CASE REPORT

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Extraskeletal osteosarcoma: a case report

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Extraskeletal osteosarcoma is a rare soft tissue sarcoma. Survival is related with the wide resection of the tumor. The role of adjuvant chemotherapy and radiation therapy remains controversial. In our study, we present a patient with extraskeletal osteosarcoma of the thigh which was initially misdiagnosed as lipoma.

Key words: Chemotherapy; extraskeletal; osteosarcoma; radiation therapy; soft tissue sarcoma; wide resection.

Extraskeletal osteosarcoma is a rare, high-grade soft tissue sarcoma, accounting for approximately 1% of all soft tissue sarcomas.[1-4] It is more prevalent in male adults in the sixth decade of life.[4,5] For a lesion to be defined as extraskeletal osteosarcoma, it must arise in the soft tissue and not be attached to the bone or periosteum, have a uniform sarcomatous pattern and produce osteoid and/or cartilage matrix.[2]

Several cases of secondary osteosarcomas arising in areas of myositis ossificans or heterotopic ossification have been reported.[2,3,6] Nonetheless, few of these cases have been histologically proven extraskeletal osteosarcomas. In most reports the excised osteosarcomas did not contain residual tissue of the previous benign condition and evidence of the benign precursor depended mainly on the clinical course and not on the pathologic and imaging features of the lesion.[6]

In this article, we present a patient with extraskeletal osteosarcoma of the thigh and discuss the clinicopathological features, diagnosis and treatment of this lesion.

Case report

A 73-year-old man presented with a 2-year history of an enlarging right thigh mass. There was no history of trauma. The lesion was initially misdiagnosed as lipoma and observation was recommended. Physical examination showed a large palpable mass at the posteromedial aspect of the right thigh. Routine laboratory analysis was within normal limits.

Plain radiographs showed a soft tissue mass with peripheral calcification at its lower border. Computed tomography showed a large soft tissue mass with an ossified rim, located closely but not attached to bone, with an interspersed soft tissue mass (Fig. 1). Magnetic resonance imaging showed a heterogeneous and relatively hypointense mass in T1-weighted images that was enhanced with gadolinium administration and a hyperintense mass in T2-weighted images (Fig. 2). Radiography and computed tomography of the chest were normal.

Biopsy of the soft tissue mass was performed. Histology showed calcified bone trabeculae and osteoid elaborated by pleomorphic anaplastic spindle cells with

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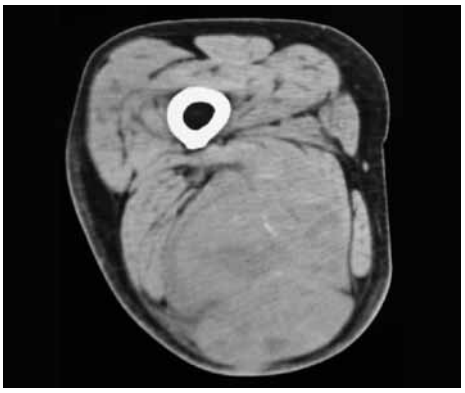

Fig. 1. Axial CT scan showing a large soft tissue mass with scarce calcifications in the right posteromedial thigh.

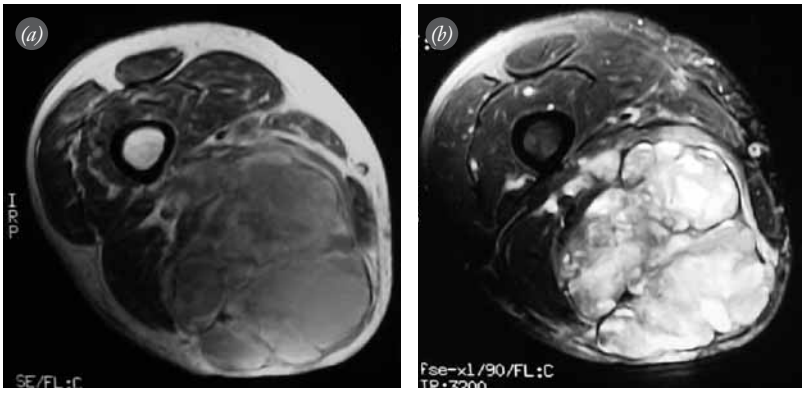

Fig. 2. Axial **(a)** T1-weighted and **(b)** T2-weighted fat-suppressed MRI showing a large soft tissue mass in the posteromedial thigh.

