

## Extraskelatal presentation of Ewing's Sarcoma

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The case of a 27-year-old Hispanic female who presented with an occipito-parietal tumor after suffering trauma to the area. A physical examination revealed no tenderness to palpation and with evidence of healing ulcerations. The biopsy was consistent with a synovial sarcoma. A wide excision of the mass (15cm x 14cm x 6cm) followed by a pericranial flap was performed. A follow-up CT showed recurrence involving the parietal sagittal sinus. After a second biopsy the mass was determined to be a small-cell sarcoma, consistent with Ewing's sarcoma. Chemotherapy included 8 cycles of doxorubicin, vincristine, and cyclophosphamide, with alternating cycles of etoposide and ifosfamide. A year later, a second wide excision of the mass was performed, followed by bilaminar skin substitute and skin graft placement for reconstruction of the soft-tissue defect. After chemotherapy, a follow-up PET scan showed no signs of re-uptake in any soft tissue or skeletal structures. After 2 years, the patient remains in complete remission. [*P R Health Sci J* 2018;37:55-57]

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Ewing's sarcoma is the second most common primary bone malignancy (in the first 2 decades of life). Its involvement includes long bones (47%), ribs and vertebrae (12%), and flat bones (29%) (1). Its incidence is around 3/100,000 in white Caucasians; it is rare in African and Asian populations (2). CNS involvement occurs in 10% to 30% of the cases, due to secondary deposits from primary extracranial manifestations (3). The skull is a rare primary site for this tumor, with an incidence 1% to 6% (4).

### Case Report

Case of a 27-year-old Hispanic woman complaining of a growing mass in the parieto-occipital region of the skull (Figure 1) after trauma to the affected area. The patient presented with dizziness, tinnitus, headaches, insomnia, and excessive pressure. A CT without contrast (Figure 2) showed a 15cm x 12cm x 4cm mass with mixed areas of low- and high-density foci representing hemorrhagic and fluid components. No evidence of intracranial extrusion or cortical destruction was noted. MRI without contrast showed a large heterogeneous mass arising in the parieto-occipital region. T1 imaging showed an isodense mass with areas of increased signal intensity. T2 imaging showed multiple cystic components. The mass appeared to be adherent to the underlying periosteum. No intracranial brain flow obstruction was evident.

Wide excision of the mass followed by a pericranial flap was performed. The gross specimen was a 15cm x 14cm x 6cm mass. Pathology evaluation showed immunostains positive for CD99, CD8/18, bcl-2, and occasional cells with CK7, favoring

the diagnosis of a poorly differentiated synovial sarcoma. Genetic studies were not done. Translocations, though useful for purposes of identification, are not always present in synovial sarcoma; translocation t(X;18) is found in 80% of such cases, while translocation t(11;22) is found in 90% of Ewing sarcoma cases. The case was revised at the NIH, and the diagnosis of small round-cell sarcoma consistent with Ewing sarcoma was confirmed as the most likely.

Follow-up MRI showed a mass extending into the right parietal superior sagittal sinus. The extra-axial lesion measured approximately 13mm x 16mm x 13mm. A filling defect of the superior sagittal sinus represented tumor thrombosis. All these findings concurred with the suspicion of tumor recurrence, with calvarium and intracranial extensions making the tumor unresectable.

A chemotherapy protocol of 5 cycles of doxorubicin, vincristine, and cyclophosphamide was given every 8 weeks in addition to etoposide with ifosfamide given for 5 consecutive days in between cycles was given. To minimize cardiotoxic side effects, doxorubicin was replaced by dactinomycin when the maximal dose of doxorubicin was reached.

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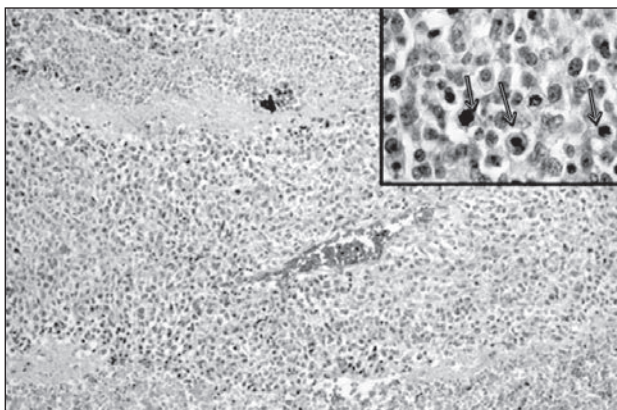


**Figure 1.** Gross View

A second wide local excision of the remaining tumor, osteotomy, and placement of bilaminar skin substitute were performed a year later. Pathology specimen showed negative margins. A skin graft was placed to repair the soft-tissue defect. PET scan showed no scintigraphic evidence of residual, recurrent, or metastatic disease.



