available at http://www.tzuchimedjnl.com/

Tzu Chi Medical Journal

ELSEVIER

Case Report

Pontine Primitive Neuroectodermal Tumor With Spinal Metastasis in a 10-year-old Girl

Yu-Ching Chang[1], Kuang-Lin Lin[1], Tang-Her Jaing[2], Alex Mun-Ching Wong[3], Chen-Kan Tseng[4]*

[1]*Division of Pediatric Neurology, Chang Gung Children's Hospital, Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taoyuan, Taiwan*
[2]*Division of Pediatric Hematology, Chang Gung Children's Hospital, Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taoyuan, Taiwan*
[3]*Department of Diagnostic Radiology, Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taoyuan, Taiwan*
[4]*Department of Radiation Oncology, Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taoyuan, Taiwan*

Article info

Article history:
Received: February 24, 2009
Revised: March 17, 2009
Accepted: April 21, 2009

Keywords:
Brain stem
Glioma
Primitive neuroectodermal tumors
Pontine tumor

Abstract

Brain tumors are the most common type of solid cancer in children. Approximately 20% of pediatric brain tumors originate from the brain stem, and most are comprised of gliomas. However, metastasis of brain stem gliomas along the neuraxis is rare. Brain stem primitive neuroectodermal tumors (PNETs) are also rare and are prone to leptomeningeal metastasis. We describe here a 10-year-old girl with a pontine tumor. Initially, she was diagnosed with a glioma because of the clinical presentation, but later pathology of a metastatic tumor in the spinal cord showed PNET. The tumor response to radiotherapy was poor and she died 6 months after diagnosis. Since biopsy of brain stem tumors is not always feasible, diagnoses other than glioma should be considered if the patient's clinical presentation is unusual. (*Tzu Chi Med J* 2010;22(1):54–57)

*Corresponding author. Division of Pediatric Neurology, Chang Gung Children's Hospital, 5, Fu-Shin Street, Kwei-Shan, Taoyuan, Taiwan.
E-mail address: lincgh@adm.cgmh.org.tw

1. Introduction

Intrinsic brain stem tumors account for 10% of all pediatric brain tumors, most of which are gliomas. The majority (85%) are composed of high-grade fibrillary gliomas, which arise predominantly in the pons and less frequently in the medulla. Low-grade gliomas (15%) are focal tumors that usually arise in the medulla or midbrain (1). Primitive neuroectodermal tumors (PNETs) are malignant embryonic tumors occurring most commonly in the cerebellum of young individuals (2). PNETs arising from the brain stem are rare and the prognosis is poor (1,2). In addition, initial detection of brain stem PNETs is difficult. Most neuro-oncologists avoid performing biopsies in children with pontine tumors because of the risk of brain stem herniation. In these situations, clinicians usually treat brain stem tumors according to their experience and imaging findings, without pathological evidence.

We describe here a 10-year-old girl with a brain stem tumor. Initially, she was diagnosed with pontine

glioma because of the clinical presentation, but later pathology of a metastatic tumor in the spinal cord showed PNET.

2. Case report

A 10-year-old girl had been healthy before February 2008, when she suffered from progressive right upper and lower limb weakness and right central facial palsy for 1 week. She had no fever, cough, rhinorrhea, headache, vomiting, or diarrhea. A hemogram showed no abnormal findings (white blood cell count, 7700/μL; hemoglobin, 14.2 g/dL; platelets, 253,000/μL; C-reactive protein, <0.5 mg/L). Brain computed tomography (CT) showed focal bulging with slightly increased density of the left side pons (Fig. 1). Brain magnetic resonance imaging (MRI) (Fig. 2) revealed a 2.6×2.1×2 cm well-defined intra-axial lesion involving the anterior aspect of the bilateral pons. The lesion was hypointense on T1-weighted images without obvious enhancement and was hyperintense on T2-weighted images. Brain stem glioma was diagnosed according to the imaging findings and clinical presentation. The patient received radiotherapy with a total dose of 3000 cGy in 20 fractions combined with temozolomide (100 mg/day for 25 days). During radiotherapy, only a mild headache and nausea were observed. Her right side weakness persisted and she underwent rehabilitation.

Three months later, the patient suffered from headaches, vomiting, and blurred vision. Bilateral lower limb weakness was also found. Follow-up brain MRI (Fig. 3) showed interval regression of the size of the pontine tumor with intratumoral bleeding, but there was an enhanced nodule over the anterior aspect of the cervical spinal cord at C3 and increased leptomeningeal contrast enhancement in the basal cisterns and cerebellar sulci, which strongly suggested tumor seeding in the cerebral spinal fluid pathway. Spinal MRI (Fig. 4) showed extensive cerebral spinal fluid tumor seeding involving the entire spinal column with multiple sites of spinal cord compression. A biopsy of the metastatic nodule in the sacral area was carried out because of this rare manifestation of brain stem glioma. The pathology showed PNET. Our initial diagnosis of brain stem glioma was changed to brain stem PNET with leptomeningeal metastasis.

