

## Case Report

# Small-cell extraskeletal osteosarcoma: case report and literature review

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**Abstract:** Small-cell extraskeletal osteosarcoma is extremely rare and consists of sheets of small round cells with variable amounts of osteoid. This tumor is often difficult to diagnose when tissue samples do not include recognizable osteoid. Only four cases have been reported in English and none in Chinese. We report a typical case of small-cell extraskeletal osteosarcoma occurring in the left leg of a 40-year-old female. Laboratory results were within normal limits. Magnetic resonance imaging demonstrated a soft tissue mass measuring 36 mm × 18 mm in the medial lateral aspect of left limb. The initial histological findings led to a misdiagnosis because the first fine-needle biopsy was randomized and incomplete. However, an open surgical specimen showed recognizable osteoid, which enabled us to make a definitive diagnosis. We also present clinical, radiologic and pathologic features of this case.

**Keywords:** Small-cell extraskeletal osteosarcoma, osteosarcoma, soft tissue

## Introduction

Extraskeletal osteosarcoma (OS) is a rare “malignant mesenchymal neoplasm that reproduces malignant osteoid bone and/or chondroid material and is located in soft tissue without attachment to bone or periosteum” [1]. Small-cell subtype OS was first described by Sim et al. as an extremely rare and distinct variant [2]. We here present the fifth case of small-cell extraskeletal OS in English literature [3-6].

## Case report

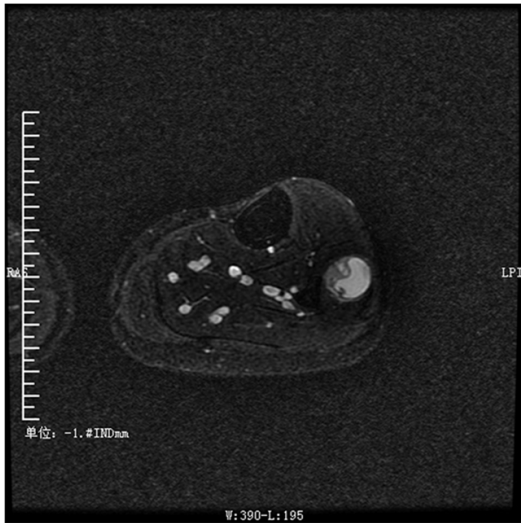
### *Clinical information*

A 40-year-old female presented with a painless palpable mass on her left leg. On physical examination, a firm mass was confirmed in the medial lateral aspect of the left leg. The patient reported pain radiating from the toe in the affected limb upon palpation. Magnetic resonance imaging (MRI) showed a subcutaneous soft tissue mass measuring 36 mm × 18 mm in diameter. No calcification or ossification was apparent, and adjacent bone and periosteum were normal (**Figures 1, 2**). The patient had no history of radiation or trauma, and further labo-

ratory findings and systemic examinations were normal.

### *Pathological analysis by aspiration biopsy*

Histopathological examination showed numerous thick- and thin- walled blood vessels and sheets of neoplastic small round cells, with indistinct cell borders, scanty eosinophilic or clear cytoplasm and round to oval hyperchromatic nuclei containing inconspicuous nucleoli (**Figure 3**). One to two mitoses were present per ten high-power fields. No osteoid or chondroid differentiation was observed. By immunohistochemistry, the tumor cells were diffusely positive for CD99 and focally positive for neuron-specific enolase, but completely negative staining for cytokeratin, vimentin, epithelial membrane antigen, CD45, desmin, myogenin, MyoD1, smooth muscle actin, S-100 protein, CD138, HMB45, synaptophysin and chromogranin A. The Ki-67 index was approximately 5% to 20%, and neoplastic cells were focally positive for PAS. Based on these findings, we diagnosed a malignant small-round-cell tumor, which was consistent with the diagnosis of an extraskeletal Ewing’ sarcoma/peripheral neuroectodermal tumor (ES/PNET). Thus, surgical treatment was recommended.



