Extraskeletal Osteosarcoma: A case report and review of the literature

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Radiology Case. 2013 Jul; 7(7):15-23 :: DOI: 10.3941/jrcr.v7i7.1245

ABSTRACT

We report an instructive case of extraskeletal osteosarcoma in a 63-year-old African American male who presented after an episode of recent trauma, with clinical and radiological features characteristic of this neoplasm. Osteosarcoma is the most common primary malignant tumor of bone in young adults, but the extraskeletal variety is very uncommon. The radiological and pathological features of this neoplasm will be discussed, along with a review of the literature.

CASE REPORT

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A 63 year old male with a past history of type II diabetes mellitus, hypertension, and hypercholesterolemia, presented to the clinic with a lemon-size painless mass in the posterior of his left thigh that he noticed following a fall down a flight of stairs. His physical exam demonstrated a non-tender firm mass at the junction of the upper and middle third of the thigh. The overlying skin was unremarkable. The surface of the mass was smooth with regular margins and the mass itself demonstrated diminished mobility and became less prominent with knee flexion. Motor strength was normal in both lower extremities and the neurological and vascular exams were both unremarkable.

Radiographs of the pelvis and femur taken at the time of initial presentation demonstrated no evidence of acute fracture or other acute osseous abnormality, but there was a very subtle soft tissue mass in the posterior aspect of his left thigh with a small focus of ossification (Figure1). Scattered radio-opaque foreign bodies were seen and not related to the current episode of trauma. An MRI without contrast was performed which showed a 5.9 x 5.4 x 5 cm mass with mixed solid, cystic, and hemorrhagic components, in the semitendinosus muscle belly at the level of middle third of the left femur suggestive of a soft tissue hematoma (Figure 2).

Two months later, a follow-up MRI with and without intravenous gadolinium revealed an enlarging enhancing mass within the semitendinosus muscle, now measuring 7 x 8 x 7.5 cm. Cystic and hemorrhage components were identified with several fluid-fluid levels, however the solid component of the mass demonstrated marked enhancement concerning for a soft tissue sarcoma. There was no involvement of the femur (Figure 3).

Approximately 6 months prior to initial presentation, the patient had a radionuclide bone scan performed for an unrelated reason which showed focal uptake of Tc99m MDP in the thigh mass indicating osteoblastic activity, and no metastasis (Figure 4).

A percutaneous core biopsy of the mass, obtained after the contrast enhanced MRI, demonstrated an osteosarcoma with chondroblastic differentiation. Subsequent wide local excision of the mass with primary closure was performed and the biopsy site was included in the elliptical incision. Final pathology confirmed an extraskeletal osteosarcoma with surgical margins that were free of tumor (Figure 5).

One week after surgery, a postoperative MRI showed edema and contrast enhancement, related to hyperemia and

granulation tissue as is typical in the postoperative bed. No new areas of mass or suspicious enhancement were seen, and there was no inguinal lymphadenopathy (Figure 6a-c). The patient had an uneventful postoperative recovery and following one course of chemotherapy at an outside facility, decided not to complete the remaining adjuvant chemo-radiation therapy due to the side-effects of nausea and emesis.

Two months later, a repeat MRI was performed which showed resolution of the postoperative change and no evidence of recurrent or residual tumor (Figure 6d). Eighteen months after diagnosis he presented to the Emergency Room with chest pain. The chest X-ray showed large bilateral pulmonary lesions, consistent with "cannonball" pulmonary metastasis, typical for osteosarcoma metastasis (Figure 7). The patient died within 2 years of diagnosis.

DISCUSSION

Soft-tissue osteosarcoma is very rare compared to its better known counterpart, the osseous osteosarcoma. In the bone, osteosarcomas are the most common primary malignant tumors of bone in adolescents and young adults, comprising about 15% of all primary bone tumors [1,2]. Osseous osteosarcomas may occur secondary to underlying osseous or genetic conditions such as Paget's disease, fibrous dysplasia, Li Fraumini, Rothmund-Thompson and retinoblastoma syndromes and following radiation therapy [1-3]. In contrast, extraskeletal lesions account for 1-2% of all soft tissue sarcomas and 4-5% of all osteosarcomas [1,4,5]. The peak prevalence occurs in patients in the 6th decade of life and males are slightly more affected.

