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# Case Report: Periosteal Ewing's sarcoma of the proximal humerus

## *Caso clínico: Sarcoma de Ewing periostal en húmero proximal*

Hari Isvara Castro Herrán[1] María Emilia Riquelme Stagnaro[2] Tomás Zamora Helo[1]
Laura Fonseca Muñoz[3] Eduardo Botello Correa[1]

[1] Department of Orthopedics and Traumatology, Pontifical Catholic University of Chile, Santiago, Chile
[2] Faculty of Medicine, Pontifical Catholic University of Chile, Santiago, Chile
[3] Department of Pediatrics, Intensive Care Unit, Pontificia Universidad Católica de Chile, Santiago, Chile

**Address for correspondence** Hari Isvara Castro Herrán, Department of Orthopedics and Traumatology, Pontifical Catholic University of Chile, Faculty of Medicine, Diagonal Paraguay 362, Santiago, Chile (e-mail: haric47@gmail.com).

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**Abstract**

Ewing's sarcoma is the third most common malignant bone tumor, occurring in patients under 20 years of age in 80% of cases. Histologically it is composed of small round cells with round nuclei with chromatin and eosinophilic cytoplasm. For its definitive diagnosis, a molecular study is necessary. It classically affects the medullary cavity of the diaphysis of long bones, however, it has less frequent presentations such as the extra osseous and the periosteal. We present a case report of a 17-year-old patient with swelling in the left proximal humerus with imaging studies compatible with a periosteal tumor lesion that spares the medullary cavity. A biopsy of the tumor was performed with histopathological and molecular confirmation of Ewing's sarcoma, which was treated with concomitant chemotherapy and radiotherapy, obtaining a progressive decrease in the size of the lesion and therefore surgery was not necessary. Periosteal Ewing's sarcoma is an extremely unusual entity, with few cases reported in the literature, which makes it important to recognize and treat these aggressive bone lesions in a timely manner.

**Keywords**

- ewing's sarcoma
- parostal ewing's sarcoma
- periostal ewing's sarcoma
- sarcoma
- bone tumor

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**Resumen**

El sarcoma de Ewing es el tercer tumor óseo maligno más frecuente, presentándose en el 80% de los casos en pacientes menores de 20 años. Histológicamente se compone de células pequeñas redondas con núcleos redondos con cromatina y citoplasma eosinofílico. Para su diagnóstico definitivo es necesario el estudio molecular. Clásicamente, afecta la cavidad medular de la diáfisis de huesos largos, sin embargo, tiene presentaciones menos frecuentes como la extra ósea y la periostal. Se presenta un reporte de caso de un paciente de 17 años con un aumento de volumen progresivo en húmero proximal izquierdo, con estudios imagenológicos compatibles con una lesión tumoral periostal que respeta la cavidad medular. Se realizó una biopsia del tumor con confirmación histopatológica y molecular de sarcoma de Ewing el cuál fue tratado con quimioterapia y radioterapia concomitante, obteniendo una disminución progresiva del tamaño de la lesión, por lo que no fue necesario realizar cirugía. El sarcoma de Ewing periostal es una entidad extremadamente inusual con pocos casos reportados en la literatura, lo que hace importante reconocer y tratar oportunamente estas lesiones óseas agresivas.

**Palabras clave**

- sarcoma de ewing
- sarcoma de ewing periostal
- sarcoma de ewing parostal
- sarcoma
- tumor óseo

## Introduction

Ewing's sarcoma (ES) is the third most common malignant bone tumor after osteosarcoma and chondrosarcoma. 80% of cases occur in patients under 20 years of age and is more prevalent in men with a ratio of 1.4:1.[1,2]

Any bone can be affected, however, it occurs mainly in the medullary cavity of the diaphysis and the metaphysial-diaphyseal junction of the long bones, the pelvis and the ribs.[2,3] Other less frequent forms of presentation are extra-skeletal ES, where there is only soft tissue involvement without affecting bone tissue, and periosteal Ewing's sarcoma (PES), which originates from the periosteum, respecting the spinal canal, with an incidence of 12% and 3% respectively.[4,5]

In 2020, the book of classifications of bone and soft tissue tumors of the World Health Organization (WHO) in its 5th edition, updates some definitions, identifying ES as a small round cell sarcoma that involves the fusion of a limb of the FET gene family (usually EWSR1) and a member of the ETS gene family.[2] One of the big changes in this new edition is that it identifies and separates as different entities all small round cell sarcomas that histologically resemble SE but lack the fusion between EWSR and ETS,[2,6–8] highlighting the role of molecular pathology in the diagnosis of these clinical entities.

