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Case Report

Ruptured Dissecting Aneurysm of the Carotid Artery 12 Years after Gamma Knife Therapy for Pituitary Adenoma

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Objective: We report a rare case of carotid artery dissection leading to fatal epistaxis 12 years after Gamma knife surgery.
Case Presentation: A 65-year-old woman underwent Gamma knife surgery for remnant pituitary adenoma adjacent to the left cavernous sinus after transsphenoidal tumor removal. After 12 years, she developed repetitive critical hematemesis subsequent to cardiopulmonary arrest, and a dissecting aneurysm of the cavernous segment of the left internal carotid artery (ICA) was identified by cerebral angiography after resuscitation and massive blood transfusion. Effective hemostasis was confirmed by endovascular embolization to occlude the affected carotid artery. She was transferred to a rehabilitation facility 1 month after onset.
Conclusion: The etiology of this pathology may have been a collapsed vasa vasorum or fibrosis of adventitia on the carotid wall adjacent to the irradiated site. We need to suspect this rare but serious pathology in patients with histories of irradiation of the cavernous region who develop massive hematemesis of unknown origin.

Keywords ▶ pituitary adenoma, Gamma knife, dissection of the internal carotid artery, carotid-cavernous fistula, epistaxis

Introduction

Approximately 30 patients with intracranial aneurysms or rupture of the intracranial vascular wall after radiotherapy have been reported. These complications are rare,[1–15] but hemorrhage from major arteries requires emergency care, leading to a fatal outcome in some cases. In this study, we report a patient in whom a dissecting aneurysm of the internal carotid artery (ICA) at the cavernous region in the irradiated area developed 12 years after Gamma knife therapy for pituitary adenoma, and its rupture induced massive epistaxis.

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Case Presentation

A 65-year-old woman underwent transsphenoidal surgery for non-functioning pituitary adenoma and subsequent radiotherapy by Gamma knife for the residual lesion in the cavernous sinus which was conducted at maximum and marginal radiation doses of 24 and 12 Gy, respectively, in 2006. Twelve years later, she was transported to the emergency department of our hospital because of the loss of consciousness after hematemesis after headache persisting for 10 days. Hematemesis (approximately 300 mL) developed 3 days before emergency admission. On arrival of the ambulance crew to her home, her blood pressure was unmeasurable due to too low level. On arrival at our hospital, consciousness was improved to clear the level and vital signs, including the blood pressure, were stable. No abnormal findings were noted on upper gastrointestinal endoscopy.

Hematemesis recurred 4 days after admission. Upper gastrointestinal endoscopy revealed an ulcer at the greater curvature of the stomach. Although there was no active hemorrhage, the ulcer was considered to be the source of hemorrhage and clipping for the visible vessels in the ulcer was performed. At this event, she went into shock and fractured her femur neck upon falling down. Femoral head replacement was performed 5 days after admission. After surgery, the administration of an anticoagulant (edoxaban) was started to prevent deep venous