An extraskeletal osteosarcoma is defined as a malignant mesenchymal neoplasm that produces osteoid, located in the soft tissues and is without (or with minimal) skeletal or periosteal attachment [6,7] . Symptoms usually include a slowly growing painless mass in an extremity and a history of prior trauma is present in 12.5% of patients [8]. The most common location for primary extraskeletal osteosarcoma is the soft tissues of the thigh (46%), followed by the upper extremity (20%) and the retroperitoneum (17%), but can occur in any part of the body [8]. Most tumors are firmly attached to the underlying fascia, but sometimes can be freely movable and confined to the dermis. Approximately 4-13% of reported cases occur secondary to radiation therapy, with the therapy taking place 2-40 years prior to presentation [5,8,9].

Radiographs may show a soft tissue mass with variable amounts of mineralization, and a lack of skeletal involvement. No calcification is seen in approximately 50% of lesions [4,5,10]. CT scans demonstrate a soft tissue mass often displacing fat planes, with variable degrees of calcification/ossification. Nonmineralized areas have muscle attenuation on CT.

MRI shows a soft tissue mass with the nonmineralized areas showing nonspecific intermediate to low signal intensity on T1 weighted images, and high signal intensity on T2 weighted images reflecting tumor edema. There is variable contrast enhancement after intravenous gadolinium [6]. Foci of hemorrhage and necrosis are also common. The tumors often appear well circumscribed and pseudoencapsulated, or infiltrative into the surrounding soft tissues.

Tc-99mMDP radionuclide scans may show increased uptake in both the primary lesion (as in our case), as well as metastatic foci, and is consistent with osteoblastic activity within the tumor. Diagnostic angiography usually displays a hypervascular mass, although angiography is rarely performed as a diagnostic tool (but may be useful for pre-operative planning).

Extraskeletal osteosarcomas are usually large at diagnosis, typically averaging 9 cm in diameter [5]. Microscopically, by definition, they display at least some osteoid and often there are variable amounts of bone or cartilage, often blending into a high-grade sarcomatous stroma.

The radiological differential includes post-traumatic myositis ossificans, and less likely a synovial sarcoma, but the presence of a mineralized soft tissue mass in a patient older than 40 should always be concerning for an extraskeletal osteosarcoma. The absence of any radiographically demonstrable osteoid material within the mass should, conversely, not exclude the diagnosis. As post-traumatic myositis ossificans can have an aggressive appearance on MRI simulating tumor with edema and contrast enhancement, and given that the history often includes trauma in these tumors, follow up imaging to assess for resolution should be performed in any patient with trauma and a soft tissue mass. Decreasing edema and mass effect on MRI will be seen in myositis ossificans, with the converse occurring in extraskeletal osteosarcomas. Histologically, myositis ossificans can be separated by its distinct zonation, organization and lack of sarcomatous stroma. Other sarcomas such as synovial sarcoma and pleomorphic sarcoma ("malignant fibrous histiocytoma") can be separated by the presence of convincing osteoid production.

The prognosis of soft-tissue (extraskeletal osteosarcoma) is poor when compared to conventional, de novo, intra-osseous osteosarcoma. More than 80-90% of patients develop local recurrences and metastasis to the lungs and bones [8,10]. The time period between surgical removal of the primary neoplasm and recurrence is between 2 months to 10 years [8].

Treatment consists of amputation or wide surgical resection with no difference in overall survival between patients treated with resection and those treated by amputation [11,12]. After surgery, patients with localized disease treated with an 'osteosarcoma-type' chemotherapy regimen consisting of doxorubicin, ifosfamide, cisplatin, and possibly methotrexate have show encouraging results with a 5 year survival rate of 66 - 77% compared to surgery alone at < 25-50% [12-14]. Tumor size is the best predictor of outcome [5,8]. If the tumor is less than 5 cm at presentation the patient has an increased chance of survival at 30 months [5]. Radiation therapy has been used when the resection has been

marginal or as a palliative treatment. Radiation therapy as the only local treatment is insufficient [12].

Extraskeletal osteosarcomas by definition are not (or minimally) associated with the underlying skeleton or periosteum. They must be distinguished from surface osseous osteosarcoma - including parosteal, periosteal and high-grade surface osteosarcoma [6,7]. Parosteal osteosarcomas account for 65% of all the surface subtypes and are usually well differentiated tumors that tend to wrap themselves around the bone and may simulate osteochondroma clinically [15,16]. These lesions are typically seen in the metaphysis of long bones (mostly distal femur) with a lobulated "cauliflower like" juxtacortical mass. Periosteal osteosarcomas make up 25% of the surface variety of osteosarcomas [15,16]. They commonly arise in the diaphysis or metadiaphysis of long bones with a perpendicular periosteal reaction extending into a soft tissue mass and are often chondroblastic. High-grade surface osteosarcomas make up about 10% of the surface lesions and histologically are similar to the usual high-grade osteoblastic osteosarcoma [16].

