Int J Clin Exp Pathol 2016;9(5):5787-5791
www.ijcep.com /ISSN:1936-2625/IJCEP0022003

Case Report

Primary intracranial neuroectodermal tumor in a pregnant woman misdiagnosed as pregnancy reaction: a case report

Chao He[1*], Jie Gong[2*], Yijie Shao[3], Leiyu Qiu[1], Ming Zhao[1]

[1]Department of Neurosurgery, Zhuji People's Hospital, Zhuji, Zhejiang, China; [2]Department of Neurosurgery, Zhejiang Hospital, Hangzhou, Zhejiang, China; [3]Department of Neurosurgery, Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China. [*]Equal contributors.

Received December 15, 2015; Accepted February 26, 2016; Epub May 1, 2016; Published May 15, 2016

Abstract: Primary intracranial neuroectodermal tumor is a very rare form of malignant neoplasm. Only few cases have been reported on the literature. Here, we report a case of a 28-years-old pregnant woman who had a chief complaint of headaches and dizziness. The patient initially misdiagnosed as having pregnancy reaction but was finally diagnosed with intracranial primary intracranial neuroectodermal tumor. The diagnosis and treatment of Primary intracranial neuroectodermal tumor is reviewed.

Keywords: Intracranial, primary intracranial neuroectodermal tumor, misdiagnosis, pregnancy reaction

Introduction

Primary neuroectodermal tumor (PNETs) are aggressive, poorly differentiated malignant neoplasm composed of small, round cells, arising in the central nervous system of adolescents and children. These tumors are associated with a peak incidence in the second decade and there is a male preponderance [1].

PNETS can be divided into two types, central PNET (cPNET, arising in the brain or spinal cord) and the peripheral Primary neuroectodermal tumor pPNET/Ewing's sarcoma family tumors, which include Ewing sarcoma, pPNET and Askin tumors [2]. pPNET usually arise within the paraverterbral region and bone. The involvement of the intracranial cavity is extremely rare. Here we describe a case of intracranial pPNET in a pregnant woman who was misdiagnosed as having pregnancy reaction.

Case report

A 28-years-old pregnant woman presented to several hospitals with a 20 days' history for headaches and dizziness. However, she was misdiagnosed as having pregnancy reaction, and no special treatment was given. Her headaches exacerbated, accompanied by projectile vomiting and changes in consciousness. She was taken to our hospital and underwent MRI of the brain. The MRI revealed a 44*58*52 mm extraaxial tumor with cystic change in the left frontotemporal region. The tumor was hypointense on T1-weighed images (**Figure 1A**) and hyperintense on T2-weighed images (**Figure 1B**), and showed multiple patchy changes with high T1 and high T2 signal. Moreover, left lateral ventricle and brainstem compression deformation were obvious. Magnetic Resonance Angiography shows the left middle cerebral artery has superior and posterior shift due to the tumor compression (**Figure 1C**). Her physical examination revealed coma, with a GCS score of 10, and dilated left pupil with no light reaction. Considering that the patient has cerebral hernia, intravenous injection of mannitol was given and an emergency craniotomy was performed.

At surgery, a solid with cystic change mass was found in the epidural space, with rich blood supply. The dura, skull and temporal muscle were all invaded by the tumor. Although it was hard to

