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IP Journal of Diagnostic Pathology and Oncology

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Case Report

Small cell osteosarcoma morphological overlap with Ewings sarcoma: A case report

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Abstract

Background: Small cell osteosarcoma is an uncommon, aggressive subtype of conventional osteosarcoma characterized by small round cell morphology. Due to its histological overlap with Ewing sarcoma, accurate diagnosis remains challenging but is crucial for determining appropriate treatment and prognosis.
Case Presentation: A 22-year-old male presented with left knee pain and swelling following trauma. Imaging revealed irregular trabecular and cortical features in the distal femur. Biopsy showed sheets of small, round tumor cells with hyperchromatic nuclei, high mitotic activity, and osteoid deposition in a lacy pattern. Given the morphological resemblance to Ewing sarcoma, immunohistochemistry was performed. The tumor cells showed strong nuclear positivity for SATB2, confirming the diagnosis of small cell osteosarcoma.
Conclusion: This case highlights the diagnostic challenges posed by small cell osteosarcoma due to its histologic similarity to Ewing sarcoma. It emphasizes the pivotal role of SATB2 immunostaining in distinguishing between these entities and underscores the need for an integrated diagnostic approach that combines clinical, radiological, histological, and immunohistochemical data

Keywords: Small cell osteosarcoma, Ewing sarcoma, SATB2.

Received: 22-04-2025; **Accepted:** 22-05-2025; **Available Online**: 04-07-2025

1. Introduction

Small cell osteosarcoma is a rare and aggressive histological variant of conventional high-grade osteosarcoma, the most common primary malignant bone tumor in adolescents and young adults.[1] Characterized by its osteogenic differentiation, small cell osteosarcoma often presents significant diagnostic challenges due to its histological resemblance to other small round cell tumors, particularly the Ewing sarcoma family of tumors.[1] Accurate distinction between these entities is crucial, as treatment protocols and prognosis differ significantly. Immunohistochemistry (IHC), especially the use of SATB2—a marker of osteoblastic differentiation—has emerged as a valuable tool in differentiating small cell osteosarcoma from Ewing sarcoma. This case report highlights the diagnostic importance of SATB2 in confirming small cell osteosarcoma.

2. Case Report

A 22-year-old male presented with a 1.5-month history of pain and swelling in the left knee, preceded by a history of trauma. Clinical examination revealed diffuse swelling over the left knee with local warmth and tenderness. There were no signs of skin changes, sinuses, ecchymosis, muscle wasting, or crepitus.

Radiographic evaluation with X-ray revealed a mild increase in soft tissue density in the anterior distal femur, with no cortical discontinuity (**Figure 1**).

Further imaging with CT scan demonstrated irregular trabecular patterns and cortical irregularity involving the metaphyseal end of the left femur (**Figure 2**).

MRI showed intramedullary signal changes appearing hyperintense on T2 and PD FAT SAT images, involving the mid and lower shaft as well as the condyles of the femur. Small intramedullary cystic areas were also noted—likely

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https://doi.org/10.18231/j.jdpo.2025.019

representing small collections. Periosteal elevation was observed with a thin rim of subperiosteal fluid, along with subarticular extension (**Figure 3**).

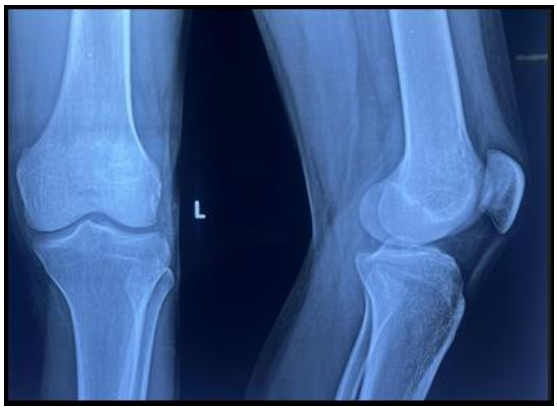

Figure 1: X-ray of left knee joint- Mild increase in soft tissue density in the anterior distal femur, with no cortical discontinuity

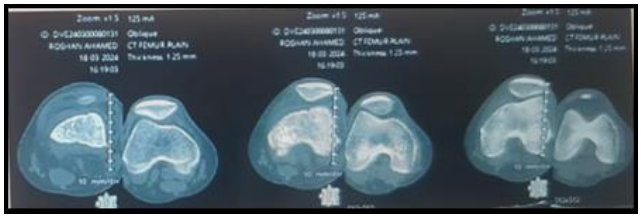

Figure 2: CT scan- irregular trabecular patterns and cortical irregularity involving the metaphyseal end of the left femur - Osteomyelitis to be considered