TEACHING POINT

Extraskeletal osteosarcomas may present as a soft tissue mass after trauma and may thus be confused with a muscle hematoma. Ossification/calcification may not be seen in the mass further complicating the diagnosis, and follow up imaging is usually required to assess the evolution of the lesion.

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FIGURES

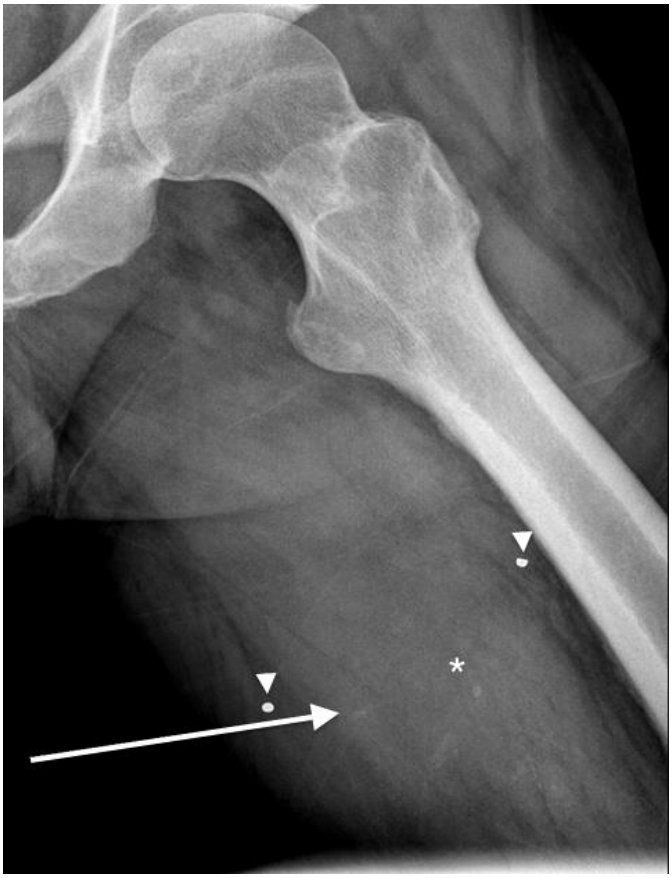
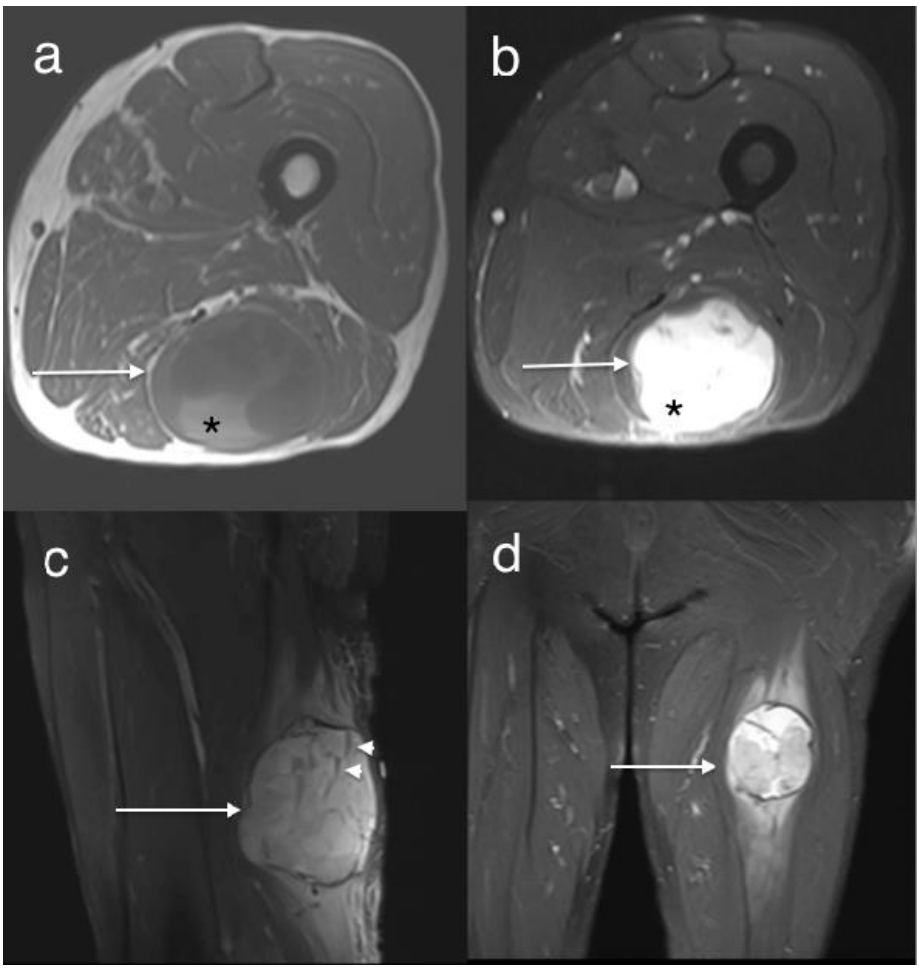