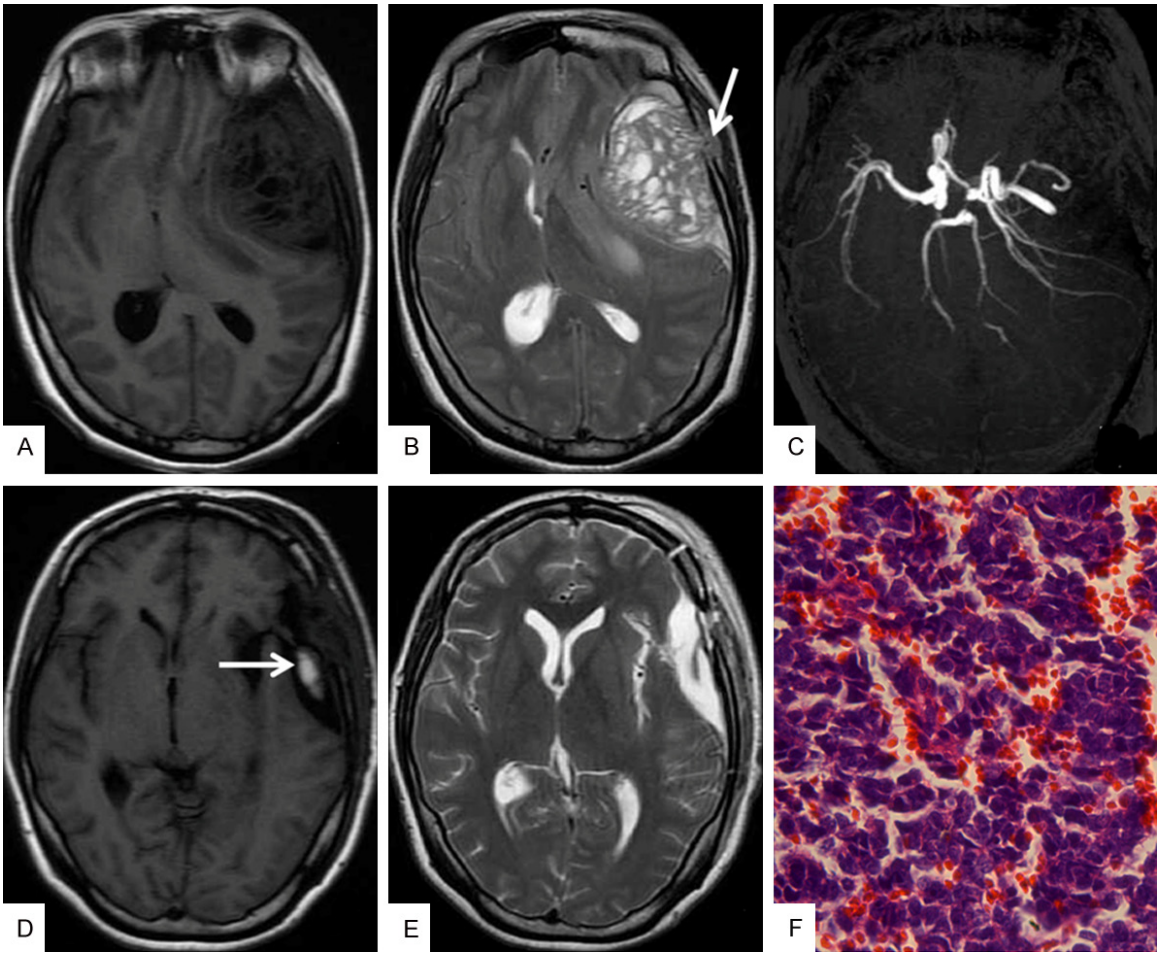

Figure 1. A: T1-weighted axial MRI reveals a 44*58*52 mm hypointense mass in the left frontotemporal region, with a well-defined margin and multiple cystic changes. B: T2-weighted axial MRI reveals a mixed hyperintense mass, which eroding the left temporal bone (slanted white arrow). C: Magnetic Resonance Angiography shows the left middle cerebral artery has superior and posterior shift due to the tumor compression. D: T1-weighted axial MRI shows mild postoperative hemorrhage (horizontal white arrow) and the preceding mass being totally removed. E: T2-weighted axial MRI shows epidural fluid accumulation in the surgical area and eased middle line shift. F: The tumor shows small, round cells with hyperchromatic nuclei, brisk mitotic figures and scant cytoplasm (Hematoxylin and Eosin, 400×).

separate the tumor from the dura, all tumor tissues were totally removed under the microscope.MRI after operation shows the mild postoperative hemorrhage and fluid accumulation in the left frontotemporal region and the preceding mass being removed (**Figure 1D**, **1E**).

