Talar Osteosarcoma in an Elderly Woman

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Although second only to myeloma as the most common primary malignant bone tumor, osteosarcoma is an uncommon diagnosis in foot and ankle pathology, particularly in elderly patients. In the United States, osteosarcoma is still considered a relatively rare disease, with approximately 600 cases diagnosed each year.[1] The distal femur and proximal tibia are the most common sites for osteosarcoma, representing 50% of all cases.[2] Osteosarcoma of the foot and ankle accounts for only 0.2% to 2.0% of all cases of osteosarcoma.[3]

Early presentation of osteosarcoma of the foot and ankle may include pain, swelling, mechanical symptoms with ambulation, difficulty wearing shoes, and sometimes a palpable mass.[4,5] The subtle clinical presentation combined with the uncommon occurrence of osteosarcoma of the foot and ankle may lower the index of suspicion and delay diagnosis in many cases. Radiographic imaging may be helpful, but there is a marked variety in the radiographic appearance of osteosarcoma of the foot and ankle. Treatment usually includes below-knee amputation and sometimes chemotherapy. As osteosarcoma of the foot and ankle is rare, information regarding prognosis is limited. However, previous reports suggest the estimated 5-year survival rate ranges from 35% to 75%.[6,7] We present the case of an 81-year-old woman diagnosed with a primary high-grade osteoblastic osteosarcoma of the talus.

Case Report

While on vacation, an 81-year-old woman presented to an internal medicine physician with complaints of pain and swelling associated with a soft-tissue prominence at the anterior right ankle. Plain x-rays showed a focal sclerotic lesion in the talus, and the patient was referred to a podiatrist. Subsequent magnetic resonance imaging (MRI) showed changes in the right talus thought to represent avascular necrosis. Surgical options were discussed, but the patient wanted to defer treatment until after she returned home from vacation. Meanwhile, her right ankle pain worsened, progressively restricting her weight-bearing activity.

After returning home from her vacation 5 months later, the patient had her ankle reevaluated. Her medical history revealed she had been in otherwise excellent health, living a very active lifestyle until the onset of the right ankle pain. She had no known family history of malignancy. Systems review revealed no appreciable weight loss, but the right ankle pain did not improve with rest and was worse at night, waking her from sleep. A 4-cm rigid nontender bony mass was palpable at the anterior aspect of the right talus. Dorsiflexion of the right ankle was limited, but distal neurovascular examination was normal. No popliteal or inguinal adenopathy was appreciated.

"The best method of disease determination is adequate tissue biopsy and thorough histologic examination."

A completely new set of imaging and diagnostic studies was obtained. Plain x-rays showed a sclerotic bone lesion in the right talus, with multiple extraosseous calcifications anterior to the talus (Figures 1, 2). MRI showed a soft-tissue mass extending out into the soft tissues directly anterior to the talus deep to the neurovascular bundle (Figure 3). A whole-body bone scan revealed isolated increased uptake in the right talus (Figures 4, 5). Additional metastatic workup included chest, abdominal, and pelvic computed tomography (CT) scans, which revealed several small pulmonary nodules and a 1.2-cm nodule in the right lower lobe (Figure 6). On positron emission tomography (PET) scan, the 1.2-cm pulmonary nodule displayed a peak standardized uptake value (SUV) of 0.7, suggesting the lesion was more likely to be an inflammatory process rather than a malignancy. Smaller pulmonary nodules displayed peak SUVs consistent with an inflammatory etiology as opposed to a malignancy. Laboratory studies, including complete blood cell count, basic chemistry, alkaline phosphate, calcium, alanine aminotransferase, and aspartate aminotransferase, were all within normal limits.

