

Pontine Malignant Astrocytoma With Hemorrhagic Onset

—Case Report—

Yosuke NISHIMUTA, Masaki NIRO, Takashi KAMEZAWA, Koichi ISHIMARU,
Shunichi YOKOYAMA, and Jun-ichi KURATSU

Department of Neurosurgery, Faculty of Medicine, University of Kagoshima, Kagoshima

Abstract

A 7-year-old boy presented with acute onset of left hemiparesis and headache, followed by disturbance of consciousness. Neuroimaging studies showed pontine hemorrhage. Surgery was performed to remove a massive hematoma. Histological examination of the wall revealed anaplastic astrocytoma. Postoperative radiation therapy and several types of chemotherapy were administered. However, the tumor recurred and he died 9 months after onset. Hemorrhagic onset of pontine glioma is rare and carries an extremely poor prognosis.

Key words: pontine glioma, hemorrhage, hemorrhagic onset, malignant astrocytoma, chemotherapy

Introduction

Pontine gliomas account for 5–15% of all pediatric brain tumors.^{4,6,15,19} The vast majority of these tumors are astrocytomas including malignant astrocytoma.^{3,15} The prognosis of pontine gliomas is poor^{6,7,15} despite the administration of radiation therapy and different regimens of combined chemotherapy. Pontine gliomas usually manifest as progressive, typically asymmetric symptoms and signs resulting in a 2- to 5-month history of ataxia and cranial nerve dysfunction.¹⁵ Presentation with an acute, stroke-like onset is rare. We treated a pediatric patient with a malignant pontine glioma manifesting as stroke-like onset and atypical imaging features due to the presence of hemorrhage.

Case Report

A 7-year-old boy suddenly developed left hemiparesis and swallowing disturbance on April 15, 1999. Two days later, he complained of headache and gradually became unconscious. His level of consciousness slightly improved after conservative treatment with osmotic agents and steroids, but dysarthria and diplopia appeared. He was transferred to our hospital on April 26.

On admission, he was somnolent. Neurological examination revealed bilateral abducens palsy dominant on the right and facial palsy, dysarthria, swallowing disturbance, cerebellar ataxia, and left hemiparesis. Computed tomography (CT) obtained 2 days after onset showed a hematoma with surrounding edema in the pons (Fig. 1). Magnetic resonance (MR) imaging on admission disclosed a hypointense area on the T₁-weighted image and a mixed hyper- and hypointense area on the T₂-weighted image in the pons. The pons was remarkably expanded and the fourth ventricle was compressed backwards (Fig. 2A, B). The lesion showed irregular ring-like enhancement by contrast medium (Fig. 2C). Cerebral angiography revealed a remarkable mass effect of the basilar artery. No tumor stain or vascular malformation was observed.

Surgery was performed to remove the hematoma and identify the bleeding origin. A midline suboccipital craniectomy was performed. A bulge was found in the floor of the fourth ventricle 2 cm above the obex. A 7 mm-long midline incision was added. Dark red clot was evacuated from 5 mm under the surface. The brain tissue surrounding the hematoma was pinkish gray and bled easily. Biopsy samples of the abnormal tissue were taken.

Histological examination confirmed high cellularity, pleomorphic tumor cells, and atypical nuclei with increased mitotic activity (Fig. 3A). Most tumor cells were glial fibrillary acidic protein-

positive and the MIB-1 labeling index was extremely high (68%) (Fig. 3B). No necrosis or endothelial proliferation was observed. The histological diagnosis was anaplastic astrocytoma.

He recovered consciousness after the operation, but the focal neurological deficits remained unchanged. Postoperatively, he received chemoradiation therapy consisting of interferon-beta (100 U/day for 15 days), ACNU (80 mg/kg), and radiation (50 Gy), otherwise called IAR therapy. However, the tumor continued to grow (Fig. 4A) and his neurolog-

ical condition worsened. Therefore, three cycles of chemotherapy with carboplatin (400 mg/m²) and etoposide (300 mg/m²) were added. Subsequently he could walk with a stick and eat by himself. MR imaging showed remarkable reduction of the tumor size (Fig. 4B).

His neurological state was relatively stable during August through September. However, he complained of headache followed by consciousness disturbance and tetraplegia in October. Imaging studies disclosed tumor growth and cerebrospinal fluid (CSF) dissemination (Fig. 4C). Another round of chemotherapy with ifosfamide, cisplatin, and etoposide was administered, followed by whole-brain radiation (21.6 Gy) against CSF dissemination. However, he died of the tumor on December 30, 1999. Autopsy was not permitted.

