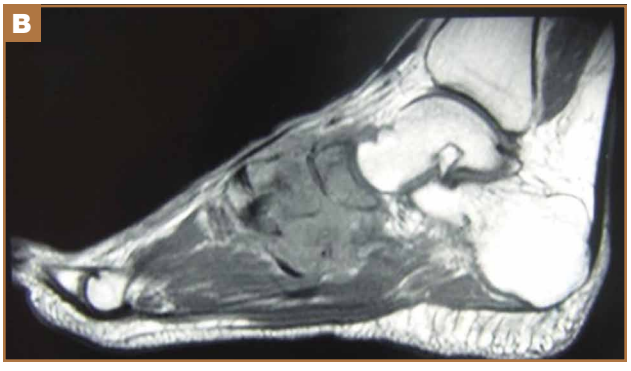


Figure 3. (A) Axial and (B) sagittal magnetic resonance imaging of left foot. T1-weighted image shows bony involvement with soft-tissue extension.

palpable mass on the dorsum of the left foot. Anteroposterior and lateral plain radiographs showed a permeative lytic lesion with cortical destruction in the left calcaneus, navicular, cuboid, and cuneiform bones and in all metatarsal bones except the first (**Figure 2**). A soft-tissue mass around the involved bones was noted as well. The talus was not involved (**Figure 3**).

CT showed permeative destruction of left foot bones, including the calcaneus, navicular, cuboid, and cuneiform bones and all metatarsal bones except the first. Invasion through the overlying cortex of the involved bones indicated aggressive biological activity of the tumor (**Figure 4**). MRI showed a destructive bony lesion of the mentioned bones associated with the soft-tissue mass (**Figure 3**).

Bone scan showed increased uptake in the involved areas (**Figure 5**). Chest plain radiographs and CT showed no distant metastasis. An incisional biopsy was performed, and histopathology showed a malignant small round cell tumor, identified as Ewing sarcoma (**Figure 6**). An immunohistochemistry study demonstrated positive CD99 and negative cytokeratin, leukocyte common antigen, desmin, and synaptophysin.

The patient was started on 4 cycles of adjuvant chemotherapy. Cycles 1 and 3 involved cyclophosphamide 2 g, vincristine 2 g, and doxorubicin 50 mg; cycles 2 and 4 involved ifosfamide 3.5 g and etoposide 200 mg. Tumor shrinkage occurred after chemotherapy. Clinical response to preoperative chemotherapy was documented by a decrease in tumor size at follow-ups. The patient underwent below-knee amputation.

Postoperative histopathology confirmed the diagnosis of

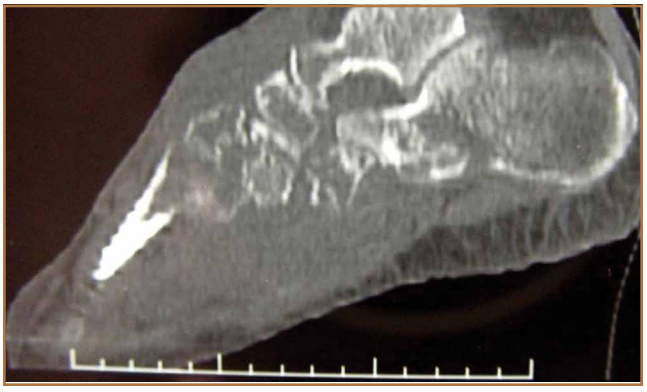


Figure 4. Sagittal computed tomography of left foot shows bony lesion with cortical destruction.

Ewing sarcoma of the calcaneus, navicular, cuboid, and cuneiform bones and all metatarsal bones except the first (**Figure 7**). At 2-year follow-up, the patient had no evidence of local recurrence or distant metastasis based on chest CT and clinical examination of the affected site.