Following completion of the radiologic imaging studies, an open biopsy was performed. The final pathology report from multiple institutions concluded that the lesion involving the right talus was a grade II osteoblastic osteo-

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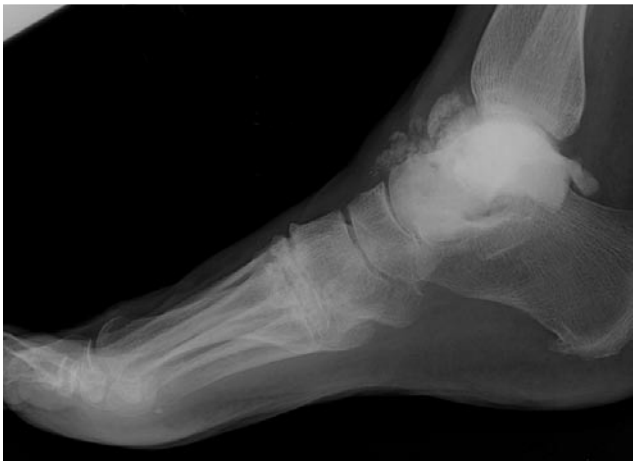

Figure 1. Lateral x-ray shows multiple extraosseous calcifications at the anterior talus with an additional extraosseous process protruding at the posterior talus. Also noted is widespread sclerotic consolidation of the talar body.

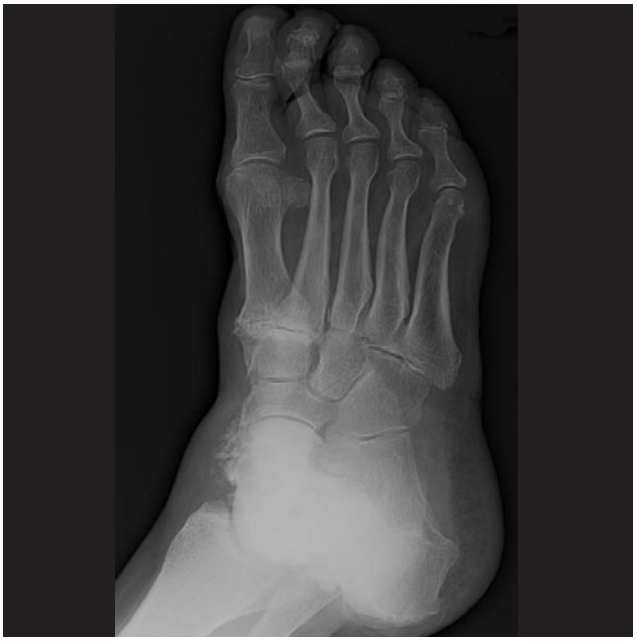

Figure 2. Anteroposterior x-ray shows extraosseous calcification at the anterior talus with sclerotic consolidation of the talar body.

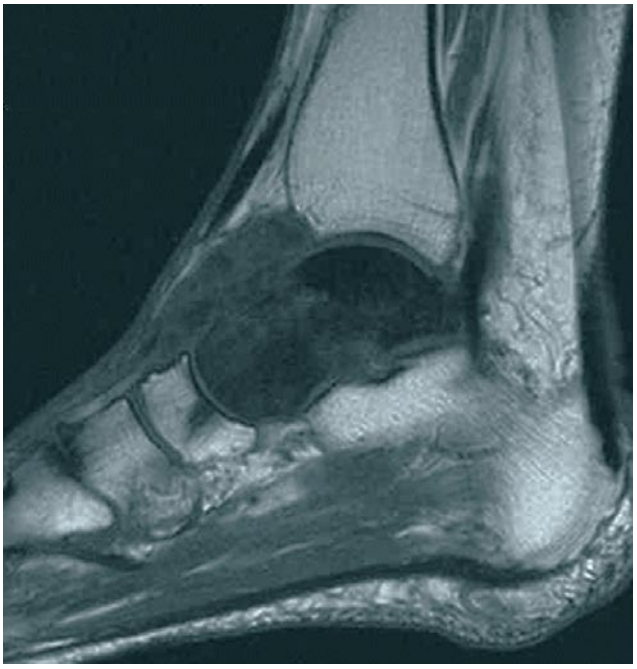

Figure 3. Sagittal T_2-weighted magnetic resonance image shows soft-tissue extension of tumor at the anterior talar surface with almost complete talar body signal change.

