MEDICAL FORUM

IMAGING CHARACTERISTICS OF PERIOSTEAL EWING SARCOMA: A RARE CASE REPORT AND THE DIAGNOSTIC CHALLENGES IN DIFFERENTIATING SURFACE-BASED BONE LESIONS

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SUMMARY

Ewing's sarcoma (ES) is a malignant small round-cell tumor that typically develops within the medullary cavity of bone. A rare variant, known as periosteal Ewing's sarcoma (PES), arises from multipotent mesenchymal cells located in the periosteum. This subtype predominantly occurs in males, with the highest incidence during the second decade of life, and most commonly affects the femur. Due to its non-specific clinical and radiological features, PES can be misdiagnosed as other surface-based bone lesions. We report a case of a 7-year-old boy who was admitted with progressively worsening right thigh pain over a two-month period. Radiographic, computed tomography (CT), and magnetic resonance imaging (MRI) revealed a destructive cortical lesion of the femur, initially suggestive of periosteal osteosarcoma (POS). The patient subsequently underwent an ultrasound-guided biopsy. Histopathological examination, combined with immunohistochemical analysis, confirmed the diagnosis of periosteal Ewing's sarcoma. This case highlights the diagnostic challenges associated with periosteal Ewing's sarcoma and underscores the importance of recognizing its imaging characteristics-particularly in differentiating it from other surface-based bone tumors-within the appropriate clinical context.

Keywords: *Ewing's sarcoma, Periosteal Ewing's Sarcoma, Periosteal Osteosarcoma, Surface-based bone tumors, MRI, CT.*

I. INTRODUCTION

Ewing Sarcoma (ES) is a rare and aggressive malignant bone tumor, first described by Dr. James Ewing in 1921. Histologically, this tumor is classified as a member of the small round cell tumor group and represents the second most common primary bone malignancy in children and adolescents, following osteosarcoma (OS). The disease typically manifests during the second decade of life and predominantly affects males. Common sites of involvement include the femur, pelvis, tibia, and other long bones [1, 2].

Epidemiologically, ES accounts for approximately 10–15% of primary bone tumors in children, with an estimated annual incidence of 2 to 3 cases per million individuals under 20 years of age. It is most prevalent among individuals aged 10–20 years, extremely rare in children under 5 years old, and uncommon in adults over 30 years. The incidence is significantly higher in Caucasians compared to other racial groups [1,2,3]Although ES typically arises within the medullary cavity of bones, rare cases may present in atypical locations. One such variant is periosteal Ewing's sarcoma (PES), in which the tumor originates from the periosteuma connective tissue layer covering the outer surface of the bone. Due to its extra-medullary location and atypical radiologic features, this variant can be mistaken for other surface bone tumors, such as periosteal chondrosarcoma, bone lymphoma, bone metastases from neuroblastoma, subperiosteal hematoma, periostitis, periosteal hemangioma, and

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particularly POS, making accurate diagnosis more challenging. [4,5].

In this article, we report a rare case of PES in a 7-year-old male patient who presents with progressively worsening pain in the right thigh over a two-month periods. Initial clinical and imaging findings suggest a diagnosis of POS. However, histopathological examination combined with immunohistochemical analysis following biopsy confirms the diagnosis of PES. This case highlights the diagnostic challenges of imaging PES and underscores the importance of recognizing its radiologic characteristics to differentiate it from other surface bone lesions within the appropriate clinical context [6].

II. CASE REPORT

A 7-year-old male patient presented with progressively worsening pain and swelling in the right thigh over a two-month period. There was no history of recent trauma. The patient's medical history was unremarkable, and physical examination revealed a well-appearing child with no notable abnormalities. Laboratory investigations were within normal limits.

Radiographic images of the right femur demonstrated an ill-defined osteolytic lesion with a characteristic deep saucerization defect located subperiosteally at the cortical surface of the distal third of the right femur, with subjacent cortical thickening beneath the lesion and an irregular periosteal reaction (Figure 1).