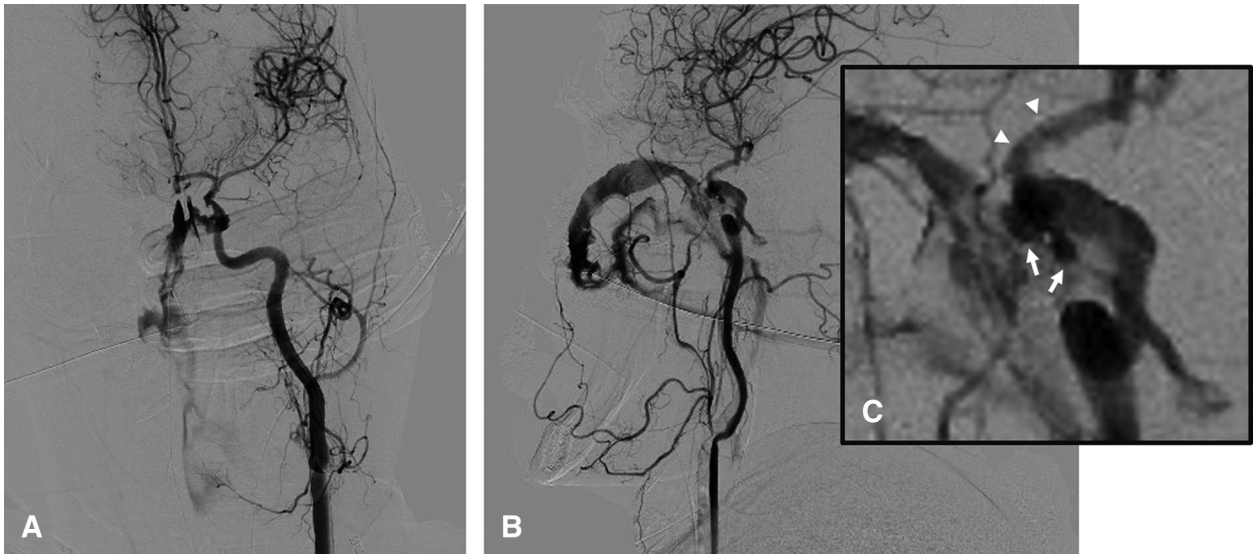

Fig. 1 Left common carotid angiograms in the anteroposterior view (**A**), lateral view (**B**), and superimposed view (**C**) showing irregularity and aneurysmal dilatation (arrows) of the ICA at the inferior wall of the cavernous segment (C3-4) associated with marked extravasation. The distal supraclinoid segment of the ICA has narrowed (arrowheads). ICA: internal carotid artery

thrombosis (DVT). After recurrent massive hematemesis 10 days after admission, electrocardiography demonstrated pulseless electrical activity and resuscitation was performed. After 10 minutes, return of spontaneous circulation was achieved. As hemorrhage from the gastric ulcer was suspected, upper gastrointestinal endoscopy was performed while maintaining systemic circulation by massive fluid replacement, blood transfusion, and balloon pumping blockage of the aorta. However, massive blood retention in the stomach made observation difficult, and abdominal endovascular embolization was selected. Abdominal arteriography did not reveal the source of hemorrhage, and epistaxis gradually became severe. Head and neck angiography demonstrated massive extravascular leakage from the cavernous sinus of the left ICA to the nasal cavity, suggesting a carotid-cavernous fistula (CCF) as an etiological factor. In the department of otorhinolaryngology, astriction was attempted, but hemostasis was difficult, and an emergency call to the department of neurosurgery was made. On left common carotid angiograms, irregularity of the inferior wall at the cavernous sinus of the ICA (C3-4) and dilation of the vascular diameter were observed, leading to a diagnosis of a ruptured dissecting aneurysm. Narrowing of the vascular diameter was observed at an area distal to the C3 segment of the ICA (**Fig. 1**).

Embolization at an area proximal to the C3 segment of the left ICA, where arterial dissection was clear, was selected. Initially, to reduce the volume of blood loss as promptly as possible, a 9Fr OPTIMO guiding catheter with a balloon (Tokai Medical Products, Aichi Japan) was inserted into the left common carotid artery to block it. This reduced hemorrhage from the CCF to the nasal cavity, and the blood pressure, which had ranged from 50 to 60 mmHg, was maintained at 80 to 90 mmHg. It was impossible to evaluate a collateral pathway for the following reasons: balloon pumping blockage of the contralateral aorta had been conducted through the left femoral artery, and marked edema of the upper limb made approaching through the upper limb difficult. A microcatheter (2.2Fr Carnelian ER microcatheter, Tokai Medical Products, Aichi, Japan) was guided to the C3 segment of the ICA distal to the site of dissection coaxially to a CHIKAI 14 200 cm (Asahi Intecc, Aichi, Japan). Regarding this site as a distal end, coil embolization was performed using three Target XL 360 soft 5 mm × 15 cm, four Target XL 360 soft 4 mm x 12 cm, and five Target XL 360 soft 3 mm × 9 cm (Stryker, Kalamazoo, MI, USA) (**Fig. 2A**). At this point, there was a decrease in the volume of blood loss, but extravascular leakage into the nasal cavity remained. Complete hemostasis should be confirmed because her systemic circulation remained unstable just after the massive hemorrhage. Therefore, additional embolization with 50% n-butyl-2-cyanoacrylate (NBCA) was performed after confirming the absence of anterograde blood flow to the distal intracranial ICA (**Fig. 2B**). Subsequently, slight extravascular leakage from the external carotid artery system was observed, but the volume was markedly small. The blood pressure became stable. Post-embolization angiograms confirmed a favorable collateral pathway mediated by the posterior communicating artery (**Fig. 3A**). Blood transfusion with 46 units of packed