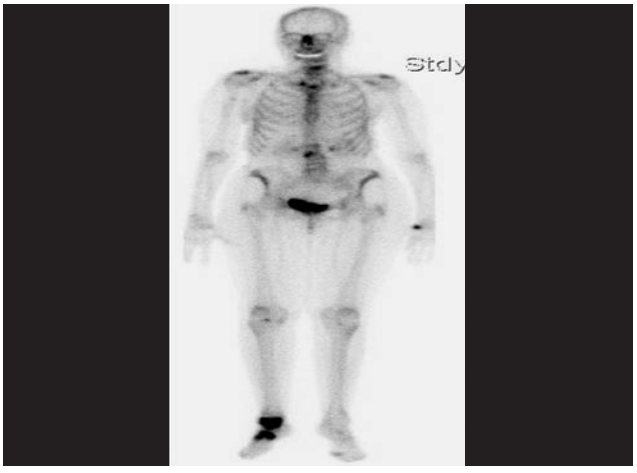

Figure 4. Whole-body bone scan shows localized hypermetabolic activity at the right talus without evidence of metastatic lesions.

sarcoma. During a review of the information, the patient was informed that the osteosarcoma seemed to be confined to the ankle and that there was no identifiable metastatic disease. Thus, it was agreed that below-knee amputation would be performed to remove the entire tumor. A lesser surgical procedure would leave a nonfunctional foot, prolonged rehabilitation, and suboptimal recovery. The below-knee amputation was performed without complication 7 months after the initial presentation of symptoms.

Gross pathology demonstrated a 5.2×4×1.3-cm tan-white firm irregular mass involving almost the entire talus (Figure 7). The mass eroded the anterior cortical surface of the talus to involve the adjacent soft tissue. The tumor showed almost complete involvement of the talus but did not involve the distal end of the tibia, fibula, or other bones of the foot and ankle. Histologically, the tumor showed many areas of prominent osteoid production with some well-formed trabeculae of woven bone (Figure 8A). In these areas, malignant osteoblasts had a spindled appearance with relatively low-grade nuclear features, but plump ovoid osteoblasts with high-grade nuclear features could still be identified. Other areas were marked by sheets of severely atypical osteoblasts with a lacelike pattern of osteoid (Figure 8B), as more typically seen in conventional osteosarcoma. In addition, the tumor involving the adjacent soft tissue showed malignant osteoblasts with high-grade

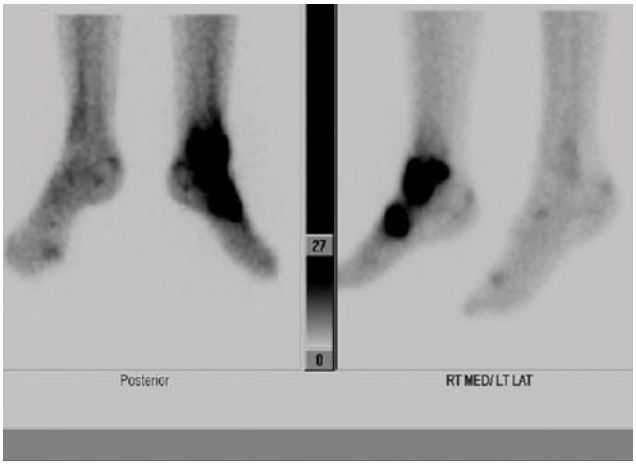

Figure 5. Extremity bone scan shows hypermetabolic activity at the right anterior ankle and talar region.

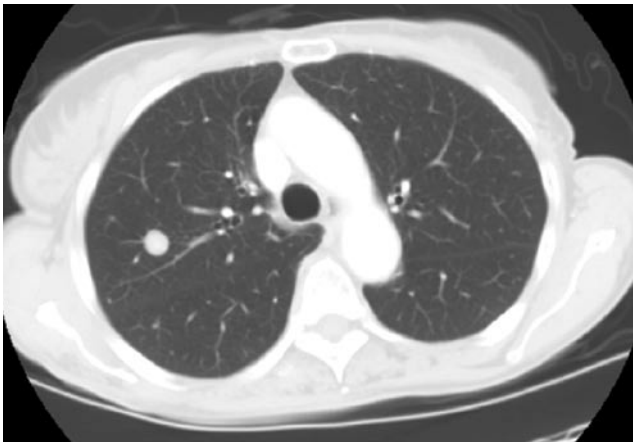

Figure 6. Chest computed tomography scan with contrast shows numerous indeterminate pulmonary nodules, with the largest, in the right upper lobe, measuring 1.2×1.3 cm.