Discussion

Unusual manifestations of pontine glioma include acute onset with pure motor hemiplegia, upbeat nystagmus, and internuclear ophthalmoplegia, which were histologically identified as glioblastoma.^{12,14,18} However, these cases were not associated with hemorrhage on CT. Only three of 1861 brain tumors were pontine gliomas associated with hemorrhage.²⁰ Pontine gliomas associated with hemorrhage identified by neuroimaging^{7,11,20} or histological study⁹) may not be very rare, but our case of pontine glioma associated with massive hemorrhage also presented with unusual stroke-like onset.

CT usually demonstrates pontine glioma as a diffuse low-density area with mass effect with or without contrast enhancement. In our case, CT ob-

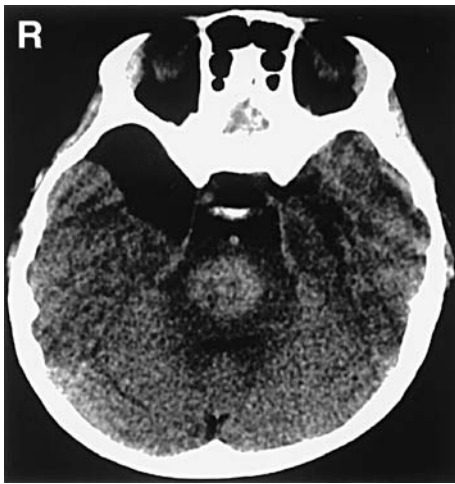


Fig. 1 Computed tomography scan obtained 2 days after onset showing a round high-density area with a surrounding low-density area in the pons. The low-density area in the anterior part of the right temporal lobe is an arachnoid cyst.

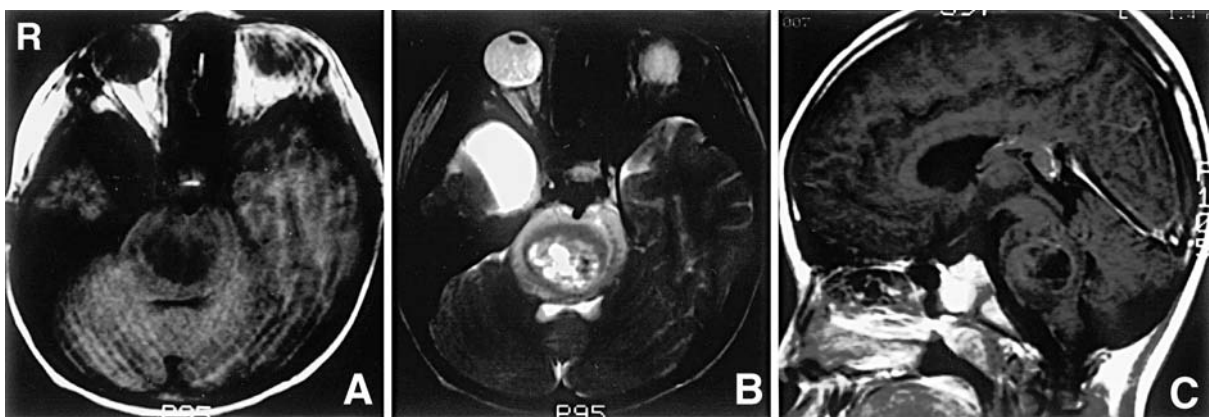


Fig. 2 Magnetic resonance images obtained on admission. (A) T₁-weighted image showing a hypointense area, (B) T₂-weighted image showing a mixed hyper- and hypointense area in the pons and the fourth ventricle compressed backwards, and (C) T₁-weighted image with contrast medium showing irregular ring-like enhancement of the lesion.