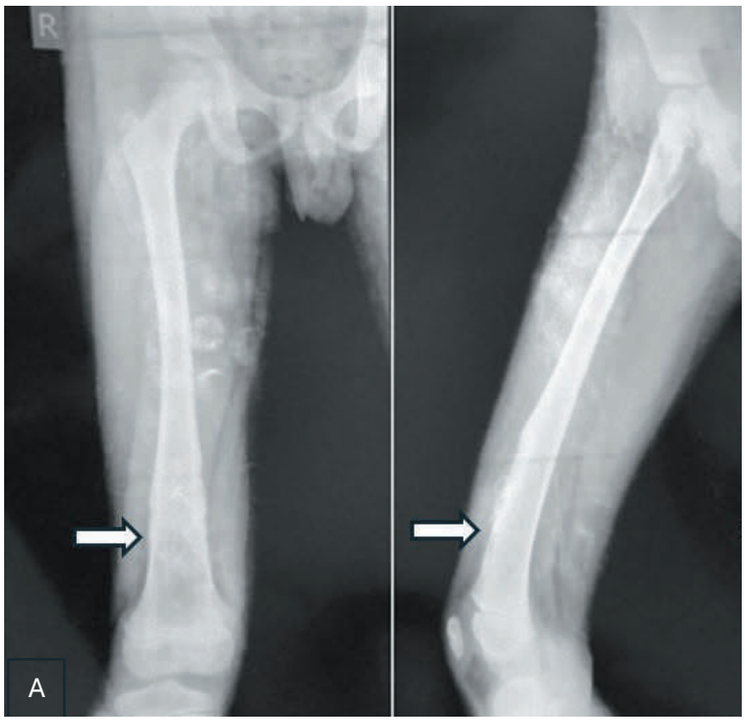

Figure 1. *Anteroposterior and lateral radiographs of the right femur revealed an ill-defined osteolytic lesion (arrows) with a deep saucerization defect located subperiosteally on the cortical surface of the distal third of the femur. The lesion was associated with subjacent cortical thickening and an irregular periosteal reaction.*

CT and MRI of the right femur demonstrated an ill-defined subperiosteal osteolytic lesion along the distal third of the femoral shaft, corresponding to the radiographic findings. The lesion was associated with cortical thickening and an irregular periosteal reaction, without evidence of mineralized matrix formation or extension into the adjacent soft tissues. The inner cortex remained intact. The underlying medullary cavity showed mild increased attenuation on CT, with corresponding high signal intensity on STIR images and strong enhancement after contrast administration on MRI. The lesion measured approximately 3.5 × 1.8 × 6.5 cm. (Figures 2, 3).

