

# Primary extraosseous intracranial Ewing's sarcoma: Case report and literature review

Krishnangshu Bhanja  
Choudhury, Shyam Sharma,  
Ramesh Kothari,  
Anjali Majumder

Department of Radiotherapy,  
IPGMER and SSKM Hospital,  
Kolkata, West Bengal, India

## Address for correspondence:

Dr. Krishnangshu Bhanja  
Choudhury,  
C-11 / 4, Green Tower,  
Golf Green, Kolkata – 700 095,  
West Bengal, India.  
E-mail: krishnangshubc@gmail.  
com

## ABSTRACT

Ewing's sarcoma / peripheral primitive neuroectodermal tumors occur most often in bone and soft tissues of children and young adults. The intracranial manifestation of the disease is rare, and when present, this is often misdiagnosed with other varieties of primary brain tumors. We report such a case of extraosseous Ewing's sarcoma, which was initially suspected to be a case of meningioma in an 11-year-old girl.

**Key words:** *Extraosseous Ewing's sarcoma, extradural, intracranial*

## INTRODUCTION

Ewing's sarcoma family of tumors are a group of small round-cell neoplasms, which include Ewing's sarcoma (EWS), Primitive neuroectodermal tumor (PNET), Askins tumor, PNET of the bone, and Extraosseous Ewing's sarcoma (ESS).<sup>[1]</sup> Ewing's sarcoma / peripheral primitive neuroectodermal tumor, presumed to be neuroectodermal in origin, most often occurs in the bone and soft tissues of children and young adults. The intracranial Extraosseous Ewing's sarcoma (CNS-ESS) is extremely rare and often misdiagnosed as central nervous system PNET (c-PNET) or as other primary intracranial neoplasms.

## CASE REPORT

An 11-year-old female presented with a history of headache for one year, which increased in intensity over the last one month. She had repeated episodes of vomiting for one month and a left temporal scalp swelling, which was gradually increasing in size. There was no history

of loss of consciousness, limb weakness or seizure. On examination there was bilateral papilledema, but no other focal neurological deficits were detected. The left temporal scalp swelling was mildly tender, firm, immobile, and non-pulsatile with ill-defined margins.

The Computed Tomography Scan (CT Scan) of the brain showed a rounded, well-defined, heterogeneously hyperdense, enhancing lesion in the left temporoparietal region, with a mass effect and destruction of the left temporal bone, extending into the scalp, suggesting the possibility of a meningioma. No evidence of calcification was noted within the lesion [Figure 1]. Magnetic resonance imaging (MRI) of the brain showed a left temporal lesion, hypointense on T1, heterointense on T2, with heterogeneous enhancement [Figure 2]. The lesion measured 6.0×4.6×7.4 cm. A significant mass effect was detected with a midline shift to the right, of 15 mm. The diffusion weighted image showed mild restriction. Magnetic resonance spectroscopy showed choline and N-Acetyl Acetate peaks.

The patient underwent left temporoparietal craniotomy and decompression of the lesion. The operative findings suggested that the lesion was extradural, with erosion of bone in some areas and involvement of the overlying temporalis muscle.

The histopathological examination showed round-to-oval cells arranged in lobules, separated by a thin vascular

### Access this article online

#### Quick Response Code:



Website:  
www.ijmpo.org

DOI:  
10.4103/0971-5851.89798

channel, having vesicular nuclei, with indistinct nucleoli. Mitotic figures were seen with focal areas of necrosis. A few bony trabeculae were seen embedded in the tumor island. Fat globules seen were positive for Periodic Acid Schiff's staining. Immunohistochemistry showed focal positivity for synaptophysin and MIC-2 [Figure 3]. It was negative for CD20, CD3, Myosin, and Glial Fibrillary Acidic Protein. The overall features were compatible with a Primitive Neuroectodermal Tumor (PNET), with a possibility of Ewing's sarcoma in the temporal region. The tumor was positive for t (11; 22) (q24; q12) translocation detected by fluorescent *in situ* hybridization (FISH) in the tumor biopsy sample. The findings of further metastatic workups, including CT Scans of the thorax and abdomen and a bone scan with Technetium Tc-99m, were negative.