nuclear features. There was no evidence of necrosis grossly or histologically. In comparison with the gross specimen, the small specimen from the open biopsy seemed to contain more well-differentiated features consistent with grade II/IV (low-grade) osteosarcoma.[8] However, the gross specimen contained multiple areas of highly malignant osteoblasts, thus receiving a more accurate grade III/IV determination. The final high-grade determination contravened the preliminary determination of low-grade II/IV osteosarcoma derived from a probable sampling error reflecting the limitations of biopsy techniques.[8]

The patient did well after surgery. Her wounds healed without incident, and she was fitted with a prosthesis. After an initial postoperative visit, she met with a medical oncologist to discuss chemotherapeutic options and the preferred means of monitoring the pulmonary lesions. She deferred chemotherapy at this time and elected to have serial CT scans to monitor the pulmonary lesions. As of August 2005, the large nodule in the right upper lobe appeared stable. A few other pulmonary

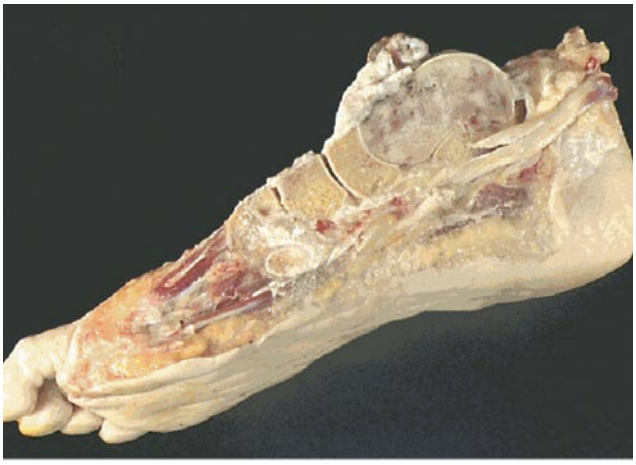

Figure 7. Gross specimen shows almost complete involvement of the tumor in the talus but no involvement in the distal tibia, fibula, or other ankle bones. The tumor did show cortical destruction and extension beyond the anterior talar surface.

nodules appeared slightly enlarged, and a new nodule was observed in the left lower lobe. These lesions will be closely monitored for progression of metastasis. Clinically, the patient progressed well with rehabilitation and described no detrimental change in health 4 months after the below-knee amputation.

Discussion

Malignant tumors are exceedingly rare in the foot and ankle. Berlin[9] reviewed 67,000 foot lesions and found less than 1% of these tumors to be malignant. Osteosarcoma is the second most common primary bone malignancy, yet it is still considered a rare tumor, with only 600 cases diagnosed in the United States annually.[1] There is a bimodal age distribution for osteosarcoma, with the first peak age of incidence occurring at 16 years for females and 18 years for males, comprising 70% of all cases.[10] In this younger population, the male:female ratio for osteosarcoma is 2:1.[1] A second peak of incidence occurs in a much older population, around 68 years, and comprises 10% to 15% of all cases.[10] More females are affected in this older population of osteosarcoma patients, with a male:female ratio of 1.3:1.[11]

Important distinctions have been found to contrast osteosarcoma diagnosed in the younger and older populations. Osteosarcoma in the adolescent population is typically primary bone tumors diagnosed in the absence of preexisting disease originating from the distal femur or proximal tibia in more than half of all cases.[1] Osteosarcoma in the older adult population usually occurs secondary to Paget disease or prior radiation treatment, with the majority of cases originating in the axial skeleton.[10] Our patient is unique in that she was elderly and had no previous medical disease but was diagnosed with a primary talar osteosarcoma.

