Small cell extraskeletal osteosarcoma: a rare case report

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Abstract

Extraskeletal osteosarcoma is a rare malignant mesenchymal neoplasm and its small cell variant is one among the rarest variant. This article describes a 60-year-old woman presenting with a large, lobulated, painful mass in left thigh with associated history of trauma since 18 months. Her magnetic resonance imaging showed a variegated mixed intensity lesion with associated cystic degeneration, necrosis and matrix arborizing nearby muscles. Fine needle aspiration cytology showed a small cell lesion with very scant osteoid. Tumor was excised and histopathological diagnosis was small cell osteosarcoma involving adjacent muscles and fat with sparing of lymph nodes. The aim of this article is to present the clinical, radiological, cyto-histological and immunohistochemical features of this extremely rare lesion.

Introduction

Extraskeletal osteosarcoma (ESOS) is a rare malignant bone forming mesenchymal neoplasm, located in the soft tissues without having any primary osseous or periosteal involvement and it constitute 1-2% of all soft tissue sarcomas. Thigh muscles are the most commonly affected, followed by the large muscles of the pelvic and shoulder girdles, retroperitoneum. Uncommon sites include larynx, tongue, mediastinum, spermatic cord, penis, pleura, lung, heart, colon, and central nervous system.[1] Among the ESOS, the small cell type is extremely rare.[2] Small cell osteosarcoma is a rare histological subtype of osteosarcoma and resembles Ewing's tumor, as both are made up of small round cells.[3] Small cell osteosarcoma is extremely rare constituting 1-4% of all osteosarcomas.[4] Approximately 12.5% to 23% reported cases are associated with history of mechanical injury but the correlation with trauma is difficult to assess.[1] We describe a 60 year old female presented with large enlarging lesion in left thigh associated with a history of trauma and it is presented for its rarity.

Case Report

A-60-years-old woman presented with large, slowly enlarging and painful lesion in left thigh since last 18 months. She gave a history of trauma at the onset. On examination the lesion was firm, non mobile, fixed to skin and underlying structures on lateral aspect of thigh. MRI showed a variegated mixed intensity lesion in antero-medial aspect of left thigh arborizing left adductor, obturator, pectineus, vasti and fringe of sartorius and ilio-psoas musculature and enclosing neuro-vascular bundles with cystic degeneration, necrosis and associated solid density lesional matrix and discrete calcific foci (Figure 1A). Patient was referred for fine needle aspiration cytology (FNAC) of lesion and smears showed diffuse sheets of small round cells with mild pleomorphism, high nuclear cytoplasmic ratio (N:C ratio) and dark fine granular chromatin without classical rosseting pattern with few foamy histiocytes and scant osteoid (Figure 1B, C). A diagnosis of small round cell tumor with possibilities of ESOS and PNET was given. The lesion was then excised and sent for histopathological examination.

Gross examination of specimen showed an irregular, infiltrating firm, grey white lobulated growth measuring 17×13.5×8.7 cm invading skeletal muscle fibers. Focal gritty areas were observed (Figure 1D).

Microscopy showed nodules and islands of tumor with focal malignant lace like as well trabecular mineralized and non-mineralized osteoid formation without any cartilage or zoning pattern (Figure 2A). Trichrome stain highlighted neoplastic osteoid (Figure 2B). Extensive areas of necrosis were also observed. Tumor cells were small, round with inconspicuous cytoplasm, dense coarse chromatin with minimal pleomorphism with 1-2 mitosis/hpf and small round cells show PAS positivity (Figure 2C). Tumor was invading attached skeletal muscle fibers and fat however the resected skin, soft tissue margins and separately sent lymph nodes were free of tumor. S100 (Figure 2D), LCA, smooth muscle actin, chromogranin, desmin, pancytokeratin and EMA were negative. Patient was monitored for 6 months and was uneventful thereafter lost for further follow up.