Figure 1 (left): 63 year old male with extraskeletal osteosarcoma. Frog leg lateral radiograph of the proximal left thigh, which demonstrates a very subtle soft tissue mass (asterisk) in the posterior aspect of the thigh. There is a tiny focal area of ossification (arrow), which corresponds with osteoid produced by the tumor. The metallic foreign bodies are from prior trauma (arrowheads).

Figure 2 (bottom): 63 year old male with extraskeletal osteosarcoma. Siemens Symphony 1.5 Tesla MRI: (a) Axial T1 (TR: 500 msec, TE 12 msec), (b) axial, (c) sagittal and (d) coronal fat saturated fast spin echo T2 weighted (TR: 3400 msec, TE 55 msec) MRI images without contrast demonstrate a 5.9 x 5.4 x 5 cm mass (arrow) with mixed solid and cystic components and hemorrhage (asterisk) in the semitendinosis muscle belly, at the level of the middle third of the left femur. Cystic and hemorrhagic components can be seen with fluid-fluid levels (arrowheads).



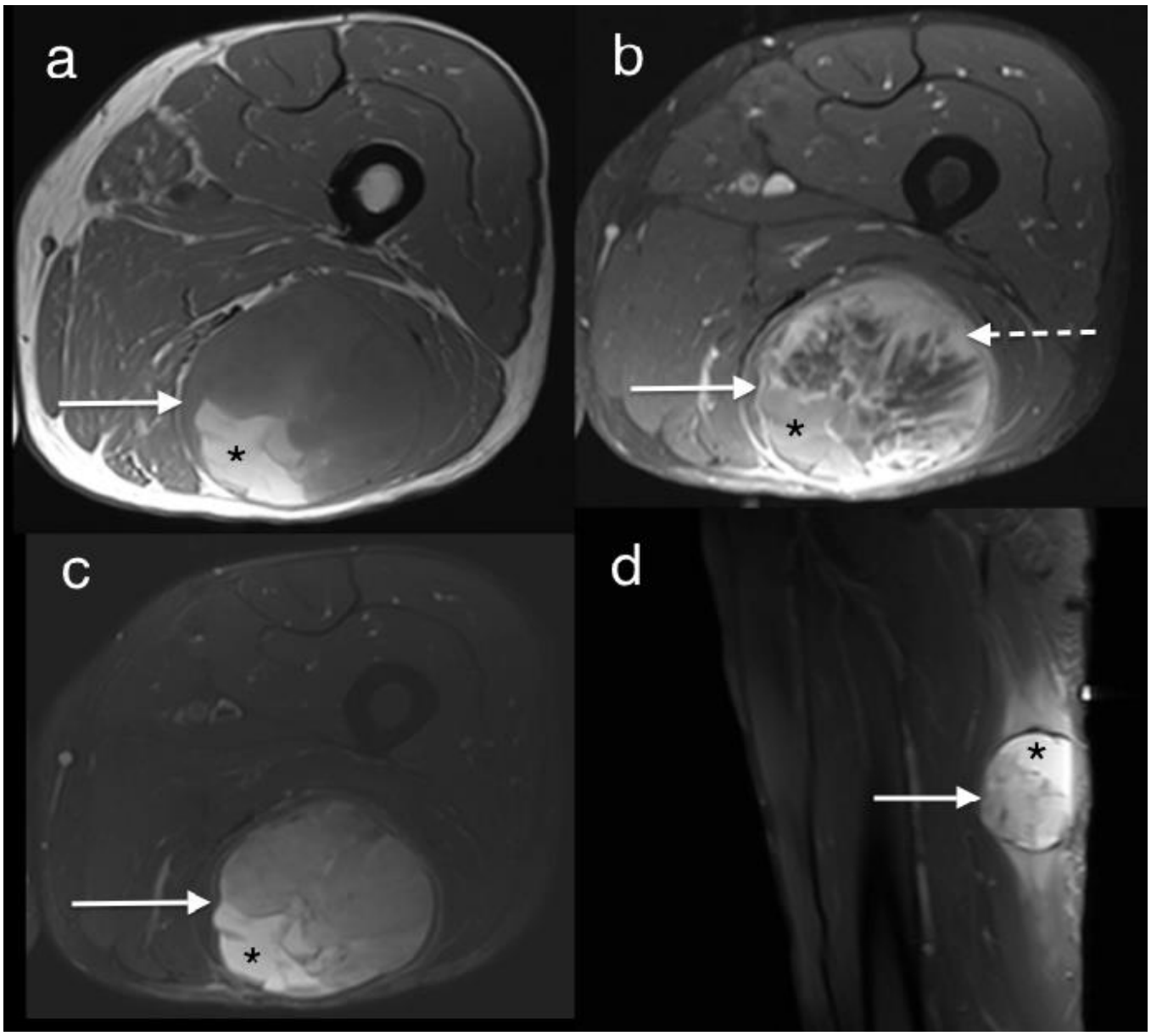


Figure 3: 63 year old male with extraskeletal osteosarcoma. Siemens Symphony 1.5 Tesla MRI: (a) Axial T1 (TR: 1140 msec, TE: 12 msec), (b) fat saturated T1 weighted image (TR: 530 msec, TE: 12 msec) after 19 cc of IV Omniscan gadolinium, (c) axial and (d) sagittal fat saturated FSE T2 weighted images (TR: 3500 msec, TE: 60 msec), demonstrate a 7 x 8 x 7.5 cm enlarged well circumscribed soft tissue mass (solid arrow) that does not involve the femur, but contains hemorrhage (asterisk) and enhancing solid component (dashed arrow).

