De Novo Aneurysm after Treatment of Glioblastoma

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A rare case of spontaneous subarachnoid hemorrhage from newly developed cerebral aneurysm in glioblastoma patient is presented. A 57-year-old man was presented with headache and memory impairment. On the magnetic resonance image and the magnetic resonance angiography, a large enhancing mass was found at right frontal subcortex and intracranial aneurysm was not found. The mass was removed subtotally and revealed as glioblastoma. He took concurrent PCV chemotherapy and radiation therapy, but the mass recurred one month later after radiotherapy. He was then treated with temozolomide for 7 cycles. Three months after the completion of temozolomide therapy, he suffered from a subarachnoid hemorrhage due to a rupture of a small de novo aneurysm at distal anterior cerebral artery. He underwent an aneurysm clipping and discharged without neurologic complication.

Key Words : Glioblastoma · Intracranial aneurysm · Subarachnoid hemorrhage · Radiation therapy · Chemotherapy.

INTRODUCTION

The brain tumor associated with intracranial aneurysm is rare (0.19-4%).9,11,15,18,20 Pituitary adenomas or meningiomas are sometimes associated with aneurysm11, but the incidence of glioblastomas associated with intracranial aneurysm is extremely rare1,3,4,13. Incidentally, the intracranial aneurysm can be identified at a glioblastoma patient before tumor surgery but not related to tumor location. In this report, we present a case of de novo pericallosal artery aneurysm that was not found in initial magnetic resonance angiography (MRA) which taken before treatment of glioblastoma.

CASE REPORT

A 57-year-old man complained headache and memory impairment for 1 month. On the magnetic resonance image (MRI), a 4.7×5.8×4.1 cm sized peripheral enhancing mass surrounded by edema was shown at the right frontal white matter and left frontal subcortex (Fig. 1A). MRA showed that the anterior cerebral artery (ACA) was deviated to the left side slightly and the distal ACA was narrowed focally. However, the intracranial aneurysm was not shown (Fig. 1B). The mass was removed subtotally by transcortical approach and the pathology was glioblastoma (WHO grade IV). In the immunologic staining, p53, glial fibrillary acidic protein, and synaptophysin were positive and Ki-67 index was about 20%. Three weeks later after the operation he was performed the concurrent PCV chemotherapy (lomustine 75 mg/m2 on day 1, procarbazine 60 mg/m2 on day 8-21, and vincristine 1.4 mg/m2, maximum 2 mg on day 8 and 28) and radiation therapy (5940 cGy/33 fractions). One month after the completion of radiation therapy, the patient suffered from the seizure. On the follow up MRI, the enhancing mass was increased slightly at the marginal area. He took temozolomides (150-200 mg/m2 at days 1-5, in a 28-days cycle) for 7 cycles and the recurred lesion was disappeared (Fig. 1C). Three months later he was transferred to the emergency room due to the drowsy mentality. On the three-dimensional computed tomographic angiography (CTA), subarachnoid hemorrhage and an intracranial aneurysm at the right distal anterior cerebral artery (ACA) were shown (Fig. 2). He underwent an aneurysm neck clipping without distal subtraction angiography (DSA) due to the patient's condition. On the microscopic finding, the small saccular aneurysm was found at the junction of the pericallosal and callosomarginal artery. The aneurysm directed posteriorly had a thrombus. This aneurysm was seen a distance from the previous tumor removal site and there was no evidence of vascular injury. On the pathologic finding around the aneurysm, there was no malignant tumor cell. The patient was discharged without any newly developed neurologic deficit after the control of aneurysmal subarachnoid hemorrhage.
computed tomography. At the junction of the pericallosal and callosomarginal artery (B). CT: precontrast CT (A). On the CT angiography, a small aneurysm is shown (Fig. 2).

Subarachnoid and intraventricular hemorrhages are shown on precontrast CT (A). On the CT angiography, a small aneurysm is shown at the junction of the pericallosal and callosomarginal artery (B). CT: computed tomography.

