Primary, Dural-Based, Ewing Sarcoma in a Pediatric Patient: Presentation of a Rare Tumor Entity with Literature Review

Ali GULER (glerali@yahoo.com)
Ankara Bilkent City Hospital, Department of Neurosurgery
Yigit Can SENOL
Ankara Bilkent City Hospital, Department of Neurosurgery

Case Report

Keywords: Primary, Cerebral, Ewing Sarcoma, Cranioplasty

Posted Date: May 25th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1614033/v1

Abstract

Primary Ewing's sarcoma originating from the calvaria bone and/or underlying Dural involvement has been reported relatively rarely in the literature. Those originating from the dura and invading the bone above it in both directions, both towards the brain parenchyma and via the dura, are even rarer.

CASE DESCRIPTION: We present a case of a 14-year-old girl with no known focal neurological deficit who presented with the complaint of vertigo for only 2 months. In neuroradiological examination, The left frontoparietal region of the brain showed the presence of a tumor originating from the dura, invading both bone and brain parenchyma. No other tumor location was discovered after radiological examination. Since the patient had a shift in the brain and progressive loss of strength on the right side, the patient was taken to surgery for tumor excision. The frozen result sent per-operatively was consistent with a round blue cell tumor. Adjuvant chemotherapy treatment was given to the patient after the definitive pathology report was compatible with Ewing's sarcoma.

CONCLUSION: The patient had an uneventful neurological recovery without permanent neurological deficit. When the patient was kept under close clinical and radiological surveillance one year after the operation, no recurrence of the disease was observed. Bone marrow biopsy results and pet computerized tomography results confirmed the case of primary intracerebral Ewing sarcoma. This case illustrates an extremely rare location of primary Ewing's sarcoma with a set of clinical signs and symptoms extremely rare for this location of this rare disease entity.

Introduction

Ewing sarcoma (EWS)/primitive neuroectodermal Tumor (PNET) is a highly malignant small round cell tumor that predominantly affects bone and soft tissue. Ewing sarcoma (EWS) is currently considered the second most common pediatric primary bone malignancy, with osteosarcoma being the most common[1–6]. It originates mainly from the long bones or the axial skeleton, including the pelvis, ribs, and vertebrae. It is defined as an undifferentiated, malignant, small round cell tumor that prefers bone and soft tissues. James Ewing first described it as "diffuse bone endothelioma" in 1921. Primary intracranial EWS has been demonstrated extremely rarely. It is considered a distinct subtype of extraosseous EWS, based on the fact that its most common origin is the dura mater and is estimated to constitute 1–4%[7–8].

Ewing sarcoma breakpoint region 1 (EWSR1) and several common gene fusions are well known. In this tumor. Approximately 85–90% of EWS/PNETs contain a t(11;22) chromosomal translocation, 10–15% have a t(11;22) chromosomal translocation. Considering the fact that it is primary intracranial, EWS is an entity that is not very well and comprehensively defined in the literature clinically and radiographically. In this case, we present a case with its symptoms, histopathological features, and follow-up results.

Historical Background

The 14-year-old girl was seen several times by the general pediatrician for dizziness for 2 months. She. After the patient had complaints of numbness and numbness on the right side for the past 1 week and weakness on the right side, magnetic resonance imaging of the patient showed a mass lesion (Fig. 1). Dural based brain parenchyma is under pressure and causing shift. A case of meningioma with heterogeneous enhancement and thought to be Dural origin was considered the patient was started on anti-epileptic therapy, levetiracetam. No tumor was found in a different part of the body in the preoperative abdominal ultrasonography and computed tomography examinations. The cranial computerized tomography showed that the bone or dura eroding the bone developed hemiparesis on the right side of the patient while he was in the hospital. The patient was taken to an urgent surgery.