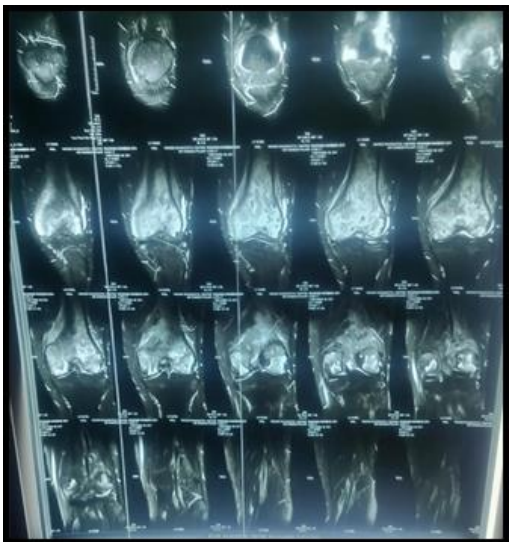

Figure 3: MRI - intramedullary signal changes appearing hyperintense on T2 and PD FAT SAT images noted involving mid lower shaft and condyles of femur. Small intramedullary cystic areas also noted within it-likely small collection. Periosteal elevation is noted with thin rim subperiosteal fluid. Subarticular extension is noted

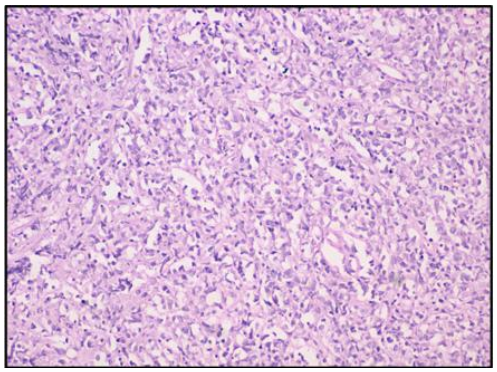

Figure 4: Tumor cells arranged in diffuse sheets (H&E 20X)

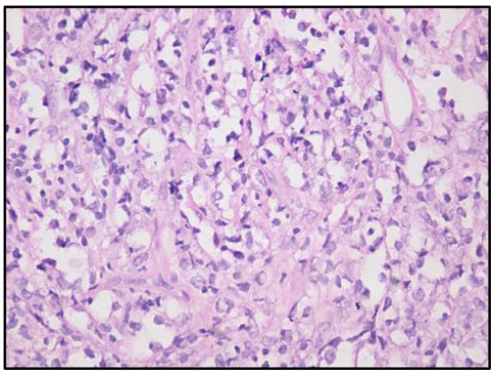

Figure 5: Osteoid deposition in between the tumour cells (H&E 40X)

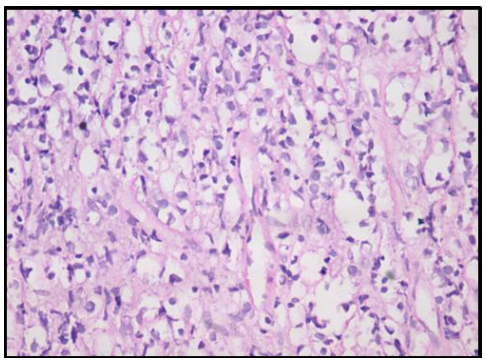

Figure 6: Osteoid deposition in between the tumour cells(H&E 40X)

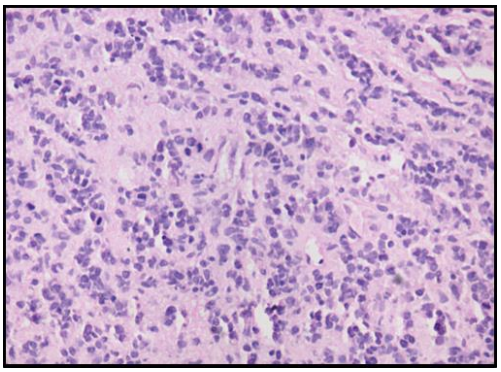

Figure 7: Small cells with hyperchromatic nucleus and inconspicuous nucleoli (H&E 40X)