Discussion

Conventional bone osteosarcoma occurs during the first two decades of life while Extraskeletal osteosarcoma (ESOS) occurs in patients older than 40 years, with mean age of 50.7 years (range 23-81 years) and with slight male predominance.[1] In present case patient was 60 years old female. Most common variants of osteosarcoma is osteoblastic variant, followed by the fibroblastic, chondroid, telangiectatic, small cell, and well differentiated types.[5] Small cell osteosarcoma is extremely rare. It consists of sheets of small round cells with variable amounts of osteoid.[4] Small cell osteosarcoma was classified by Ayala *et al*. into Ewing's-like, large cell lymphoma-like, and spindle cell patterns.[6] On FNAC, small cell osteosarcoma is composed of mildly pleomorphic, small to intermediate-sized cells with round nuclei, high N:C ratio and dark fine granular chromatin. Cytoplasmic vacuoles, numerous mitoses, abundant karyorrhectic nuclei and scant osteoid may also be seen.[7] In present case, smears showed diffuse presence of small round cells with scanty to moderate cytoplasm showing very occasional cytoplasmic vacuoles, mild pleomorphism insignificant mitosis and minimal scanty osteoid. No rossetting was appreciated in this case to rule out PNET. Histologically, small cell osteosarcoma shows sheets of uniform, round nuclei and minimal cytoplasm with at least focal presence of lace like mineralized osteoid.[2,7,8] Present case showed similar appearance but lacked numerous mitosis and abundant karyorrectic nuclei. PAS staining has been of limited help as in this case with positivity observed by Ayala *et al*.[6] whereas Sim *et al*. found all their cases to be PAS negative.[3] Similarly reticulin stain also has been of variable pattern from intercellular network to paucireticular,[3] as in this case. Immunohistochemically, the tumor shows CD99 and neuronspecific enolase positivity and is negative for S100 protein, smooth mus-

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cle actin, chromogranin, Ki-67, leukocyte common antigen, epithelial membrane antigen, CD30 and desmin as in this case.[2,7,8] However CD99 can also be positive in Ewings sarcoma.[7] CD 99 was not available in our lab.

Differential diagnosis includes PNET, non-Hodgkin lymphoma, mesenchymal chondrosarcoma, myositis ossificans, rhabdomyosarcoma, desmoplastic small round cell tumor and other sarcomas with neoplastic bone formation and neuroblastoma.[7,8]

Ewing's sarcoma is composed by more uniform cells and nuclei than small cell osteosarcoma, without osteoid formation and the diagnosis of Ewing's sarcoma/PNET is supported by presence of Homer Wright rosettes,[3] pseudorosettes and CD99 positivity however, CD99 positive staining is not always helpful in distinguishing the two.[7,8]

The malignant lymphoma generally shows larger nuclei than small cell osteosarcoma with vesicular chromatin, irregular nuclear membranes and prominent nucleoli. Moreover, lymphomas are common leukocyte antigen positive and negative in small cell osteosarcoma and lack osteoid.[7] Mesenchymal chondrosarcoma shows solid areas of round or spindle shaped mesenchymal cells interspersed with well-differentiated cartilage and with hemangiopericytic pattern of multiple vascular spaces and also lack osteoid.[6,7]

Myositis ossificans is a benign extra osseous bone forming lesion located in muscles of extremities in 80% of cases often following local trauma.[9] It also presents as painful, enlarging lesion but has characteristic radiological picture of circumferential calcification with a lucent center and a radiological cleft that separate lesion from cortex of adjacent bone along with typical histological zonal organization in form of peripheral well organized mature lamellar bone, intermediate osteoid region and central immature non osteoid cellular focus and this was clearly absent in this case.[10] Desmoplastic small round cell tumor consist of small round cells of primitive appearance with vimentin, synaptophysin, CD99 (MIC2 protein), and FLI-1 positivity and detection of the reciprocal chromosomal translocation, t(11;22)(p13;q12), which is uniquely associated with this tumor.[9] Neuroblastoma metastasis mimics small cell osteosarcoma histologically but the age of presentation and presence of Homer Wright rosettes or pseudorosettes supports a diagnosis of neuroblastoma over small cell osteosarcoma. Neuroblastomas are immunoreactive for synaptophysin and chromogranin, negative in this case and are virtually never immunoreactive for CD99.[7]

Combination of radical surgery, radiotherapy, and sequential preoperative or postoperative chemotherapy are treatment of choice to improve the survival in ESOS.[1]

