Primary Intracranial Ewing Sarcoma/peripheral primitive neuroectodermal tumor: A Case Report

[redacted]
Department of Radiology1Department of Radiology, Affiliated Hospital of Southwest Medical University,
feifei wang
Department of Radiology1Department of Radiology, Affiliated Hospital of Southwest Medical University,
huan huang
Department of Radiology1Department of Radiology, Affiliated Hospital of Southwest Medical University,
GuangCai Tang (✉ 2483267576@qq.com)
Affiliated Hospital of Southwest Medical University

Case Report

Keywords: Ewing sarcoma, peripheral primitive neuroectodermal tumors, diagnosis, treatment

Posted Date: February 22nd, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1374795/v1

Abstract

Background: Primary intracranial Ewing sarcoma/peripheral primitive neuroectodermal tumor (EWS/pPNET) is exceedingly rare; and easy to misdiagnose.

Case presentation: We report a case of a 23-year-old male who presented with headache and vomiting. The preoperative imaging examination of the brain revealed an irregular mass in the left parietal lobe, which was misdiagnosed as a meningioma, but the surgical specimen was diagnosed as primary intracranial EWS/pPNET. The patient underwent a total tumor resection, followed by adjuvant chemotherapy and radiotherapy. No recurrence or distant metastasis was found 18 months post-surgery. In addition, the clinical manifestations and treatment prognosis of primary intracranial EWS/pPNET were explored through a literature review.

Conclusions: When the imaging features of young patients' lesions are solid, aggressive, and unevenly enhanced masses, physicians should be aware of the possibility of primary intracranial EWS/pPNET, and if possible, gross total resection (GTR) and intensive chemotherapy and radiotherapy are recommended.

Background

Primary intracranial EWS/pPNET is exceedingly rare, undifferentiated, small, round, blue-cell neoplasms, originating from long bones and soft tissue. It is the second most common primary malignant bone tumor in children and adolescents[1-3]. The most common chromosome translocation in EWS/pPNET is chromosome t(11,22)(q24;q12) translocation, which accounts for approximately 90% of EWS/pPNET[4]. Primary intracranial location is extremely rare, with only 80 cases reported previously. Primary intracranial EWS/pPNET differs from central primitive neuroectodermal tumors (cPNET) in terms of potential genetics, treatment, and prognosis[5]. Given the rarity of primary intracranial EWS/pPNET, especially in terms of prognosis and treatment, we report our experience.

Case Presentation

A 23-year-old male presented to the hospital with a 1-week history of headache and vomiting. The patient did not exhibit neurological deficits nor signs or symptoms of systemic illness. His medical history and family history were normal. The physical examination was normal, and the other examinations and laboratory examinations were also normal. CT revealed an irregular mass with a slightly higher density with clear borders in the left parietal lobe with surrounding edema (Figure 1). MRI discovered a large space-occupying lesion of the left parietal lobe measuring 5.8×4.5×6.1 cm. The lesion displayed isointense-to-hypointense signals on a T1WI scan, and T2WI exhibited hypointense-to-hyperintense signals (Figure 1). The tumor mass appeared to have invaded and disrupted the dura mater, and after contrast, the lesion showed a heterogeneous enhancement (Figure 1). The preoperative clinical diagnosis was a meningioma, and the patient underwent surgery to remove the lesion. The tumor specimen was

grayish-white, firm, rich in blood supply, having a specific boundary with the surrounding brain tissue, and had invaded into the adjacent dura mater. The lesion was completely resected with no residue.

Histological Analysis: The tumor was composed of small round cells with hyperchromatic nuclei, scant cytoplasm, granular chromatin (Figure 2). Immunohistochemical examination revealed that the neoplastic cells were positive for CD99, FLI1, INI, Syn, and negative for S-100, myoD1, CGa, GFAP, LCA, TdT, CK, EMA, TLE (Figure 2). Moreover, the genetic analysis was positive for the EWSR1 rearrangement diagnostic of EWS and showed > 20% of split signals confirming the diagnosis of primary intracranial EWS/pPNET (Figure 2). The postoperative period was uneventful, and a CT of the thorax and abdomen was performed, as well as bone scans; all results were negative. One week after the operation, the brain MRI indicated that the lesion had been entirely removed, with no residual or recurrent tumor evidenc. The patient's parents decided to accept adjuvant therapy, including chemotherapy and focal radiation. Chemotherapy drugs included Vincristine, Cyclophosphamide, Doxorubicin, alternating with Ifosfamide and Etoposide, followed by focal radiation with a total dose of 50 Gy. During the final follow-up, 18 months after diagnosis, the patient's imaging features indicated no evidence of recurrence or metastasis.