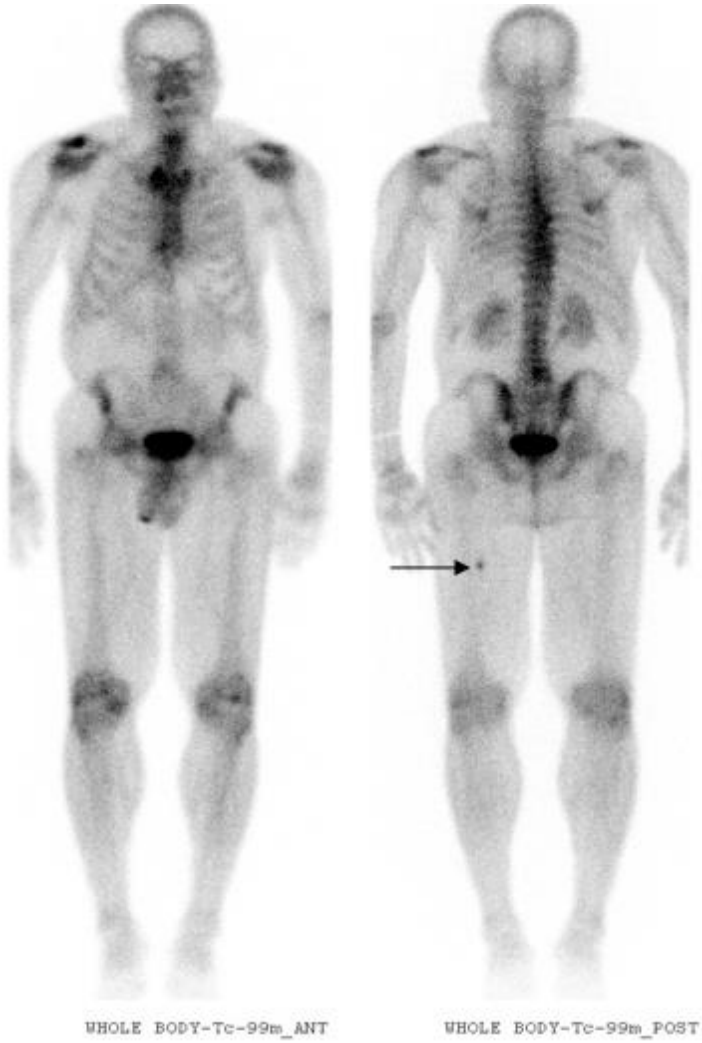


Figure 4 (left): 63 year old male with extraskeletal osteosarcoma. Technetium 99m MDP labeled radionuclide bone scan (20 mCi) using a General Electric SMV DST-XLi Dual Detector Gamma Camera with Large Field of View Low Energy High Resolution Collimator. There is a focal area of osteoblastic activity (arrow), which corresponds with the plain film findings, and reflects new bone formation in the soft tissues. There is no evidence of metastatic disease in the lungs at this time.