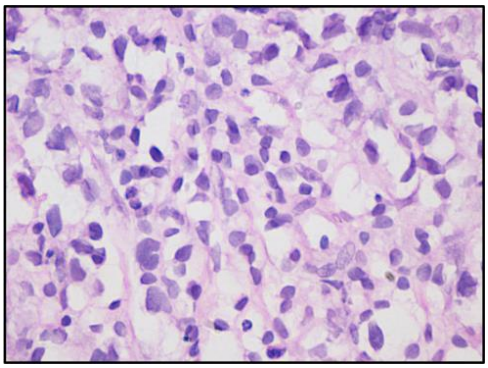

Figure 8: Small cells with hyperchromatic nucleus and inconspicuous nucleoli(H&E 40X)

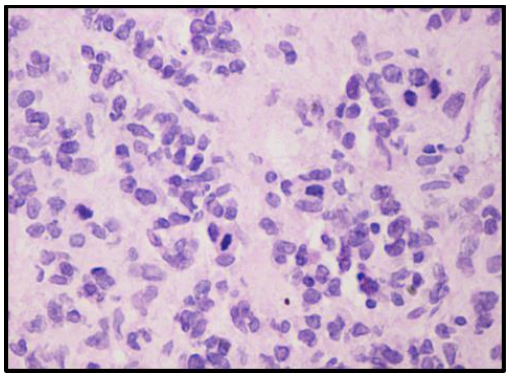

Figure 9: Atypical mitoses (H&E 40X)

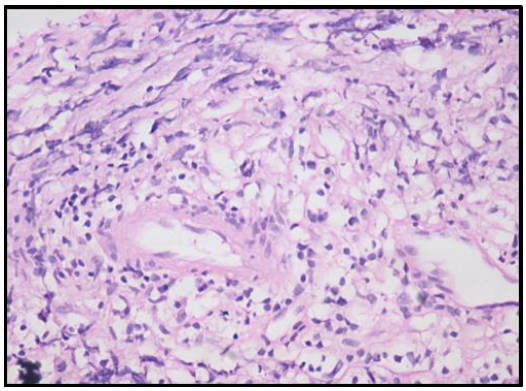

Figure 10: Tumour cells around the blood vessels (H&E 40X)

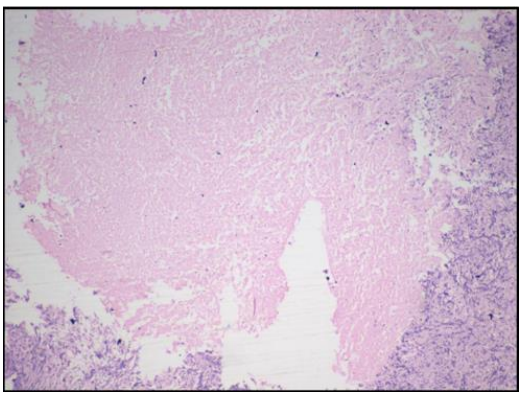

Figure 11: Areas of necrosis (H&E 40X)

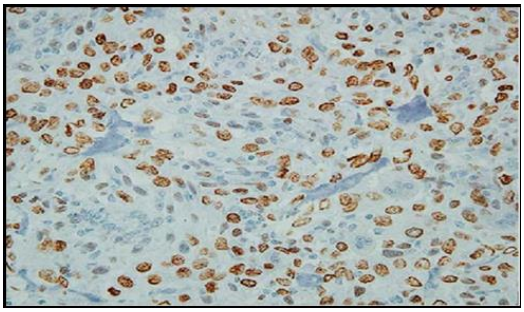

Figure 12: SATB2- Nuclear positive in small cell variant of osteosarcoma

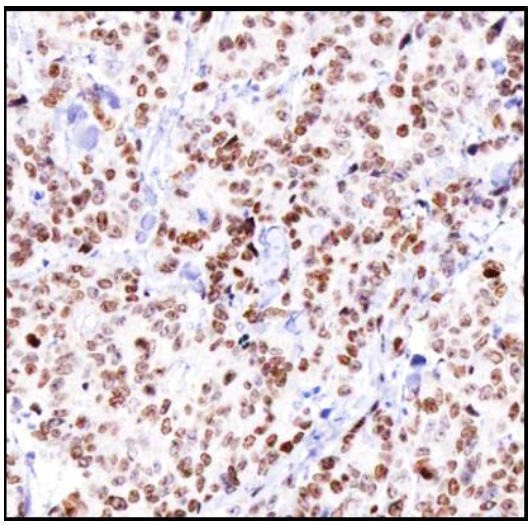

Figure 13: SATB2- Nuclear positive in small cell variant of osteosarcoma

Histopathological examination of the biopsy specimen showed sheets of small round tumor cells (**Figure 4**) with hyperchromatic nuclei, inconspicuous nucleoli (**Figure 7**, **Figure 8**), high mitotic activity (**Figure 9**,**Figure 10**), and areas of necrosis (**Figure 11**). Notably, osteoid deposition was observed in a delicate, lacy pattern surrounding the tumor cells (**Figure 5**, **Figure 6**) and tumour cells around the blood vessels (**Figure 4**)