**DISCUSSION**

According to the literatures, brain tumors associated with the intracranial aneurysm are very rare (0.19-4%). The true incidence of the association of these two pathologic conditions seems higher than what is reported in the literature because angiographies are rarely done for brain tumors. Among them, cases of glioblastoma associated with intracranial aneurysm are extremely rare and can be categorized to 3 groups; simultaneous development of glioblastoma and aneurysm, glioblastoma after the treatment of aneurysm, and aneurysm after the treatment of glioblastoma (Table 1). Some investigators have postulated that postradiotherapy aneurismal formation is developed by endothelial damage as shown at the radiation-induced vasculopathy. This endothelial damage leads to thrombosis, intimal narrowing, and atherosclerosis. Other report presented that the aneurysm may be occurred by the idiopathic trauma like a retraction. Unintended luminal shearing force to the artery makes focal arterial dissection leading to aneurysm formation. The direct invasion of malignant glioma can produce the intracranial aneurysm. Malignant glioma causes endothelial proliferation, telangiectasia, and fibrosis on adjacent small vessels. Aneurysmal dilatation was demonstrated at weakened arterial wall by the infiltration of tumor cells.

In our case, the intracranial aneurysm was not found before the tumor treatment. After the operation, chemotherapy, and radiotherapy, a pathologic circumstance for an aneurysm formation was developed. Because there were no vascular injury during the tumor resection and no evidence of tumor invasion to the aneurysm, we postulated two possibilities for de novo aneurysm; hemodynamic change after tumor resection or radiation effect. After the subtotal removal, most intratumoral shunting system may be removed without the removal of extratumoral feeding vessels. Pathologic high-pressure may be developed at the feeding artery leading to new aneurismal formation at the weak point. Radiation may cause the aneurysm formation considering the radiation field for glioblastoma.

**CONCLUSION**

De novo aneurysm can be developed while treating glioblastoma patient, although the accurate pathophysiology is still unknown. If the tumor is located near the major cerebral artery, the cerebral vessel study such as MRA, CTA, and DSA should be checked serially.

**References**

2. Bourekas EC, Newton HB, Figg GM, Slone HW: Prevalence and rupture rate of cerebral aneurysms discovered during intra-arterial chemo-

### Table 1. Reported cases of glioblastoma associated with intracranial aneurysm

<table>
<thead>
<tr>
<th>Study</th>
<th>Age/Sex</th>
<th>Tumor location</th>
<th>RTx (dose)</th>
<th>CTx (regimen)</th>
<th>Aneurysm location</th>
<th>Aneurysm rupture</th>
<th>Therapy of aneurysm</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
<td>Pia et al.</td>
<td>55/M</td>
<td>P, Rt.</td>
<td>N/D</td>
<td>N/D</td>
<td>PCoA, Rt</td>
<td>Yes</td>
<td>Observe</td>
<td>Die</td>
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<tr>
<td>N/D</td>
<td>Hemisphere</td>
<td>N/D</td>
<td>N/D</td>
<td>MCA</td>
<td>No</td>
<td>Clipping</td>
<td>Die</td>
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<td>T-O, Lt.</td>
<td>N/D</td>
<td>N/D</td>
<td>ACoA</td>
<td>Yes</td>
<td>Clipping</td>
<td>No deficit</td>
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<td>Gökalp et al.</td>
<td>50/M</td>
<td>F, Lt.</td>
<td>No</td>
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<td>Clipping</td>
<td>Die</td>
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<tr>
<td>Cheng and Shen</td>
<td>67/F</td>
<td>F, Lt.</td>
<td>Yes (40 Gy)</td>
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<td>No deficit at 1 yr</td>
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<td>Yes</td>
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<tr>
<td>Cohen et al.</td>
<td>53/F</td>
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<td>N/D</td>
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<td>52/F</td>
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<td>N/D</td>
<td>N/D</td>
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*De Novo Aneurysm after Treatment of Glioblastoma* | WS Yoon, et al.