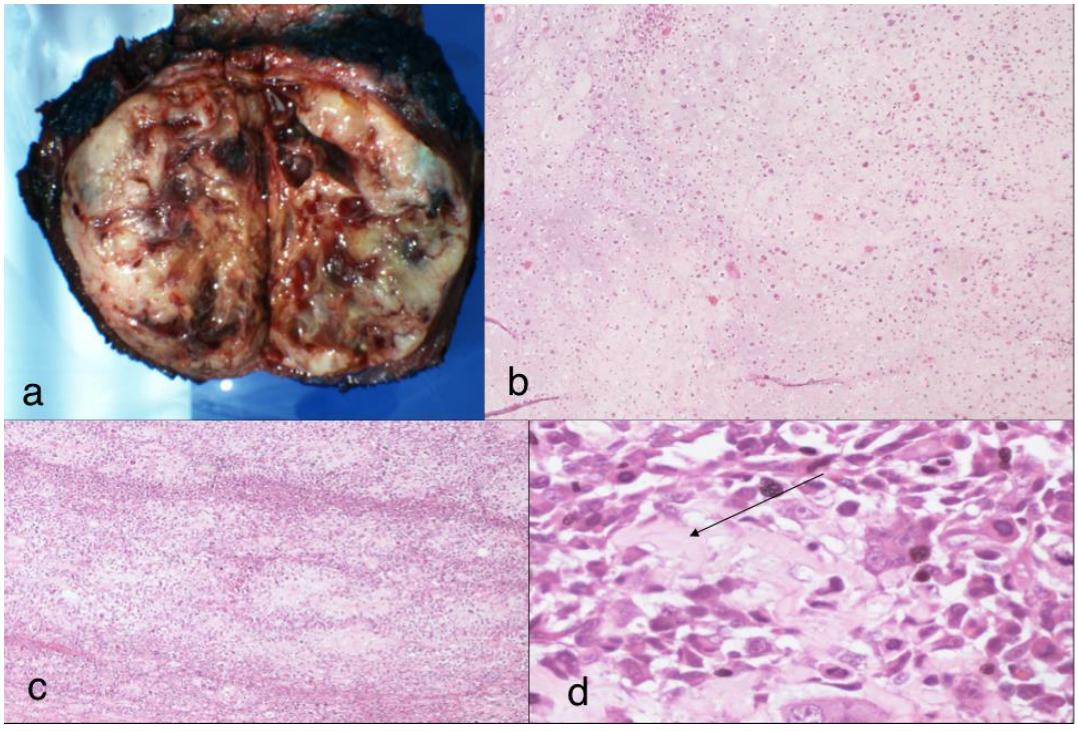


Figure 5: 63 year old male with extraskeletal osteosarcoma. (a) Gross surgical specimen cut section, (b) 40X H and E low power microphotograph showing chondroblastic differentiation, (c) 40X H and E low power microphotograph showing osteoid and spindle cells, (d) 400X H and E high power microphotograph of areas seen in (c) showing osteoid (arrow) and highly atypical sarcomatous cells.

