

Solid Tumour Section

Short Communication

Soft Tissue Tumors: Extraskkeletal osteosarcoma

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Abstract

Short communication on extraskkeletal osteosarcoma with data on clinics.

Identity

Other names

Soft tissue osteosarcoma

Note

Extraskkeletal osteosarcoma is a high-grade malignant mesenchymal soft tissue neoplasm composed of neoplastic cells (osteoblastic, chondroblastic and fibroblastic) that produce osteoid, neoplastic bone or chondroid matrix and has a clinically aggressive course. For a lesion to be defined as extraskkeletal osteosarcoma, it must arise in the soft tissue and not attached to bone or periosteum, have a uniform sarcomatous pattern, and produce osteoid and/or cartilage matrix. In contrast to the more common osteogenic sarcoma (osteosarcoma), extraskkeletal osteosarcoma is a rare tumor occurring mainly in adults. Often it arises at the site of prior radiation therapy. Response to treatments (mainly chemotherapy) is worse and prognosis is much poorer compared to that for primary osteosarcoma of bone.

Clinics and pathology

Epidemiology

Extraskkeletal osteosarcoma accounts for 1% to 2% of all soft tissue sarcomas and approximately 2% to 4% of all osteosarcomas. It typically affects patients

between 50 and 70 years of age. The reported male to female ratio is 1.9:1.

Clinics

Most extraskkeletal osteosarcomas are deep seated; <10% are superficial, originating in the dermis or subcutis. The most common location is the lower extremity (75%; thigh and buttock), followed by the upper extremity (15%-23%, shoulder girdle), and the retroperitoneum (17%). A progressively enlarging soft tissue mass, rarely causing pain or tenderness is the most common clinical presentation.

Imaging

Plain radiographs, CT and MRI usually reveal a large deep-seated soft tissue mass with variable mineralization. By definition, extraskkeletal osteosarcomas arise in the soft tissue and are not attached to bone or periosteum; however, they may secondarily involve the periosteum, cortex or medullary canal.

- Radiography: Shows a mass, possibly with peripheral, chunky or linear and mature calcification similar to mature bone or heterotopic ossification.

- Computed tomography: Shows a mass with ossified rim. The mass is close to the bone but not attached to it; a soft tissue mass is interposed between the bone and the ossified mass.

- MR imaging: The unmineralized portion of the tumor shows heterogeneous and relatively hypointense signal intensity on T1-weighted images and hyperintense signal intensity on T2.

- Scintigraphy: Shows intense accumulation of radioactivity in the tumor.