Management And Prognosis

With a bi-coronal skin incision, a wide fronto-parieto-occipital craniotomy flap crossed to the opposite side was used. Per-operative image of the mass showed Dural-based and penetrating brain parenchyma, Due to its proximity to the sagittal sinus, preoperative magnetic resonance venography (MRV) imaging was performed on the patient (Fig. 2). MRV showed sagittal sinus was intact and functional. The mass was excised gross totally and the tissues around the intact sagittal sinus were left (Fig. 3). The Dural parts and bone to which the mass was attached were excised and sent to pathological examination. Per-operative histopathological examination result was compatible with malignancy consisting of small blue round cells. Duraplasty and cranioplasty were performed in the same session using synthetic dura graft (Duragen, Integra, USA) and titanium mesh. Postoperative contrast enhanced MRI revealed that the mass was gross totally excised and there was no intracranial hemorrhage (Fig. 4**).** Preoperative right-sided weakness continued in the postoperative period, and intravenous 3% sodium solution was given for 1 week as anti-edema treatment. After the anti-edema treatment, the patient's neurological deficits improved at the end of the 1st week.

At the end of the 3rd postoperative week, the patient's pathological examination was completed and the EWS was confirmed. Bone marrow biopsy and peripheral blood smear tests were performed on the patient. However, no tumor was detected in any part of his body. The patient was given adjuvant chemotherapy. The patient, who did not have any neurological complaints, came to the 6th month follow-up. Contrast-enhanced cranial magnetic resonance imaging was performed (Fig. 5). No recurrence was detected in MRI, and the patient was included in the follow-up list after receiving the consultations of the pediatric hematology and oncology departments. No additional chemotherapy or radiotherapy was given.

Results

The patient received additional therapy consisting of chemotherapy and radiotherapy as is commonly used in patients with EWS. Chemotherapy included a combination of vincristine, cyclophosphamide, doxorubicin, and etoposide alternating with ifosfamide. No additional radiotherapy was given to the patient. Additional imaging evaluation was performed 3 months after surgery and then every 3 months

until the completion of the 1-year follow-up period. In all serial magnetic resonance scans, after intravenous contrast administration, no pathological contrast administration that could be sensitive to possible local tumor recurrence was detected. Neurological examination was repeated at each follow-up, but no change was observed in the neurological examination.

Cranioplasty of the patient was performed in the same session, since it was difficult to repair the resected bone flap with allogeneic graft material due to the toxicity of chemotherapy reported in previous cases[10]. Cranioplasty was performed by placing a titanium mesh. However, as reported in other cases, antiedema treatment was continued for 1 week in the postoperative period. The patient was followed up for 1 year postoperatively.

Discussion

EWS/PNET is a malignant tumor of bone and soft tissues. This pathology, which occurs in childhood and young adults, is seen equally in men and women. This aggressive neoplasm is a treatable malignancy with a good prognosis in patients younger than 16 years of age[11].

Primary EWS is relatively rare. Although EWS looks the same as PNET under the microscope, these tumors differ in histogenesis, molecular features, and clinical behavior. They described the imaging features of the primary intracranial EWS. Dural adhesion, containment, lobularity, and intense diffuse enhancement were consistent features of intracranial EWS, according to their review[12]. Histologically, they are like other small round blue cell tumors in general and PNET in particular and are often misdiagnosed as secondary. Immunohistochemistry for CD99 encoded by the MIC2 gene is usually positive in the primary intracranial EWS and in most cases helps distinguish it from PNET that does not express this antigen. However, it is worth noting that this antigen is not entirely specific and can be encountered in several other CNS tumors, including hemangiopericytoma.

Recent advances in the molecular classification of PNET and intracranial EWS have allowed a clear pathological distinction between these 2 entities. It shows diagnostic chromosomal translocations involving a fusion of the intracranial EWS with a member of the EWS gene with a member of the Ets family of transcription factors, leading to expression of chimeric fusion oncoproteins. This characteristic feature is not found in PNET. Instead, the most common molecular abnormalities involve isochromosome 17q and myc gene amplifications in patients with medulloblastoma or, less commonly, supratentorial PNET[13].

Our case shows radiological and histological features similar to several primary intracranial EWS cases previously described in the literature. No tumor was seen in chest, abdomen, or pelvis on computed tomography. In addition, bilateral bone marrow biopsies and technetium-99m bone scan were negative, confirming the case was primary EWS.