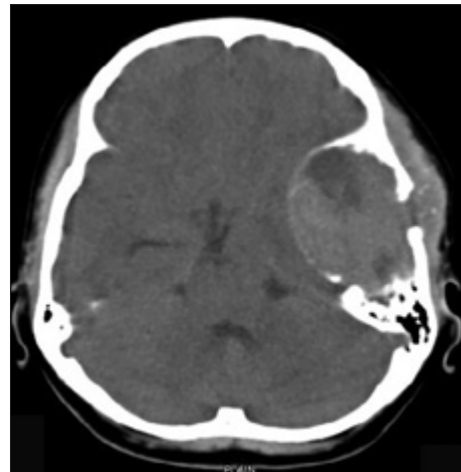
A postoperative CT scan of the brain revealed a large extradural and subdural hematoma in the left frontotemporal region, with a postoperative craniotomy defect and scalp edema. The child went on to receive 12 weeks of chemotherapy with vincristine, doxorubicin, and cyclophosphamide, alternated with ifosfamide and etoposide. Radiation with a dose of 56 Gray was prescribed at the local site. The treatment was completed with the same combination of chemotherapeutic drugs for another 24 weeks. The child is doing well and is under post treatment surveillance.

## DISCUSSION

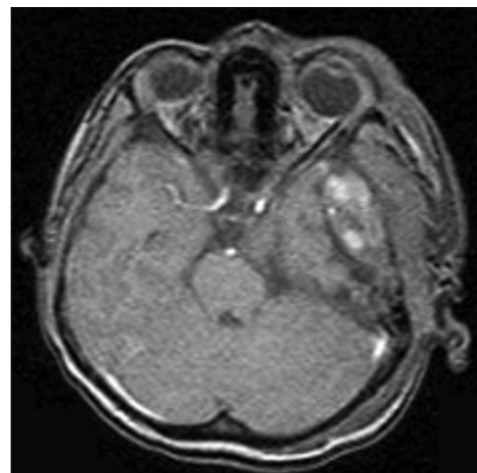
James Ewing (1866–1943) first described the tumor, establishing that the disease was different from lymphoma and other types of cancer known at that time.<sup>[2]</sup> In 1921, he described a lethal primary bone lesion that affects children and young adults and most frequently originates in the long bones (47%), pelvis (19%) or ribs (12%).<sup>[3]</sup> The skull is rarely involved, probably in less than 4% of the cases, with the frontal and parietal bones being the most commonly affected.<sup>[4,5]</sup>

Extraosseous Ewing's sarcoma (EES) has been recognized as a distinct disease entity that afflicts young adults in the second and third decades of life, with equal sex predilection. The EES commonly involves the paravertebral regions of the spine and in rare instances, these lesions arise in the intracranial compartment, where they have been commonly misdiagnosed as c-PNET, because of the similarity in their histological appearance.<sup>[6]</sup>

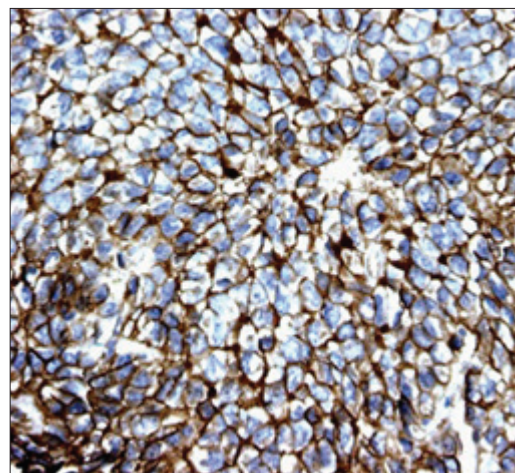
Very few cases of the central nervous system extraosseous Ewing's sarcoma (CNS-EES) have been reported in pathology literature.<sup>[6-11]</sup> *Jay et al.* was probably the first to describe a patient with an isolated posterior fossa mass



**Figure 1:** Preoperative CT scan of the brain showed a rounded, well-defined, heterogeneously hyperdense, enhancing lesion in the left temporoparietal region, with a mass effect and destruction of the left temporal bone extending into the scalp, suggesting the possibility of meningioma. No evidence of calcification was noted within the lesion



**Figure 2:** Preoperative MRI of the brain showed a left temporal lesion, hypointense on T1, heterointense on T2, with heterogenous enhancement



**Figure 3:** EWS / PNET's are characterized by immunoreactivity to the surface antigen CD99 / MIC2, which is expressed in up to 97% of the cases

that histologically resembled a medulloblastoma, but demonstrated the t(11;22) (q24;q12) translocation, which confirmed CNS-EES.<sup>[7]</sup> As far as our knowledge goes, this is the seventh case we are reporting.