**Figure 1.** MRI scans of the lower limb showing an absence of contact between the fibula and tumor (axial view).



**Figure 2.** T1-weighted MRI scans of the lower limb showing a soft tissue mass arising from the fascia between the peroneus longus and brevis and extensor digitorum longus, with heterogeneous signal intensity on T2-weighted images (coronal view).

### Operation findings

A relatively elliptical tumor measuring 4.0 cm × 2.0 cm was observed in the superficial peroneal nerve. The highly friable tumor was well circumscribed with a fuscous, somewhat gelatinous appearance, no true capsule and a small amount of clear fluid leakage. The resection margins were negative for rapid frozen section examination.

### Postoperative pathological findings

Grossly, a pile of cracked soft tissues with irregular shapes, measuring 3.5 cm × 2.5 cm × 2.0 cm, shows mixed yellowish-white and greyish-white fish-flesh areas. Microscopically, the subsequent examination showed focal areas of tumor osteoid with irregular calcification (**Figure 4**), in addition to areas resembling ES. Conclusive pathological diagnosis: Small-cell extraskeletal osteosarcoma.

### Treatment and follow-up

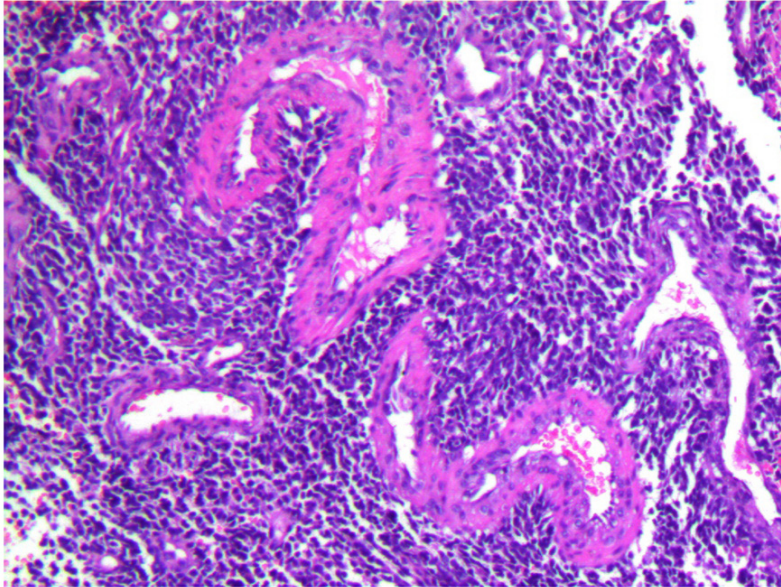
The patient accepted surgery with a wide margin resection, followed by two cycles of postoperative chemotherapy with doxorubicin. No signs of regional recurrence or distant metastasis were observed during the follow-up period of 3 years.

