

# A primitive neuroectodermal tumor in an adult

## Case report of a unique location and MRI characteristics

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### Abstract

**Rationale:** Central nervous system primitive neuroectodermal tumors (CNS PNETs) mostly occur in children and present as cerebellar medulloblastoma. A few cases of PNETs occur in the cerebral hemisphere. The presence of a PNET in ventricles is extremely rare. The prognosis of CNS PNET is extremely poor, and the 5-year survival rate does not exceed 35%. In the present study, we describe the first case of a PNET in the ventricles with good prognosis.

**Patient concerns:** The case of a 36-year-old man is reported, who presented with a progressively worsening headache for 2 months.

**Diagnoses:** Magnetic resonance imaging (MRI) revealed multiple tubercula on the walls of the lateral and third ventricles. Histopathologic analysis revealed a hypercellular tumor with small round cells containing hyperchromatic nuclei and a high nucleus:cytoplasm ratio. The analysis was consistent with PNET.

**Interventions:** Radiation therapy covering the entire craniospinal axis was administered, with Temozolomide for synchronous auxiliary treatment.

**Outcomes:** The patient was follow-up for a year and showed no signs of recurrence.

**Lessons:** We present the first CNS PNET located in the ventricles with good prognosis. In this case, radiotherapy with Temozolomide auxiliary treatment presented good efficacy and safety to treat PNET. Additional studies on biomarkers may be useful in predicting personalized therapeutic response.

**Abbreviations:** CNS = central nervous system, DWI = diffusion-weighted images, EMA = epithelial membrane antigen, MRI = magnetic resonance imaging, NSE = neuron-specific enolase, PNET = primitive neuroectodermal tumor, Syn = synaptophysin.

**Keywords:** adult, brain tumor, malignant, primitive neuroectodermal tumor, ventricle

## 1. Introduction

Primitive neuroectodermal tumor (PNET) originates from primitive neuroepithelial cells and occurs in the central nervous system (CNS) and the surrounding muscles, bones, and organization. PNET is a primitive, undifferentiated small round cell malignant tumor. On the basis of different sites of the tumor, PNET is divided into central and peripheral types.<sup>[1]</sup> Central PNET mostly occurs in children and accounts for only 1% of primary CNS tumors. Ventricular primary PNET is extremely rare; to the best of our knowledge, only 4 cases of recurrence have been reported in the English literatures<sup>[2–5]</sup> In this study, we present the first case of the PNET occurring in a 36-year-old man in his ventricles. The standard treatment for CNS PNETs consists

of major surgical resection when feasible, followed by radiotherapy and chemotherapy, but survival rates are consistently lower in spite of multimodal therapy. In our case, the patient obtained 1-year progression-free survival by radiotherapy and chemotherapy. This is the first case that highly responds to radiotherapy and chemotherapy.

## 2. Case report

This is a case report and informed consent was obtained from the patient. A 36-year-old male presented to our hospital complaining of a headache, dizziness, and forgetfulness without an obvious cause. There were no sensory or cranial nerve deficits. Magnetic resonance imaging (MRI) of the brain revealed multiple nodules on the wall of the bilateral and third ventricles. The nodules were hypointense on T1-weighted images and hyperintense on T2-weighted images, with high signal on diffusion-weighted images (DWIs) (Fig. 1A–D). Postcontrast T1-weighted image showed homogeneously enhancement. Because of the depth of the lesion site and the vicinity of complex neurovascular structures, surgical access to lesions of petroclival region represented a challenge. So, this patient underwent a biopsy. Histologically, the tumor was hypercellular with small round cells containing hyperchromatic nuclei with a high nucleus:cytoplasm ratio (Fig. 2 A and B). Many cells contained irregular nuclei. According to immunohistochemical analysis, the tumor was positive for neuron-specific enolase (NSE), CD99, CD56, and S-100 expression (Fig. 2C–F) and negative for Synaptophysin (Syn), Vimentin, and epithelial membrane antigen (EMA)

Editor: Shizhang Ling.