Diagnosis requires a histopathological examination, immunohistochemistry, and cytogenetics. The differential diagnosis of an intracranial round cell tumor is primitive neuroectodermal tumor (neuroblastoma), lymphoma, rhabdomyosarcoma, and Ewing's sarcoma.

The histological examination reveals that these tumors are composed of small, undifferentiated neuroectodermal cells and frequently demonstrate immunohistochemical and/or electron microscopic features of glial or neuronal differentiation.<sup>[12]</sup> Recent advances in the molecular classification has allowed a clear pathological distinction between c-PNET and CNS-EES. CNS-EES is known to demonstrate in 97% of the patients, a strong membrane expression of the MIC-2 gene product, designated CD99, which is specifically recognized by the monoclonal antibodies O13 and HBA71.<sup>[13-16]</sup> In addition, the chromosomal translocation t(11, 22)(q24;q12), detected by FISH, is found in more than 90% of EES. This nonrandom translocation is not found in the central primitive neuroectodermal tumors (c-PNET) such as the medulloblastoma and supratentorial PNET.

Although, CNS-EES is histologically similar to c-PNETs such as the medulloblastoma, it differs significantly in clinical behavior, treatment, and prognosis.<sup>[17,18]</sup> The treatment options available for patients with CNS-EES are similar to those of EES elsewhere in the body and include multimodality treatment comprising of surgery, chemotherapy, and radiation. Patients with c-PNET also require surgery; however, the chemotherapeutic and radiation therapy protocols differ from those used for CNS-EES. Chemotherapy forms the backbone of the multimodality treatment of localized Ewing's sarcoma. Multiagent chemotherapy regimens including cyclophosphamide, ifosfamide, doxorubicin, dactinomycin, and etoposide have been shown to be effective in localized Ewing's sarcoma, in various trials.<sup>[19,20]</sup> The primary treatment for localized ESS consists of neoadjuvant chemotherapy, with a combination of vincristine, doxorubicin, and cyclophosphamide, alternating with ifosfamide and etoposide, given for 12 to 24 weeks, followed by definitive local treatment of surgery or radiation, or surgery and postoperative radiation directed at the primary site.<sup>[21]</sup> The treatment is completed with administering chemotherapy with a similar combination for a total of 36 to 49 weeks. Because of the small number of patients, the prognosis of CNS-EES is not clearly known, although it has been suggested

that patients with EES that arises from structures within or around the CNS may have a more favorable outcome than patients with c-PNET.<sup>[22]</sup>

