Primary Ewings Sarcoma of Cavernous Sinus in an Infant: A Case Report and Review of Literature

ABSTRACT

Ewing's / peripheral primitive neuroectodermal tumor (pPNET) of the cavernous sinus are extremely uncommon. We present clinical, radiological, pathological findings of Ewing's/pPNET involving the cavernous sinus in an eleven-month-old infant presenting with proptosis and 6th nerve palsy. MRI Contrast scans showed a well-defined, homogenously enhancing mass involving the right cavernous sinus location. Histopathology and immunohistochemical features were consistent with Ewing's/pPNET. The patient succumbed to disease in spite of starting chemotherapy. The clinical, radiological and pathological findings of previously reported cases of Ewing's sarcoma / pPNET involving the cavernous sinus are summarized. The histological differential diagnosis of primary intracranial Ewing's sarcoma / pPNET are discussed.

Keywords: Ewing's sarcoma, Peripheral primitive neuroectodermal tumor, Cavernous sinus

INTRODUCTION

Ewings sarcoma is the second most common bone tumor presenting in childhood. Ewing's Sarcoma (ES)/ peripheral primitive neuroectodermal tumor (pPNET) are considered together as a single ES/ pPNET family group as both types share common histopathological, immunophenotype and genetic abnormalities (1, 2). These can occur at several extraosseous sites like chest wall, head, neck, soft tissues of extremities and in any viscera. Primary intracranial ES/ pPNET has been uncommonly reported at jugular foramen, cerebellopontine angle, frontal dura, tentorium and cavernous sinus (3, 4, 8, 10). Cavernous sinus location is extremely uncommon with only a few cases reported in literature till date (3, 4, 8, 10). We present clinical, imageological and pathological findings of one such case in an eleven month old infant along with review of previously reported cases.

CASE REPORT

An eleven month old infant was brought by parents with a 10 days history of proptosis and medial deviation of right eye. Examination confirmed right sixth nerve palsy with proptosis. Complete haemogram was done and the values were in normal range. Bone marrow biopsy was done which was showing normal morphology. CT scan and MRI Contrast scans showed a well defined, homogenously enhancing mass measuring 1.8 x 3 x 2.1 cm involving the right cavernous sinus location with mass effect over adjacent right medial temporal lobe. The lesion was abutting and posteriorly displacing right trigeminal nerve (Figure 1A, B). Radiological differential diagnosis included neuroblastoma,
hemangioma, lymphoma, undifferentiated small round cell tumor and meningioma.

Debulking of the tumor was done by right frontotemporal craniotomy through subtemporal approach. The lesion was found in the cavernous sinus after opening the parkinsons triangle in the lateral wall. The tumor was vascular, non suckable. Frozen section revealed small round cell tumor. Patient had an uneventful postoperative period and was discharged on fourth post operative day. Histopathological examination revealed a highly cellular tumor comprised of sheets of monotonous round cells with round hyper chromatic nuclei and scant cytoplasm (Figure 2A, B). Mitotic activity as well as foci of necrosis was noted. On immunohistochemistry, the tumor cells showed diffuse strong membrane positivity for CD99 (Figure 3A) but were negative for CD 45 (Figure 3B), terminal deoxynucleotidyl transferase (TdT), glial fibrillary acidic protein (GFAP) and desmin (Figure 3C). These features were consistent with diagnosis Ewings sarcoma/pPNET. EWS-FLI 1 genetic analysis confirmed the diagnosis of Ewing’s Sarcoma/pPNET.

Post-operative scans done 2 weeks later showed residual tumor confined to right cavernous sinus. Bone scan, CT scan of chest, abdomen & pelvis, bone marrow aspiration, MRI scan of spine and CSF cytology showed no evidence of systemic involvement.

The patient advised adjuvant chemotherapy consisting of alternating cycles of doxorubicin, vincristine and cyclophosphamide with ifosfamide and etoposide according to pediatric oncology group protocol. Patient received one dose of doxorubicin, vincristine and cyclophosphamide regimen. The patient died on 37th post operative day at his home due to status epilepticus according to patient attendants.

