



## Case Report

# Intracranial Ewing Sarcoma – A case report

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Received : 12 April 2020

Accepted : 08 May 2020

Published : 30 May 2020

### DOI

10.25259/SNI\_178\_2020

### Quick Response Code:



## ABSTRACT

**Background:** Intracranial Ewing's sarcoma (ES) is a rare entity with <15 cases reported in the literature. It belongs to a family of round-cell neuroectodermally derived tumors bearing many similarities to peripheral primitive neuroectodermal tumor (pPNET). There is currently no established treatment protocol. Reported cases are treated with either surgery alone or surgery with adjuvant chemotherapy and radiation.

**Case Description:** We describe a case of intracranial left frontal ES in a 19-year-old patient who presented with change in behavior. Diagnosis was unclear based on radiological findings on MRI and CT alone. MRI brain with contrast demonstrated a large extra-axial ovoid heterogeneously enhancing left frontal convexity mass. The patient underwent gross total resection with adjuvant chemotherapy and radiation. No local or systemic recurrence was found at 12 months postoperatively.

**Conclusion:** Intracranial ES/pPNET is rare tumor with nonspecific clinical presentation and radiological findings. They are locally invasive. Surgery with adjuvant chemoradiation is the mainstay treatment. Distinction of pPNET and cPNET is important for therapeutic and prognostic purposes.

**Keywords:** Ewing's sarcoma, Meningeal tumor, Neuro-oncology, Peripheral primitive neuroectodermal tumor, Soft-tissue tumor

## INTRODUCTION

Ewing's sarcoma and peripheral primitive neuroectodermal tumor (ES/pPNET) belongs to a family of round-cell neuroectodermally derived tumors. They are overlapping entities with the same histological origin but different degree of neuroectodermal differentiation (absent for ES, definite for pPNET).<sup>[7]</sup> They can occur at both osseous and extraosseous sites and are most commonly found in the axial skeleton (pelvis, vertebrae, and ribs) as well as peripheral soft tissue. They are locally aggressive and are prone to dissemination. Primary ES/pPNET is exceedingly rare and even more so at an intracranial location. ES/pPNET is distinct from central primitive neuroectodermal tumors (cPNETs), which are central nervous system embryonal tumors most commonly arising in the supratentorial parenchyma. The distinction between these two entities is important in terms of underlying genetics, immunochemistry, treatment, and long-term prognosis.

We report a rare case of intracranial Ewing sarcoma. The case presentation, imaging findings, operative approach, and postoperative treatment plan are discussed, with a summary of the literature.

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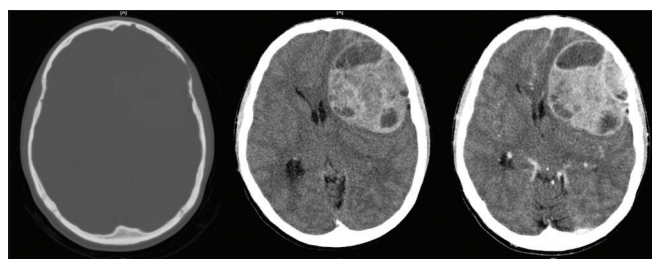
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## CASE DESCRIPTION

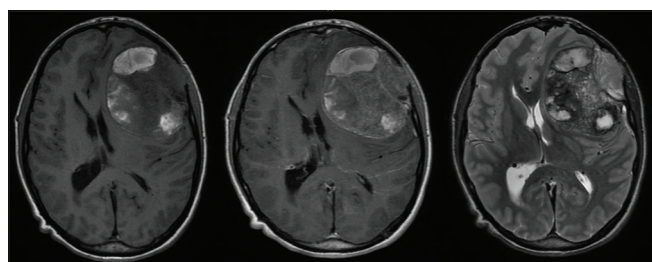
A 19-year-old male with no medical history was referred to our service with approximately 2 weeks of headache and 2 episodes of vomiting. Detailed history from his parents revealed a change in behavior, including apathy and uncharacteristically poor university grades, over the prior 12 months. With the exception of a right pronator drift, his neurological examination was normal. CT brain revealed a large extra-axial heterogeneous mass involving the left frontal and temporal lobes with well-defined lobulated margins and avid enhancement of the high-density areas. The lesion eroded the inner table of the left frontal bone with the outer table almost completely eroded [Figure 1]. MRI brain with contrast demonstrated a large extra-axial ovoid heterogeneously enhancing left frontal convexity mass measuring 6.2 cm × 7.1 cm × 7 cm [Figure 2]. There was considerable susceptibility artifact, suggesting calcification and/or hemorrhage. There was also evidence of destruction and erosion of the calvarium, and a small extracranial component of the tumor was noted. The diagnosis of hemangiopericytoma was entertained and surgery planned.