The authors declare no of conflict of interest.

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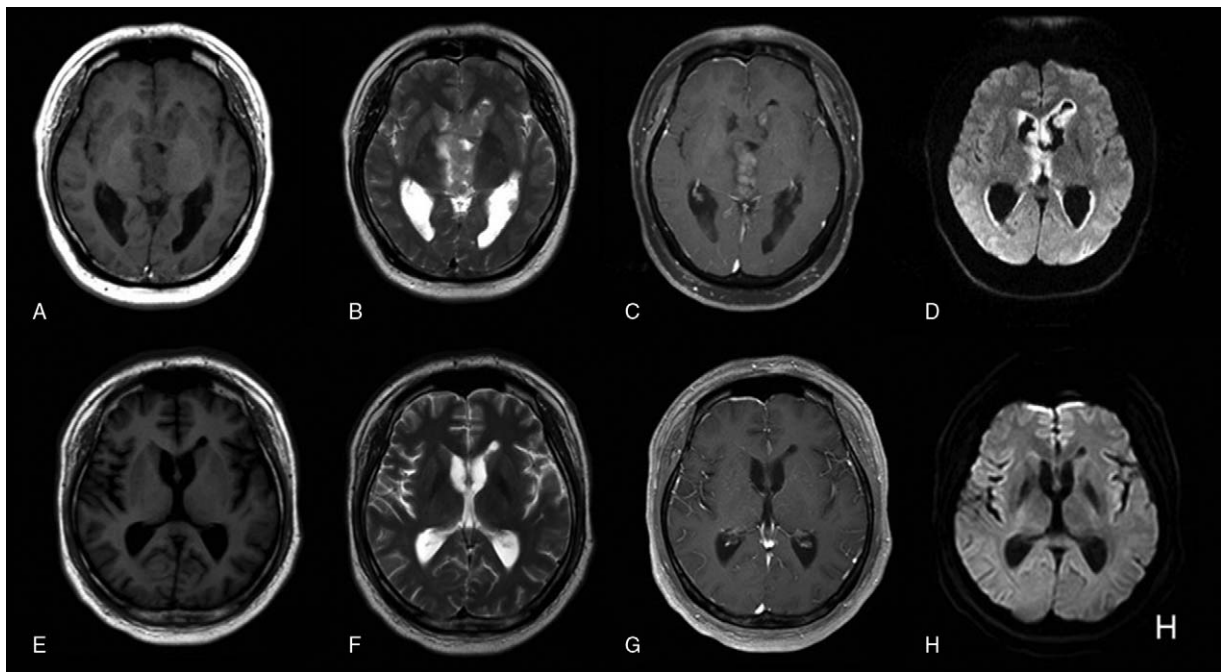
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Medicine (2018) 97:7(e9933)

Received: 11 December 2017 / Accepted: 29 January 2018

<http://dx.doi.org/10.1097/MD.00000000000009933>



**Figure 1.** (A~D) before radiotherapy and chemotherapy, the MRI revealed multiple tubercle on the wall of lateral and third ventricle, which were hypointense on T1-weighted images, hyperintense on T2-weighted images, and hyperintense on diffusion-weighted images (DWIs). (E~H) After 1 month remedy, MRI showed completely disappear of the tumor.

expression. The Ki-67 index was 70%. On the basis of these findings, this tumor was diagnosed as a PNET.

Next, radiation therapy covering the entire craniospinal axis was administered. On the third day of radiation therapy, 160 mg/day temozolomide was administered for synchronous auxiliary treatment. Radiotherapy of the entire craniospinal axis was performed 20 times. A followed MRI showed that the tumor had disappeared (Fig. 1 E–H). Further definitive management consists of cerebral local intensity modulated treatment; however, radiotherapy was suspended after the third iteration because of thrombocytopenia, so the patient received leukocyte and thrombopoietin injections. After the patient's thrombocyte count stabilized, the whole radiotherapy plan was completed. Meanwhile, temozolomide auxiliary treatment was also suspended. The patient underwent follow-up for a year and showed no signs of recurrence.