**DISCUSSION**

Ewing’s Sarcoma is an undifferentiated small cell neoplasm, sharing immunoreactivity and several fusion genes with pPNET, but pPNET is defined as having further differentiation (1, 2). Both ES/pPNET family tumors believed to be derived from neural crest cells (5). Primitive neuroectodermal tumors can be broadly divided into 3 categories, namely, peripheral PNETs, central PNETs, and neuroblastomas, including tumors arising from autonomic nerves. World Health Organization classification of tumors on nervous system recommend the use of PNET selectively to the Medulloblastoma (PNET-MB) and other round cell tumors in nervous system are called as pPNET.

Primary intracranial ES/pPNET is uncommon and cavernous sinus involvement as noted in our case is exceptionally rare (3, 4, 8, 10). The clinical, Imageological and pathological findings of previously reported cases of ES/pPNET involving cavernous sinus are summarized in Table I.

Out of the four cases reported in literature two were male and two were female with age ranging from 13 to 48 years, our case is peculiar in view of extremely young age at presentation. Of the four reported cases one of them was considered to be metastatic (10) as patient was found to have similar tumor with...
Figure 2A, B: Histological section showing a highly cellular tumor comprised of sheets of monotonous round cells with round hyper chromatic nuclei and scant cytoplasm. (H&E stain; AX100, BX200).

Figure 3: Immunohistochemistry with (A) CD 99 showing diffuse strong membrane positivity in the tumor cells and negative staining (B) CD 45 and (C) desmin. (Polymer-HRP; X 200).
### Table I: Clinical, Imageological, Immunohistochemistry, Treatment and Follow Up Details of Previously Reported ES/pPNET of Cavernous Sinus