**Figure 2.** Preoperative CT without contrast



**Figure 3.** Viable neoplastic cells surrounding a central blood vessel (blue cells), with necrosis at the periphery (in pink) (H&E, 100x). Inset: High magnification of neoplastic cells with several mitotic figures, red arrows (H&E, 100x).

## Discussion

Primary Ewing's sarcoma of the cranial bone usually involves the frontal and parietal bones. The reported peak incidence is between 5 and 13 years of age (5). Occipital bone involvement has been reported (4). The male-to-female ratio is 1.6:1 (6).

The presence of distant metastases at the time of diagnosis is the most unfavorable prognostic factor. Older age at presentation, tumor size, the tumor's having a median location, and low efficiency of chemotherapy are other poor prognostic factors (7). Cranial involvement offers the best prognosis.

Headache (100%), intracranial pressure (75%), and skull swelling are the main symptoms and also the most commonly reported (5). Lesions of the petrous temporal bone are characterized by facial paralysis and hearing loss. Cuneiform bone involvement causes ocular deficits and trigeminal nerve disturbance.

Ewing's sarcoma can develop metastases within 2 years. The most affected sites are the lungs (57%), bones (34%), and skull (4%) (8). Metastases in cranial tumors are uncommon.

Ewing's sarcoma is the second most common bone tumor; it usually manifests during the first 2 decades of life. The skull is a rare primary site for this tumor, with an incidence of only 1% to 6% of all the reported cases (3, 4). In our patient, the late presentation with an unlikely location added to the diagnostic challenge.

James Ewing first described Ewing's sarcoma in 1921 as a "diffuse hemangioendothelioma of bone." Data show that this neoplasm "may be neuroectodermally derived from the primitive neural tissue" (9). Small round cells with round nuclei exhibiting fine chromatin and scanty cytoplasm and Homer Wright rosettes may be present; necrosis with viable cells (usually perivascular in distribution) are features of Ewing's sarcoma. The presence of PAS (periodic acid-Schiff staining)-positive grains in the cytoplasm is a typical pathomorphological feature. This indicates the presence of glycogen and helps in the differentiation from other tumors, such as lymphoma, rhabdomyosarcoma, and metastatic neuroblastoma (2).

Markers, including CD99, vimentin, and transmembrane proteins encoded by MIC-2, help in the verification of diagnosis (8). Many types of sarcomas are characterized by specific chromosomal translocations. The  $t(11;22)(q24;q12)$  and  $t(21;22)(q22;q12)$  translocations are considered to be specific for PNET/ES, and the  $t(X;18)(p11;q11)$  translocation is specific for synovial sarcoma (10). Primary and metastatic tumor manifestations can look identical, immunohistochemically. The Ki-67 proliferation marker can help in the identification of metastases.

Chemoradiation combined with surgery has been reported as having good outcome, both in primary and metastatic cases. Most physicians use radical tumor excision, systemic chemotherapy, and radiotherapy for local control. The main goal is to reduce tumor size before invasive procedures are

performed. Despite morbidity rate of en-bloc osteotomy the procedure was considered for this patient, ultimately being rejected because of the high-risk involvement of the superior sagittal sinus.

Chemotherapy is essential in the treatment regimen. Radiotherapy and surgery alone confer a 5-year survival rate of 8 to 15% (7). For decades, a 4-drug combination including vincristine, doxorubicin, cyclophosphamide, and actinomycin-D has been the standard treatment. Some studies have replaced cyclophosphamide with ifosfamide or have added ifosfamide and/or etoposide (11). Studies have shown that VACAc plus an ifosfamide/etoposide regimen offers the best survival rate (12) in poor responders. Employing modern regimens, the overall survival (OS) for ES of the extremities is around 80% for patients with localized disease (13).

### Resumen

Caso de una mujer hispana de 27 años que presenta un tumor en el área occipito-parietal después de haber sufrido trauma en el área afectada. Evaluación física mostró no dolor a palpación y ulceraciones en diferentes estadios. Biopsia fue consistente con sarcoma sinovial. Escisión (15cm x 14cm x 6cm) con márgenes amplios fue ejecutada seguida de un colgajo pericranial. CT demostró recurrencia del tumor envolviendo el seno parieto-sagital. Segunda biopsia reportó sarcoma de célula pequeña, consistente con sarcoma de Ewing. Quimioterapia incluyó 8 ciclos de Doxorubicina, Vincristina, Ciclofosfamida en adición a ciclos alternantes de Etoposido con Ifosfamida. Al año siguiente, una segunda escisión de masa seguido por la implantación de una malla de sustituto de piel bilaminada con injerto de piel. Después de completada la quimioterapia, un PET-SCAN de seguimiento no demostró señales en tejidos blandos o ninguna otra estructura ósea. Dos años después, la paciente se encuentra en total remisión.

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