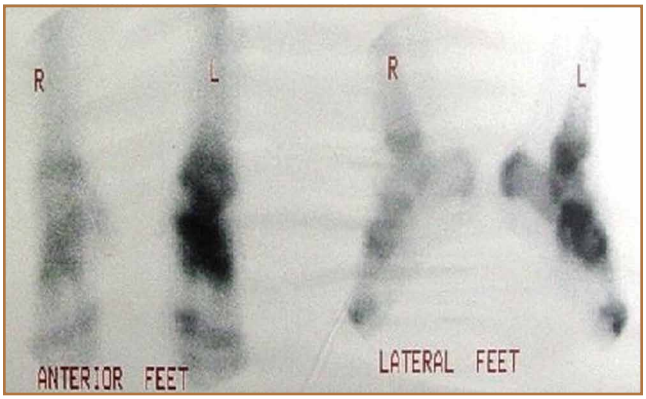


Figure 5. Bone scan of left foot shows increased uptake in involved areas.

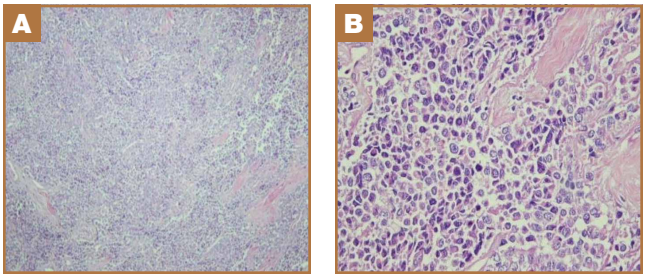


Figure 6. Biopsy of lesion shows malignant small round cell tumor in favor of diagnosis of Ewing sarcoma. Hematoxylin-eosin: (A) original magnification ×10 and (B) original magnification ×40.

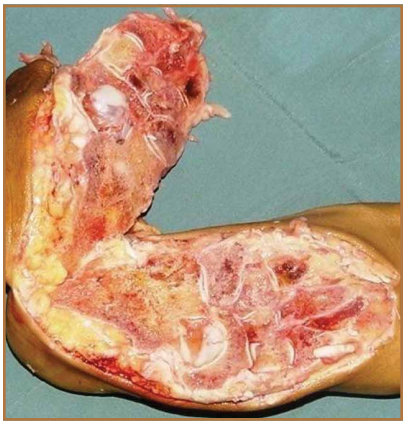


Figure 7. Postoperative view of left foot lesion.

Discussion

Ewing sarcoma is the prototype of round small cell malignancies that arise from the long bones and the flat bones. It seldom involves the hands or feet. To our knowledge, this is the first report of Ewing sarcoma of the foot with multiple-bone involvement. Our literature review found a case of Ewing sarcoma of the first phalanx of the third toe, the second metatarsal bone, the cuneiform, the cuboid, and the talus, with lesser soft-tissue extension compared with our patient's case.[9]

As this foot tumor is rare, there are few reports on its clinical aspects, appropriate treatment, and long-term outcome. For treatment of nonmetastatic Ewing sarcoma, limb-salvage surgery is advised if response has been good and there is a reasonable expectation of negative margins and good functional results.

Radiation and surgery may be part of the overall treatment plan. Radiation without surgery has a unique role in pelvic Ewing sarcoma, in contrast to extremity Ewing sarcoma. In our opinion, margins and histologic necrosis in the resection specimen are examined after surgery, and, if the margins are widely negative and histologic response is good, no further local control is advised. If the margin is positive, postoperative radiation therapy is recommended.[1] Amputation has gradually become a (rare) choice in the treatment of extremity sarcomas.[9] In our patient's case, surgery was preferred over radiation therapy after chemotherapy because of the low risk of local side effects and the expected high efficacy. In addition, radiation at such high doses for Ewing sarcoma in the foot causes functional impairment. Because of the multiple-bone involvement, a salvage procedure was not possible for our patient. Given the calcaneal involvement, however, below-knee amputation was considered safer than ankle disarticulation.