Discussion

James Ewing was the first to report Ewing's sarcoma (EWS), and theorized that EWS originated from the vascular endothelium[6]. In 2002, the World Health Organization classified EWS and peripheral primitive neuroectodermal tumor (pPNET) as a single pathological entity[7]. EWS/pPNET is the second most common primary bone tumor after osteosarcoma in adolescents and children, which usually occurs in the long bones of limbs and pelvis and most often appears in the second decade of life. There are no significant gender differences[8, 9]. Primary intracranial locations are extremely rare, with only approximately 80 cases of primary intracranial EWS/pPNET reported in English, with a relatively high number of male patients. The clinical presentation of primary intracranial EWS/pPNET is varied and is usually determined by the tumor's site, location and size. In the reported cases, headache and vomiting are the most common clinical symptoms related to increased intracranial pressure (ICP), followed by cranial nerve damage, seizures, and a cranial mass[10, 11]. In this case, the main symptoms were headache and vomiting, which are common signs of raised ICP.

Previous studies have demonstrated that the tumor commonly exhibits iso-to-hypointense signals on T1WI scan and iso-to-hyperintense signals on T2WI scan. As far as enhancement is concerned, it can be expressed as moderate, heterogeneous, and intense enhancement, with heterogeneous enhancement being the most common[10]. The performance of this case is consistent with the literature report. However, due to the non-specific and variable radiological characteristics, it is difficult to make any confident radiological diagnosis; it is easily misdiagnosed as rhabdomyosarcoma hemangiopericytoma or metastatic tumors, especially malignant meningioma. Hence its final diagnosis depends on immunohistochemistry and gene detection.

Previous studies have reported that the MIC2 gene product (CD99) immune expression is important for EWS/PNET diagnosis [12]. The sensitivity of CD99 is 93%, and the specificity is 80%[13]. A central primitive neuroectodermal tumor (cPNET) that is negative for the MIC2 gene and CD99 can be used in the differential diagnosis[14]. However, CD99 can be found in other small blue round cell tumors, including lymphoma, neuroblastoma, and rhabdomyosarcoma [14, 15]. Thus at present, the final diagnosis must be confirmed by the translocation of EWS gene. The most common translocation is t (11, 22)(EWS-FLI-1), which accounts for >90% of EWS/pPNET. The second is ESW/ERG t(21, 22) (EWS-ERG), with less common translocations including EWS-ETV1, EWS-E1AF, and EWS-FEV, with an incidence of each case being less than 1%[16].

Primary intracranial EWS/pPNET and cPNE are both primitive ectoderm tumors. However, the cell-of-origin is different, cPNET originates from granular cells in the outer cerebellum, subventricular stromal cells of the fourth ventricle, or pineal precursor cells[17]. Primary intracranial EWS/pPNET is mainly derived from the dura mater, and the cells of its origin are not yet clear. It is theorized that it originates from neural crest cells[15] (neural crest cells are involved in meningeal embryonic development). It is important to distinguish between primary intracranial EWS/pPNET and cPNET as treatment and prognosis are entirely different. The reported[18] disease-free survival period of cPNET is short, and the long-term disease-free survival period of primary intracranial EWS/pPNET is nine months to eight years, much longer than cPNET.

Due to the rarity of primary intracranial EWS/pPNET there is a lack of understanding of treatment options for primary intracranial EWS/pPNET. The current treatment recommendation from the National Comprehensive Cancer Network (NCCN) is local treatment (surgery and/or radiotherapy) plus chemotherapy[16, 19]. A gross total resection (GTR) can improve patient quality of life, improve long-term survival and reduce local recurrence. The prognosis of patients who did not receive GTR was worse than those who received GTR [4, 10]. Chen et al. [11] reported that patients treated with partial resection had a shorter median survival time than those treated with GTR. Chemotherapy is one of the most important treatments for primary intracranial EWS/pPNET. A previous study showed that adjuvant chemotherapy improved the 5-year survival rate from 5 to 10% to >65%[17, 20]. Current systemic chemotherapy drugs include vincristine-doxorubicin-cyclophosphamide and dactinomycin alternating with ifosfamide-etoposide[10]. Local radiotherapy is generally used for tumors that cannot be removed by surgery or those with residual tumors. Chen et al. [11] reported that adjuvant radiotherapy can improve the patients' 1-year and 2-year survival rate (from 60.0% to 88.9%, 0 to 66.7%, respectively). We have observed that patients undergoing surgery, radiotherapy and chemotherapy may have the best prognosis. Michael et al. [21] reported that a young female patient that received GTR, systemic chemotherapy, and focal radiation had a survival time of 10.5 years. Our case has received surgery, radiotherapy, chemotherapy, and thus far, no indication of recurrence or metastasis.