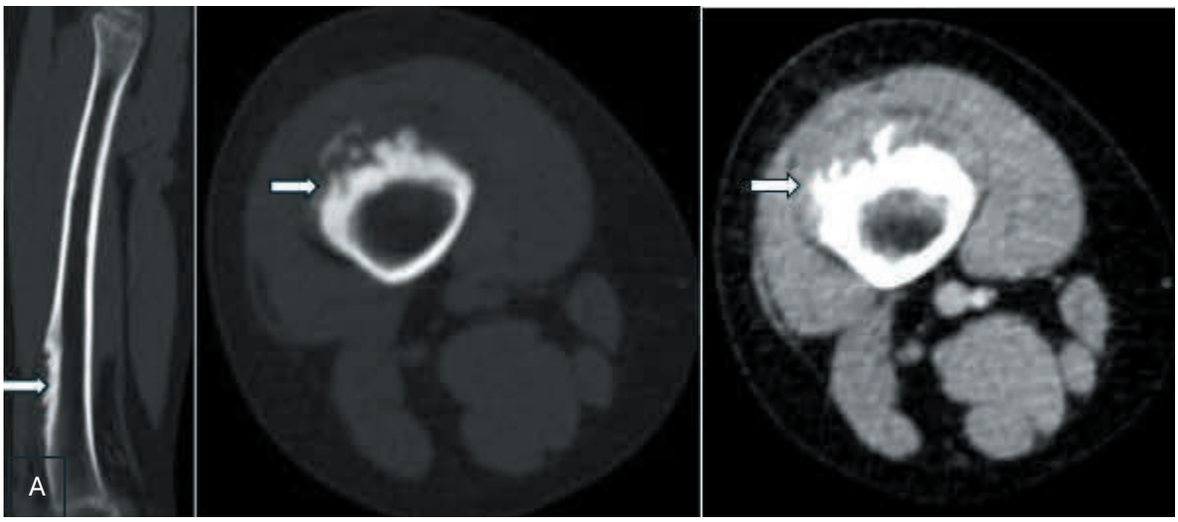

Figure 2. *CT images of the right femur revealed an ill-defined subperiosteal osteolytic lesion with heterogeneous attenuation along the cortical surface of the distal third of the femoral shaft. The lesion was associated with subjacent cortical thickening and an irregular periosteal reaction. A slight increase in attenuation was observed in the anterior portion of the underlying medullary cavity at the level of the lesion. No evidence of mineralized matrix formation was presented, and there was no extension into the adjacent soft tissues.*

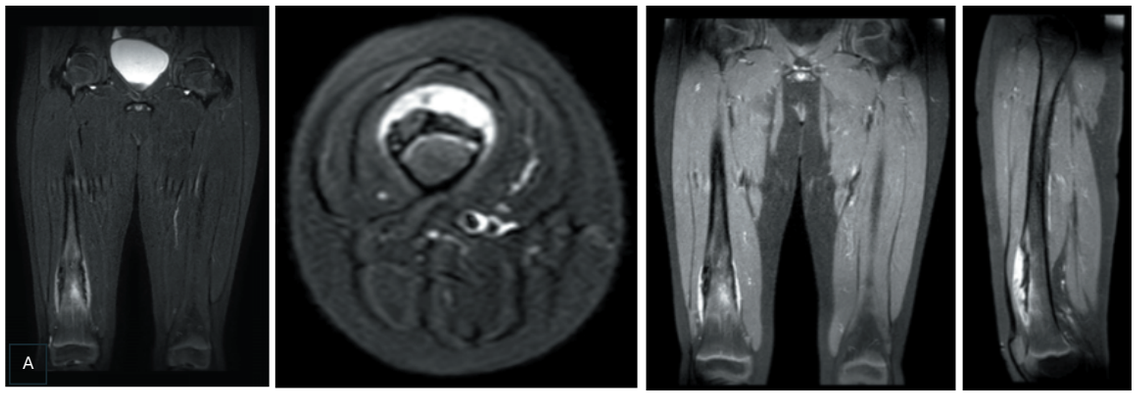

Figure 3. *MRI of the right femur revealed an osteolytic lesion (arrow) with high signal intensity on STIR sequences (Figures A, B) and contrast enhancement post-gadolinium administration (Figures C, D), located subperiosteally on the cortical surface of the distal third of the femur. This was accompanied by subjacent cortical thickening and an irregular periosteal reaction. Bone marrow edema was also observed, showing high signal intensity on STIR (Figures A, B) and contrast enhancement (asterisk) (Figures C, D). No evidence of invasion into surrounding soft tissues was noted.*

On the basis of the imaging findings, a preliminary diagnosis of periosteal osteosarcoma (POS) was suggested. The differential diagnosis included periosteal chondrosarcoma, bone lymphoma, metastatic neuroblastoma, periostitis, and periosteal hemangioma, with POS considered the most likely. However, histopathological examination and immunohistochemical analysis of the ultrasound-guided biopsy specimen (Figure 4) confirmed the diagnosis of PES (Figure 5).