extracellular osteoid matrix production (Fig. 3). These findings were consistent with extraskeletal osteosarcoma.

We performed angiography for possible embolization and preoperative radiation therapy at a total radiation dose of 50 Gy, aiming for tumor reduction and demarcation of the margins. Angiography did not show increased vascularity of the lesion and embolization was not performed (Fig. 4). One month after radiation therapy, tumor resection was performed, with dissection and preservation of the sciatic nerve (Fig. 5a). At surgery, the tumor extended under the skin in close proximity with the sciatic nerve. Surgical resection was marginal at the proximity with the sciatic nerve and wide in the remaining areas; brachytherapy was decided. After tumor resection, the tumor bed was covered with a set of plastic tubes placed parallel at 1.5-2.0 cm intervals (Fig. 5b). The tumor specimen was grossly encapsulated with areas of hemorrhage and necrosis. The central part was cystic, whereas the periphery was firm. Specks of calcification were observed (Fig. 5c). The soft tissue defect was reconstructed with a free vascularized latissimus dorsi musculocutaneous flap (Fig. 6a).

A computed tomography was performed 48 hours after surgery; data was transferred to the Radiation Treatment Planning System for optimization of dosimetry, and computerized after-loading iridium-192 brachytherapy was administered at a dose of 20 Gy.

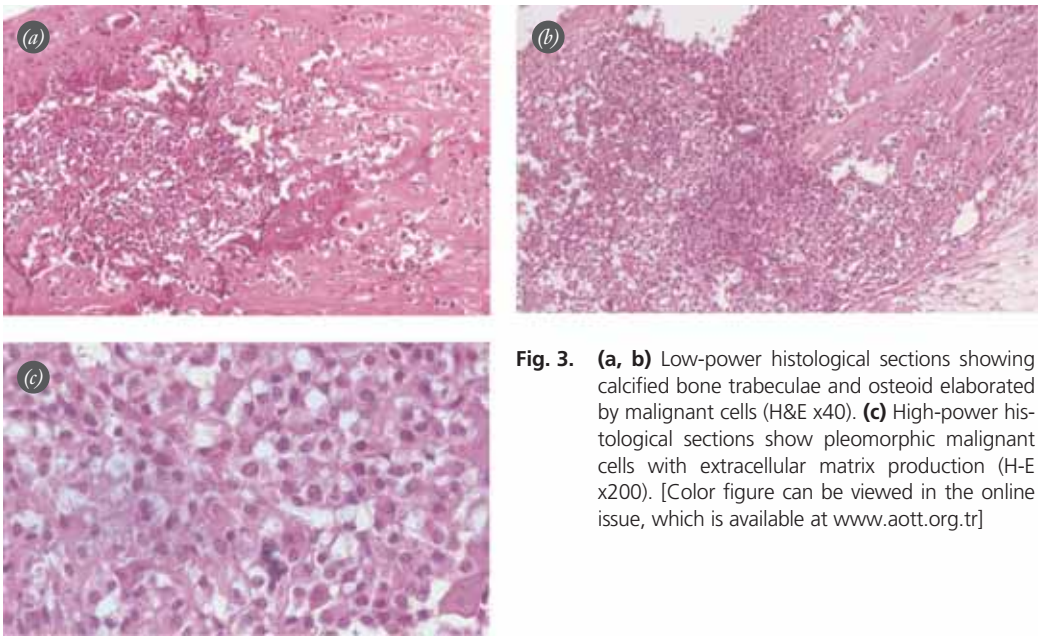

Fig. 3. **(a, b)** Low-power histological sections showing calcified bone trabeculae and osteoid elaborated by malignant cells (H&E x40). **(c)** High-power histological sections show pleomorphic malignant cells with extracellular matrix production (H-E x200). [Color figure can be viewed in the online issue, which is available at www.aott.org.tr]