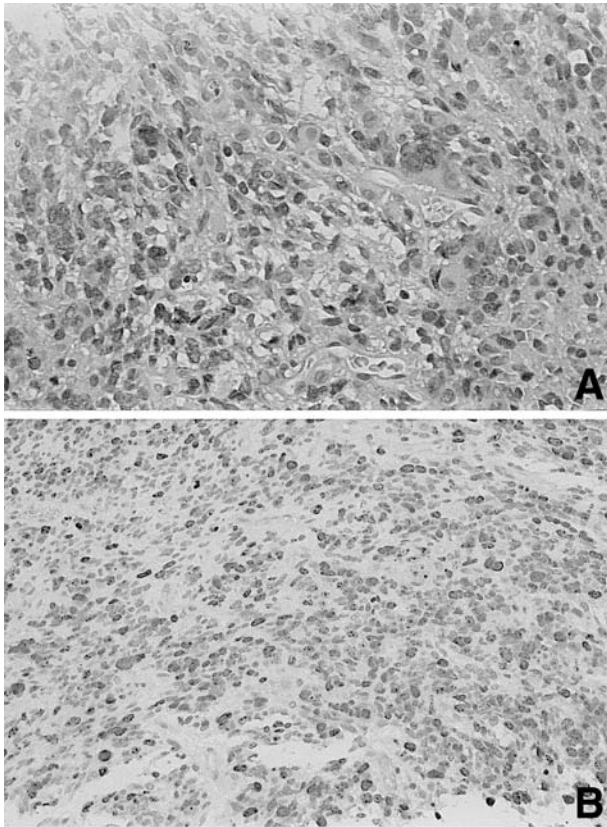


Fig. 3 Photomicrographs of the hematoma wall showing pleomorphic astrocytic tumor cells, increased cellularity, and atypical nuclei with increased mitotic activity (A: hematoxylin-eosin stain, $\times 100$); and Ki-67 staining showing an extremely high number of positive nuclei with a MIB-1 labeling index of 68% (B: $\times 50$).

tained 2 days after onset revealed a high-density area in the central part of the tumor, which reflected the presence of hemorrhage. Lesions with mixed hypo- and hyperintensity on both T_1 - and T_2 -weighted MR imaging may reflect intratumoral hemorrhage.^{5,11)} In our case, the signal intensity on T_1 -weighted imaging was not typical of intratumoral hemorrhage, but the presence of a massive, fluid-containing hematoma was confirmed intraoperatively.

The indications for surgery in patients with pontine glioma are restricted because the tumor usually diffusely infiltrates the brain stem. Therefore, the ablation of diffuse-type brain stem tumors is usually abandoned unless the tumor extends exophytically or is present in both poles of the brain stem.^{6,16)} Biopsy is sometimes performed to confirm tumor histology and the degree of malignancy,^{10,17)} but this entails additional and unnecessary risks. Therefore, the diagnosis of pontine gliomas should be established by imaging studies.^{2,6)}

The onset and imaging findings were atypical for pontine glioma in our case, so we performed hematoma removal and open biopsy to establish the differential diagnosis from vascular malformations such as cavernous angioma. Histologically, the biopsy specimens identified a highly malignant astrocytic tumor, but diagnosis was anaplastic astrocytoma due to the absence of necrosis and endothelial proliferation. The microscopic pathology of brain stem tumors is often inhomogeneous.^{3,19)} Our specimens were small and few in number, so we could not confirm necrosis. However, the histologically verified malignancy and the extremely high MIB-1 labeling index suggested that the tumor was a highly malignant anaplastic astrocytic tumor, i.e. a gli-



Fig. 4 Serial T_1 -weighted magnetic resonance images with contrast medium (A) after the course of radiochemotherapy showing growth of the tumor, (B) after three cycles of chemotherapy with carboplatin and etoposide showing reduction of the enhanced area and less compression of the fourth ventricle, and (C) 2 months later showing increased tumor size and cerebrospinal fluid dissemination.

blastoma. Therefore, we conclude that pontine gliomas with hemorrhagic- and stroke-like onset are highly malignant and carry a very poor prognosis.

Spontaneous hemorrhage from brain tumors is associated with malignant brain tumors, such as glioblastoma, oligodendroglioma, and metastatic brain tumor.^{1,8,20)} Excluding pituitary adenoma, the incidence of hemorrhage from brain tumor was 2.4–5.4% macroscopically^{1,8,9,20)} and 9.2% microscopically.⁸⁾ The incidence of hemorrhage in pediatric patients was higher, at 5.3%²⁰⁾ and 10%,¹³⁾ respectively, than in adults. The site of the hemorrhage varies. Our case was intratumoral hemorrhage as in three previous patients with pontine astrocytoma.²⁰⁾ The histological features of tumors with intratumoral hemorrhage include tumor necrosis as well as vascular changes such as vessel-wall hyalinization, degeneration or necrosis of vessel walls, thrombosis, and presence of many thin-walled vessels and ruptured vessels.⁸⁾ Our surgical specimens were too small to clarify the pathological mechanisms of bleeding from the tumor. The high MIB-1 labeling index suggested that rapid tumor growth may have caused vessel compression and/or distortion, and additional tumor invasion of the vessel walls may have resulted in the intratumoral hemorrhage. The incidence of hemorrhagic onset in the patients with brain tumor is not high, but direct proof of the hemorrhagic origin is necessary for the diagnosis and treatment planning for an intracerebral hematoma with atypical location, imaging findings, or clinical course.

Irradiation is the main therapy for pontine gliomas, but cannot improve the prognosis satisfactorily. IAR therapy is one of the most widely accepted postoperative treatment modalities for astrocytic tumors in Japan. However, some tumors are resistant to this treatment, as in our case. Radiochemotherapy achieved only temporary remission despite the addition of carboplatin and etoposide treatment. Development of a new treatment approach is needed to improve the currently dismal prognosis of patients, such as ours, with brain stem gliomas that exhibit malignant behavior.