## REFERENCES

1. Toskos M. Peripheral primitive neuroectodermal tumors. diagnosis, classification and prognosis. *Perspect Pediatr Pathol* 1992;16:27-98.
2. Ewing J. Diffuse endothelioma of bone. *Proc N Y Pathol Soc* 1921; 21: 17-24.
3. Falk S, Alpert M. The clinical and Roengen aspects of Ewing's sarcoma. *Am J Med Sci* 1965;250:492-508.
4. Bhansali SK, Desai PB. Ewing sarcoma observation on 107 cases. *J Bone Joint Surg.* 1963; 45: 541–553.
5. Steinbok P, Flodmark O, Norman MG, Chan KW, Flyer CJ. Primary Ewing's sarcoma of the base of the skull. *Neurosurgery* 1986;19:104-7.
6. Dedeurwaerdere F, Giannini C, Sciot R, Rubin BP, Perilongo G, Borghi L, *et al.* Primary peripheral PNET / Ewing's sarcoma of the dura: A clinicopathologic entity distinct from central PNET. *Mod Pathol* 2002;1:673-8.
7. Jay V, Zielenska M, Lorenzana A, Drake J. An unusual cerebellar primitive neuroectodermal tumor with t(11;22) translocation: pathological and molecular analysis. *Pediatr Pathol Lab Med* 1999;16:119-28.
8. Mazur MA, Gururangan S, Bridge JA, Cummings TJ, Mukundan S, Fuchs H, *et al.* Intracranial Ewing's sarcoma. *Pediatr Blood Cancer* 2005;45:850-6.
9. Katayma Y, Kimura S, Watanabe T, Yoshino A, Koshinaga M. Peripheral-type primitive neuroectodermal tumor arising in the tentorium: Case report. *J Neurosurg* 1999;90:141-4.
10. Antunes NL, Lellouch-Tubiana A, Kalifa C, Delattre O, Pierre-Kahn A, Rosenblum MK. Intracranial Ewing sarcoma / 'peripheral' primitive neuroectodermal tumor of dural origin with molecular genetic confirmation. *J Neurooncol* 2001;51:51-6.
11. Papotti M, Abbona G, Pagani A. Primitive neuroectodermal tumor of the meninges: An histology, immunohistochemical, ultrastructural and cytogenetic study. *Endocr Pathol* 1998;3:275-80.
12. Rorke LB, Hart MN, McLendon RE. Supratentorial primitive neuroectodermal tumor (PNET). In: Kleihues PCW, ed. *Tumors of the nervous system.* Lyon, France: IARC Press; 2000. p.141-4.
13. Sandberg AA, Bridge JA. Updates on cytogenetics and molecular genetics of bone and soft tissue tumors: Ewing sarcoma and peripheral primitive neuroectodermal tumors. *Cancer Genet Cytogenet* 2000;123:1-26.
14. Gu M, Antonescu CR, Guiter G, Huvos AG, Ladanyi M, Zakowski MF. Cytokeratin immunoreactivity in Ewing's sarcoma: prevalence in 50 cases confirmed by molecular diagnostic studies. *Am J Surg Pathol* 2000;24:410-6.
15. Fellingner EJ, Garin-Chesa P, Triche TJ, Huvos AG, Rettig WJ. Immunohistochemical analysis of Ewing's sarcoma cell surface antigen p30 / 32MIC2. *Am J Pathol* 1991;139: 317-25.
16. Ladanyi M, Lewis R, Garin-Chesa P, Rettig WJ, Huvos AG, Healey JH, *et al.* EWS rearrangement in Ewing's sarcoma and peripheral neuroectodermal tumor: Molecular detection and correlation with cytogenetic analysis and MIC2 expression. *Diagn Mol Pathol* 1993;2:141-6.
17. Schmidt D, Hermann C, Jurgens H, Harms D. Malignant peripheral neuroectodermal tumor and its necessary distinction from Ewing's sarcoma: A report from Kiel pediatric tumor registry. *Cancer* 1991;68:2251-9.
18. Dirks PB, Harris L, Hoffman HJ, Humphreys RP, Drake JM, Rutka JT. Supratentorial primitive neuroectodermal tumors in

- children. *J Neurooncol* 1996;29:75-84.
19. Subbiah V, Anderson P, Lazar AJ, Burdett E, Raymond K, Ludwig JA. Ewing's sarcoma: Standard and experimental treatment options. *Curr Treat Options Oncol* 2009;10: 126-40.
  20. Paulussen M, Craft AW, Lewis I, Hackshaw A, Douglas C, Dunst J, *et al.* Results of the EICESS-92 Study: Two randomized trials of Ewing's sarcoma treatment – cyclophosphamide compared with ifosfamide in standard risk patients and assessment of benefit of etoposide added to standard treatment in high-risk patients. *J Clin Oncol* 2008;26:4385-93.
  21. Grier HE, Krailo MD, Tarbell NJ, Link MP, Fryer CJ, Pritchard DJ, *et al.* Addition of ifosfamide and etoposide to standard chemotherapy for Ewing's sarcoma and primitive neuroectodermal tumor of bone. *N Engl J Med* 2003;348: 694-701.
  22. Hadfield MG, Quezado MM, Williams RL, Luo VY. Ewing's family of tumors involving structures related to the central nervous system: A review. *Pediatr Dev Pathol* 2000;3: 203-10.

**How to cite this article:** Choudhury KB, Sharma S, Kothari R, Majumder A. Primary extraosseous intracranial Ewing's sarcoma: Case report and literature review. *Indian J Med Paediatr Oncol* 2011;32:118-21.  
**Source of Support:** Nil, **Conflict of Interest:** None declared.