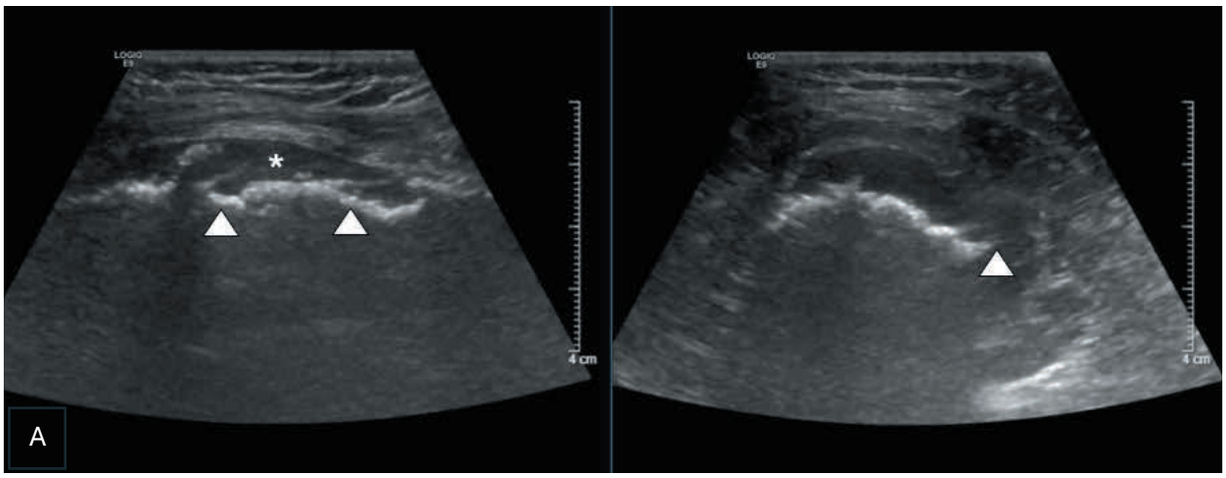

Figure 4. *(A) Panoramic longitudinal US view demonstrated aggressive destruction of the right femur (arrowheads) by a large hypoechoic tumor mass (*). (B) Transverse US of the right femur showed irregular periosteal reaction (arrowheads).*

