Spontaneous Regression of a Primary Cerebral Tumor Following Vasospasm Caused by Subarachnoid Hemorrhage Due to Rupture of an Intracranial Aneurysm
—Case Report—

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Abstract
A 40-year-old man demonstrated spontaneous regression of a malignant glioma following vasospasm caused by subarachnoid hemorrhage due to rupture of an intracranial aneurysm. The patient had been treated under a diagnosis of malignant glioma for 5 years. He presented with a ruptured aneurysm manifesting as subarachnoid hemorrhage. Single photon emission computed tomography with N-isopropyl-p-123I-iodoamphetamine and diffusion-weighted magnetic resonance (MR) imaging revealed severe flow reduction due to vasospasm in the bilateral temporoparietal cortical regions, including the tumor. MR imaging performed 5 months later showed marked tumor regression. The present case suggests that treatment targeting angiogenesis of malignant gliomas may be effective as a part of multimodality treatment.

Key words: malignant glioma, spontaneous regression, subarachnoid hemorrhage, vasospasm

Introduction
Supratentorial malignant glioma is a common primary tumor of the adult central nervous system. Unfortunately the currently available multimodal approach has not improved the poor prognosis for patients with this tumor, with a median survival time of less than several years.4) Malignant glioma is highly vascularized, so treatment strategies targeting the angiogenesis have been investigated recently. We report a rare case of spontaneous regression of a malignant glioma associated with severe blood flow reduction following vasospasm after subarachnoid hemorrhage due to rupture of an intracranial aneurysm.

Case Report
A 40-year-old man presented with visual disturbance. Ophthalmological examination showed left upper homonymous quadrantanopsia. Head magnetic resonance (MR) imaging in November 1994 showed a 3 × 3 cm heterogeneously enhanced mass in the right parahippocampal gyrus (Fig. 1A). Angiography was not performed. The clinical diagnosis was malignant glioma. The patient refused any surgery so biopsy could not be performed to obtain a histological diagnosis. He received involved field radiotherapy with a total dose of 50.4 Gy given by conventional factionation. Follow-up MR imaging with gadolinium showed a marked decrease in the volume of the tumor. He maintained a high Karnofsky performance status (100%) until tumor recurrence.

About 4 years after the radiotherapy, the patient was reevaluated because of left limb weakness. Head MR imaging showed tumor progression (Fig. 1B). He refused any tumor-specific treatment and received medical treatment with anticonvulsant as an outpatient.

The patient remained in good condition until August 8, 1999, when he was admitted to our hospital due to sudden onset of severe headache and
Fig. 1 Axial T₁-weighted magnetic resonance (MR) images with gadolinium-diethylenetriaminepenta-acetic acid. (A) MR image at the first manifestation of the disease, showing the heterogeneously enhanced tumor in the right parahippocampal gyrus. (B) Follow-up MR image 4 years after radiotherapy, showing tumor progression. (C) Fluid-attenuated inversion recovery MR image 5 months after the ictus of subarachnoid hemorrhage, showing tumor regression. (D) Follow-up MR image one month before death, showing regrowth of the tumor.

Fig. 2 Computed tomography scans taken soon after the sudden onset of severe headache and vomiting, revealing subarachnoid hemorrhage of Fisher grade III.

Fig. 3 (A) Left internal carotid angiogram, anteroposterior view, showing an aneurysm at the bifurcation of the middle cerebral artery. (B) Left vertebral angiogram, lateral view, showing an aneurysm of the vertebral-posterior inferior cerebellar artery.

vomiting followed by transient loss of consciousness. Brain computed tomography showed subarachnoid hemorrhage of Fisher grade III (Fig. 2). Angiography showed aneurysms of the left middle cerebral artery and the left vertebral-posterior inferior cerebellar artery (Fig. 3). These locations of aneurysms were unrelated to the tumor lesion. His consciousness suddenly deteriorated to coma. Emergency surgery was performed to clip the left middle cerebral artery aneurysm on the day of admission (Day 0). The left vertebral-posterior inferior cerebellar artery aneurysm was embolized using Guglielmi detachable coils (Target Therapeutics, Fremont, Calif., U.S.A.) on Day 3.