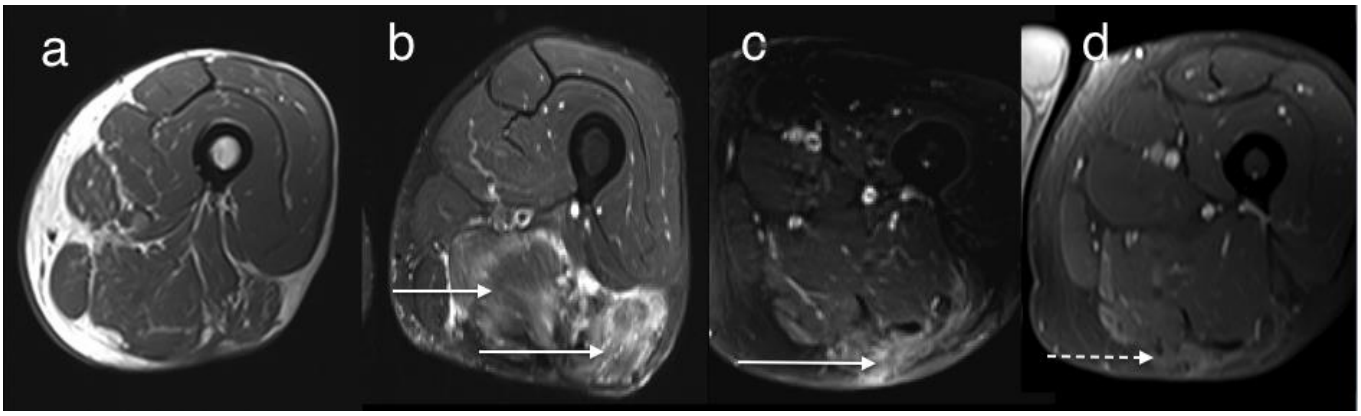


Figure 6: 63 year old male with extraskeletal osteosarcoma. Siemens Symphony 1.5 Tesla MRI: 1 week postoperative: (a) Axial T1 (TR: 1140 msec, TE: 12 msec), (b) axial fat saturated FSE T2 weighted image (TR: 5280 msec, TE: 76 msec), (c) axial fat saturated T1 weighted images (TR: 391 msec, TE: 10 msec) after injection of 20 cc IV Omniscan gadolinium show interval resection of the mass and expected postoperative edema and contrast enhancement in the operative bed (solid arrows). 2 months postoperative: (d) Axial fat saturated T1 weighted image (TR: 720 msec, TE: 12 msec) with 20 cc of IV Omniscan gadolinium shows resolution of the postoperative changes, and no evidence of residual or recurrent tumor (dashed arrow).

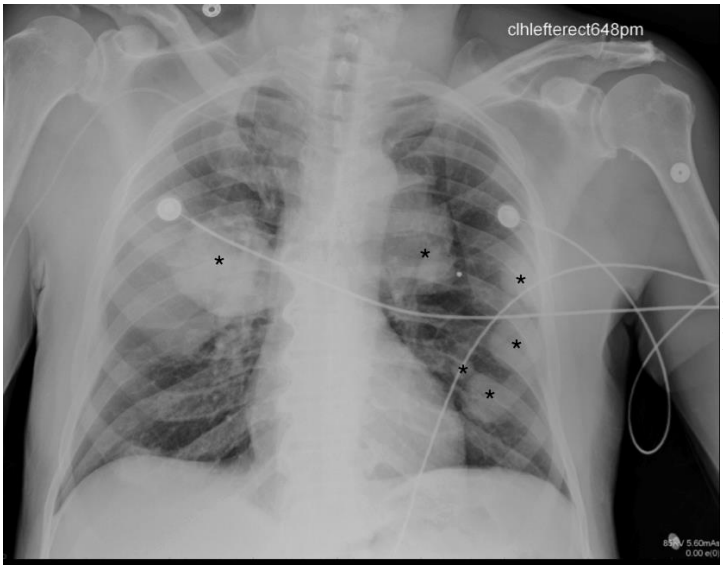


Figure 7 (left): 63 year old male with extraskeletal osteosarcoma. AP Chest X-ray one and half years after initial presentation shows the development of multiple large pulmonary masses, consistent with "cannonball" metastasis (asterisks).