Following brachytherapy, the tubes were removed and 4 cycles of adjuvant chemotherapy with doxorubicin, ifosfamide and cisplatin were administered. Wound healing was uncomplicated (Fig. 6b). However, 6 months after surgical treatment and chemotherapy the patient experienced local recurrence and lung metastases and died 6 months later.

Discussion

Although extraskeletal osteosarcoma can occur in any part of the body, approximately 75% of tumors are located in the lower extremities, particularly the thigh and the buttocks, followed by the upper extremities and the retroperitoneum.[3,7-12] Post-irradiation extraskeletal osteosarcomas have also been reported.[6] Distant metastases are common and usually located in the lungs (>80%),[2] followed by the regional lymph nodes, bone, brain, liver and skin.[3,6,7] Plain radiographs usually show a mass with peripheral, chunky or linear and mature calcification similar to mature bone or heterotopic ossification. Computed tomography shows an ossified rim close but not attached to the bone with an interspersed soft tissue mass. Magnetic resonance imaging shows a heterogeneous and relatively hypointense mass in T1-weighted and hyperintense in T2-weighted images.[7] Angiography may demonstrate hypervascularity of the tumor.[7-8,13]

Macroscopically, the tumor is deep-seated and firmly attached to the fascia without attachment to the skeleton; rarely, it may lie in contact with the periosteum.[13] A tough, connective tissue capsule usually surrounds these tumors and adheres to the surrounding structures, making dissection difficult. The central part is usually cystic; areas of hemorrhage and necrosis are common.[13] The tumor has a remarkable ability to infiltrate the surrounding tissues; occasionally it can be confined to the subcutis or dermis, or ulcerate the overlying skin.[13] Invasion of blood vessels is not common.[1,13]

Histologically, extraskeletal osteosarcoma is characterized by a malignant, anaplastic spindle cell proliferation with an osteoid matrix or immature bone formation. A mitotic count of >10 mitoses per 10 high-power fields and extensive areas of necrosis are usually observed. The tumor cells are arranged in nodules containing spindle and giant cells, frequently arranged in cords similar to fibrosarcoma.[1,13] According to the predominance of the type of matrix, osteoblastic, chondroblastic, fibroblastic, telangiectatic, and rarely, small cell histological patterns can be observed.[1,13,14] The histological differential diagnosis should include myositis ossificans, synovial and epithelioid sarcoma, liposarcoma with metaplastic bone, chondrosarcoma (conventional and extraskeletal), malignant fibrous histiocytoma, malignant mesenchymoma, osteosarcoma (conventional, high-grade surface, parosteal and periosteal), rhabdomyosarcoma, hamartoma and malignant schwannoma.[3,13,15]

Immunohistochemically, extraskeletal osteosarcoma cells are positively stained for alkaline phosphatase. The tumor cells can be positive for vimentin, and occasionally for desmin, actin, S-100 protein, epithelial membrane

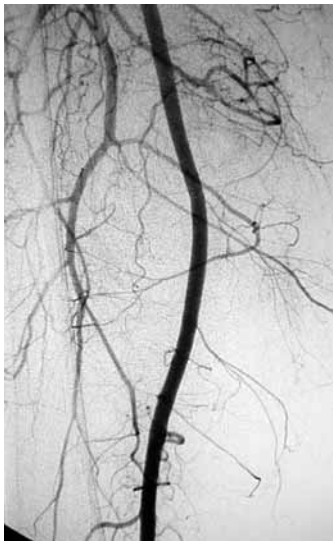

Fig. 4. Angiography of the right thigh showing poor vascularity of the tumor.