The risk factors associated with worse prognosis in primary intracranial EWS/pPNET include tumor location, surgical margins, radiotherapy, chemotherapy, and with or without metastasis. Distant

metastasis are a poor prognostic factor, with extrapulmonary metastases having the worst prognosis[22]. However, age, gender, and the occurrence of symptoms does not influence the prognosis [4, 10-12].

Conclusion

Primary intracranial EWS/pPNET is rare and is easily misdiagnosed. Genetic evaluation is the standard for primary intracranial EWS/pPNET diagnosis. When the imaging features of young patients lesions are solid, aggressive, and unevenly enhanced masses, physicians should be aware of this rare tumor, and if possible, GTR and intensive chemotherapy and radiotherapy are recommended.

Abbreviations

ES: Ewing Sarcoma; PpNET: peripheral primitive neuroectodermal tumor; CPNET : central primitive neuroectodermal tumors ; GTR : gross total resection; CT: Computed tomography ; MRI: Magnetic resonance imaging; CD99: Anti-CD99 antibody; EWSR1: Ewing sarcoma breakpoint region 1 gene

Gy Gray absorbed dose; H&E: hematoxylin-eosin staining; ICP: increased intracranial pressure

T1WI: T1 weighted imaging; T2WI: T2 weighted imaging; MIC : MHC class chain-related Gene ;

NCCN: the National Comprehensive Cancer Network

Declarations

Acknowledgements

The authors thank the Department of Pathology, Southwest Medical University Hospital for technical support

Authors' contributions

shigang luo: drafting of the manuscript, analysis of image performance

huang huan feifei wang : acquisition of data;

guangcai tang: read and approved the fnal manuscript.

Funding

None

Availability of data and materials

The authors confrm the data and materials are available.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the Ethics Committee of the Southwest Medical University Hospital. Written informed consent was obtained from the patient prior to submission

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Competing interests

The authors declare that they have no competing interests

Author details

[1]Department of Radiology, Affiliated Hospital of Southwest Medical University, 25 Taiping Street, Jiangyang District, Luzhou City, Sichuan Province, China

References

1. Ke C, Duan Q, Yang H, Zhu F, Yan M, Xu SP, et al. Meningeal Ewing sarcoma/peripheral PNET: Clinicopathological, immunohistochemical and FISH study of four cases. Neuropathology. 2017; 37:35-44.
2. Mattogno PP, Nasi D, Iaccarino C, Oretti G, Santoro L, Romano A. First case of primary sellar/suprasellar-intraventricular Ewing sarcoma: Case report and review of the literature. World Neurosurg. 2017; 98:861-9.
3. Yim J, Lee WS, Kim SK, Kang HJ, Bae J, Park SH. Intracranial Ewing sarcoma with whole genome study. Child Nerv Syst. 2019; 35:547-52.
4. Jiang Y, Zhao L, Wang Y, Liu X, Wu X, Li Y. Primary intracranial Ewing sarcoma/peripheral primitive neuroectodermal tumor mimicking meningioma: A case report and literature review. Front Oncol. 2020; 10:528073.
5. Salunke PS, Gupta K, Malik V, Kumar N, Henke LE, Cai C, et al. Primary Ewing's sarcoma of cranial bones: analysis of ten patients. Acta Neurochir. 2011; 153:1477-85.
6. Ewing J. The classic: Diffuse endothelioma of bone. Clin Orthop Relat Res. 2006; 450:25-7.
7. Yip CM, Hsu SS, Chang NJ, Wang JS, Liao WC, Chen JY, et al. Primary vaginal extraosseous Ewing sarcoma/primitive neuroectodermal tumor with cranial metastasis. J Chin Med Assoc. 2009; 72:332-5.
8. Potratz J, Dirksen U, Jürgens H, Craft A. Ewing sarcoma: clinical state-of-the-art. Pediatr Hemat Oncol. 2012; 29:1-11.