Conclusion

Intradural and concurrent extradural extension with erosion of adjacent frontal and parietal bone associated with Dural invasion and intraparenchymal extension is an extremely rare condition for primary EWS. The overall clinical scenario is further complicated by the rare combination of clinical and neurological manifestations that lead to the diagnosis of the disease. The aim of this article is to compile the cases of primary intracranial EWS previously reported in the literature and to compare them with their results, to emphasize the fact that early diagnosis and effective treatment strategy of primary EWS is imperative and highly recommended to achieve a good overall outcome.

More specifically, regarding the contribution of our article to the scientific community, we would like to talk about some of the features of our case compared to other previously described cases in the literature. Unlike other cases, the first clinical symptom in our case was hemiparesis. Due to the rapid development of this focal neurological deficit seen with the anatomical localization of the tumors, our patient had to be operated without pre-operative tumor investigation. The differences are as follows (Table 1.). Based on a detailed MEDLINE search. It has been well reviewed in a recent article[10].

Declarations

Ethics approval and consent to participate: An informed consent was taken from the child's parents.

Consent for publication: Permission for publication was obtained from her family.

Availability of data and materials: The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement: All of the authors report that there are no known conflicts of interest associated with this publication concerning the materials and methods used or the finding specified in this paper and report no disclosure.

Authors' contributions: All authors contributed equally to the work**.**

Acknowledgements: Not applicable.

Author's information: Not applicable.

ETHICS DECLARATION STATEMENT

Approval was obtained from the ethics committee of University C. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

References

1. Jay V, Zielenska M, Lorenzana A, et al. An unusual cerebellar primitive neuroectodermal tumor with t(11;22) translocation: pathological and molecular analysis. Pediatr Pathol Lab Med. 1999;16:119–128.
2. Katayama Y, Kimura S, Watanabe T, et al. Peripheral-type primitive neuroectodermal tumor arising in the tentorium: case report. J Neurosurg. 1999;90:141–144.
3. Papotti M, Abbona G, Pagani A, et al. Primitive neuroectodermal tumor of the meninges: an histology, immunohistochemical, ultrastructural and cytogenetic study. Endocr Pathol. 1998;3: 275–280.
4. Dedeurwaerdere F, Giannini C, Sciot R, et al. Primary peripheral PNET/Ewing's sarcoma of the dura: a clinicopathologic entity distinct from central PNET. Mod Pathol. 2002;1:673–678.
5. Mazur M, Gururangan S, Bridge J, et al. Intracranial Ewing's sarcoma. Pediatr Blood Cancer. 2005;45:850–856.
6. Antunes NL, Lellouch-Tubiana A, Kalifa C, et al. Intracranial Ewing sarcoma/'peripheral' primitive neuroectodermal tumor of dural origin with molecular genetic confirmation. J Neurooncol. 2001;51:51–56.
7. Yang MJ, Whelan R, Madden J, et al. Intracranial Ewing sarcoma: four pediatric examples. Childs Nerv Syst. 2018;34:441-448.
8. Salunke PS, Gupta K, Malik V, et al. Primary Ewing's sarcoma of cranial bones: analysis of ten patients. Acta Neurochir. 2011;153:1477-1485.
9. Turc-Carel C, Aurias A, Mugneret F, et al. Chromosomes in Ewing's sarcoma. I. An evaluation of 85 cases and remarkable consistency of t(11;22)(q24;q12). Cancer Genet Cytogenet. 1988;32: 229–238.
10. Panagopoulos D, Themistocleous M, Apostolopoulou K, Sfakianos G. Primary, Dural-Based, Ewing Sarcoma Manifesting with Seizure Activity: Presentation of a Rare Tumor Entity with Literature Review. World Neurosurg. 2019 Sep;129:216-220.
11. Ahmad R, Mayol B, Davis M, et al. Extraskeletal Ewing's sarcoma. Cancer. 1999;85:725–731
12. Kazmi SA, Perry A, Pressey JG, Wellons JC, Hammers Y, Palmer CA. Primary Ewing sarcoma of the brain: a case report and literature review. Diagn Mol Pathol. 2007 Jun;16(2):108-11.
13. Jay V, Squire J, Zielenska M, et al. Molecular and cytogenetic analysis of a cerebellar primitive neuroectodermal tumor with prominent neuronal differentiation: detection of MYCN amplification by differential polymerase chain reaction and Southern blot analysis. Pediatr Pathol Lab Med. 1995;5:733–744