<table>
<thead>
<tr>
<th>Case</th>
<th>Source</th>
<th>Age/sex</th>
<th>Clinical Findings</th>
<th>Imaging</th>
<th>IHC results/ Genetic analysis</th>
<th>Treatment</th>
<th>Follow-up</th>
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<tr>
<td>1</td>
<td>Elias et al, 2002</td>
<td>27/M</td>
<td>Left Retro-orbital headache &amp; 3rd nerve paresis.</td>
<td>Inhomogeneous contrast enhancing mass involving left parasellar region and CS. Size: 9mm</td>
<td>Vimentin and CD 99-positive, S-100, GFAP, CAM 5.2, CK 7, Melan-A, CD 1a, CD 20, CD 21, CD 30, CD 35, CD 45, CD 43, and CD 68-negative. MIB 1 &gt;10% EWS-FLI1 negative by FISH</td>
<td>Trans sphenoidal debulking, followed by Gamma Knife RT for residual tumor and CT</td>
<td>Diagnosed to have ES of distal left fibula 2m later with multiple metastases involving spine, ribs and extremities. NED at 12m.</td>
</tr>
<tr>
<td>2</td>
<td>Idrees et al, 2005</td>
<td>46/M</td>
<td>Headache, nausea, and vomiting. Right ophthalmoplegia, right ptosis, perception of light in right eye positive and V1, V2 involvement of 2 weeks duration.</td>
<td>T1-W isointense, heterogeneously enhancing lesion occupied the right cavernous sinus, sellar and suprasellar area. Size: 2.3 x 2.0 x 1.0 cm</td>
<td>CD99, NSE, CK (AE1/AE3), and synaptophysin-positive. CD45, CD3, CD20, desmin, MSA, SMA, NF, S-100 and Chromogranin-negative</td>
<td>Trans-sphenoidal and supraorbital craniotomy for tumor biopsy. Vincristine CT followed by RT (5400 rad)</td>
<td>NA</td>
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<td>3</td>
<td>Khusen et al, 2005</td>
<td>13/F</td>
<td>Orbital apex syndrome of 1 week duration</td>
<td>Right CS mass, extended to clivus posteriorly, SOF anteriorly and crossed midline to involve left CS, Extension into sphenoid sinus Size: 5.3 x 9.2 x 2.7 cm.</td>
<td>CD99, NSE, CK (AE1/AE3), and synaptophysin-positive. CD45, CD3, CD20, desmin, MSA, SMA, NF, S-100 and Chromogranin-negative</td>
<td>Trans-sphenoidal biopsy, followed by 3D CRT (5060 cGy) followed by 11 cycles of Adriamycin based in CT in two combinations, Autologous BMT.</td>
<td>Metastatic work up using CT scan Head &amp; Neck mass in thyroid with right neck node, underwent total thyroidectomy + ERT to thyroid bed and mediastinum Hip metastasis at 16m Death at 18m.</td>
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<tr>
<td>4</td>
<td>Attabib et al, 2006</td>
<td>48/F</td>
<td>CN 3, V1, V2, 6 involvement of 6m duration</td>
<td>Intensely enhancing lesion in left CS extending to ACF and PCF Size: 4 cm</td>
<td>CD99, synaptophysin, NSE and CD57-positive. CD34, GFAP, S-100, NF and EMA-negative EWS-FLI1 positive by RT-PCR</td>
<td>Debulking through perional craniotomy. Postoperative RT (54 Gy) followed by CT with alternative cycles of Doxorubicin, cyclophosphamide and vincristine with ifosfamide and etoposide every 3 weeks.</td>
<td>Residual tumor with no FND at 14m.</td>
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<tr>
<td>5</td>
<td>Present case</td>
<td>11m/M</td>
<td>Right CN 6 involvement and Proptosis of 10 days duration</td>
<td>Homogenously enhancing tumor in CS with extension to superior orbital fissure, compressing ICA, Temporal lobe. Size: 1.8 x 3 x 2.1 cm</td>
<td>CD99-positive. CD 45, Desmin, GFAP-negative. TdT negative EWS-FLI1 positive by RT-PCR</td>
<td>Debulking by right frontotemporal craniotomy through subtemporal approach, followed by CT-one cycle Doxorubicin, cyclophosphamide, vincristine</td>
<td>Patient died on 37th post operative day due to status epilepticus</td>
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**Abbreviations:** 3D CRT- 3 dimensional conformational RT, ACF- Anterior Cranial Fossa, BMT- Bone marrow transplantation, CK- cytokeratin, CT- Chemotherapy, CN- Cranial nerve, CS- cavernous sinus, EMA- epithelial membrane antigen, ERT- external beam radiotherapy, FISH- fluorescence in situ hybridization, FND- focal neurological deficits, GFAP- glial fibrillary acidic protein, Gy- grey, m- months, MCF- Middle cranial fossa, MRI- magnetic resonance imaging, MSA- muscle specific actin, NA- not available, NED- no evidence of disease, NF- neurofilament, NSE- neuron specific enolase, RT- Radiotherapy, RT-PCR-reverse transcriptase polymerase chain reaction, SMA- smooth muscle actin, V1- ophtalmic division of 5th CN, V2- Maxillary division of 5th CN.
ES/pPNET family tumor is aggressive in nature and warrants the time of diagnosis (4). Radical removal is not possible in cavernous sinus in view of its highly vascular nature and close association with cranial nerves, so debulking is the possible modality (4). Role of radiotherapy is mainly for the residual tumor and usual radiation is 56 Gy (5). In view of patient age and deleterious side effects of radiotherapy on developing brain we planned multiagent chemotherapy with alternating cycles of Doxorubicin, vincristine and cyclophosphamide with ifosfamide and etoposide, which had shown favorable results in previous studies (5). Unfortunately, our patient died after receiving only one cycle of chemotherapy. Bone scan, CT scan of chest, abdomen & pelvis, bone marrow aspiration, CSF cytology and MRI scan of spine should be done to rule out metastasis before initiating the treatment (3). The follow-up period in the reported cases has ranged from 12 to 18 months, with death at 18 months in one due to multiple metastases (4). Of the other two cases where follow-up is available one was doing well without evidence of disease at 12 months, whereas the other was symptom free with residual tumor at 14 months. In our case patient died on 37th post operative day with status epilepticus. The number of cases of cavernous sinus ES/ pPNETs reported is few and follow up period has been too short to draw any conclusion regarding the prognosis of these lesions.

REFERENCES