CASE REPORT

Small cell osteosarcoma of the parietal region: a unique case at an unusual site

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SUMMARY

Small cell osteosarcoma is a rare tumour that histologically mimics Ewing sarcoma, mesenchymal chondrosarcoma and lymphoma, the presence of osteoid being diagnostic. This variant needs different management protocol, being non-radiosensitive and behaving more aggressively than conventional osteosarcoma. The aim of this article is to highlight such an entity at an unusual site—the parietal region—with unique diagnostic, treatment and prognostic considerations in a 16-year-old girl.

BACKGROUND

Primary osteosarcoma (OS) is the second most common primary bone malignancy, the first being multiple myeloma. OS occurs in the second decade, with a predilection for ends of long bones. Head and neck involvement is seen in 2–9% with extracranial craniofacial bones in 1–2% of cases.¹ Small cell OS (SCO) constitutes 1.3–4% of all OS, skeletal distribution and age range being similar.^{2–3}

Skull-based OS clinically presents as scalp swelling, pain or both, with a duration of a few weeks to months. Non-specific radiological features may pose a diagnostic difficulty.^{2–4} The characteristic ‘sunburst’ roentgenographic pattern of OS of long bones may not be evident in flat bones. Histologically, demonstration of osteoid formation directly from tumour cells is diagnostic of OS. SCO shows a predominant population of malignant small round cells, instead of the much more common spindle cells, with foci of bone formation. However, extensive tissue sampling may be required for osteoid demonstration. The problem in diagnosis is further compounded as its immunohistochemical profile overlaps with other more common malignant small round cell tumours (MSRCTs), including Ewing sarcoma (ES), mesenchymal chondrosarcoma and lymphoma.^{2–3} Rare locations, such as the skull, and lack of awareness of this rare histological subtype, may lead to erroneous diagnosis. A unique case of primary SCO involving the parietal bone is presented along with a brief literature review.

CASE PRESENTATION

A 16-year-old girl presented with a 12-month history of gradually increasing swelling over the right side of her head and three recent episodes of vomiting. The swelling had been partially excised 4 months earlier, but no previous records were available. General and systemic examinations were within normal limits. Local examination revealed a

4×4 cm firm, non-tender, non-mobile swelling over the right parietal region.

INVESTIGATIONS

Routine haematological and biochemical investigations were within normal limits.

MRI of the brain showed a large heterogeneous lesion in the right parietal region. Overlying parietal bone was not visualised. The mass was intracranial with subgaleal extension and had an enhancing soft tissue component with areas of calcification. There was associated vasogenic oedema. On radiology, possibility of metastasis, meningioma or OS was suggested (figure 1A–C).

Histopathological examination revealed a MSRCT, the cell nuclei being 3–4 times the size of adjoining lymphocyte (figure 2A). Focal presence of lace-like material (osteoid) in between the cells was noted (figure 2B). Periodic acid-Schiff stain failed to reveal intracytoplasmic glycogen (figure 2C). Immunohistochemically, the cells were positive for vimentin, osteopontin (figure 2D) and MIC2 (figure 2E), but negative for synaptophysin (figure 2F), chromogranin (figure 2G) and pan-cytokeratin (figure 2H).

DIFFERENTIAL DIAGNOSIS

Histologically, SCO is a MSRCT with differential diagnoses of ES, mesenchymal chondrosarcoma and lymphoma; however, presence of a mineralised tumour matrix and immunoreactivity for osteopontin distinguishes it from the others. Presence of intracytoplasmic glycogen does not rule out the possibility of SCO.³ Immunohistochemistry for FLI1, or demonstration of EWSR1-FLI1 fusion gene or t(11:22) (q24;q12), will help in diagnosing ES, but these may not be available at all centres. However, diagnosis of SCO is based chiefly on histomorphology, as there is no definite diagnostic marker. Three histological patterns of this rare tumour have been described by Ayala *et al*³—ES like, lymphoma like and small spindle-cell like.³ The ES-like pattern is most common, having nuclei 3–4 times the size of an erythrocyte or a mature lymphocyte. In the lymphoma-like pattern, the nuclei are 4–5 times larger than a lymphocyte, with more abundant cytoplasm.³ The current case was categorised as ES-like SCO.

TREATMENT

The patient received three cycles of cisplatin 60 mg and doxorubicin 40 mg injections.

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Figure 1 T1-weighted (A), T2-weighted (B) and postcontrast (C) MRI showing a mass lesion involving the right parietal region with non-visualised (postoperative) overlying parietal bone. The mass is intracranial with subgaleal extension and has an enhancing soft tissue component with an area of calcification (arrow). The mass is associated with oedema (star).