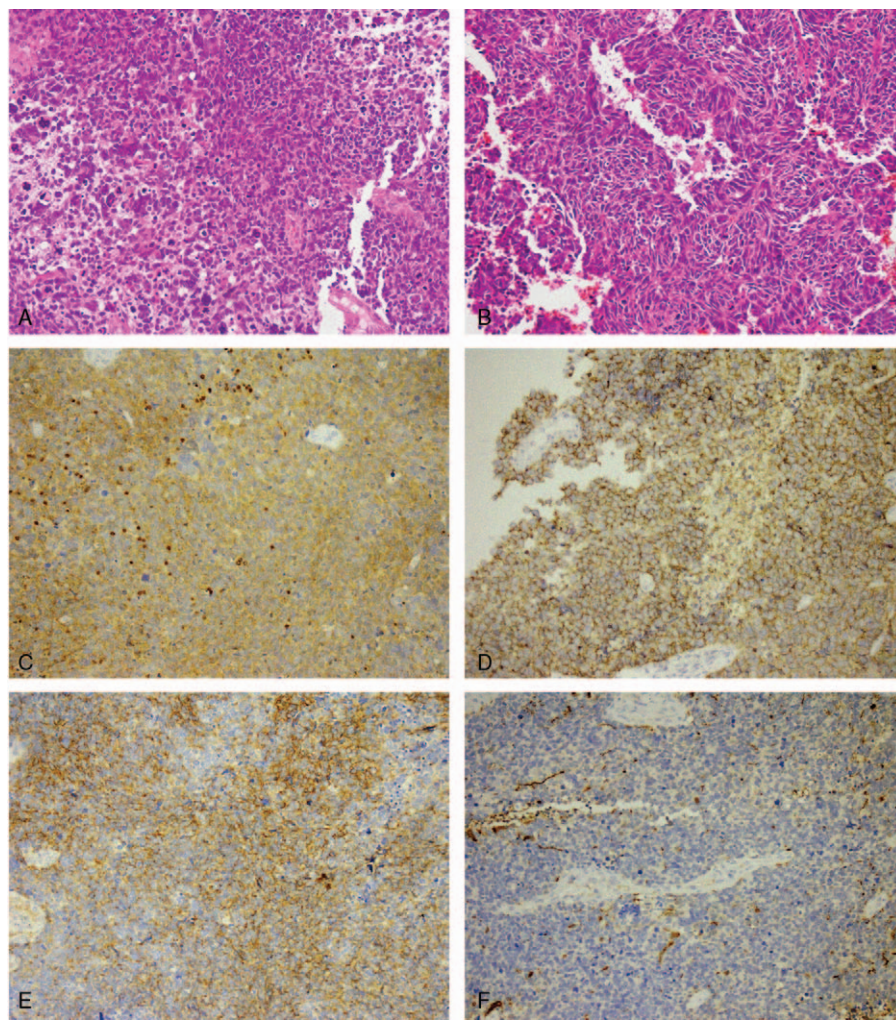
### 3. Discussion

PNET, a term coined in 1973 by Hart and Earle, is a malignant tumor that originates from primitive neuroepithelial cells and occurs in the CNS and the surrounding muscles, bones, and organization.<sup>[5]</sup> Clinically, intracranial PNET is common in children but rarely occurs in adults, accounting for only 0.46% of adult cranial tumors.<sup>[3]</sup> Intracranial PNET is often located in the cerebral hemisphere. Ašmoniene et al<sup>[3]</sup> reviewed the literature and described 57 adult PNETs. The tumor is uniformly distributed in the frontal lobe, temporal lobe, and parietal lobe, and is greater than 6cm in size. To our knowledge, only 4 cases in ventricles have been reported in the literature, but lesions in those cases presented as isolated solid mass. Patients with multiple lesions in the ventricles have not been reported in the previous published literatures. In our case, the tumor has multiple lesions and was distributed along

the ventricular wall, possibly related to the residual neuroectodermal cells near the ventricle. These cells did not differentiate into normal neurons, leading to a “primitive” tumor. The clinical manifestations are associated with the site of the tumor, which is often characterized by high cranial pressure, and may be associated with epilepsy, abnormal mental disorders, and mild hemiplegia.<sup>[6,7]</sup>