Given the morphology of small round blue cells with nuclear atypia, high mitotic activity, and osteoid production, a provisional diagnosis of small cell osteosarcoma was made. However, due to its resemblance to Ewing sarcoma, immunohistochemistry was performed. The tumor cells showed strong nuclear positivity for SATB2 (**Figure 12**, **Figure 13**), confirming the diagnosis of small cell osteosarcoma**.**

The patient expired following completion of surgical and chemotherapeutic management due to disease progression and associated complications.

3. Discussion

Small cell osteosarcoma (SCO) remains a rare and aggressive variant of conventional osteosarcoma that poses significant diagnostic challenges due to its morphological and radiological resemblance to other small round cell tumors, most notably Ewing sarcoma. The index case presented in this report—a 22-year-old male with distal femoral involvement—demonstrates typical features of SCO, including small, round hyperchromatic tumor cells and delicate osteoid deposition, necessitating immunohistochemical confirmation to avoid misdiagnosis.

The primary diagnostic dilemma lies in distinguishing SCO from Ewing sarcoma, which shares overlapping features such as round cell morphology, a high nuclear-to-cytoplasmic ratio, and an aggressive clinical presentation. However, accurate classification is crucial due to significant differences in therapeutic protocols and prognosis. While Ewing sarcoma typically responds well to multi-agent chemotherapy and is defined by EWSR1 translocation, SCO requires osteosarcoma-specific treatment regimens.

In our case, the use of SATB2—a marker of osteoblastic differentiation—proved essential. The tumor cells demonstrated strong nuclear positivity for SATB2, supporting the diagnosis of SCO.

This finding is consistent with the work of Machado et al. (2016), who emphasized the utility of SATB2 in distinguishing osteosarcomas from their histological mimics, particularly when conventional morphological criteria are ambiguous. In that study, SATB2 was expressed in the majority of SCO cases but not in Ewing sarcomas, highlighting its diagnostic specificity.[2]

Hiemcke-Jiwa et al. (2024) further corroborated these findings in a comparative study of SCO and fusion-driven round cell sarcomas. They demonstrated that, although SCO is morphologically similar to Ewing sarcoma, it lacks hallmark molecular rearrangements such as EWSR1 and instead shows SATB2 positivity alongside osteoid production—features that were evident in our case.[3]

Ewing sarcoma typically exhibits membranous CD99 positivity and is negative for SATB2, reinforcing the necessity of a panel-based immunohistochemical approach. This diagnostic algorithm is endorsed by the WHO 2020 classification of bone tumors, which emphasizes the integration of histopathology, immunohistochemistry, and molecular studies in complex cases.

Thus, this case reinforces the importance of a multimodal diagnostic strategy that includes clinical-radiological correlation, histopathological evaluation, and selective immunohistochemical testing. SATB2, in particular, emerges as a pivotal marker in resolving diagnostic uncertainty between SCO and Ewing sarcoma, thereby enabling timely and appropriate therapeutic intervention.

Other differential diagnosis for this case included mesenchymal chondrosarcoma**,** Non-Hodgkin lymphoma, and metastatic small round cell tumors. Mesenchymal chondrosarcoma was ruled out due to the absence of cartilaginous areas.[4] Non-Hodgkin lymphoma may present as sheets of small atypical lymphoid cells but typically lacks osteoid.[5] Desmoplastic small round cell tumor and metastatic neuroblastoma can resemble small cell osteosarcoma histologically but are distinguished by specific features such as rosette formation, desmoplastic stroma, and absence of osteoid deposition.[6-8]

Lack of EWSR1 molecular testing is a limitation of this study.

4. Conclusion

Small cell osteosarcoma poses a diagnostic dilemma due to its overlapping radiological and histological features with Ewing sarcoma. A combination of clinical findings, site of involvement, radiological features, and histopathological examination with immunohistochemistry is essential for accurately diagnosing the neoplastic lesion. This case underscores the critical role of SATB2 in differentiating the small cell variant of osteosarcoma from its mimics, reinforcing the importance of a multimodal diagnostic approach.

5. Source of Funding

None.

6. Conflict of Interest

None.

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Cite this article: Sundaram S, Pagidyala R, Ashwini HN. Small cell osteosarcoma morphological overlap with Ewings sarcoma: A case report. *IP J Diagn Pathol Oncol*. 2025;10(2):82-86.