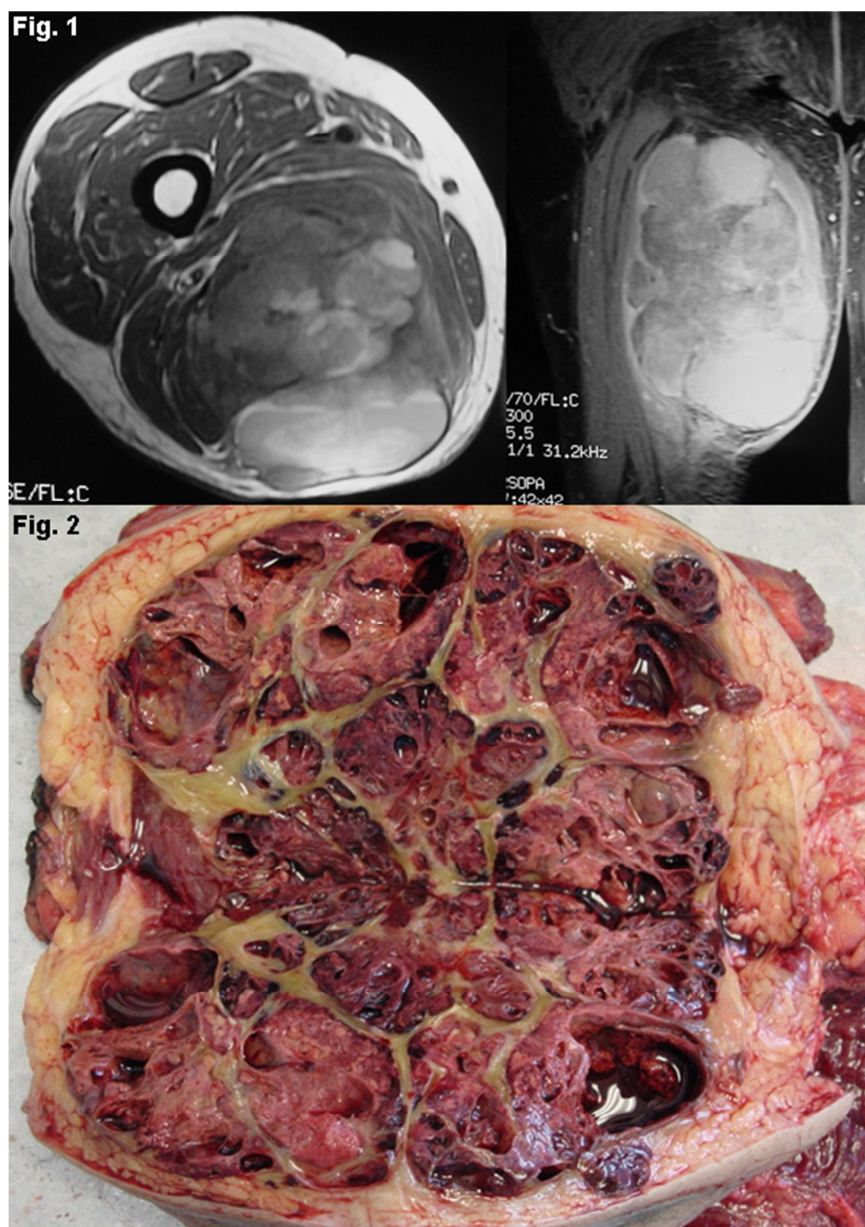


Figure 1. Axial T1-weighted (left) and coronal T2-weighted fat suppression (right) MR imaging show a large soft tissue mass in the postero-medial thigh. The tumor is not attached to bone. **Figure 2.** Tumor specimen of an extraskeletal osteosarcoma.

- Angiography: May show hypervascularity of the tumor.

Pathology

Pathogenesis unknown. The majority develops de novo; in approximately 10% extraskeletal osteosarcomas may be radiation induced.

Gross pathology: Extraskeletal osteosarcomas may grow up to 50 cm (mean, 8-10 cm). Macroscopically, the tumors are hemorrhagic and focally necrotic, and firmly attached to the fascia without attachment to the skeleton; rarely, it may lie in contact with the periosteum; >30% appear grossly encapsulated, and >10% may exhibit extensive haemorrhagic cystic changes. A tough connective tissue capsule usually surrounds the

tumors and adheres to the surrounding structures, making dissection difficult. 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. Invasion of blood vessels is not common.

Micro pathology: Extraskeletal osteosarcoma is characterized by anaplastic spindle cell proliferation with the presence of osteoid matrix or immature bone formed by the neoplastic cells. The tumor cells are spindle or polyhedral with cytological atypia, malignant chondroid areas, extensive areas of necrosis, mitotic activity (>10 mitoses per 10 high-power fields), and atypical mitotic figures.

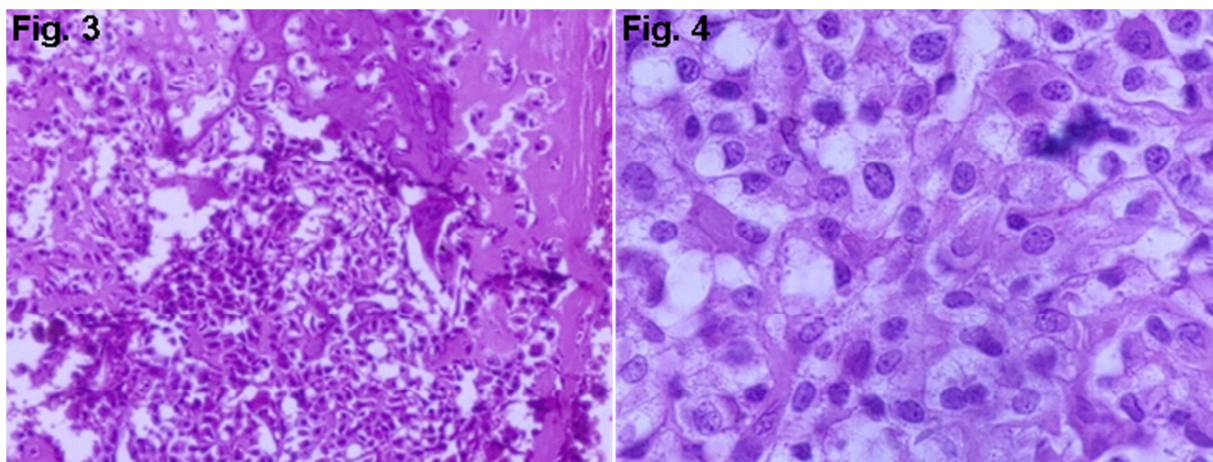


Figure 3. Low power histological sections show calcified bone trabeculae and osteoid elaborated by malignant cells (Stain, hematoxylin and eosin; original magnification, 40x). **Figure 4.** High power histological sections shows pleomorphic malignant cells with extracellular matrix production (Stain, hematoxylin and eosin; original magnification, 200x).