9. Womer RB, West DC, Krailo MD, Dickman PS, Pawel BR, Grier HE, et al. Randomized controlled trial of interval-compressed chemotherapy for the treatment of localized Ewing sarcoma: a report from the Children's Oncology Group. J Clin Oncol. 2012; 30:4148.
10. El Asri AC, Benzagmout M, Chakour K, Chaoui MF, Laaguili J, Chahdi H, et al. Primary intracranial pPNET/Ewing sarcoma: diagnosis, management, and prognostic factors dilemma–a systematic review of the literature. World Neurosurg. 2018; 115:346-56.
11. Chen J, Jiang Q, Zhang Y, Yu Y, Zheng Y, Chen J, et al. Clinical features and long-term outcome of primary intracranial Ewing sarcoma/peripheral primitive neuroectodermal tumors: 14 cases from a single institution. World Neurosurg. 2019; 122:e1606-14.
12. Mishra S, Parida D, Senapati S, Patra S. Multifocal Ewing's sarcoma, presenting radiologically as extradural hematoma. Neurol India. 2012; 60(3):361.
13. Zhang Y, Li H, Li Z, Liu M, Yang L, Fan L, et al. Synthetic treatment of intracranial peripheral primitive neuroectodermal tumor with multiple metastasis: a case report. OncoTargets Ther. 2016; 9:3327.
14. Velivela K, Rajesh A, Uppin MS, Purohit AK. Primary intracranial peripheral PNET"-A case report and review. Neurol India. 2014; 62:669.
15. Kumar V, Singh A, Sharma V, Kumar M. Primary intracranial dural-based Ewing sarcoma/peripheral primitive neuroectodermal tumor mimicking a meningioma: A rare tumor with review of literature. Asian J Neurosurg. 2017; 12:351.
16. Biermann JS. Updates in the treatment of bone cancer. J Natl Compr Canc Ne. 2013; 11:681-3.
17. Abboud A, Masrouha K, Saliba M, Haidar R, Saab R, Khoury N, et al. Extraskeletal Ewing sarcoma: Diagnosis, management and prognosis. Oncol lett. 2021; 21:1-6.
18. Huang JH, Ghent F, Levingston R, Scholsem M. Intracranial Ewing Sarcoma–A case report. Surg neurol int . 2020; doi:10.25259/SNI_178_2020.
19. Casali PG, Bielack S, Abecassis N, Aro HT, Bauer S, Biagini R. Bone sarcomas: ESMO–PaedCan–EURACAN clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2018; 29:79-95.
20. Peabody TD, Attar S. Orthopaedic oncology: primary and metastatic tumors of the skeletal system. London: Springer; 2014.
21. Yang MJ, Whelan R, Madden J, Levy JMM, Kleinschmidt-DeMasters BK, Hankinson TC, et al. Intracranial Ewing sarcoma: Four pediatric examples. Child Nerv Syst. 2018; 34:441-8.
22. Haeusler J, Ranft A, Boelling T, Gosheger G, Braun-Munzinger G, Vieth V, et al. The value of local treatment in patients with primary, disseminated, multifocal Ewing sarcoma (PDMES). Cancer-Am Cancer Soc. 2010; 116:443-50.