Pathologically, PNET is densely cellular with undifferentiated, small, and hyperchromatic small round cells. The nuclei are short and round or spindle-shaped with less cytoplasm. Mitosis is usually observed. The characteristic feature is “Homer-Wright rosettes.”<sup>[8,9]</sup> Immunohistochemical examination PNET may show glial, neuronal, and ependymal direction differentiation or the coexistence of multiple directions of differentiation.<sup>[10]</sup>

According to several published reports, the MRI features of AMFB have been summarized. Typically, the mass reveals a low signal intensity on T1-weighted image, and high signal intensity on T2-weighted image. The mass shows acidic enhancement after contrast MRI scan. The tumor signal is not uniform, mostly due to necrosis and cystic changes, or accompanied by hemorrhage and calcification in the tumor. Although the location of this PNET was unique, the MRI signal characteristics of this case were similar to those of tumors occurring in the brain hemisphere, such as nonperitumoral edema, and well-defined borders. One possible reason for these characteristics is that the main mechanism of PNET growth is proliferation, which is different from the infiltrative growth observed in other malignant brain tumors. The enhanced extent of the tumor was associated with the number of blood vessels in the tumor.<sup>[11]</sup> The solid composition in DWI can help identify the solid component of the tumor.<sup>[12]</sup> In this case, the tumor had high signal in DWI and obviously enhanced, which shows more densely arranged tumor cells with a rich blood supply, which has certain significance in differential diagnosis.



**Figure 2.** (A) H&E-stained biopsy revealed that this tumor was hypercellular with small round cells containing hyperchromatic nuclei and a high nucleocytoplasmic ratio. (B) High magnification shows cell clusters around a fibrinoid matrix (Homer–Wright rosettes). (C~F) Immunohistochemical examination showed positive reaction for NSE, CD56, CD99, and s-100, respectively.

A treatment strategy for PNETs has not yet been established. In accordance with the patient's clinical status, maximum resection of the tumor, chemotherapy, and radiotherapy were performed as standard procedures.<sup>[3]</sup> However, in our case, because of the special location, the treatment is different from the traditional strategies for the tumor could not be removed by surgery. Radiation of the entire craniospinal axis has also been recommended on the basis of CNS dissemination risk and improved prognosis. Gaffney recommends radiotherapy at a dose of 50 to 55 Gy for the tumor site for 7 to 8 weeks, which is in accordance with our plan.<sup>[13]</sup> Note that the tumor in our case was in the ventricles, making it easier to disseminate through the cerebrospinal fluid to the whole brain and spinal canal. So, radiotherapy of the entire craniospinal axis was administrated. Currently, the role of chemotherapy in CNS PNET treatment is controversial.<sup>[5,14,15]</sup>

The 5-year survival rate of adults with PNET is less than 35%.<sup>[3,5,16]</sup> Nonetheless, the prognosis of patient in our case is very good, because the tumor was highly sensitive to radiation and chemotherapy. Some studies discovered some molecular markers affecting resistance against radiation therapy, and Rad51 is one of these key proteins. Tumors with high expression

of either LIN28 or OLIG2 or elevated level of Rad51 were significantly associated with poorer prognosis. Predictive biomarkers could discriminate patients who are most likely to be sensitive to radiotherapy and avoid unnecessary surgery. Thus, additional studies on biomarkers may be useful in predicting personalized therapeutic response.<sup>[14–20]</sup>

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