Multiple-bone involvement occurs in the advanced stage of Ewing sarcoma, usually after visceral and pulmonary metastases are detected.[9] The case reported by Rammal and colleagues[9] had both multiple-bone involvement in the foot and pulmonary metastasis. The authors indicated that hematogenous spread of the tumor was discerned because the lesions were noncontiguous.[9] Our patient had no distant metastases. We think his tumor originated in a tarsal or midtarsal bone and extended to adjacent bones. Therefore, it probably spread through its capsular and ligamentous attachment among tarsal and midtarsal bones, as the involvement was contiguous rather than distinct.

Average delay from symptom onset to diagnosis was reported to be 34 weeks.[3] Average physician delay from initial visit to correct diagnosis was reported to be 19 weeks.[3] Patients may have erythema, fever, and swelling, suggestive of osteomyelitis.[3] Laboratory results may show increased white blood cell count and elevated ESR and CRP level.[3] In addition, needle biopsy of the tumor may reveal an appearance grossly similar to that of pus.[3] Therefore, physicians may send all the tissue out for microbiological analysis (according to the erroneous diagnosis of infection) and none out for pathologic analysis. The situation can be further complicated when Ewing sarcoma occurs in the foot, an uncommon site. In this special case, multiple-bone involvement can present a misleading clinical picture of infection.[10] In other words, infection is one of the best choices in the differential diagnosis.[7] Also to be considered are multicentric giant cell tumor, fibrosarcoma,[11] and osteosarcoma.[12]

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References

1. Herring JA. Malignant tumors of bone. In: Herring JA, ed. *Tachdjian's Pediatric Orthopaedics*. Philadelphia, PA: Saunders Elsevier; 2008:2324-2327.
2. Cavazzana AO, Miser JS, Jefferson J, Triche TJ. Experimental evidence for a neural origin of Ewing's sarcoma of bone. *Am J Pathol*. 1987;127(3):507-518.
3. Canale ST, Beaty JH. Malignant tumors of bone. In: Canale ST, ed. *Campbell's Operative Orthopaedics*. Philadelphia, PA: Mosby Elsevier; 2008: 910-913.
4. Unni KK. Ewing sarcoma. In: Unni KK, ed. *Dahlin's Bone Tumor: General Aspects and Data on 11087 Cases*. Philadelphia, PA: Lippincott-Raven; 1996:121-142.
5. Casadei R, Magnani M, Biagini R, Mercuri M. Prognostic factors in Ewing's sarcoma of the foot. *Clin Orthop*. 2004;(420):230-238.
6. Greenspan A, Jundt G, Remagen W. Bone-forming (osteogenic) lesions. In: Greenspan A, Jundt G, Remagen W, eds. *Differential Diagnosis in Orthopaedic Oncology*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:114.
7. Metcalfe JE, Grimer RJ. Ewing's sarcoma of the foot masquerading as osteomyelitis. *Foot Ankle Surg*. 2004;10(1):29-33.
8. Hoffmann C, Ahrens S, Dunst J, et al. Pelvis Ewing sarcoma: a retrospective analysis of 241 cases. *Cancer*. 1999;85(4):869-877.
9. Rammal H, Ghanem I, Torbey PH, Dagher F, Kharrat K. Multifocal Ewing sarcoma of the foot. *J Pediatr Hematol Oncol*. 2008;30(4):298-300.
10. Ledermann HP, Morrison WB, Schweitzer ME. MR image analysis of pedal osteomyelitis: distribution, patterns of spread, and frequency of associated ulceration and septic arthritis. *Radiology*. 2002;223(3):747-755.
11. Dhillon MS, Prabhudev Prasad AP, Virk MS, Aggarwal S. Multicentric giant cell tumor involving the same foot: a case report and review of literature. *Indian J Orthop*. 2007;41(2):154-157.
12. Baraga JJ, Amarami KK, Swee RG, Wold L, Unni KK. Radiographic features of Ewing's sarcoma of the bones of the hand and feet. *Skeletal Radiol*. 2001;30(3):121-126.