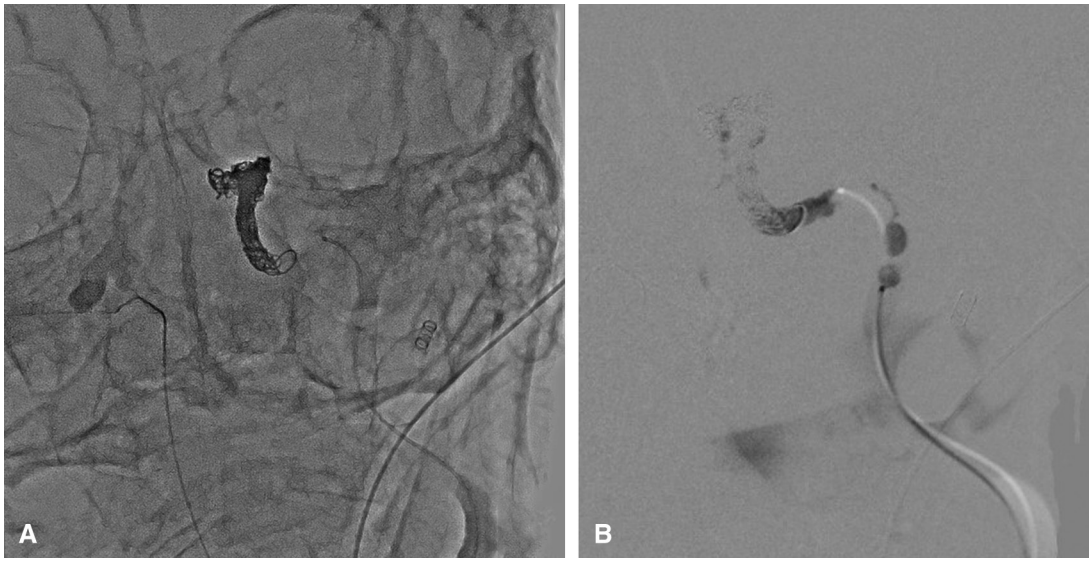

Fig. 2 Fluoroscopic images of the anteroposterior view after parent artery occlusion showing coils placed from the C4 portion to the petrous portion of the ICA (**A**), and injection of 50% n-butyl 2-cyanoacrylate into the same portion of the ICA (**B**). ICA: internal carotid artery