Table

Table-1 Review of Demographic, Neurological and Location Characteristics of Previously Referred Pediatric Cases of Primary Sarcoma Ewing

Data	All Patients	Our Patient
Age(Median) years	15	14
Sex	27 Male – 21 Female	Female
Acute subacute mode of installation	%58	(+)
Elevation of intracranial pressure	%50	(+)
Cranial nerve palsies	%27	(-)
Seizure	%9-13	(-)
Supratentorial Location	%77-83	(+)
Greatest Tumor Diameter	47-51mm	55mm

Figures

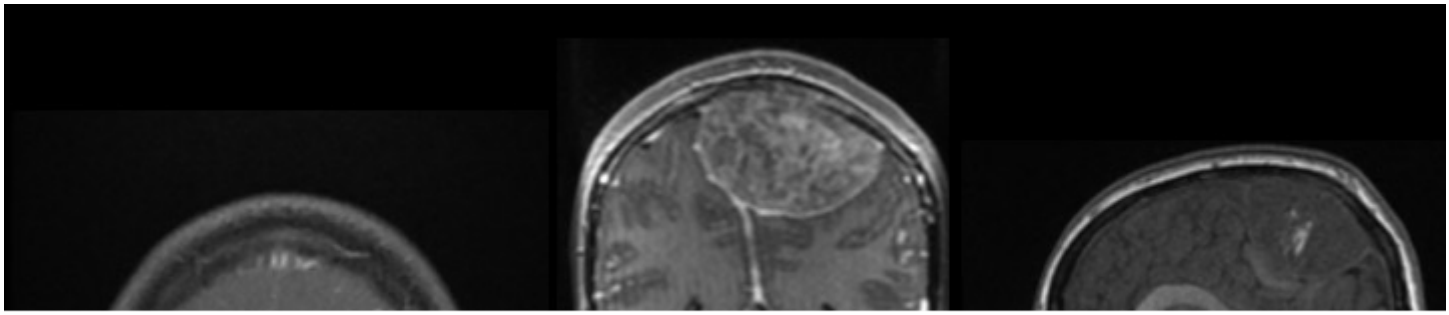

Figure 1

A: In the t1 section with axial contrast, a lesion close to the sinus with the widest diameter of 55 mm is seen. B: In contrast enhanced T1 coronal section, it is seen that the mass shifts due to the compression effect. C: T1 section with sagittal contrast shows compression on the brain parenchyma and edema of the mass.

Figure 2

Magnetic Resonance Venography (MRV), Anterior posterior(A) and Lateral(B) view; Although the mass has surrounded the sagittal sinus, minimally filling is seen in the sinus.

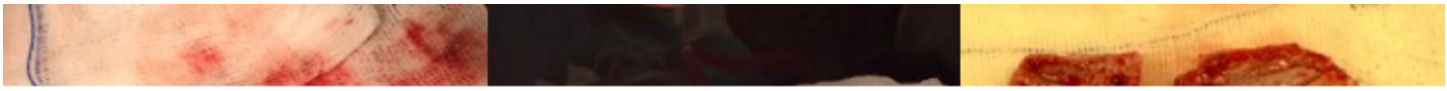

Figure 3

A: Intradural extension of the mass is seen after craniotomy B: Adherent parts of the mass to the sagittal sinus were left in order not to damage the sinus. C: Extraaxial parts of the mass that invade the bone are seen. D: It did not cause any damage to the brain parenchyma after gross total excision. Only a small piece around the sinus had to be left. E: Duraplasty was performed with the synthetic dura graft Duragen (Integra, USA). Bone structure was excised and titanium mesh was placed in the same session and cranioplasty was performed.