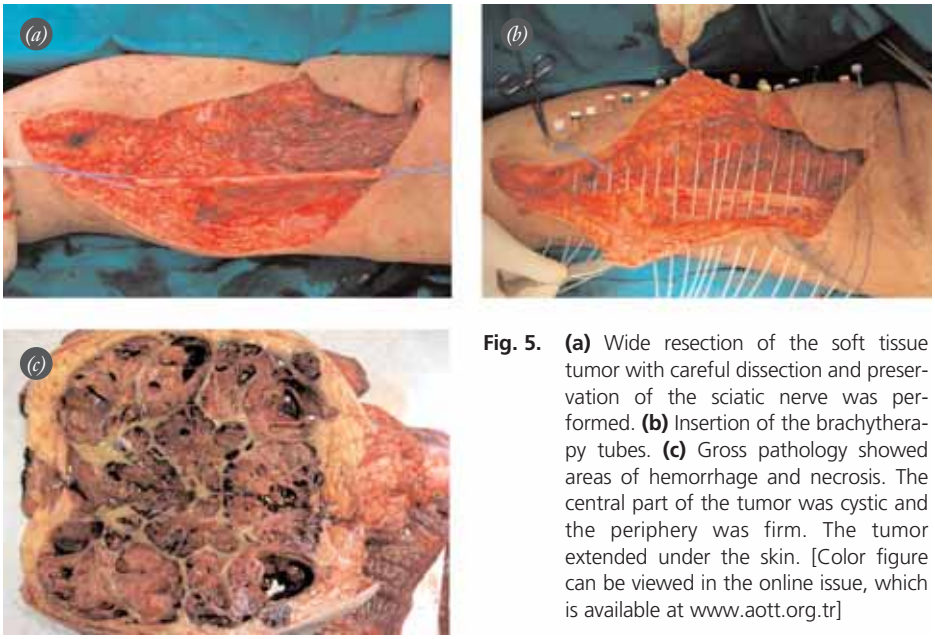

Fig. 5. **(a)** Wide resection of the soft tissue tumor with careful dissection and preservation of the sciatic nerve was performed. **(b)** Insertion of the brachytherapy tubes. **(c)** Gross pathology showed areas of hemorrhage and necrosis. The central part of the tumor was cystic and the periphery was firm. The tumor extended under the skin. [Color figure can be viewed in the online issue, which is available at www.aott.org.tr]

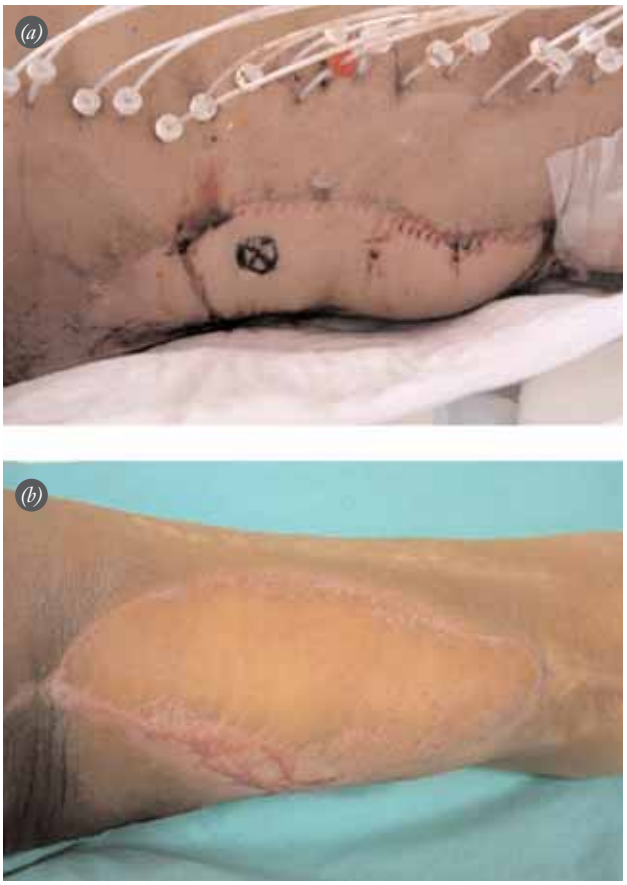

Fig. 6. **(a)** Wound closure using the ipsilateral free latissimus dorsi musculocutaneous flap. **(b)** Uncomplicated wound closure 2 months after tumor resection. [Color figure can be viewed in the online issue, which is available at www.aott.org.tr]