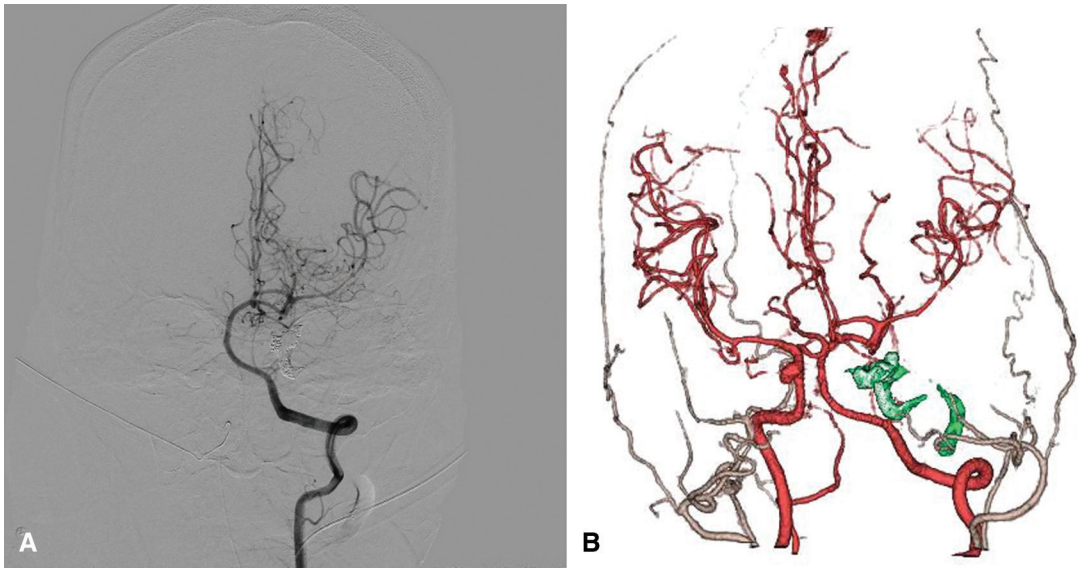

Fig. 3 Right vertebral angiogram in the anteroposterior view (**A**) after endovascular treatment showing cross flow via the posterior communicating artery. CT angiogram in the anteroposterior view (**B**) after endovascular treatment showing complete occlusion of the left ICA and blood flow to the peripheral middle cerebral artery. CT: computed tomography; ICA: internal carotid artery

red blood cells, 30 units of fresh frozen plasma, and 20 units of platelet concentrate was required before the completion of hemostasis.

Three-dimensional computed tomography angiography (CTA) the day after surgery revealed occlusion of the left ICA and a collateral pathway mediated by the left posterior communicating artery (**Fig. 3B**). Perfusion computed tomography (CT) suggested a reduction in watershed area blood flow in the left cerebral hemisphere (there were increases in the cerebral blood flow [CBF], cerebral blood volume [CBV], and mean transit time [MTT] in the watershed area), but revascularization surgery was impossible due to the general condition after resuscitation and massive blood transfusion. After endovascular treatment, cerebral and systemic circulation were intensively managed. Magnetic resonance imaging (MRI)-diffusion-weighted image (DWI) revealed fresh infraction in the same area as the above watershed ischemia (**Fig. 4**). The watershed infarction