The periosteal variant of ES (PES) is extremely unusual, with few reports identified in the international literature, which often makes its diagnosis complex and late.[1] The objective of our report is to present a new case of this rare diagnosis, molecularly proven, along with a literature review. Additionally, we aim to contribute to the timely recognition and differential diagnosis of aggressive bone surface lesions and provide insights into the management of patients affected by PES. We have obtained the patient's consent and received approval from the ethics committee of the Pontificia Universidad Católica de Chile to publish this clinical case.

## Clinical case

17-year-old male patient, previously healthy, who consulted in October 2019 due to a rapidly progressive increase in volume in the proximal third of the left humerus, without pain or other associated symptoms. A study was initiated with radiographs that showed thinning of the external cortex of the proximal diaphyseal region of the humerus, associated with discontinuous periosteal reaction and extensive soft tissue mass (►**Fig. 1**). Magnetic resonance imaging (MRI) was performed confirming the presence of a periosteal mass of approximately $6.4 \times 3.4 \times 4.7$ cm, which determines elevation of the humeral periosteum and respective the spinal cavity (►**Fig. 2**).

A core puncture biopsy performed under computed axial tomography (CT) had inconclusive results, so an incisional pavilion biopsy was then performed, showing a tumor made up of sheets of uniform, small round, blue cells with little clear cytoplasm, rounded, vesicular nucleus and small nucleolus (►**Fig. 3**). Immunohistochemical stains for CD99 and FLI-1 were diffusely positive; Focal positive BCL2. FISH was performed to detect translocations at the 22q12.2 locus of the EWSR1 gene, with a positive result.

The staging study using positron emission tomography (PET-CT) shows no evidence of distant dissemination. The patient is finally diagnosed with PES of the left proximal humerus without metastatic lesions, therefore, stage IIA according to the AJCC.

In December 2019 and April 2020, the evolution of the tumor was monitored with MRI, showing a progressive decrease in its size (►**Fig. 4**), so it was decided to complete the chemotherapy protocol initiated. In June 2020, it entered the follow-up stage, with PET-CT that did not show hypermetabolic lesions of local or distant disease, with controls every three months during the first two years. Currently, the patient

 

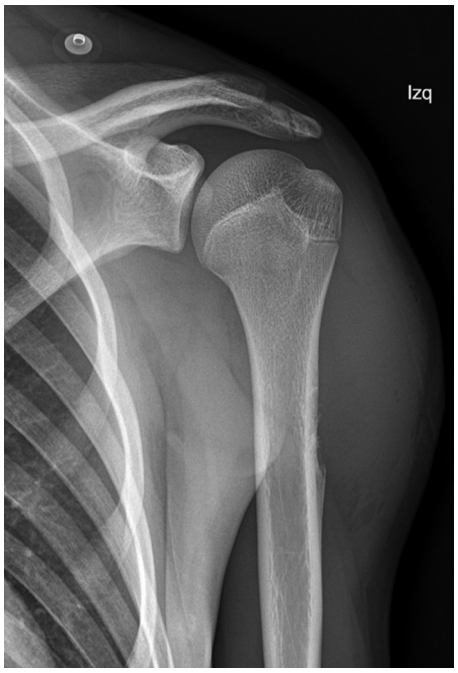


**Fig. 1** Anteroposterior radiograph of the left proximal humerus, showing a metaphysio-diaphyseal lesion located in the lateral cortex of the humerus, associated with a discontinuous periosteal reaction and soft tissue mass. No defined matrix mineralization pattern observed.

has been followed for two years with chest CT and shoulder MRI, stable, with no changes or signs of recurrence. In addition to this, he has excellent shoulder function, with a Musculoskeletal Tumor Society Functional Scale (MSTS) score of 93%.

## Discussion

In 1921, James Ewing identified a form of primary malignant bone tumor, which he defined as diffuse endothelioma or entodothelial myeloma, today known as ES,[9] being the second most common primary malignant bone tumor in the pediatric population and young adults. Our report highlights a rare variant of ES, molecularly proven and successfully treated with the combination of chemotherapy and radiotherapy without the need for surgery.