The patient's condition progressed, her consciousness became disorientated, and follow-up brain CT

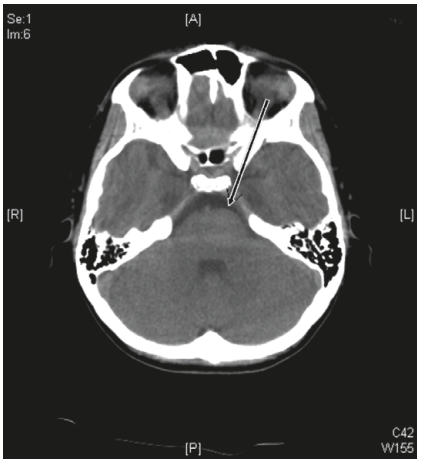

Fig. 1 — Brain computed tomography shows focal bulging of the left pontine region (arrow) with slight hyperdensity.

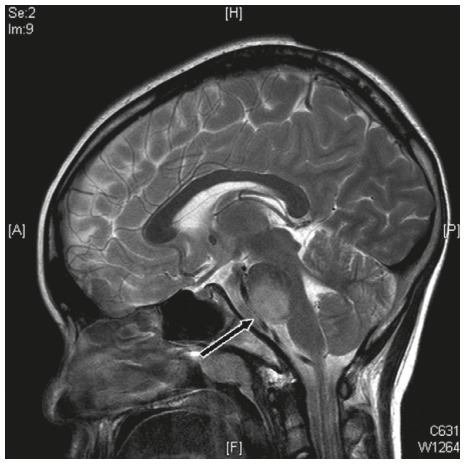

Fig. 2 — Brain magnetic resonance imaging shows a well-defined 2.6×2.1×2 cm intra-axial lesion in the anterior pons (arrow), with hyperintensity on T2-weighted imaging.

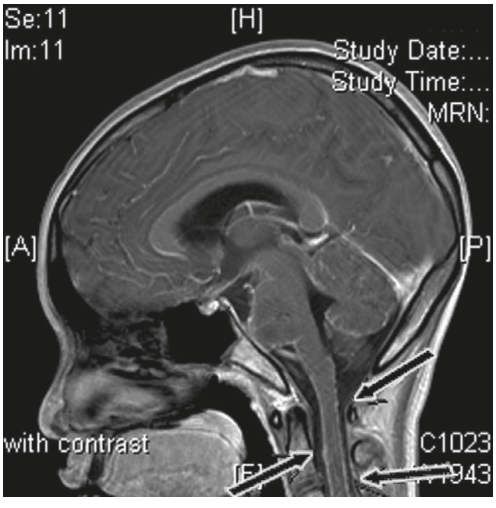

Fig. 3 — Brain magnetic resonance imaging shows an enhanced nodule over the anterior aspect (arrows) of the cervical spinal cord at the C3 level.

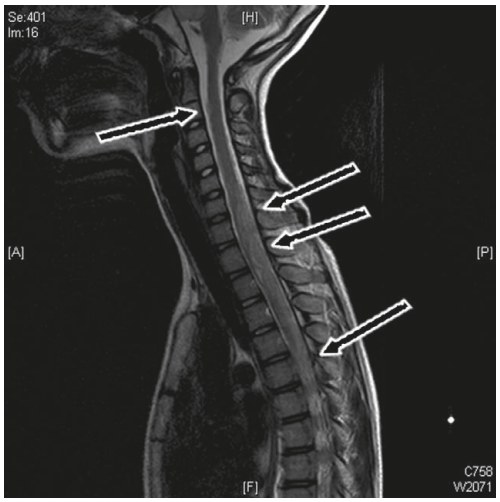

Fig. 4 — Spinal magnetic resonance imaging shows extensive cerebral spinal fluid tumor seeding involving the entire spinal column with multiple sites of spinal cord compression (arrows).

showed hydrocephalus; for this reason, her parents refused insertion of a ventriculoperitoneal shunt. She received only palliative radiotherapy of the brain and whole spine, but chemotherapy was not performed because of her unstable condition. One month later, the patient died due to cardiopulmonary failure.

3. Discussion

The term PNET was first introduced by Hart and Earle in 1973 to describe tumors that are clinically defined by their aggressive behavior. PNETs are malignant embryonic tumors occurring most commonly in the cerebellum of young individuals [2]. Ten percent of central nervous system PNETs arise outside the cerebellum, and there have only been a few case reports of brain stem PNETs [1,3–5].