Osteosarcoma of the talus is extremely rare; only a few cases have been documented in the world literature. According to a review of 1929 patients diagnosed with osteosarcoma from 1911 to 1992, the tumor was localized to

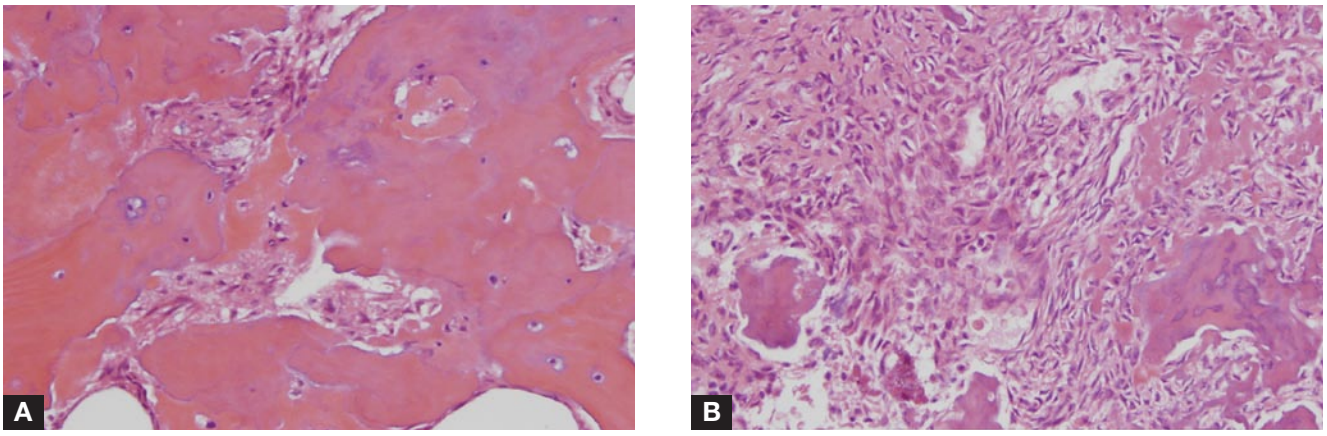

Figure 8. Histologic specimens. (A) Prominent osteoid production, with some sections even showing well-formed trabeculae of woven bone. In these areas, some of the malignant osteoblasts had a spindled appearance with relatively low-grade nuclear features, but plump ovoid osteoblasts with high-grade nuclear features could still be identified. (B) Sheets of severely atypical osteoblasts with a lacelike pattern of osteoid are more typically seen in conventional osteosarcoma. In addition, the tumor involving the adjacent soft tissue showed malignant osteoblasts with high-grade nuclear features.

the talus in only 3 cases, representing 0.16% of all osteosarcomas in the study.[7] (Only 12 below-ankle cases were identified.) Mean age for these 3 patients with talar osteosarcoma was 43.7 years. Of the 3 patients, 2 had high-grade osteoblastic osteosarcoma (1 died from disease 18 months after diagnosis; the other showed no evidence of disease after 10 years); the third patient, with high-grade telangiectatic osteosarcoma, died from disease 2 years after diagnosis.[7] The other osteosarcoma cases in this study were localized to the calcaneus (50%, 6/12), metatarsals (17%, 2/12), and cuboid (8%, 1/12). Another study, which reviewed more than 13,000 tumors in a national registry between 1904 and 1988, revealed only 11 below-ankle osteosarcomas.[12] Similarly, tumors were localized to the talus (27%, 3/11), calcaneus (45%, 5/11), tarsus (18%, 2/11), and metatarsals (9%, 1/11). In another single-institution report, osteosarcoma was diagnosed below the ankle in only 14 patients between 1941 and 1991, with the tumor localized to the talus in only 1 case. [12] The patient was an 8-year-old boy who had high-grade osteoblastic osteosarcoma and died from disease 23 months after below-knee amputation. The other osteosarcoma cases in this study were localized to the calcaneus (76%, 11/14), metatarsals (7%, 1/14), and phalanges (7%, 1/12).