### Operative management

Intraoperatively, the tumor was found to have breached the dura and as suggested by preoperative imaging, had invaded bone [Figure 3]. The involved bone (including the lateral sphenoid wing) and a generous cuff of dura were resected. The tumor was soft and moderately vascular. The tissue plane between tumor and brain was easily developed



**Figure 1:** Bone window (left), noncontrast (middle), and postcontrast (right) CT brain.



**Figure 2:** T1 FLAIR pre- (left) and postgadolinium (middle) and T2 (right).

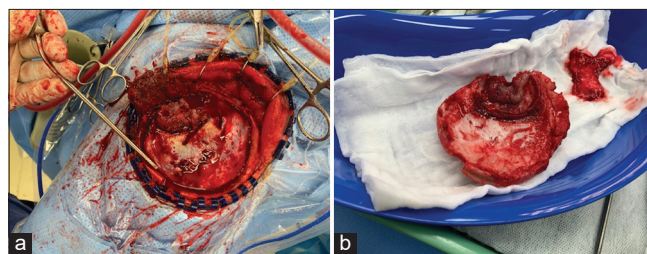
using standard microsurgical technique. A gross total resection was achieved. The dural defect was repaired with pericranial graft, and titanium mesh used to repair the bony defect.

The patient's postoperative recovery was uneventful and he was discharged home day 5 after surgery. Postoperative MRI revealed no evidence of residual tumor. PET scanning did not reveal any other lesions. The patient was referred to a local specialist sarcoma unit for adjuvant chemotherapy with VIDE (vincristine, ifosfamide, doxorubicin, and etoposide), to be followed by focal irradiation and second round of chemotherapy with VAI (vincristine, dactinomycin, and ifosfamide).

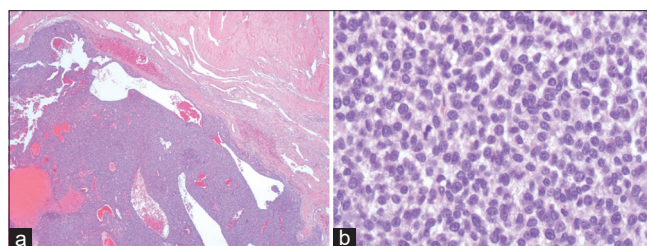
The patient is now 1-year postsurgery with no clinical or radiological evidence of recurrence or metastatic disease.

### Histopathology

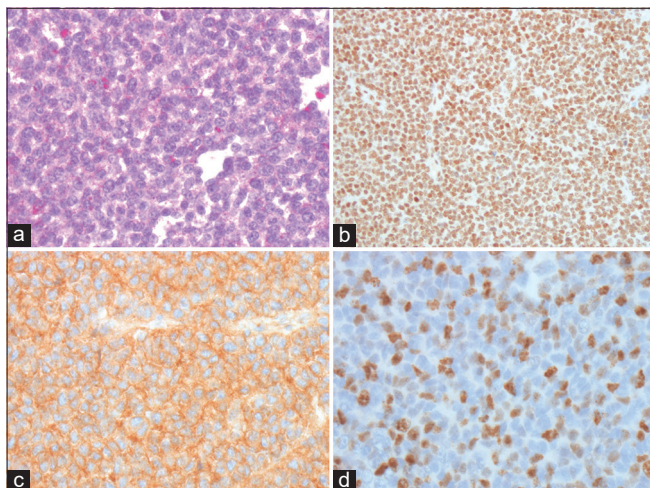
Under light microscopy, the specimen showed a durally based, highly cellular tumor composed of relatively monotonous small blue cells with slightly irregular nuclei and thin rims of cytoplasm [Figure 4] displaying PAS-positive material [Figure 5]. The mitotic rate was high at 34 mitoses per 10 high-power fields. There were numerous vessels, some displaying thrombosis and there were areas of hemorrhage and hemosiderin deposition. There was no necrosis. The tumor cells were positive for FLI-1, MIC-2, and vimentin [Figure 5]. The cells were negative for STAT6, CD 34, DUX-4, WT1, desmin, myogenin, ERG, synaptophysin, chromogranin A, pan-CK, EMA, P40, CK8/18, LCA, SOX10, CD 20, CD3, and TDT. Ki67 was positive in 30% of the cells,



**Figure 3:** (a) Intraoperative photograph of the tumour breaching dura, (b) The tumour had extended through the skull.



**Figure 4:** (a) Hematoxylin and eosin stain (high-power view), (b) hematoxylin and eosin stain (low-power view).



**Figure 5:** (a) PAS positive, (b) FLI-1 positive, (c) MIC-2 positive, (d) Ki67 30% positive by visual estimation.

visually estimated. The specimen was sent for FISH and tested positive for EWSR1 (22q12) rearrangement.

## DISCUSSION

ES/pPNET is neuroectodermal tumors with common histopathological features and a unifying immunophenotypical and genetic profile.<sup>[2]</sup> They account for 1% of all pediatric malignancies, and incidence peaks in the second decade of life then decline, with 80% of patients diagnosed before 20 years of age.<sup>[12]</sup> Intracranial extraosseous ES/pPNET is a rare entity with <15 cases reported in the literature. Among the reported cases, the most common presenting clinical symptom is seizure followed by other signs of raised intracranial pressure including headache, vomiting, and reduced level of consciousness.