Histologically, the tumor consisted of small, round, malignant cells with hyperchromatic nuclei, scant cytoplasm, and brisk mitotic figures (**Figure 1F**). Immunohistochemically, the tumor cells showed intense membrane expression of CD99 (+++), Syn (+), and the Ki-67 index was 20% (+). Thus the diagnosis of primitive neuroectodermal tumor was established.

Since the patient's decision of giving birth to her baby, neither radiotherapy nor chemotherapy was given after surgery. She received traditional Chinese medicine treatment until the baby was born about 4 weeks after surgery. 6 weeks after surgery, she received radiotherapy for 1 month. But unfortunately, MR showed tumor relapse at the end of the course of radiotherapy (a total dose of 5000 cGy in 25 fractions) (**Figure 2A-C**). PET scan also showed tumor metastases to the spine. So the patient received further chemotherapy (vincristine, cyclophosphamide and epirubicin) for 6 cycles. And MR reexamination revealed the tumor to have significantly reduced (**Figure 2D-F**). At

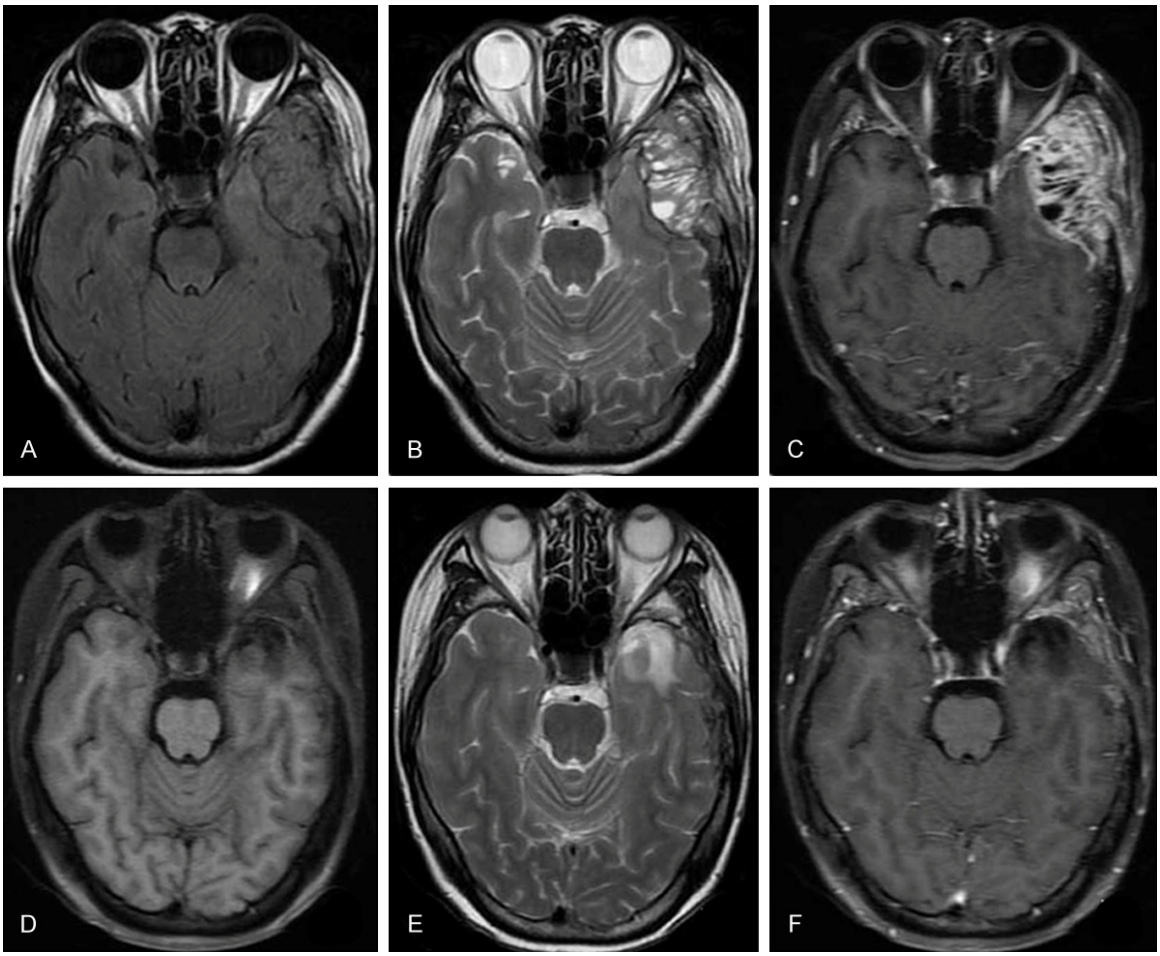

Figure 2. A: T1-weighted axial MRI reveals a 55*24 mm iso- and hypointense mass in the left temporal base, with a wide base adhering to the temporal bone. B: T2-weighted axial MRI reveals a mixed hyperintense mass, which erode left temporal bone. C: T1-weighted gadolinium-enhanced MRI image shows an irregular contrast enhancement in the tumor and part of temporal bone. D: T1-weighted axial MRI shows the mass had obviously contracted, though there is small encephalomalacia on part of the left temporal lobe. E: T2-weighted MRI shows encephalomalacia on part of left temporal lobe with high signal. F: T1-weighted enhanced axial MRI shows there is no evidence of tumor exists except a mild enhancement in part of left temporal bone.

12-months telephone follow-up, the patient had no significant symptoms and was clinically stable.

Discussion

Pregnancy reaction is a common phenomenon which arises in the pregnant women during the pregnant period due to the increased level of HCG. The symptoms include headaches, vomiting, nausea and so on. All these symptoms are similar to the symptoms which are caused by increased intracranial pressure, such as hemorrhage, brain tumor and hydrocephalus. On the other hand, intracranial neoplasm may manifest for the first time during pregnancy, because considerable tumor expansion and edema can develop with intracellular and extracellular