The patterns observed from these reports reveal that osteosarcoma very seldom occurs below the ankle, but in these exceptional cases the bone most often affected is the calcaneus, followed by the talus, metatarsals, and phalanges. Moreover, compared with conventional osteosarcoma, osteosarcoma of the foot and ankle seems more commonly a primary tumor affecting more of an older population. In most documented cases of talar osteosarcoma, mean patient age is 35 years, much younger than our patient's age (81 years).

The clinical presentation of osteosarcoma of the foot and ankle may be very subtle, commonly delaying an accurate diagnosis. For 6 months before presentation, our patient had painful ankle swelling followed by development of a rigid prominence at the anterior ankle. Other cases have presented similarly: Pain and swelling were present for several months, but most patients deferred evaluation until a palpable mass was detected, shoe wear was limited, or weight-bearing activity was limited. Late presentation may also affect survivability, with mortality rates of osteosarcoma of the foot and ankle higher than originally predicted.[6] In other cases, death from high-grade disease was caused by pulmonary metastasis 18 months to 2 years after surgery.[6] The older age of diagnosis and more aggressive high-grade histotype suggest that below-ankle osteosarcoma may represent a variant with pathophysiology different from that of conventional osteosarcoma, which customarily originates from the metaphysis of long bones in adolescents and young adults.

Radiologic Signs

Radiologic studies may be limited in providing additional information in many cases of osteosarcoma originating below the ankle. The hallmark radiographic features of osteosarcoma, such as the sunburst and the Codman triangle, may not be present in tumors below the ankle. One study indicated that osteosarcoma localized to the calcaneus, tarsus, and talus demonstrated more commonly densely sclerotic lesions with ill-defined borders and extracompartmental bone production.[7] However, osteosarcoma in metatarsals and phalanges may have densely sclerotic features or may demonstrate expansive osteolysis with thinning cortex. Each of the different histotypes of talar osteosarcoma seemingly displays unique radiologic features, though unreliably. Osteoblastic osteosarcoma mainly exhibited a sclerotic pattern but in another case appeared purely lytic.[7] The single case of telangiectatic osteosarcoma appeared as an expansile lytic lesion with cortical thinning and erosion. The 2 case reports of parosteal osteosarcoma demonstrated a well-defined and densely ossified mass protruding off the anterior talar surface with an intervening radiolucent line between cortex and tumor.[13,14] In our patient's case, x-rays revealed extraosseous calcification with dense sclerosis of the talus, which at initial outside evaluation was considered posttraumatic and related to avascular necrosis.

The various radiologic features of osteosarcoma of the foot and ankle may mimic different benign and malignant processes. Other imaging studies, including MRI, whole-body bone scans, PET, and CT of extremity, chest, abdomen, and pelvis, offer additional details at the site of origin, as well as evidence of distant metastases. These studies may further delineate whether a lesion is benign or malignant, localized or metastatic, and in some cases may offer enough information for accurate diagnosis. A broad differential diagnosis is considered, and, depending on the specific histotype of osteosarcoma, may include osteoblastoma, Paget disease, reactive fracture callus, heterotopic ossification, chronic osteomyelitis, solitary exostosis, osteochondroma, metastatic carcinoma, chondroblastoma, giant cell tumor, Ewing sarcoma, intraosseous ganglion, and aneurysmal bone cyst.[15]

Diagnosis and Treatment

The best method of disease determination is adequate tissue biopsy and thorough histologic examination. Although a universal grading system has yet to be developed, most histologic grading of osteosarcomas is based on degree of cellular differentiation. Tumors are separated into 4 categories, I to IV, with grade IV being the least differentiated.[8] In our patient's case, the initial limited biopsy results were reviewed by multiple institutions and deemed to represent a well-differentiated, low-grade (II/IV) osteosarcoma. After amputation, however, the gross specimen allowed more sampling, which revealed many areas of osteoid interspersed with malignant osteoblasts displaying high-grade (III/IV) nuclear features.