Zagzag et al retrospectively reviewed 146 pediatric patients with brain stem tumors, among which PNET was histologically diagnosed in seven patients (4.8%). Two of these PNETs were located in the pons. The median age of the patients was 2.7 years (range, 1.0–8.0 years) [1]. All seven patients relapsed and had progression at the primary site, and six had additional documented leptomeningeal dissemination. Only two patients responded to therapy. The median survival was 7 months (range, 3–17). Other reports of brain stem PNETs include one series of four cases originating in the pons [3], another series of two cases in the medulla and two cases in the region of the third cranial nerve [4], and an additional report of two cases with brain stem PNETs [5].

For our patient, we considered the possibility of two coexistent primary tumors (brain stem glioma and spinal PNET). There have not been any other such case reports of these two coexisting primary tumors. Zagzag et al reviewed a patient in whom PNET was pathologically proven throughout the subarachnoid space, but the pontine tumor had the appearance of a low-grade glioma [1]. At autopsy, they found that the neoplasm in the pons represented a zone of advanced astrocytic differentiation of the PNET. Thus, a diagnosis of brain stem PNET with spinal cord metastasis was more favored than two independent primary tumors. In addition, in our patient, the tumor in the spinal cord was of a metastatic pattern rather than a primary pattern, which also supported our diagnosis.

There are no definite clinical characteristics distinguishing brain stem glioma from PNET. In brain MRI, both tumors are mostly hypointense on T1-weighted images with/without enhancement and hyperintense on T2-weighted images. PNETs are prone to leptomeningeal metastasis (42–100%), which occurs less frequently in brain stem gliomas (5–30%) [6]. Patients with brain stem PNETs are thought to be younger and have a higher tendency to have hydrocephalus at diagnosis than patients with gliomas [2]. A definite diagnosis is still dependent on histological findings.

Treatment of PNET/medulloblastoma consists of radiotherapy and chemotherapy, which provide long-term progression-free survival in over 50% of children with PNETs arising in the cerebellum. Nevertheless, the prognosis of PNET in the brain stem is much poorer than that of PNET in the cerebellum [7]. From previous reports, patients with brain stem PNETs have a poor response to radiotherapy and chemotherapy, and no survival past 18 months has been reported [8]. Our patient received temozolomide treatment. Although adult studies with larger cohorts have confirmed a high response to temozolomide for both low-grade and high-grade astrocytomas and other gliomas, overall pediatric data suggest that temozolomide activity may be less robust in children. However, a complete response was noted in one patient with PNET/medulloblastoma [9], and thus further study into the use of temozolomide for treatment of children with medulloblastoma and other PNETs may be warranted.

Fangusaro et al reported two patients with brain stem PNETs initially treated with induction chemotherapy, and then consolidative chemotherapy followed by autologous hematopoietic cell rescue [8]. Both patients received craniospinal irradiation with a boost to the primary tumor after hematopoietic rescue and remained long-term survivors at 32 and 38 months with stable disease.

In conclusion, although the most common brain stem tumor is glioma, PNET might be the primary

pathology of brain stem tumors with spinal metastasis. Close follow-up and spinal cord surveys are mandatory for diagnosis when initial pathology in the brain stem is not available.

References

1. Zagzag D, Miller DC, Knopp E, et al. Primitive neuroectodermal tumors of the brainstem: investigation of seven cases. *Pediatrics* 2000;106:1045–53.
2. Hart MN, Earle KM. Primitive neuroectodermal tumors of the brain in children. *Cancer* 1973;32:890–7.
3. Behnke J, Mursch K, Bruce W, Cristen HJ. Intra-axial endothytic primitive neuroectodermal tumors in the pons: clinical, radiological, and immunohistochemical aspects in four children. *Childs Nerv Syst* 1996;12:125–9.
4. Zimmerman RA. Neuroimaging of pediatric brain stem diseases other than brain stem glioma. *Pediatr Neurosurg* 1996;25:83–92.
5. Molloy PT, Yachnis AT, Rorke LB, et al. Central nervous system medulloepithelioma: a series of eight cases including two arising in the pons. *J Neurosurg* 1986;84:430–6.
6. Gururangan S, McLaughlin CA, Brashears J, et al. Incidence and patterns of neuraxis metastases in children with diffuse pontine glioma. *J Neurooncol* 2006;77:207–12.
7. Packer RJ, Sutton LN, Rosenstock JG, et al. Pineal region tumors of childhood. *Pediatrics* 1984;74:97–102.
8. Fangusaro JR, Jubran RF, Allen J, et al. Brainstem primitive neuroectodermal tumors (bstPNET): results of treatment with intensive induction chemotherapy followed by consolidative chemotherapy with autologous hematopoietic cell rescue. *Pediatr Blood Cancer* 2008;50:715–7.
9. Nicholson HS, Kretschmar CS, Krailo M, et al. Phase 2 study of temozolomide in children and adolescents with recurrent central nervous system tumors. *Cancer* 2007;110:1542–50.