ES, at a general level, has an incidence of 1 case every 1.5 million inhabitants.[10] Its main clinical presentation is localized pain and a sensation of a palpable mass.[2,5] The presence of fever or pathological bone fracture is common in advanced disease or metastasis.[2]

Histologically, small uniform round cells are evident that are analogous to medullary and extra-skeletal forms, containing a round nucleus with chromatin and eosinophilic cytoplasm, with cytoplasmic membranes.[1] ES cells are immunoreactive to vimentin and the membrane protein CD99, which is constantly expressed, and is also characterized by a reciprocally balanced translocation, which encodes an oncogenic transcription factor, the most frequent being EWS-FLI1, due to the translocation t(11;22) (q24;q12), present in 85% of cases.[1] Molecular diagnosis through fluorescence in situ hybridization (FISH) is increasingly used to identify the EWSR1 gene fusion, which confirms the diagnosis of ES.[1,2]

Radiographic studies show osteolytic, permeative and poorly defined lesions with the presence of an aggressive discontinuous periosteal reaction, in relation to a subperiosteal soft tissue mass.[2,4] Additional studies with MRI are useful to more precisely evaluate the primary lesion, its extension to soft tissues, presence of Saltatory metastases, involvement of the medullary cavity and the absence of mineralization of the matrix.[2,4,11–13]

As differential diagnoses, other sarcomas with a periosteal presentation must be taken into account, such as osteosarcoma, which has similar radiological characteristics, but with the presence of mineralization of the matrix, and periosteal chondrosarcoma.[11,14]

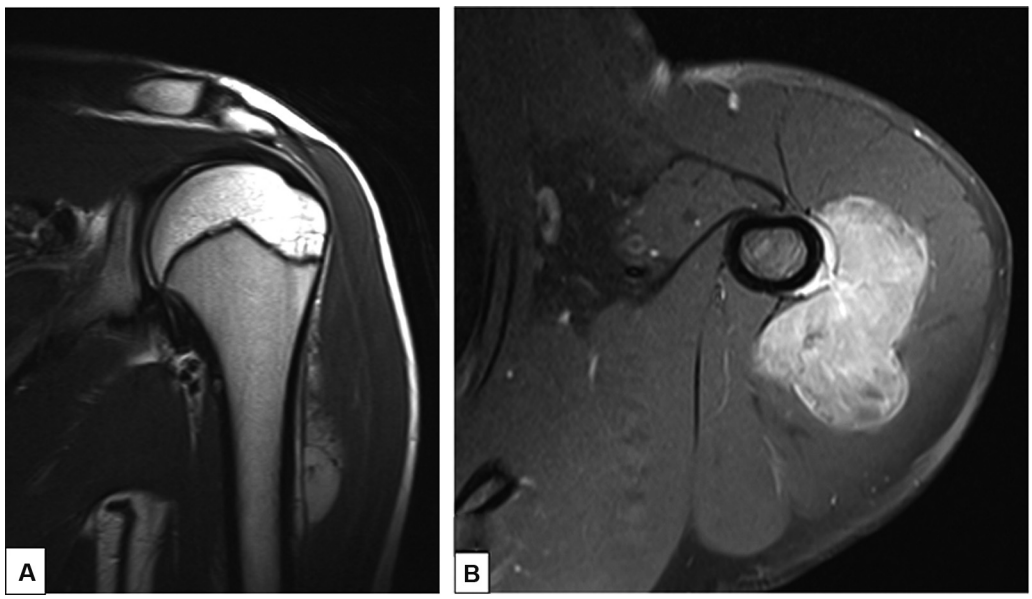


**Fig. 2** (**A**) Coronal T2 reconstruction showing the lesion with a hyperintense component, mainly extraosseous. (**B**) Post-gadolinium saturated axial reconstruction, where a soft tissue component derived from the periosteal region of the humerus is observed.

 

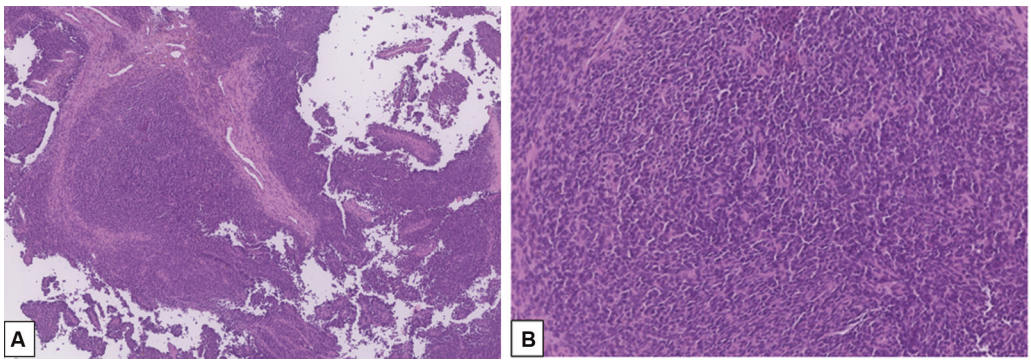


**Fig. 3** Histological sections (**A**) and (**B**) showing fragments of tumor made up of sheets of uniform, round, small, and blue cells. There is little clear cytoplasm and a rounded, vesicular nucleus and small nucleolus are observed. There is some mitosis and little stroma.