All the major subtypes of osteosarcoma of bone have been reported in extraskelatal osteosarcoma. Common to all variants is the presence of neoplastic bone deposited in a lacy, trabecular or sheet-like pattern. In contrast to myositis ossificans the bone is usually most prominent in the centre of the tumor.

- Osteoblastic extraskelatal osteosarcoma: the most common variant; the tumor cells resemble malignant osteoblasts. Bone matrix is abundant.
- Fibroblastic extraskelatal osteosarcoma: the second in frequency; the tumor cell are spindle cells arranged in a herringbone or storiform pattern.
- Chondroid extraskelatal osteosarcoma: malignant cartilage predominates in the tumor matrix.
- Telangiectatic extraskelatal osteosarcoma: it contains numerous large blood filled spaces lined by malignant cells.
- Small cell extraskelatal osteosarcoma: the tumor cells are arranged in sheets of small round cells that mimic Ewing's sarcoma or lymphoma.
- Well differentiated extraskelatal osteosarcoma: rare variant; it contains abundant bone deposited in well formed trabeculae, surrounded by a minimally atypical spindle cell component similar to parosteal osteosarcoma.

Immunohistochemistry: Several studies indicate that the immunophenotype of extraskelatal osteosarcoma is similar to osteosarcoma of bone; CD99 is expressed in all types of osteosarcoma; stain for ALP is positive with a very strong reaction; osteocalcin is the most specific antigen for extraskelatal osteosarcomas expressed in the malignant cells and matrix in 82% and 75% of cases, respectively. Extraskelatal osteosarcomas are uniformly positive for vimentin, 68% express smooth muscle actin, 25% desmin, 20% S100 protein, 52% EMA, 8% keratin, and 0% PLAP. The stain for the Ki-67 analogous MIB-1 shows high proliferative activity with values around 25%.

Differential diagnosis: Myositis ossificans; Synovial and epithelioid sarcoma; Extraskelatal chondrosarcoma; Malignant fibrous histiocytoma; Rhabdomyosarcoma; Hamartoma; Malignant schwannoma; Malignant mesenchymoma; Liposarcoma with metaplastic bone.

Cytogenetics

Systematic genetic differences between extraskelatal and bone osteosarcomas have not been documented. Three cases with clonal chromosomal aberrations have been reported; two tumors showed highly complex aberration patterns, whereas the third showed a moderately hyperdiploid karyotype with relatively few chromosomal abnormalities.

Treatment

Wide margin surgical resection is the treatment of choice for extraskelatal osteosarcoma. Resection can be with amputation of limb salvage surgery if microscopically negative margins can be achieved. Adjuvant chemotherapy and/or preoperative radiation therapy may be useful, although extraskelatal osteosarcoma seems relatively chemoresistant compared to osseous osteosarcomas. Radiation may be delivered by external beam, intraoperative, and brachytherapy. Given the high grade malignant tumor and poor prognosis, aggressive treatment with preoperative radiation therapy and surgical resection for local tumor control, and (neo-)adjuvant multi-agent chemotherapy to improve survival are current treatments of choice for the patients with extraskelatal osteosarcomas. Aggressive thoracotomy and resection of the pulmonary metastases may be necessary in patients with lung metastases.

Note: The role of (neo-)adjuvant chemotherapy or radiation therapy is controversial. Disease-specific clinical trials are required to improve the outcome of these patients.

Prognosis

The prognosis of the patients with extraskelatal osteosarcoma is poor; the 5-year survival ranges from 10% to 46%. More than 50% of the patients experience multiple local recurrences and distal metastases. Distal metastases are usually to the lungs (>80%), followed by the regional lymph nodes, bone, brain, liver and skin.

Note: Reported factors associated with a better outcome include size <5 cm (the most important), fibroblastic or chondroblastic histological subtype, and diminished proliferative activity as measured by Ki-67 index. However, the validity of these prognostic factors has not been confirmed in large studies. The well differentiated variant may behave in a more indolent manner; however, too few cases have been reported to draw definitive conclusions regarding their biologic potential.

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