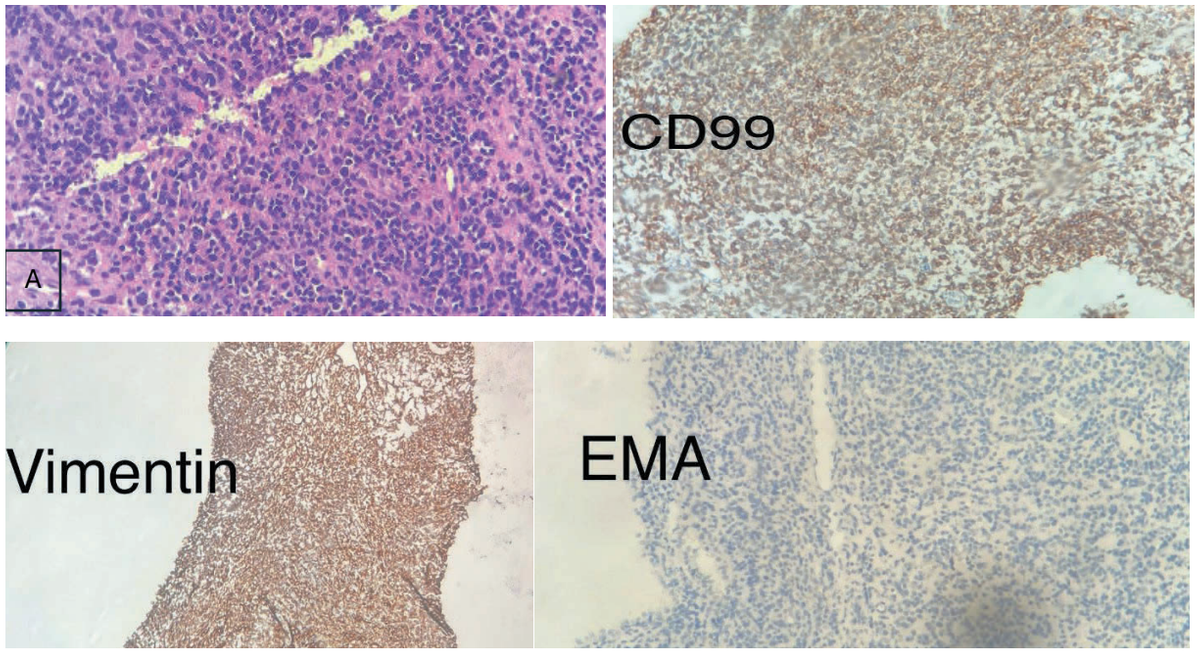

Figure 5. *Histopathological evaluation, performed using Hematoxylin and Eosin (H&E) and Periodic Acid-Schiff (PAS) staining, revealed a tumor composed of small round cells with lightly eosinophilic cytoplasm and round, hyperchromatic nuclei. The tumor cells were arranged in a pattern suggestive of Homer Wright rosettes. Immunohistochemical analysis demonstrated that the tumor cells were positive for CD99, FLI1, and Vimentin, and negative for CD20, CD38, and EMA. These morphological and immunohistochemical features were consistent with PES.*

The patient underwent surgical curettage of the femoral lesion followed by internal fixation to restore structural stability and prevent pathological fracture. Post-intervention computed tomography (CT) imaging demonstrated the expected postoperative changes, including curettage of the intralesional components and appropriate positioning of the fixation hardware. These findings confirmed adequate removal of the tumor tissue and satisfactory alignment of the femoral cortex following surgical management.

III. DISCUSSION

PES is a rare subtype of ES that arises from the periosteum, unlike the classic medullary form. It primarily affects adolescents and young adults, with an age range from 11 to 36 years and a mean age of approximately 16.8 years. A male predominance is reported, with a male-to-female ratio of 2.2:1. The femur, humerus, tibia, fibula, and scapula are among the most commonly affected sites. Clinically, PES presents with progressive localized pain, and sometimes a palpable mass [7].

In our case, a 7-year-old male presents with features consistent with PES. The age is younger than the typical age range, emphasizing the need to consider PES in the differential diagnosis of surface bone lesions in pediatric patients, despite its rarity.

Imaging Features

Radiologic evaluation plays a central role in characterizing PES. On radiographs, typical findings include subperiosteal bone erosion and the Codman triangle, which indicates of periosteal elevation. Importantly, there is often a lack of mineralized matrix, which helps distinguish PES from osteogenic or chondrogenic tumors [8].

CT imaging is useful for evaluating cortical bone destruction and confirming the lesion's subperiosteal origin. In early stages, there is usually no medullary involvement. MRI provides excellent soft tissue contrast and is essential for assessing extraosseous tumor spread. PES typically shows homogeneous high signal intensity on T2-weighted images and strong, uniform post-contrast enhancement [9]. Nevertheless, imaging findings are non-specific, and histological confirmation is necessary.

Differential Diagnosis

Differentiating PES from other surface bone tumors can be challenging due to overlapping imaging characteristics. Key differential diagnoses include both benign and malignant conditions such as POS, periosteal chondrosarcoma, periosteal hemangioma, subperiosteal hematoma, and periostitis.

The absence of chondroid-type calcifications helps exclude periosteal chondrosarcoma. Periosteal lymphoma typically presents with diffuse periosteal thickening, homogeneous T2 signal, and mild contrast enhancement, but generally lacks the degree of soft tissue extension observed in PES. The lack of a known primary neuroblastoma and the presence of a solitary femoral lesion rendered metastatic neuroblastoma unlikely in this case. Although periosteal hemangioma, subperiosteal hematoma, and periostitis can show imaging features similar to PES on radiographs, the absence of flow voids on CT/MRI and the lack of a clinical history of trauma or infection make these diagnoses less probable [10].