Radiologically, ES/pPNET often presents as a large, contrast-enhancing, well-circumscribed lesion with dural or bony involvement, mimicking the appearance of a meningioma. They are usually solid but can also have a cystic component. Two patterns of meningeal involvement have been described in the literature.<sup>[4]</sup> The first type is diffuse involvement of the cranial and spinal leptomeninges without focal intraparenchymal or meningeal tumor. The other type is characterized by a durally based mass, as in our case. The implication of the pattern of dural involvement on prognosis and survival remains unclear, but it would serve to reason that patients with diffuse leptomeningeal disease fare worse. Limited literature exists on the specific signal intensities this entity on MR. These tumors are often hyperdense on CT and the typical appearance on MR is hypo-/isointensity on both T1 and T2 with enhancement which can be either homogeneous or inhomogeneous. Diffusion restriction is variable, having been reported present or absent.<sup>[3]</sup> Due to

these nonspecific and variable radiological characteristics, making a radiological diagnosis with any certainty is difficult. In addition, other, more likely differential diagnoses for dural and leptomeningeal neoplasms such as meningioma, hemangiopericytoma, solitary fibrous tumor, smooth muscle tumors, and hemangioblastoma are usually considered first.<sup>[1]</sup> T1 hypo- or isointensity is a common feature among hemangiopericytoma, smooth muscle tumors, and hemangioblastoma.<sup>[1]</sup> However, hemangioblastoma and smooth muscle tumors tend to exhibit T2 hyperintensity, whereas hemangiopericytoma can appear isointense to gray matter on T2.<sup>[9]</sup> Features suggesting hemangiopericytoma are flow voids and heterogeneous enhancement due to rich blood supply.<sup>[9]</sup> T2 hypointensity appears to be a feature of ES/pPNET.

The genetic abnormality of ES/pPNET is characterized by the fusion of EWSR1 gene on chromosome 22q12 with a number of other genes, most commonly with the FL11 gene on chromosome 11q24 forming a t(11; 22) (q24; q12) translocation.<sup>[8,11,12]</sup> This is present in 90–95% of cases. This translocation is responsible for dysregulation of cell proliferation, differentiation, apoptosis, angiogenesis, invasion, and metastasis.<sup>[6]</sup> This genetic abnormality can be detected with fluorescence *in situ* hybridization (FISH) and reverse transcriptase polymerase chain reaction (rtPCR). CD99, a cell surface glycoprotein and gene product of MIC 2, is highly sensitive for peripheral pPNET but not specific as it can be present in other small, blue round cells tumors such as lymphoblastic lymphomas and ependymomas.<sup>[7,10]</sup> cPNET does not exhibit the abnormality of the EWSR1 gene or expresses MIC2 gene and thus can be differentiated from ES/pPNET.<sup>[12]</sup>

The distinction between ES/cPNET has therapeutic and prognostic importance. cPNETs are embryonal tumors composed of undifferentiated or poorly differentiated neuroepithelial cells with possible divergent differentiation along neuronal, astrocytic, muscular, and melanocytic lines. They are poorly circumscribed and can occur in any region of CNS, but rarely metastases elsewhere. Involvement of cerebrospinal fluid is reported in 10–30% of cases. The treatment of cPNET involves intrathecal methotrexate followed by systemic chemotherapy and radiotherapy. Reported long-term disease-free survival for ES/pPNET ranges from 9 months to 8 years, which is much shorter for cPNET.

There is currently no established treatment protocol for intracranial ES/pPNET. In most cases, the extra-axial location of the tumor enables gross total resection with removal of the dura and bone involved. Most centers follow with adjuvant chemotherapy and focal irradiation.<sup>[11]</sup> In the reported cases, approximately half were treated with surgery alone and others with surgery and adjuvant chemotherapy



and focal radiation.<sup>[11]</sup> No comparable survival data are available. The standard chemotherapy agents are vincristine, ifosfamide, doxorubicin, and etoposide. In systemic ES, there is a role for neoadjuvant therapy to achieve cytoreduction, local control of tumor, and assess tumor response to chemotherapy.<sup>[5]</sup> ES/pPNET usually only requires focal radiation, unlike cPNET in which full craniospinal irradiation and boost to tumor bed are necessary.<sup>[12]</sup>

## CONCLUSION

Intracranial ES/pPNET is rare tumors with nonspecific clinical presentation and radiological features. It is locally aggressive and requires multimodality treatment with surgery and adjuvant chemoradiation therapy. Distinction of pPNET and cPNET is important for therapeutic and prognostic purposes. We have presented a case of frontal ES extending through the cranial vault which was treated with primary resection and adjuvant chemoradiation.

## Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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**How to cite this article:** Huang J, Ghent F, Levingston R, Scholsem M. Intracranial Ewing Sarcoma – A case report. *t. Surg Neurol Int* 2020;11:134.