Etiology	Usually de novo
Incidence	1-2 % of all soft tissue sarcomas 4-5% of all osteosarcomas
Age	Peak prevalence in 6th decade of life
Male/Female Ratio	Males slightly more affected
Risk Factors (Osteosarcomas overall)	Paget's Disease, Fibrous Dysplasia, Radiation Therapy, Underlying genetic conditions
Treatment	Wide surgical excision with adjuvant chemotherapy and/or radiation
Prognosis	Poor, >50% die within 2-3 years
Imaging Findings	CT: soft tissue mass displacing fat planes with variable degrees of calcification/ossification MRI: nonmineralized areas intermediate to low on T1 and high signal on T2 with variable contrast enhancement

Table 1: Summary table of extraskeletal osteosarcoma

	X-ray/CT	MRI	Pathology
Extraskeletal Osteosarcoma	-Often displaces fat planes -Variable degrees of calcification/ossification -Nonmineralized portions have muscle attenuation	-Intermediate to Low signal T1 -High T2 signal -Variable Enhancement - Hemorrhage and necrosis common	-Generally > 5cm, well defined -Hyperchromatic, pleomorphic cells of osteoblastic phenotype that produce lacelike and delicate osteoid -Various subtypes; osteoblastic osteosarcoma is the most common subtype
Extraskeletal Chondrosarcoma	-Well circumscribed multinodular mass -Lower attenuation than muscle -Calcification is uncommon -Can have periosteal reaction	-Heterogeneously isointense to muscle on T1 -T2 is hyperintense -Necrosis, fluid-fluid levels -Enhancement more intense around periphery	-True extraskeletal chondrosarcomas are rare, most examples represent the so called "myxoid chondrosarcoma", which is of uncertain lineage and may not be a true chondrosarcoma. This tumor is generally a large intramuscular tumor with gelatinous and hemorrhagic appearance -Multiple myxoid lobules intervened by fibrous septa, hemorrhage is common -Cords of tumor cells in a net-like or linear pattern; -Positive for vimentin, can be positive for cytokeratins or EMA and may show neuroendocrine differentiation by immunostains or electron microscopy -t(9;22)(q22;q12) in more than 75% of extraskeletal myxoid chondrosarcoma corresponding to the EWS-CHN fusion
Undifferentiated high grade pleomorphic sarcoma (Malignant Fibrous Histocytoma)	-Heterogeneously enhancing mass -Attenuation similar to muscle -Hemorrhage or necrosis common	-T1 isointense to muscle -Heterogeneously hyperintense on T2 -Heterogeneous enhancement	-Large solitary, lobulated tumor -Deep seated, often involves fascia or the substance of a skeletal muscle -Pleomorphic cellular tumor with storiform growth pattern -Abundant mitotic activity; may show atypical mitoses -Several morphologic variants
Myositis Ossificans	-Appearance correlates with age of lesion -Starts as low attenuating mass -Amorphous bone by 4wks. -Peripheral organized rim mineralization by 6wks -After 8wks mature bone usually has trabeculae	-Early to Intermediate: T1 iso to muscle, T2 hyperintense with curvilinear low areas or "halo" of cortical rim -Decreasing edema and mass effect over time -Late stage has signal close to mature bone	-Solitary tender mass, usually involves the extremities and often associated with trauma -Well-circumscribed, with a white and gritty cut surface -Zonal maturation of bone from center to periphery: central cellular fibroblastic proliferation, intermediate region composed of immature osteoid, and peripheral with mature lamellar bone
Synovial Sarcoma	-Well-defined to partially infiltrative soft tissue mass -Can have calcification -May contain cystic and hemorrhagic regions -Pulmonary metastases may calcify	-T1 signal iso to hypointense to muscle -Possible thin rim of fat around mass due to origin near neurovascular bundle -T2 Heterogeneously hyperintense. -"Bowl of grapes" multiloculated appearance with internal septa -Prominent heterogeneous enhancement	-Usually affects the lower extremities, grows close to tendon sheaths and bursae but not in the joint space or synovial membrane -Well-circumscribed with a gray-white or variegated cut surface -Wide histologic spectrum, including monophasic spindle cell pattern and biphasic with spindle and epithelioid cells -Ossifying form contains lamellar bone mimicking osteosarcoma -Positive for keratin, EMA, CD99 and bcl-2 -t (X;18)(p11;q11) in more than 90% tumors, corresponding to the SYT-SSX1 or SYT-SSX2 fusion

Table 2: Differential diagnosis table of extraskeletal osteosarcoma

ABBREVIATIONS

CT: Computed Tomography
FSE: Fast Spin Echo
H&E: Hematoxylin and Eosin
IV: Intravenous
MDP: Methylene Diphosphate
MFH: Malignant Fibrous Histiocytoma
MRI: Magnetic Resonance Imaging
T: Tesla
TE: Echo Time
TR: Repetition Time

KEYWORDS

osteosarcoma; extraskeletal osteosarcoma; myositis ossificans