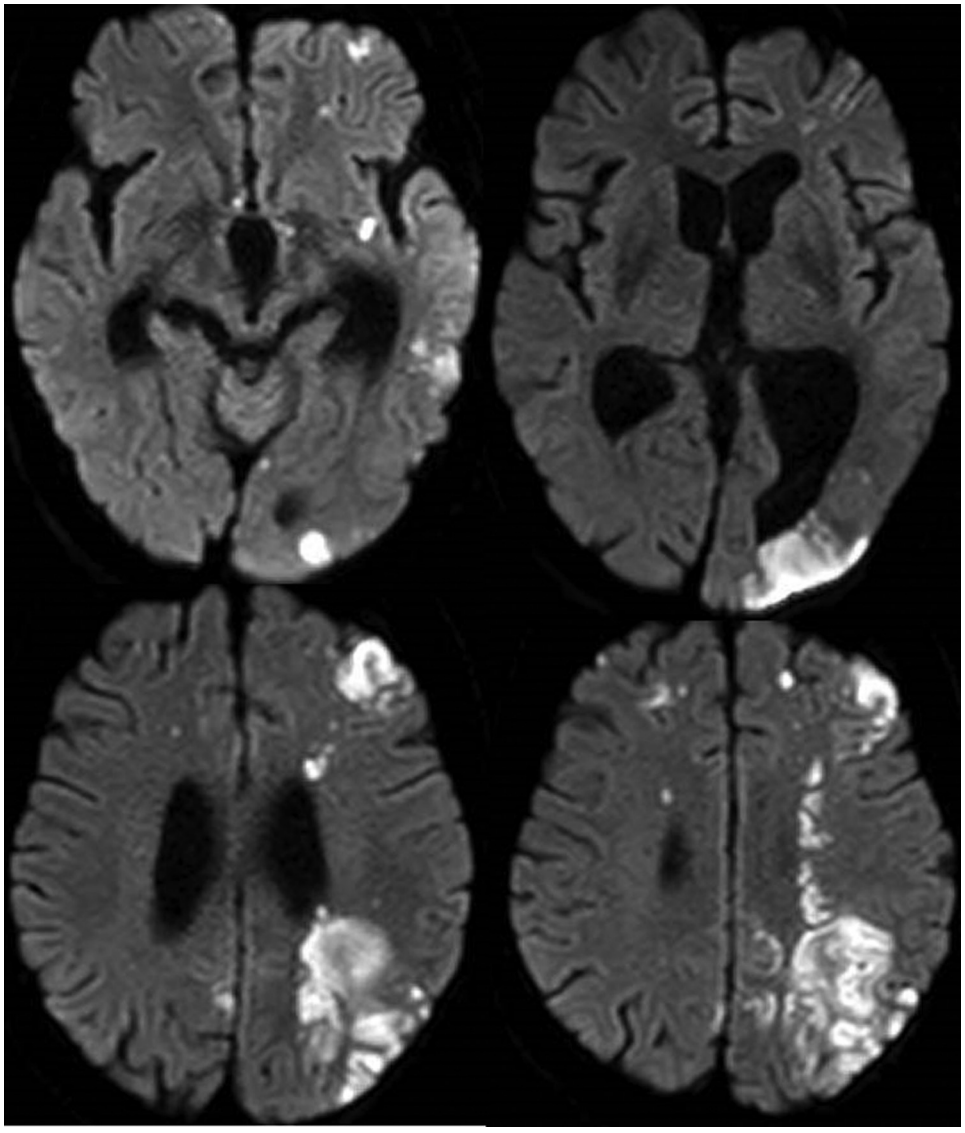

Fig. 4 Axial diffusion-weighted magnetic resonance image one day after endovascular treatment showing ischemic lesions in the watershed area of the middle cerebral artery.

related to hemorrhage-associated hypoperfusion of the left ICA, which had persisted for 6 hours until hemostasis was achieved, was suggested. Postoperative antithrombotic therapy was not performed considering the risk of rebleeding. Conservative treatment for acute ischemic stroke and rehabilitation were performed. One month after endovascular treatment, the consciousness level was evaluated as E4V3M6 using the Glasgow Coma Scale (GCS) and the manual muscle testing (MMT) score was 4/5. Motor aphasia and incomplete paralysis of the right upper and lower limbs remained. She was transferred to a rehabilitation hospital with a modified Rankin Scale (mRS) score of 3.

Discussion

Nine patients with aneurysm formation and rupture in the intracranial arteries associated with stereotactic radiotherapy have been reported.[1,2,6–8,12,14,15] In four patients, aneurysms of the anterior inferior cerebellar artery developed after Gamma knife therapy for acoustic neuroma,[12,14,15] whereas massive epistaxis from the ICA developed after stereotactic radiotherapy for tumors involving the parasellar region to skull base in the other five patients,[2,6–8] similar to the present patient.

Many studies have reported necrotic rupture of the cervical carotid artery wall after radiotherapy for malignant cervical