OUTCOME AND FOLLOW-UP

On follow-up, the patient developed frequent seizure episodes. She subsequently discontinued treatment and succumbed to the illness about 6 months after diagnosis.

DISCUSSION

Primary OS is the most common primary high-grade sarcoma of the skeleton, and has a bimodal age distribution, with most patients presenting in the second decade and about 40% being

Figure 2 Photomicrograph showing a malignant small round cell tumour; the nuclei are moderately pleomorphic and are about 3–4 times the size of a mature lymphocyte (arrow) ((A) H&E $\times 400$). Lacy osteoid was noted focally between the cells ((B) H&E $\times 200$). The tumour cells lack presence of periodic acid-Schiff (PAS)-positive material in the cytoplasm ((C) PAS $\times 400$). They are immunopositive for osteopontin ((D) immunohistochemistry (IHC) $\times 200$) and MIC2 ((E) IHC $\times 200$), but negative for synaptophysin ((F) IHC $\times 200$), chromogranin ((G) IHC $\times 200$) and pan-cytokeratin ((H) IHC $\times 200$). MIB-1 labelling index was about 3% (arrow) ((I) IHC $\times 200$).

older than 40 years of age.^{1–3} Bishop *et al*⁵ described cytopathological features of five cases of SCO. Significantly, in their series, pain was the most common clinical manifestation, being present in all, with duration of pain ranging from 1 to 20 months.⁵ However, in the series by Ayala *et al*,³ pain and swelling of the affected area were the most common symptoms.³ In the case under discussion, the symptoms were swelling and vomiting, the latter owing to intracranial extension. Long bones of extremities, namely, the distal femur (30%), proximal tibia (15%) and proximal humerus (15%), are the preferred sites, however, craniofacial bones are affected in 2–9% of cases.¹ Hence OS can be categorised on the basis of site of origin, that is, an intramedullary type, the majority (90%) of which are high grade, and a surface type, which includes periosteal and parosteal subtypes. The histomorphological subtypes are conventional (osteoblastic, chondroblastic and fibroblastic), telangiectatic, small cell, giant cell-rich, osteoblastoma-like, chondroblastoma-like, epithelioid and clear cell variants. Skull OS are rare, with only three large series.^{6–8} Most cases are sporadic.⁷ In the largest series, by Nora *et al*,⁶ 14 of the 21 cases (67%) included were de novo in origin.⁶ Radiographically, OS of flat bones may show non-specific features including intra/extra axial lesion with expansile osteolytic/osteoblastic/mixed patterns and areas of calcification, making diagnosis more challenging.^{2–4} In the index case, owing to lack of clinical suspicion of OS, and symptoms suggestive of neurological disease, the patient was subjected to MRI of the brain, on which a range of possibilities was suggested.

SCO of bone was first described by Sim *et al*,⁹ in 1979, as a small round monomorphic tumour with cells separated by a fibrous component, occurring mainly in the second decade of life.⁹ The WHO defines it as a high-grade malignant neoplasm composed of small cells, with a variable degree of osteoid formation. Metaphysis of long bones (90%) is the predominant site of involvement, however, flat bones such as the skull, jaw, pelvis, ribs, clavicle and scapula can be involved in 10% of cases. Rarity of SCO involving skull bones is highlighted by the fact that none of the cases studied by Huvos *et al*⁷ were of a small cell subtype. Their cases showed osteoblastic (9), chondrosarcomatous (3), telangiectatic (2), fibrohistiocytomatous (2) and mixed (3) patterns.⁷

Awareness of this morphological subtype of OS is important. Exact diagnosis is mandatory owing to poorer outcome than conventional OS and ES. Being non-radiosensitive, aggressive radical surgery with multiagent adjuvant chemotherapy constitutes the main treatment modality. A local recurrence rate of 26–69% and 5-year survival rate of 25–37% have been observed

for craniofacial OS, the former being the major cause of death.^{1 7 10} In contrast to the established role of prechemotherapy in conventional OS management, its impact in cranial OS is not yet proven.

Learning points

- Small cell osteosarcoma (SCO) is an extremely uncommon entity that mainly involves the metaphysis of long bones and, rarely, the skull.
- Histopathology is the key to establishing the correct diagnosis, including subtyping for appropriate management and prognostication, as radiological features are not specific.
- Being non-radiosensitive, aggressive radical surgery with multiagent adjuvant chemotherapy constitutes the main treatment modality.

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Competing interests None declared.

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