References

- 1) Albert FK: [Tumor hemorrhage in intracranial tumors]. *Neurochirurgia (Stuttg)* 29: 67–74, 1986 (Ger)
- 2) Albright AL, Packer RJ, Zimmerman R, Rorke LB, Boyett JM, Hammond GD: Magnetic resonance scans should replace biopsies for the diagnosis of diffuse brain stem gliomas: a report from the Children's Cancer Group. *Neurosurgery* 33: 1026–1030, 1993
- 3) Burger PC: Pathology of brain stem astrocytomas. *Pediatr Neurosurg* 24: 35–40, 1996
- 4) The Committee of Brain Tumor Registry of Japan: Report of Brain Tumor Registry of Japan (1969–1993), ed 10. *Neurol Med Chir (Tokyo)* 40 Suppl: 14–33, 2000
- 5) Destian S, Sze G, Krol G, Zimmerman RD, Deck MD: MR imaging of hemorrhagic intracranial neoplasm. *AJR Am J Roentgenol* 152: 137–144, 1989
- 6) Epstein F, Constantini S: Practical decisions in the treatment of pediatric brain stem tumors. *Pediatr Neurosurg* 24: 24–34, 1996
- 7) Kaplan AM, Albright AL, Zimmerman RA, Rorke LB, Li H, Boyett JM, Finlay JL, Wara WM, Packer RJ: Brainstem gliomas in children. A Children's Cancer Group review of 119 cases. *Pediatr Neurosurg* 24: 185–192, 1996
- 8) Kondziolka D, Bernstein M, Resch L, Tator CH, Fleming JFR, Vanderlinden RG, Schutz H: Significance of hemorrhage into brain tumors: clinicopathological study. *J Neurosurg* 67: 852–857, 1987
- 9) Kothbauer P, Jellinger K, Falment H: Primary brain tumour presenting as spontaneous intracerebral haemorrhage. *Acta Neurochir (Wien)* 49: 35–45, 1979
- 10) Kratimenos GP, Thomas DGT: The role of image-directed biopsy in the diagnosis and management of brainstem lesions. *Br J Neurosurg* 7: 155–164, 1993
- 11) Kuroiwa T, Numaguchi Y, Rothman MI, Zoarski GH, Morikawa M, Zagardo MT, Kristt DA: Posterior fossa glioblastoma multiforme: MR findings. *AJNR Am J Neuroradiol* 16: 583–589, 1995
- 12) Lahat E, Lanzieri C, Wallace SA, Aron AM: Pediatric brain stem tumor presenting as a pure motor hemiparesis. *Clin Neurol Neurosurg* 91: 61–63, 1989
- 13) Laurent JP, Bruce DA, Schut L: Hemorrhagic brain tumors in pediatric patients. *Childs Brain* 8: 263–270, 1981
- 14) Levitt LP, Selkoe DJ, Frankenfield B, Schoene W: Pure motor hemiplegia secondary to brain-stem tumor. *J Neurol Neurosurg Psychiatry* 38: 1240–1243, 1975
- 15) Maria BL, Rehder K, Eskin TA, Hamed LM, Fennell EB, Quisling RG, Mickle JP, Marcus RB, Drane WE, Mendenhall NP, McCollough WM, Kedar A: Brainstem glioma: 1. Pathology, clinical features, and therapy. *J Child Neurol* 8: 112–128, 1993
- 16) Pierre-Kahn A, Hirsch J-F, Vinchon M, Payan C, Sainte-Rose C, Renier D, Lelouch-Tubiana A, Fermanian J: Surgical management of brain-stem tumors in children: results and statistical analysis of 75 cases. *J Neurosurg* 79: 845–852, 1993
- 17) Rajshekhar V, Chandy MJ: Computerized tomography-guided stereotactic surgery for brainstem masses: risk benefit analysis in 71 patients. *J Neurosurg* 82: 976–981, 1995
- 18) Rothman SJ, Olanow CW: Brain stem glioma in childhood: acute hemiplegic onset. *Can J Neurol Sci* 8: 263–264, 1981
- 19) Russel DS, Rubinstein LJ: *Pathology of Tumors of Central Nervous System*, ed 5. London, Edward Arnold, 1989, pp 149–152

- 20) Wakai S, Yamakawa K, Manaka S, Takakura K:
Spontaneous intracranial hemorrhage caused by
brain tumor: Its incidence and clinical significance.
Neurosurgery 10: 437-444, 1982

Address reprint requests to: Y. Nishimuta, M.D., Department of Neurosurgery, Faculty of Medicine, University of Kagoshima, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan.
e-mail: yosuke-ns@po.minc.ne.jp