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Case Report

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 aneurysm[11], but the incidence of glioblastoma associated with intracranial aneurysm is extremely rare[1,3,14,15]. 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/m^2 on day 1, procarbazine 60 mg/m^2 on day 8-21, and vincristine 1.4 mg/m^2, 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/m^2 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 emergent aneurysmal 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.

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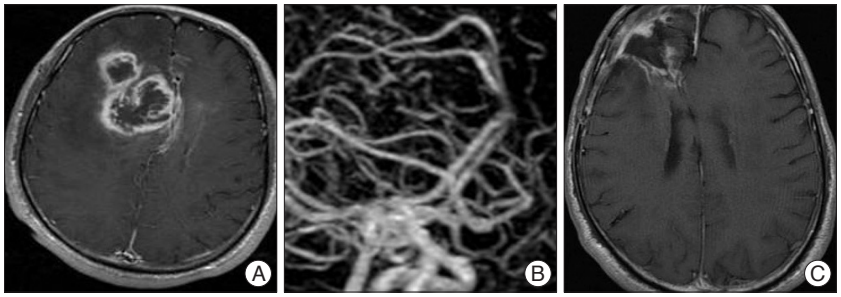

Fig. 1. A 4.7×5.8×4.1 cm sized mass is shown at the right frontal white matter extending to the subcortical region. The mass is enhanced heterogeneously and has irregular margin (A). On the MRA, the distal ACA is narrowed focally but the intracranial aneurysm is not found (B). After 7 cycles of adjuvant chemotherapy with temozolomides, tumor size is decreased definitely (C). MRA : magnetic resonance angiograph, ACA : anterior cerebral artery.

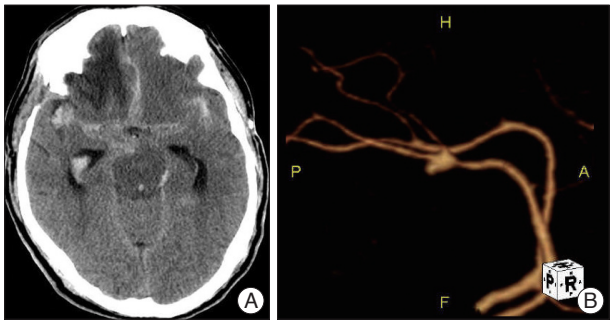

Fig. 2. Subarachnoid and intraventricular hemorrhages are shown on precontrast CT (A). On the CT angiography, a small aneurysm is shown at the junction of the pericallosal and callosomarginal artery (B). CT : computed tomography.

DISCUSSION

According to the literatures, brain tumors associated with the intracranial aneurysm are very rare (0.19-4%)[9,11,15,18,20]. But 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)[1-4,6,8,10,15].

Many theories explain the pathophysiology of intracranial aneurysm development in the brain tumor. Pia et al.[15] reported a high predominance of middle cerebral aneurysms with convexity tumors and internal carotid aneurysms with basal tumors. They postulated that aneurysms seem to be related to the arteries which supply the brain tumors. Increased blood flow to the brain tumors may induce secondary changes in the arterial wall directly and thus facilitate the formation of intracranial aneurysms. Therefore, the tumors having high vascularity like meningiomas are frequently associated with aneurysms. Hashiguchi et al.[10] reported that glioblastoma that had an increased flow through the feeding vessel and intratumoral shunting. In such condition, the aneurysm may develop at the feeding artery in similar to the aneurysm formation on arteriovenous malformation. Hormone like a growth factor can also cause intracranial aneurysm formation especially in the pituitary adenoma[12,13,19]. In the review of 150 pituitary tumors, Jakubowski and Kendall[12] found that the growth hormone-producing adenomas had intracranial aneurysm significantly compared with the chromophobe adenomas (13.8% vs. 5.1%, $p<0.005$). Radiation therapy to the brain tumor is also one of the rare causes of de novo aneurysm. 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[16,17]. 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[7]. The direct invasion of malignant glioma can produce the intracranial aneurysm. Malignant glioma causes endothelial proliferation, telangiectasia, and fibrosis on adjacent small vessels. Aneurismal dilatation was demonstrated at weakened arterial wall by the infiltration of tumor cells[1,5].

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.

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Table 1. Reported cases of glioblastoma associated with intracranial aneurysm

Study	Age/Sex	Tumor location	RTx (dose)	CTx (regimen)	Aneurysm location	Aneurysm rupture	Therapy of aneurysm	Outcome
Simultaneous development of glioblastoma and intracranial aneurysm								
Pia et al.[15]	55/M	P, Rt.	N/D	N/D	PCoA, Rt	Yes	Observe	Die
	N/D	Hemisphere	N/D	N/D	MCA	No	Clipping	Die
	54/M	T-O, Lt.	N/D	N/D	ACoA	Yes	Clipping	No deficit
Gökalp et al.[8]	50/M	F, Lt.	No	No	ACoA, Lt.	Yes	Clipping	Die
Cheng and Shen[3]	67/F	P, Lt.	Yes (40 Gy)	N/D	ICA, Lt.	No	Clipping	No deficit at 1 yr
Bourekas et al.[2]	N/D	N/D	N/D	Yes (N/D)	N/D	No	N/D	Die
Development of glioblastoma after the treatment of intracranial aneurysm								
Andrews et al.[1]	53/F	T, Lt.	N/D	N/D	MCA, Lt.	Yes	Clipping	No deficit
De Chiara et al.[6]	52/F	T, Rt.	Yes (N/D)	N/D	ICA, Rt.	Yes	Clipping	No deficit at 1yr
Development of intracranial aneurysm after the treatment of glioblastoma								
Cohen et al.[4]	35/F	F, Rt.	N/D	N/D	ACA, Lt.	Yes	Coiling	Die
Hashiguchi et al.[6]	44/F	F, Lt.	Yes (60 Gy)	Yes (ACNU)	MCA, Lt.	No	Observe	Vegetable state at 3 mo
This present	57/M	F, Rt.	Yes (59.4 Gy)	Yes (PCV, TMZ)	distal ACA, Rt.	Yes	Clipping	No deficit

P : parietal, T-O : temporooccipital, F : frontal, T : temporal, N/D : not described, PCoA : posterior communicating artery, MCA : middle cerebral artery, ACoA : anterior communicating artery, ICA : internal cerebral artery, ACA : anterior cerebral artery

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