fluid compartment expansion during pregnancy [3]. Moreover, there were some reasons that would promote tumor progression during pregnancy. First, during pregnancy, maternal immunity is reduced due to a hormonal imbalance [4]. Second, pregnancy may promote tumor growth through hormonal regulation [3]. The incidence of various primary brain tumors are higher among pregnant women, compared to age-matched nonpregnant women, with gliomas being the most common, followed by meningiomas and acoustic neuromas [5]. In our case, there were no symptoms before the patient's pregnancy, and all the tumor-related symptoms such as headaches,

nausea and vomiting appeared after pregnancy. So when she went to hospital, none of gynecologists considered she needed any examination of the brain, and no treatments were given. When she came to our hospital and underwent the MRI examination, it was too late for abortion. After careful consideration, she and her family decided to have the baby. This promoted tumor progression and might have led to her early relapse to some content. Therefore, MRI examination should be considered undertaken if a patient's symptoms did not improve. MRI is a highly sensitive and relatively safe diagnostic imaging detection method for use in pregnancy [6]. However, because of potential thermal tissue damage due to the high magnetic field, the National Radiological Protection Board recommends that pregnant women should avoid MRI examination during the first trimester [4]. Anyway, if a pregnant woman presents with severe or prolonged symptoms of intracranial hypertension, including headaches and dizziness, a systematic assessment by neurosurgeon should be considered to avoid misdiagnosis and delay of treatment.

Primary neuroectodermal tumor (PNET) is a rare, highly malignant small round cell tumor. It can be divided into 2 categories, namely peripheral PNETs (pPNET), central PNETs (cPNET) [7]. cPNET and pPNET may have common clinicopathologic features, but differ from each other in immunohistochemical staining, tumor location and chromosome translocation. On the other hand, Ewing sarcoma (ES), pPNET, and Askin tumor are the most important members of this family of tumors and are commonly collectively termed the ES/pPNET family of tumors. pPNET and Ewing's sarcoma previously belonged to different tumor types while now these two tumor types are considered the two ends of the spectrum of the same entity, which named ES family [8].