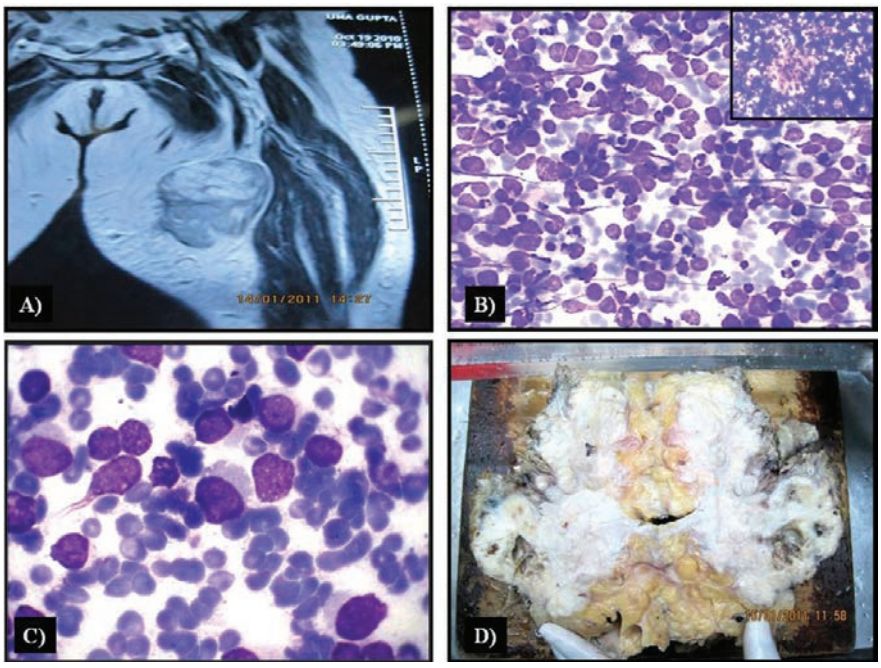

Figure 1. A) Magnetic resonance imaging thigh showing extraskeletal origin of tumor with no zonal pattern; B) fine needle aspiration smears showing small round cells with matrix (Inset, 400×); C) fine needle aspiration smears showing cytoplasmic vacuolization in small round cells (1000×); D) Gross: infiltrating grey white firm growth with areas of cystic degeneration.

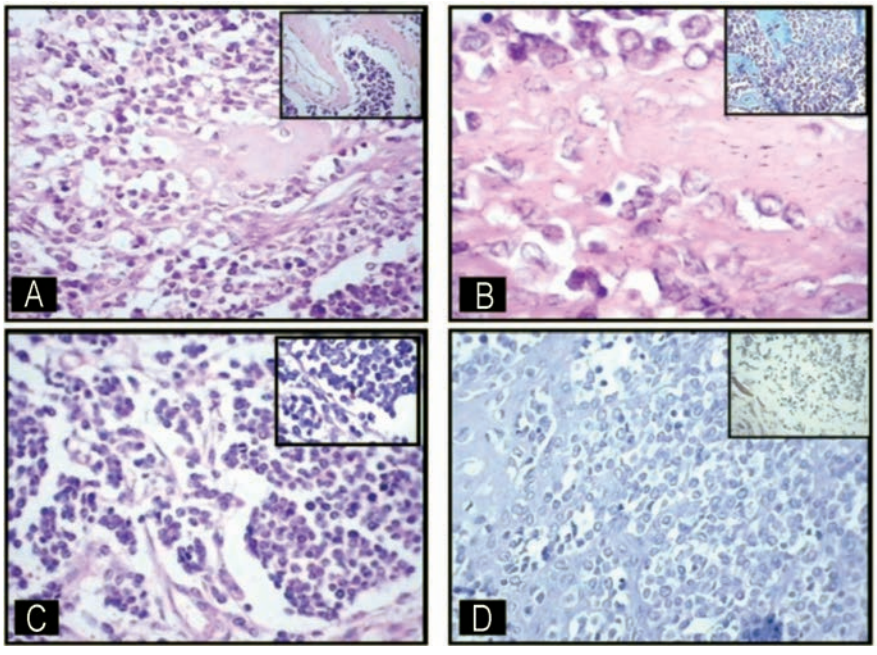

Figure 2. A) Small round cells surrounding malignant fine osteoid and mineralized osteoid (Inset, 400×); B) small round cells surrounding malignant fine osteoid (100×) with trichrome stain highlighting osteoid (Inset, 400×); C) small round cells in nesting pattern with PAS positivity (400×); D) negative S100 stain in tumor cells as well as in matrix with paucireticular pattern (Inset, 400×).

Conclusions

Extraskeletal osteosarcoma is a rare malignant mesenchymal neoplasm and its small cell variant is among the rarest variant. The diagnosis of Extraskeletal osteosarcoma should be considered when a large soft tissue mass shows intratumoral calcification or ossification with history of trauma.

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