antigen, cytokeratin and p53 protein; these features can also be observed in other pleomorphic sarcomas.[15,16] Staining for the Ki-67 analogous MIB-1 shows high activity with values around 25%.16 Scrape and fine-needle aspiration biopsy smears of extraskeletal osteosarcomas reveal moderate cellularity, cell clusters and individual cells closely associated with dense, homogeneous, non-cellular matrix. Although the lesions can easily be distinguished as high-grade sarcomas using either technique, the scrape smears usually contain large fragments of osteoid matrix.[12,15,16]

Wide resection or amputation is the treatment of choice for extraskeletal osteosarcoma.[1,3,4,17] Aggressive thoracotomy and resection of the pulmonary metastases have been reported.[3,17] Adjuvant chemotherapy and/or preoperative radiation therapy may be useful,[17] although extraskeletal osteosarcoma seems relatively chemoresistant compared to osseous osteosarcomas.[3,6,8] In a study of 60 patients with extraskeletal osteosarcoma, 27 patients were treated with doxorubicin-based chemotherapy.[17] The overall response rate was 19%, with 2 complete and 3 partial responses. For patients with localized disease, the 5-year local recurrence-free survival rate was 82%, the distant recurrence-free was 64%, the event-free was 47%, and the overall survival rate was 46%. For patients with metastatic disease, the 5-year disease-specific survival rate was 10% and the mean survival period was 8 months.[17] Radiation may be delivered by external beam, brachytherapy or intraoperatively. Our patient received combined preoperative radiation therapy and brachytherapy at a total dose of 70 Gy. Brachytherapy refers to encapsulated radionuclides delivered within or close to the tumor bed by a high-dose rate after-loading device that uses an Ir-192 source. Following dose optimization by a treatment planning software, radiation is delivered in multiple daily fractions through a short treatment time. The advantages of brachytherapy include a higher dose directly to the tumor bed, shorter overall treatment time with less patient discomfort and inconvenience, and relative sparing of the surrounding normal tissues. Brachytherapy has been associated with improved local control versus surgery alone for high-grade soft tissue sarcomas.[18-20]

Although partial spontaneous regression of extraskeletal osteosarcoma has been reported,[21] prognosis is usually poor. Approximately 50% of the tumors recur locally and lung metastases develop within 3 years after diagnosis; the 5-year survival rate is 37% or less.[2,9-12] Tumor size is an important prognostic factor. Patients with tumors >5 cm usually have an unfavorable clinical course. In a group of 16 patients with tumors >5 cm, 14 died of the disease and 2 were still alive with disease.[5] Other authors did not correlate the small size of the lesions with favorable prognosis or long-term survival.[1,2] The histological subtypes of extraskeletal osteosarcoma have also been related to prognosis. The fibroblastic and chondroblastic subtype may have a slightly better prognosis compared to the other subtypes,[2] although not all studies correlated the histological pattern with prognosis.[1,5] Other features such as deep, intramuscular or superficial tumor growth, and p53 positivity do not significantly affect prognosis. A significant difference in survival of patients with MIB-1 values >24% has been shown.[1]

In conclusion, limb salvage surgery with wide resection or amputation is recommended in the treatment of the high-grade soft tissue extraskeletal osteosarcoma, as the benefit of adjuvant chemotherapy and perioperative radiation therapy is controversial.

Conflicts of Interest: No conflicts declared.

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