Definitive diagnosis of pPNET and Ewing's sarcoma relies on pathological assessment and the translocation of t (11; 22) (q24; q12) [9]. Although other tumors may also incidentally harbor this fusion gene, disruption of the EWS (Ewing sarcoma breakpoint region 1) gene makes the diagnosis of extraosseous Ewing sarcoma (EES)/pPNET highly probable [10].

MIC-2 (CD99) is another specific marker for pPNET and Ewing's sarcoma family and is useful for the differential diagnosis of these two types of tumor [10]. Other tumors such as meningioma, schwannoma, metastasis, lymphoma, and ependymoma should be included in the differential diagnosis.

Immunohistochemically, neuroblastoma would be positive for CD56, and a monoclonal lymphoid population would support the diagnosis of lymphoma [11]. The ependymal true rosettes or pseudorosettes and a papillary arrangement of cuboidal or columnar tumor cells are morphological characteristics of ependymoma [1]. It is worth mentioning that intracranial primitive neuroectodermal tumor is often misdiagnosed as meningioma, and chemotherapy and radiation therapy were delayed. It may significantly affect the prognosis of pPNET, for surgical treatment may require early additional chemotherapy and radiation therapy, in contrast to meningioma.

pPNETs need multimodality treatment to have a good outcome. Surgery is certainly much more important for tumor control. Wide surgical resections with negative margins at the time of primary surgery have markedly reduced local recurrences [12]. It has been shown that the degree of surgical resection is one of the most important prognostic factors [13]. Therefore, we should remove the tumor as wide as possible within safe limits, followed by chemoradiation. This may lead to improvement of prognosis [14]. Adjuvant treatment consisting of focal radiotherapy and chemotherapy are also important to improve the prognosis. Drugs used for chemotherapy include vincristine, cyclophosphamide, doxorubicin, ifosfamide, and etoposide [1]. In our case, adjuvant radiotherapy and chemotherapy were not conducted in time after surgery because of pregnancy. The tumor relapsed both locally and distantly during the course of radiotherapy after giving birth. But after further chemotherapy the tumor was significantly reduced. So we can conclude that chemotherapy plays an important role in the control of intracranial pPNET.

Furthermore, prognosis depends on several characteristics, such as types of EWS-FLI1 gene, tumor location, extension, resectability, and the presence of metastases at the time of diagnosis [7]. pPNET is an aggressive type of tumors with a high incidence of recurrence and metastases [15], so follow up should be undertaken routinely in order to find recurrence or metastasis as soon as possible. Salvage che-

motherapy and radiotherapy in patients with recurrence may help to control the disease effectively [14].

Intracranial EES/pPNET is an extremely rare entity. Intracranial EES/pPNET needs to be considered in the differential diagnosis of intracranial lesions. Moreover, patient's response to therapy is driven by different factors [16], so accurate diagnosis is important and may help early treatment with appreciate methods. The case presented and reviewed emphasize that we should keep in mind that also very rare, EES/pPNET must be include in the differential diagnosis of intracranial mass lesions, and prompt treatment should be performed when the diagnosis is established.

Acknowledgements

This work was supported by a grant from Zhejiang Provincial administration of Traditional Chinese Medicine (2016ZQ004).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jie Gong, Department of Neurosurgery, Zhejiang Hospital, 12 Lingyin Road, Hangzhou 310013, Zhejiang, China. Tel: +86-571-81595277; Fax: +86-571-87980175; E-mail: orchidwave@163.com

References

[1] Mobley BC, Roulston D, Shah GV, Bijwaar, KE, McKeever PE. Peripheral primitive neuroectodermal tumor/Ewing's sarcoma of the craniospinal vault: case reports and review. Hum Pathol 2006; 37: 845-53.