Table 1 Reported cases of ICA ruptured aneurysm after stereotactic radiotherapy

Authors (year)	Age Sex	Diagnosis	RT course and dose	Period from the final RT to bleeding	Aneurysm location	Treatment	Outcome (follow-up)
Auyeung et al. (2003)	52 M	Nasopharyngeal carcinoma	1. Conventional RT (not described) 2. SRS (not described)	3 months	Petrous	Stent	Good (3 months)
Cheng et al. (2008)	57 M	Nasopharyngeal carcinoma	1. Conventional RT (70.4 Gy) 2. 3DCRT (40 Gy) + brachytherapy (18 Gy)	7 months	Petrous	None (self-thrombosis)	Good (18 months)
Endo et al. (2011)	62 F	Pituitary adenoma	1. SRS (25–35 Gy) 2. Conventional RT (55.2 Gy)	13 years	Petrous	Coil + EC-IC bypass	Good (2 months)
Fujita et al. (2014)							
Case1	29 M	Ewing PNET	1. SRT (45.0–54.9 Gy) 2. SRT (53.5–62.3 Gy) 3.SRT (52.8–60.0 Gy)	6 months	Petrous	Coil, PAO	Death (6 months, tumor relapse)
Case2	61 M	Atypical meningioma	1. SRS (12.0–25.0 Gy) 2. SRT (30.0–47.6 Gy)	6.4 years	Cavernous	Coil, PAO	Good (24 months)
Our case (2019)	65 F	Pituitary adenoma	SRS (12.0–24.0 Gy)	12 years	Cavernous	Coil, PAO	Moderate disability, mRS 3 (3 months)

3DCRT: three-dimensional conformal radiation therapy; EC-IC bypass: external carotid artery–internal carotid artery bypass; ICA: internal carotid artery; mRS: modified Rankin scale score; PAO: parent artery occlusion; PNET: primitive neuroectodermal tumor; RT: radiotherapy; SRS: stereotactic radiosurgery; SRT: stereotactic radiation therapy

tumors, but pathologically, neutrophil or eosinophil infiltration in the arterial wall and all-layer necrosis may be involved.[11] As etiological factors, occlusion of the vasa vasorum and the early progression of fibrous or arteriosclerotic changes in the adventitia have been suggested.[9,11,16,17] If an area adjacent to the cavernous sinus of the ICA is irradiated with high-dose radiation, a condition, as demonstrated in the present case, may develop in the presence of transsphenoidal surgery, sellar base defects related to adenoma progression, or inflammatory changes. Many physicians, including neurosurgeons and radiologists, should recognize the presence of this condition, which may lead to a fatal outcome. Regarding follow-up using MRI after surgery for skull base lesion including pituitary tumors, no criteria have been established, but the postoperative state should be regularly evaluated using magnetic resonance angiography (MRA). If vascular irregularity or aneurysm formation is suspected, CTA or angiography should be considered.

Furthermore, in the present case, the oral administration of an anticoagulant was started to prevent DVT. We cannot deny the fact that this induced fatal hemorrhage.

When confirming this condition, prompt management is necessary. However, endovascular treatment was selected in all previously reported patients with this condition.[2,6–8] In one patient, hemostasis was achieved through spontaneous occlusion at the stenotic site during surgery. In one patient, stenting was performed. In the other patients, including ours, coil embolization of a parent blood vessel was conducted. In one of these, this procedure was combined with bypass (**Table 1**). The prognosis was favorable except in one who died of the tumor. In the present case, cardiopulmonary arrest occurred and massive blood transfusion was required after resuscitation. Concomitant cerebral infarction was present, but the mRS score on discharge was 3. In the present case, it was difficult to evaluate the possibility of revascularization surgery in detail in the critical vital signs just after the resuscitation. However, if a collateral pathway and CBF can be sufficiently evaluated in a stable condition of vital sign, low- or high-flow revascularization surgery may lead to a better prognosis.

To achieve this, this pathognomonic condition should be suspected earlier based on the patient's medical history or diagnostic imaging findings, and earlier treatment should be performed before fatal hemorrhage.

Conclusion

We report a patient in whom a dissecting ICA aneurysm developed after radiotherapy for a pituitary tumor, inducing

massive epistaxis. Although such cases are rare, hemorrhage may be fatal; therefore, prompt diagnosis and treatment are necessary. Occlusion of the parent vessels with the detailed assessment of a collateral pathway for revascularization is necessary. However, if massive hemorrhage develops, as demonstrated in the present case, detailed examination may be difficult. Therefore, physicians should recognize findings of this pathology and suspect it earlier based on the patient's medical history or imaging findings for early diagnosis. This may lead to a favorable prognosis.

Disclosure Statement

The authors declare no conflicts of interest.

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