Intracranial Peripheral-Type Primitive Neuroectodermal Tumor

—Case Report—

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Abstract

A 15-year-old man presented with headache. Magnetic resonance (MR) imaging revealed a large extraaxial tumor with cyst at the right frontotemporal region. The solid part of the tumor was homogeneously enhanced on T₁-weighted MR imaging after injection of gadolinium. Digital subtraction angiography of the external carotid artery revealed sunburst appearance corresponding to the tumor, which was fed by the right middle meningeal artery. His headache worsened and computed tomography revealed enlargement of the tumor and intracystic hemorrhage, so emergent operation was performed. At surgery, the tumor strongly adhered to the dural membrane, and was obviously extraaxial. The tumor and cyst were gross totally removed. The attachment site at the dura mater was resected. Histological examination showed solid growth of small round cells with uniform round nuclei and minimal cytoplasm. Immunohistochemical staining showed the cells were positive for MIC-2 (CD99). The MIB-1 labeling index was 53%. The histological diagnosis was peripheral-type primitive neuroectodermal tumor (pPNET). Following surgery, radiation therapy and chemotherapy were given. Ewing's sarcoma and pPNET form a family of small round cell tumors arising in the bone or soft tissue. MIC-2 is a useful marker in the differential diagnosis. Good prognosis may be attained if complete surgical excision of intracranial pPNET is achieved.

Key words: peripheral-type primitive neuroectodermal tumor, MIC-2 antigen, cystic meningioma

Introduction

Primitive neuroectodermal tumor (PNET) was first described by Hart and Earle⁶⁾ in 1973 as predominantly undifferentiated tumor of the cerebrum which did not meet the diagnostic criteria for neuroblastoma, ependymoblastoma, medulloblastoma, or pineal parenchymal tumors. PNET is a malignant, embryonal neoplasm consisting of poorly differentiated neuroepithelial cells occurring in children and young adults.⁵⁾ The first case was found in association with the ulnar nerve¹⁹⁾ but cases are known in almost every organ of the body. Recently, these tumors were divided into central nervous system PNET (cPNET), originating in the central or sympathetic nervous system, and peripheral-type PNET (pPNET), originating in the soft tissue or

bone. These two types have different prognoses.²⁾

pPNET and Ewing's sarcoma form a family of tumors with a common cytogenetic translocation t(11;22)(q24;q12) and the same highly consistent pattern of protooncogene expression. MIC-2 is a specific marker for this family and is useful in the differential diagnosis of the two types of PNETs. pPNET could theoretically arise within the intracranial cavity. However, intracranial pPNET is rare, with only 15 cases of pPNET originating in the intracranial soft tissue.^{1,3,7-11,14-18,20)}

We describe a case of intracranial pPNET mimicking a cystic meningioma.

Case Report

A 15-year-old man presented to another clinic with a

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Fig. 1 Preoperative axial T₁-weighted magnetic resonance image with gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA) (A), axial T₂-weighted image (B), and sagittal T₁-weighted image with Gd-DTPA (C) demonstrating a well-enhanced extraaxial tumor with cyst.

Fig. 2 Digital subtraction angiograms demonstrating the tumor was fed by the right middle meningeal artery with sunburst appearance.

1-week history of headache. Magnetic resonance (MR) imaging revealed a large intracranial mass lesion, and he was referred to our hospital. On admission, the patient was alert and oriented. Neurological examination revealed no deficits. Laboratory data were within normal limits. MR imaging revealed a $6.6 \times 2.6 \times 6.0$ -cm extraaxial tumor with cyst in the right frontotemporal region (Fig. 1). The

Fig. 3 Axial computed tomography scan demonstrating enlargement of the tumor and the cyst, and intracystic hemorrhage (arrow).

Fig. 4 Photomicrograph of tissue section demonstrating small round cells and mitoses. Hematoxylin and eosin stain, original magnification $\times 200$.

Fig. 5 Photomicrograph revealing diffuse immunohistochemical staining of the tumor cells for antibodies against MIC-2 protein. Original magnification $\times 200$.

solid part of the tumor was homogeneously enhanced on T₁-weighted MR imaging after injection of gadolinium. No perifocal edema was noted. Digi-

tal subtraction angiography of the external carotid artery revealed sunburst appearance corresponding to the tumor, and identified the feeding artery as the right middle meningeal artery (Fig. 2).