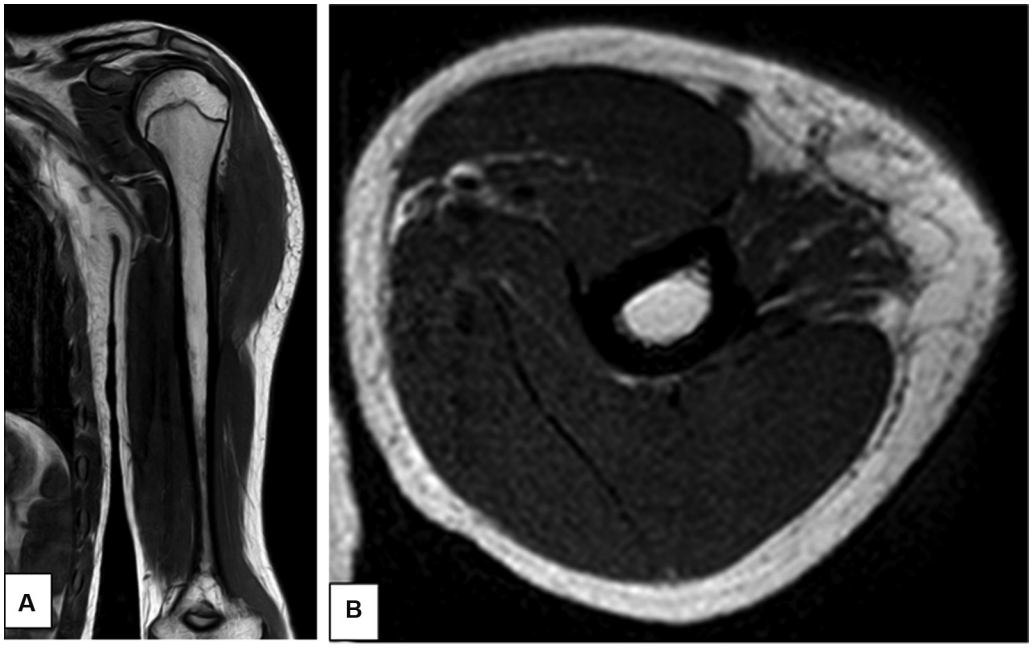


**Fig. 4** Coronal (**A**) and axial (**B**) reconstruction in T1, showing significant regression of the periosteal mass of the lateral cortex of the humerus after treatment with chemotherapy and radiotherapy. Persists with absence of spinal cord involvement.

PES was initially described in 1956 by Sherman and Soong, who reported and described different radiological variations of the disease from 111 cases of ES, obtained from the archives of the Memorial Center, New York.[9] Currently, there is limited information about PES in the literature; It is known that its prognosis is more favorable than central ES, it is more prevalent in men, it usually does not present metastases and it has less aggressive clinical and radiological characteristics, frequently affecting the proximal aspect of the extremities.[1,3–5,9,11,13,15]

There is a retrospective study that evaluated the proportion of medullary, periosteal and extra-skeletal ES in 126 patients, finding that 88.9% of cases corresponded to the medullary variant while only 4.8% of cases were periosteal. Furthermore, a prognostic and therapeutic impact was distinguished according to the topographic categories, reaffirming better survival and prognosis rates in PES.[10]

The 5-year survival of patients with spinal ES without metastasis is approximately 60% and in patients with metastases, it drops to 22%.[1] The age of presentation varies between 11 years and 36 years, however, there are case reports of PES in people over 65 years of age, with worse general results, usually attributed to the lower possibility of giving higher doses of chemotherapeutic agents.[1]

Prior to the chemotherapy era, less than 20% of ES patients survived and it was common for them to die within the first 2 years due to metastasis.[16] Currently, treatment protocols are based on systemic management with chemotherapy, using protocols such as VCD and local management with radiotherapy and/or surgery, the latter being a topic of debate today.[1,16]

To our knowledge, this rare case report represents a PES with a classic presentation, managed according to established protocols with chemotherapy and radiotherapy, resulting in a satisfactory clinical evolution, without the presence of metastasis and progressive disappearance of the tumor lesion. This is how it was finally decided not to

 

subject the patient to additional surgical treatment. Despite the infrequency of this pathology, it should always be suspected when faced with aggressive periosteal and soft tissue involvement, in order to achieve a timely diagnosis and optimize the prognosis of the patient to be treated.

Conflict of Interest
None.

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