Among differential diagnoses, POS is the most challenging entity to differentiate from PES, due to shared location and age group, as both are surface-based malignant bone tumors predominantly affecting adolescents and young adults. However, several imaging and pathological features can assist in their distinction (Table 1):

Table 1. Differential Diagnosis between Periosteal Ewing Sarcoma and Periosteal Osteosarcoma [11,12,13]

Feature	Periosteal Ewing Sarcoma	Periosteal Osteosarcoma
Age group	11–36 years (rare <10)	15–25 years
Onset	Rapidly progressive pain	Slower progression
Radiographs	Cortical erosion; Codman triangle; no mineralization	Sunburst periosteal reaction; irregular calcification
CT findings	Lytic subperiosteal lesion; intact medulla	Cortical thickening; early medullary invasion
MRI (T2-weighted)	Homogeneous hyperintensity	Heterogeneous signal due to osteoid matrix

Feature	Periosteal Ewing Sarcoma	Periosteal Osteosarcoma
MRI (post-contrast)	Strong, uniform enhancement	Heterogeneous or patchy enhancement
Medullary involvement	Late (if any)	Early medullary invasion
Soft tissue extension	More prominent, possible extracortical mass	Typically limited
Histology	Small round blue cells; CD99+, FLI1+	Malignant osteoid with neoplastic osteoblasts

Notably, PES invades the medullary cavity later than POS, but tends to show greater extracortical soft tissue extension, possibly due to its neuroectodermal origin. In contrast, POS more frequently produces mineralized osteoid matrix, which is often visible on radiographs or CT as irregular calcification or sunburst appearance-serving as a key distinguishing feature.

MRI findings further aid differentiation. PES usually demonstrates homogeneous hyperintensity on T2-weighted images and strong, uniform enhancement after contrast, while POS often shows heterogeneous T2 signal due to the presence of osteoid matrix and patchy enhancement post-contrast [11,12,13].

In this patient, MRI demonstrates bone marrow edema without significant soft tissue invasion surrounding the lesion, making differentiation from periosteal osteosarcoma particularly challenging. Therefore, when imaging features are equivocal, biopsy with histopathological and immunohistochemical evaluation remains essential for accurate diagnosis and appropriate management.

Histopathology and Immunohistochemistry

Histologically, PES consists of small round blue cells with round nuclei, fine chromatin, scant cytoplasm, and sometimes Homer-Wright rosettes. Necrosis and limited stroma are common [14].

Immunohistochemistry is essential. CD99 shows strong membranous positivity in most ES cases. FLI1 and Vimentin are often positive, while lymphoid (CD20, CD38) and epithelial (EMA) markers are negative-helping exclude lymphoma and carcinoma.[15] In our patient, the immunophenotype (CD99+, FLI1+, Vimentin+, CD20–, CD38–, EMA–) was consistent with PES.

Reatment and Prognosis

The management of PES mirrors that of classical ES and involves neoadjuvant chemotherapy, wide surgical excision, and adjuvant chemotherapy, with or without radiotherapy depending on surgical margins and tumor spread.[16] In cases with localized periosteal disease, surgery combined with chemotherapy offers the best chance for long-term disease control and improved survival. However, long-term follow-up is essential, as late recurrence and distant metastasis have been reported [17].

Early and accurate diagnosis is essential, as PES-despite being a malignant and potentially aggressive tumor-generally carries a more favorable prognosis than medullary ES or POS, yet a worse prognosis than benign periosteal lesions such as periosteal hemangioma or subperiosteal hematoma. Therefore, proper identification and differentiation are critical to guiding appropriate therapeutic strategies.

IV. CONCLUSION

PES is a rare subtype of ES, with clinical and radiologic features that often mimic other surface bone lesions, particularly POS. Although predominantly seen in adolescent males, PES can also occur in younger children, as illustrated by the case of a 7-year-old boy reported here. Therefore, PES should be considered in the differential diagnosis of subperiosteal lesions, especially when the tumor is confined to the periosteum without medullary or soft tissue involvement.

Definitive diagnosis of PES requires a multidisciplinary approach integrating clinical evaluation, imaging studies, histopathology, and immunohistochemistry. Early detection and timely initiation of multimodal treatment-including systemic chemotherapy combined with surgical resection—can lead to favorable therapeutic outcomes and improved long-term prognosis.

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