[2] Cole M, Parajuli S, Laske D, Goldstein L, Morrison T, Mukherjee A, Tumelty K, Tetzlaff E, von Mehren M, Inniss S. Peripheral primitive neuroectodermal tumor of the dura in a 51-year-old woman following intensive treatment for breast cancer. Am J Case Rep 2014; 15: 294-9.

[3] Sheth SS, Sheth KN. Treatment of neurocritical care emergencies in pregnancy. Curr Treat Options Neurol 2012; 14: 197-210.

[4] Yoshida M, Matsuda H, Furuya K. Successful Prognosis of Brain Abscess during Pregnancy. J Reprod Infertil 2013; 14: 152-5.

[5] Stevenson CB, Thompson RC. The clinical management of intracranial neoplasms in pregnancy. Clin Obstet Gynecol 2005; 48: 24-37.

[6] Lu CH, Chang WN, Lui CC. Strategies for the management of bacterial brain abscess. J Clin Neurosci 2006; 13: 979-85.

[7] Gessi M, von Bueren A, Treszl A, zur Mühlen A, Hartmann W, Warmuth-Metz M, Rutkowski S, Pietsch T. MYCN amplification predicts poor outcome for patients with supratentorial primitive neuroectodermal tumors of the central nervous system. Neuro Oncol 2014; 16: 924-932.

[8] Yan Y, Xu T, Chen J, Hu G, Lu Y. Intraspinal Ewing's sarcoma/primitive neuroectodermal tumors. J Clin Neurosci 2011; 18: 601-6.

[9] Furuno Y, Nishimura S, Kamiyama H, Numagami Y, Saito A, Kaimori M, Nishijima M. Intracranial peripheral-type primitive neuroectodermal tumor. Neurol Med Chir (Tokyo) 2008; 48: 72-6.

[10] dos Santos Rubio EJ, Harhangi BS, Kros JM, Vincent AJ, Dirven CM. A primary extraosseous Ewing sarcoma in the cerebellopontine angle of a child: review of relevant literature and case report. Neurosurgery 2010; 67: E1852-6.

[11] Zhao M, Zhang B, Liang F, Zhang J. Primary spinal intradural extraskeletal Ewing sarcoma mimicking a giant nerve sheath tumor: case report and review of the literature. Int J Clin Exp Pathol 2014; 7: 9081-5.

[12] Asano K, Kikuchi J, Munakata A, Ohkuma H, Kubo O. An infant case of intracranial peripheral-type primitive neuroectodermal tumor with long-termsurvival. Brain Tumor Pathol 2007; 24: 69-74.

[13] Müller K, Diez B, Muggeri A, Pietsch T, Friedrich C, Rutkowski S, von Hoff K, von Bueren AO, Zwiener I, Bruns F. What's in a name? Intracranial peripheral primitive neuroectodermal tumors and CNS primitive neuroectodermal tumors are not the same. Strahlenther Onkol 2013; 189: 372-9.

[14] Haresh KP, Chinikkatti SK, Prabhakar R, Rishi A, Rath GK, Sharma DN, Julka PK. A rare case of intradural extramedullary Ewing's sarcoma with skip metastasis in the spine. Spinal Cord 2008; 46: 582-4.

[15] Arpaci E, Yetisyigit T, Seker M, Uncu D, Uyeturk U, Oksuzoglu B, Demirci U, Coskun U, Kucukoner M, Isıkdogan A, Inanc M, Alkis N, Ozkan M. Prognostic factors and clinical outcome of patients with Ewing's sarcoma family of tumors in adults: multicentric study of the Anatolian Society of Medical Oncology. Med Oncol 2013; 30: 469.

[16] VandenHeuvel KA, Al-Rohil RN, Stevenson ME, Qian J, Gross NL, McNall-Knapp R, Li S, Wartchow EP, Mierau GW, Fung KM. Primary intracranial Ewing's sarcoma with unusual features. Int J Clin Exp Pathol 2015; 8: 260-74.