### Discussion

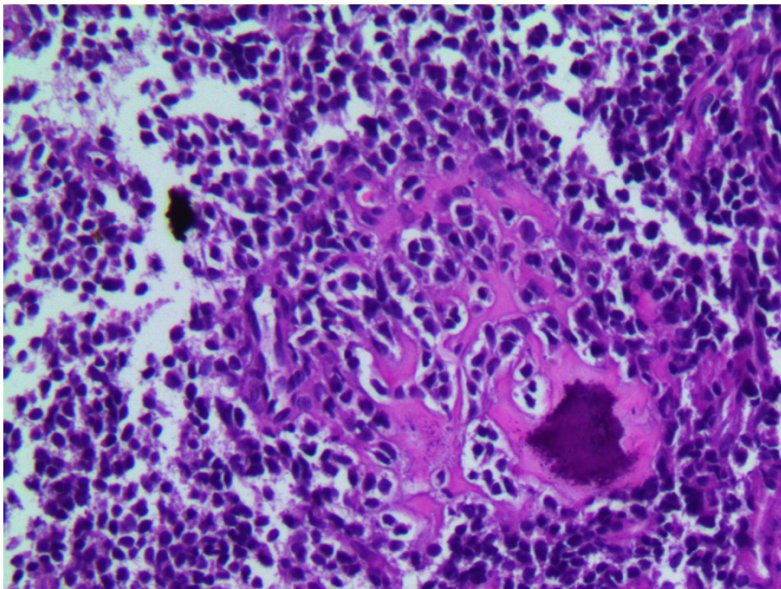
To our knowledge, only five cases of small-cell extraskeletal OS, including the present one, have been reported in English literature [3-6], and of these cases, clinicopathological review information is not available for two cases. The remaining three cases are summarized in **Table 1**. Unlike typical intraskeletal OS, which occurs predominantly during the first two decades of life, small-cell extraskeletal OS occurs most often in middle-aged patients (at 30 years, 31 years and 40 years respectively), with 1 male-to-2 female. Tumor sizes ranged from 3.6 cm to 10 cm. Presentation was usually with a growing, painless, soft tissue mass, occasionally with swelling or tenderness, but this depended on tumor size and location. Without exception, the reported anatomical locations involved the left lower extremities, including thigh, leg and foot. No evidence of any documented predisposing factors, including radiation and trauma, were observed in the three patients, and neither calcification nor ossification was visualized during imaging.

Because of the negative immunohistochemistry reported above, other small round cell malignant neoplasms, including several tumors that can create reactive or metaplastic bone (for example, synovial sarcoma, epithelioid sarcoma and malignant peripheral nerve sheath tumor), should all be ruled out during diagnosis.





**Figure 3.** Tumor composed of many open blood vessels and sheets of small round cells resembling those of ES ( $\times 100$ , H&E).



**Figure 4.** Photomicrograph showing a calcified neoplastic osteoid among round-to spindle-shaped tumor cells ( $\times 200$ , H&E).

However, immunohistochemistry is not reliable for distinguishing small-cell OS from ES/PNET. Moreover, similar to that in ES/PNET, the presence of cytoplasmic glycogen has been reported in small-cell OS [7], which is consistent with our findings. Therefore, the presence of convincing osteoid or bone in the three cases is a key component for diagnosing small-cell OS

and represents a unique feature for differentiation from ES/PNET.

The malignant potential of small-cell extraskeletal OS is relatively high, and little is known about the variables that may affect its prognosis. However, all three patients were observed to be disease-free, although the follow-up period was short (9 months to 3 years).

In conclusion, the prevailing therapeutic approach to small-cell extraskeletal OS is a radical *en bloc* excision with negative margins, which may even include total amputation. Although surgical excision is followed by postoperative chemotherapy to help control metastasis, such therapeutic efficacies are not well established because of the rarity of cases of small-cell extraskeletal OS. In the case presented here, the patient is currently disease-free and attends regular follow-ups.

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#### Disclosure of conflict of interest

None.

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## Small-cell extraskeletal osteosarcoma

**Table 1.** Review of literature describing cases of small-cell extraskeletal OS

Author (reference)	Age/ Sex	Symptoms	Loca- tion	Size (cm)	Imaging (calcifica- tion or ossification)	Morphology (os- teoid or bone)	Therapy	Follow-up
Robinson LH et al. [5]	30/F	Swelling and tightness	Foot	5.0 × 2.5	NO	Present	Amputation	9 months CDF
Yang JY et al. [6]	31/M	Tingling	Thigh	10 × 6	NO	Present	<i>en bloc</i> excision and chemotherapy	2 years CDF
Ming Z et al. (Present study)	40/F	Absent	Leg	3.6 × 1.8	NO	Present	<i>en bloc</i> excision mainly	3 years CDF

Abbreviation: CDF, continuously disease-free.

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