Preoperative embolization and surgery were planned under a diagnosis of cystic meningioma. However, his headache worsened on the 12th day of hospitalization. Computed tomography (CT) revealed enlargement of the tumor and intracystic hemorrhage (Fig. 3), so emergent operation was performed on the same day. The patient underwent right frontotemporal osteoplastic craniotomy, followed by removal of the tumor. The tumor strongly adhered to the dural membrane, and was obviously extraaxial. The cyst was readily removed leaving the arachnoid membrane intact. The tumor and cyst were gross totally removed. The attachment site at the dura mater was resected.

Histological examination showed solid growth of small round cells with uniform round nuclei and minimal cytoplasm (Fig. 4). Immunohistochemical staining showed the cells were positive for MIC-2 (CD99) (Fig. 5), carcinoembryonic antigen, synaptophysin, and S-100 protein, but negative for leukocyte common antigen and glial fibrillary acidic protein. The MIB-1 labeling index was 53%. The final diagnosis was pPNET. MR imaging of the spine was normal, and examination of the cerebrospinal fluid was negative for malignant cells. No tumor was visualized by CT of the chest and abdomen. Following surgery, we started radiation therapy and chemotherapy. He is alive with no evidence of disease at 6 months following diagnosis.

Discussion

Table 1 shows the 16 reported cases of intracranial pPNET including the present case. The eight male and eight female patients were aged between 5 months and 67 years (mean 19 years). The tumors were located in the supratentorial dura mater in seven cases including our case, frontal skull base in two cases, cavernous sinus in one case, cerebellopontine angle or tentorium in five cases, and frontal lobe in one case. Gross total removal was performed in 10 cases, partial removal in three cases, and open biopsy in two cases. The follow-up period was 9 days to 10 years (mean 2.6 years), and three patients died.

pPNET and Ewing's sarcoma were previously believed to be different tumors. However, a specific balanced translocation involving the Ewing's sarcoma gene on chromosome 22 has been demonstrated in both of these tumors and pPNET is now considered part of the spectrum of round cell sarcoma, in-

cluding Ewing's sarcoma.⁴⁾ The most common translocation is t(11;22)(q24;q12).^{10,13)} Immunoreactivity to HBA-71, which recognizes the cell surface glycoprotein p30/32 (a product of the MIC2 gene), is a highly sensitive histochemical marker of this family of tumors.^{3,10,13)} The diagnosis of cPNET can be confirmed by absence of MIC2 expression and t(11;22) translocation. MIC-2 is a specific marker for pPNET/Ewing's sarcoma family and is useful for the differential diagnosis of these two types of tumor. To make a diagnosis more exactly, it is recommended to confirm the presence of t(11;22)(q24;q12) translocation by reverse transcriptase-polymerase chain reaction and fluorescent in situ hybridization, if it is possible.

The neuroimaging differential diagnosis of pPNET includes meningioma, neurinoma, metastasis, and lymphoma, but no characteristic signs are known. pPNET was misdiagnosed as meningioma and hemangiopericytoma, so chemotherapy and radiation therapy were delayed and only performed for local recurrence and metastasis 9 years after the first diagnosis.¹⁷⁾ pPNET should be considered in the differential diagnosis of meningeal tumor, because surgical treatment may require early additional chemotherapy, in contrast to meningioma.

In our case, tumor was associated with intracystic hemorrhage. In Cases 10 and 13, the tumors also had hemorrhagic changes on MR imaging. Although the frequency of tumoral hemorrhage in pPNET is unknown, we should keep in mind that tumoral hemorrhage may cause symptomatic deterioration in patients with pPNET.

pPNET requires multimodality treatment. Surgery is important for tumor control. Wide surgical resection margins at the first surgery have markedly reduced local recurrences. The prognosis of pPNET has markedly improved with adjuvant chemotherapy and radiotherapy.^{7,12)} Long-term survival is uncommon among patients with cPNET, and many die within 1 year of diagnosis despite combined surgery, radiation therapy, and chemotherapy.^{3,6,10)} The median survival of cPNET was reported as 23 months, and 2, 3, and 5-year survivals as 50%, 34%, and 18%, respectively.⁵⁾ In our review of 16 cases, 11 patients were followed up over 1 year and only one patient died within 1 year (1-year survival of 91%). Eight patients were followed up over 2 years, and two died within 2 years (2-year survival of 75%). Four patients were followed up over 5 years, and two died within 5 years (5-year survival of 50%) (Table 1). The clinical course of intracranial pPNET is clearly more favorable than that of cPNET, so distinction of these two types is very important.