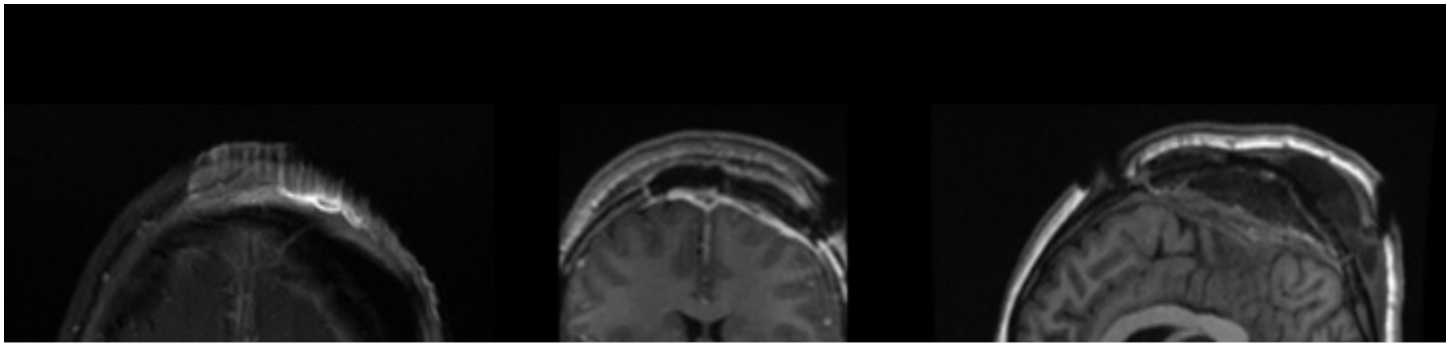

Figure 4

T1-weighted magnetic resonance imaging with intravenous contrast at the postoperative 24th hour. Axial (A), coronal (B) and sagittal (C) images show subcutaneous collection, and gross total resection of the mass is seen despite the artifact due to the titanium mesh plate.

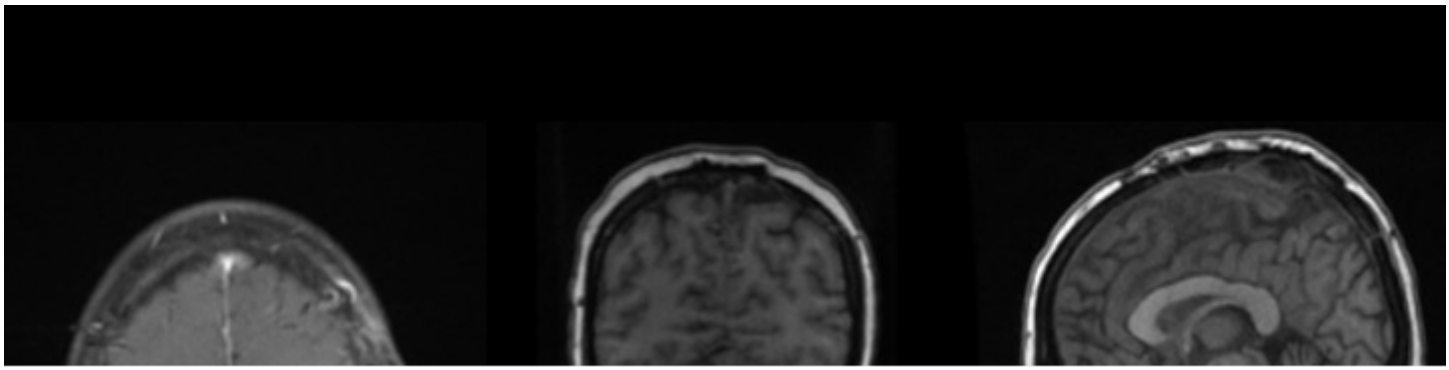

Figure 5

Axial (A), coronal (B) and sagittal (C) T1-weighted magnetic resonance images taken with intravenous contrast at the 6th month follow-up, and after adjuvant chemotherapy was given to the patient, no increase in residual mass size was observed