Although single photon emission computed tomography with N-isopropyl-p-¹²³I-iodoamphetamine (IMP-SPECT) on Day 7 demonstrated preserved cerebral blood flow (Fig. 4A), angiography on Day 10 showed moderate vasospasm of the bilateral internal carotid artery terminal segments, the bilateral middle cerebral artery M₁ segments, and basilar artery trunk. He became semicomatose with right hemiparesis on Day 13. IMP-SPECT revealed severe flow reduction in the bilateral temporoparietal cortical regions, including the tumor (Fig. 4B left). Diffusion-weighted MR
Fig. 4 Single photon emission computed tomography scans with N-isopropyl-p-123I-iodoamphetamine (IMP-SPECT) taken 7 days (A), 13 days (B, left), and 18 days (C) after the onset of subarachnoid hemorrhage. IMP-SPECT scan taken 13 days after onset of subarachnoid hemorrhage (B, left) demonstrates severe flow reduction in the bilateral temporoparietal regions, including the tumor. Axial diffusion-weighted magnetic resonance image on the same day (B, right) demonstrates multiple high intensity areas in those regions.

Hypertensive hypervolemic hemodilution therapy and hyperbaric oxygen therapy were performed. IMP-SPECT on Day 18 revealed normalized perfusion in the bilateral temporoparietal cortical regions (Fig. 4C). Subsequently, his right motor weakness improved and he was discharged with mild sensory aphasia 2 months after admission. Follow-up MR imaging 3 months later showed a marked decrease in the volume of the tumor (Fig. 1C).

MR imaging showed no evidence of tumor regression during the first 12 months' follow up in our outpatient department, but demonstrated tumor enlargement after another 8 months' follow-up (Fig. 1D). He died of tumor progression 7 years after the initial diagnosis.

Discussion

Spontaneous tumor regression has been occasionally reported in pituitary adenomas and intracranial lymphomas, as well as spontaneous shrinkage of pituitary adenoma. Silent infarction of the adenoma is the most likely cause for such tumor regression. Regression of a large pituitary macroadenoma was also observed after pituitary apoplexy. In this case, symptomatic infarction of a pituitary macroadenoma occurred after cardiac surgery. The abnormally tenuous vasculature of pituitary adenoma may result in spontaneous infarction under the hypoxic conditions which often occur during cardiac surgery. Transient spontaneous regression occurred in four patients with intracranial lymphomas.

Although the mechanism was not clear, histological studies in these cases demonstrated that perivascular infiltration by tumor cells and vessel invasion may have resulted in a spontaneous decrease in tumor activity caused by vascular changes such as infarction or hemorrhage in the tumor tissue.

Recently, the first case of spontaneous regression of recurrent oligodendroglioma was observed following infarction in the territory of the feeding artery. The excellent tumor control indicated the potential of endovascular therapies in patients with malignant gliomas. Our case demonstrated the spontaneous regression of a malignant tumor secondary to cerebral infarction due to vasospasm after subarachnoid hemorrhage. The tumor growth may have been inhibited indirectly by inhibiting the progressive neovascularization of tumor. This observation suggests that inhibition of neovascularization may provide a novel approach for treating tumors by manipulation of the tumor environment.

Clinical studies with systemically administered antiangiogenic agents, such as thalidomide, have shown modest efficacy in terms of response in recurrent malignant gliomas. The development of antiangiogenic agents and techniques certainly opens pathways to further treatment options for patients with these tumors. The tumor devascularization technique is intended to obliterate the vascular supply of the tumor and enhance the ease and effectiveness of resection, such as therapeutic embolization for extra-axial tumors including meningiomas. However, no therapeutic embolization
technique for gliomas has yet been established. Our case suggests that microvascular injection of an effective devascularizing and sclerosing agent may provide therapeutic effects. Furthermore, gene therapies related to the neovascularization of tumors may result in longer symptom-free periods than offered by currently available treatment modalities.

References


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