Figures

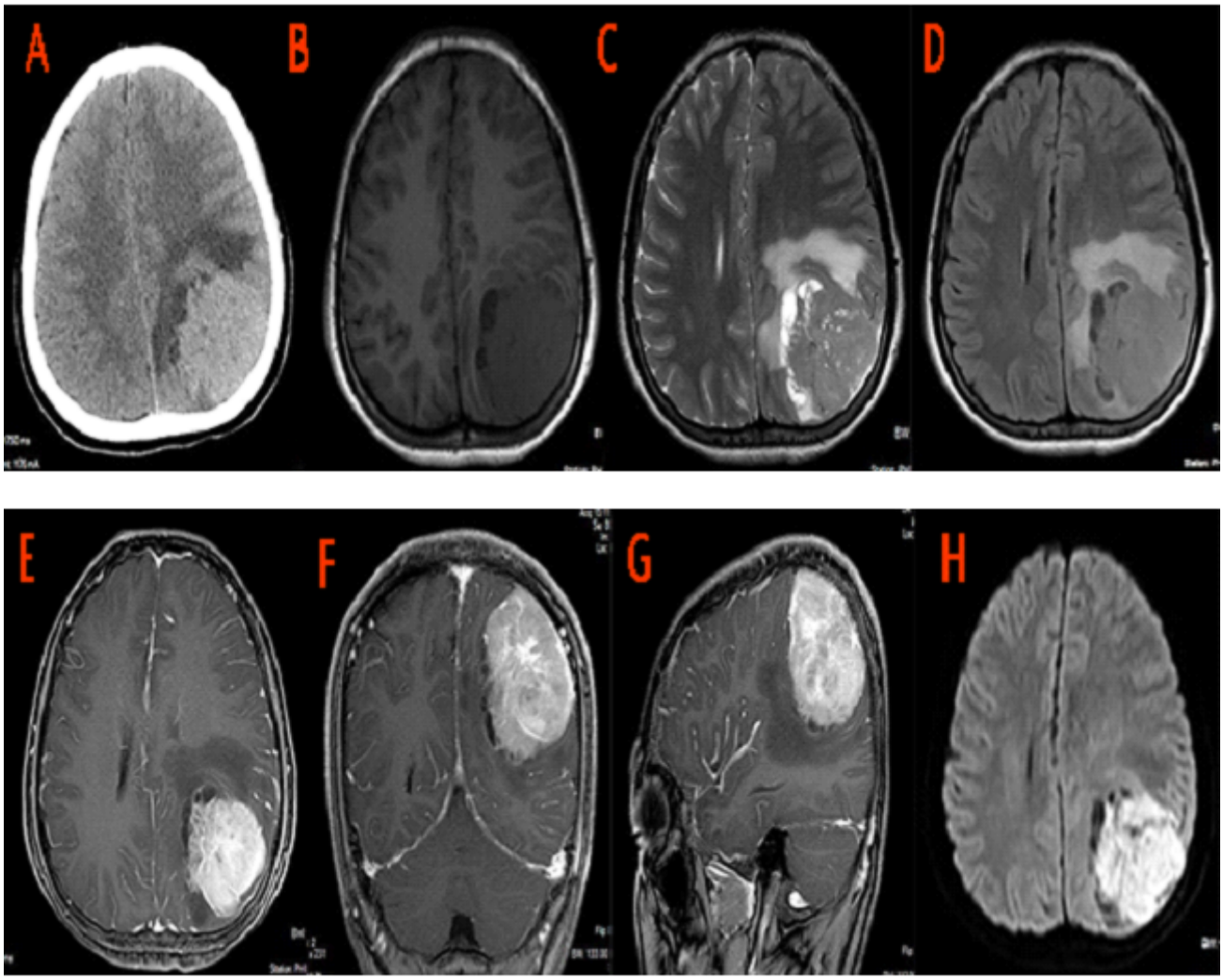

Figure 1

Preoperative CT and MRI demonstrate a large contrast-enhancing tumor in the left parietal lobe. (A) axial CT. (B) T1-weighted axial MRI. (C) T2-weighted non-contrast axial MRI. (D) Fluid attenuated inversion recovery- (FLAIR-) weighted axial MRI. (E) T1-weighted contrast-enhanced axial MRI. (F) T1-weighted contrast-enhanced coronary MRI. (G) T1-weighted contrast-enhanced sagittal MRI. (H) Diffusion-weighted imaging axial MRI.

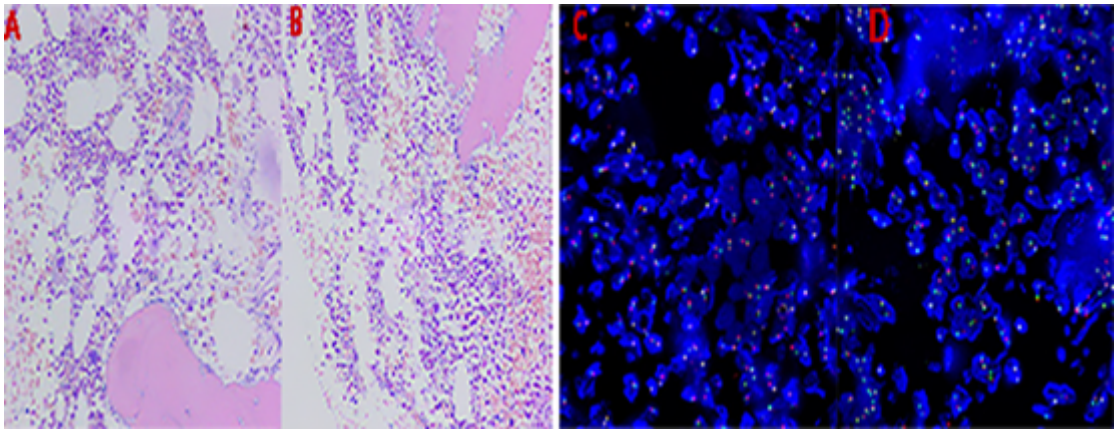

Figure 2

(A, B) H&E staining showing a small blue cell tumor. (C, D) FISH showing EWSR1 rearrangement.