In general, the 3 major histotypes of classical osteosarcoma are osteoblastic, chondroblastic, and fibroblastic. Choong and colleagues[6] demonstrated that, below the ankle, the most common histotype is osteoblastic (24/52), followed by fibroblastic (15/52), then chondroblastic (13/52). Specific histotypes will likely correspond to certain radiographic appearances, with osteoblastic osteosarcoma appearing more densely sclerotic, while fibroblastic and chondroblastic may appear more osteolytic. One of the 2 cases of parosteal osteosarcoma of the talus revealed sclerotic sections with osteoblastoma-like and aneurysmal areas, and the other displayed well-formed osseous trabeculae in a fibrous stroma contained in a cartilaginous cap.[13,14] Although relatively few cases of talar osteosarcoma have been identified, certain radiographic patterns seem to correspond to certain histotypes of osteosarcoma, but consistent relationships can be more reliably determined only with further studies.

The low incidence of osteosarcoma of the talus translates to few detailed reports on the nature of malignant tumors arising from this unique location. In 1980, Amini and Colacecchi[16] described the case of a 21-year-old man who was identified as having high-grade talar osteosarcoma after initial misdiagnoses and was treated with above-knee amputation but died 19 months after surgery from pulmonary metastases. In 1993, Matsumoto and colleagues[15] reported the case of a 20-year-old man who was diagnosed with high-grade osteoblastic osteosarcoma of the talus and was treated with below-knee amputation and chemotherapy but died from pulmonary metastases 17 months after surgery. Three other reports in the radiology literature discussed the difficulty in accurately identifying osteosarcoma of the foot and ankle stemming from 2 patients diagnosed with parosteal osteosarcoma. The first case involved a 19-year-old man treated with below-knee amputation and chemotherapy after postresection recurrence without any final report on outcome.[13] The second case involved a 2-year-old girl without any report on treatment or outcome.[14]

"According to Simon and Enneking,[17] osteosarcoma of the foot and ankle is not amenable to limb salvage surgery, and below-knee amputation is the recommended treatment."

According to Simon and Enneking,[17] osteosarcoma of the foot and ankle is not amenable to limb salvage surgery, and below-knee amputation is the recommended treatment. Below-knee amputation poses no risk for local recurrence and often allows for quick recovery and facilitates pursuit of other adjuvant therapy. One study found that the 5-year survival rate for malignant bone lesions in the foot and ankle treated with amputation and chemotherapy was 60% to 70%.[4]

Chemotherapy may also have a role in managing talar osteosarcoma, but the overall benefit is yet to be determined. At the time this report was written, our patient was recovering nicely from a below-knee amputation and elected to forego additional chemotherapy. The general philosophy regarding foot and ankle tumors purports that distal tumors display lower-grade histopathology and thus provide a more favorable outcome.[4] The high-grade talar osteosarcoma identified in our patient seemed contrary to this earlier study. However, in another study, the Mayo Clinic reported on 52 cases of osteosarcoma of the foot and ankle in which 85% of the tumors were high-grade lesions.[6] Thus, the original hypothesis, that malignant tumors localized below the ankle were considered more often low-grade lesions, may be incorrect. High-grade below-ankle osteosarcomas also demonstrate higher mortality than first considered. One report found that the 10-year survival rate for high-grade below-ankle osteosarcoma was 42%, while that for low-grade below-ankle lesions was 100%. The high mortality rate associated with high-grade osteosarcoma of the foot and ankle suggests that the prognosis may be less favorable than originally thought. Overall, the prognosis for

talar osteosarcoma seems dependent on grade, stage, and extent of the tumor's invasion of adjacent tissue.

Conclusions

Osteosarcoma of the talus is very rare. The ability to obtain an early and accurate diagnosis is complicated by subtle clinical and radiologic features. Sound biopsy techniques are needed to procure sufficient representative tissue samples to provide thorough pathologic examination. Although low-grade malignant tumors may be more common in the foot and ankle, high-grade osteosarcomas appear to be as aggressive as proximal lesions. Once identified, osteosarcoma of the foot and ankle is best treated surgically with below-knee amputation. Additional chemotherapy may prove beneficial, but current data are limited. The patient in our report was an 81-year-old woman with a high-grade osteoblastic talar osteosarcoma treated with a below-knee amputation. Four months after surgery, she was learning to live with her prosthesis and was considered disease-free but had pulmonary lesions, which we will continue to follow closely.

Authors' Disclosure Statement

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.