This case was first diagnosed as cystic meningio-

Table 1 Reported cases of intracranial peripheral neuroectodermal tumor

Case No.	Author (Year)	Age/Sex	Symptoms and signs	Location	Maximum diameter (cm)	Surgery	Postoperative therapy	Follow up
1	Papotti et al. (1998) ^[7]	30 yrs/F	headache, vertigo	rt frontal dura mater (two lesions)	7.0 and 4.0	gross total removal	radiation therapy and chemotherapy when local recurrence was seen	died 10 yrs after diagnosis
2	Katayama et al. (1999) ^[10]	5 yrs/M	vomiting, lt abducent nerve palsy	lt tentorium	not mentioned	gross total removal	radiation therapy and intrathecal chemotherapy	no evidence of disease 7 yrs after surgery
3	Antunes et al. (2001) ^[1]	6 yrs/M	vomiting, lethargy	rt frontal dura mater	not mentioned	gross total removal	radiation therapy and chemotherapy	no follow-up available
4	Kalamarides et al. (2001) ^[9]	34 yrs/F	vertigo, pulsatile tinnitus	lt CPA, acoustic facial bundle	1.8	partial removal	radiation therapy	no recurrence of tumor 1 yr after diagnosis
5	Niwa et al. (2001) ^[6]	5 mos/F	lt exophthalmos, bloody nasal discharge	frontal skull base	6.0	gross total removal	not done	died 9 days after surgery
6	Simmons et al. (2001) ^[18]	67 yrs/F	rt facial pain, facial palsy, hearing disturbance	rt CPA	not mentioned	open biopsy	radiation therapy	died 13 mos after diagnosis
7	Dedeurwaerdere et al. (2002) ^[3]	17 yrs/M	headache	rt frontal dura mater	5.0	gross total removal	local radiation therapy	no progression of tumor 12 mos after diagnosis
8		12 yrs/M	severe headache, lt neck, arm, and chest paresthesia	frontal dura mater	4.5	gross total removal	radiation therapy and chemotherapy	no evidence of disease 27 mos after diagnosis
9	Izycka-Swieszevska et al. (2003) ^[8]	26 yrs/F	headache, vertigo, dysarthria	lt CPA, tentorium, dura mater	5.0	gross total removal	radiation therapy	no evidence of disease 3 yrs after surgery
10	Utsunomiya et al. (2004) ^[20]	7 yrs/M	headache, vomiting	frontal base dura mater	5.0	gross total removal	radiation therapy and chemotherapy	no evidence of disease 2 yrs after surgery
11	Idrees et al. (2005) ^[7]	46 yrs/M	headache, vomiting, lt oculomotor and trigeminal nerve palsy	rt cavernous sinus, sella	2.3	open biopsy	radiation therapy and chemotherapy	no follow-up available
12	Mazur et al. (2005) ^[14]	8 yrs/F	headache, nausea, vomiting	rt tentorium	not mentioned	partial removal	radiation therapy and chemotherapy	no evidence of disease 2 yrs following diagnosis
13		7 yrs/F	headache, vomiting	rt frontal lobe	8.0	not mentioned	radiation therapy and chemotherapy	no follow-up available
14	Mobley et al. (2006) ^[15]	21 yrs/M	headache, double vision, lt partial homonymous hemianopia	parafalcine region of the rt occipital lobe	3.5	partial removal	radiation therapy and chemotherapy	recurrence of disease 18 mos after surgery
15	Kazmi et al. (2007) ^[11]	7 yrs/F	headache	frontal skull base	6.2	gross total removal	radiation therapy and chemotherapy	no follow-up available
16	Present case	15 yrs/M	headache	rt frontotemporal dura mater	6.6	gross total removal	radiation therapy and chemotherapy	no evidence of disease 6 mos after diagnosis

CPA: cerebellopontine angle.

ma. At surgery, the tumor was gross totally resected and the attachment site at the dura mater was resected with a wide surgical margin. The correct diagnosis of pPNET was then established, and radiation therapy and chemotherapy were given. Good prognosis is expected, but recurrence or metastases of the tumor remain possible.

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