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Development of a Carotid Cavernous Aneurysm after Medical Treatment of a Prolactinoma: A Case Report

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Abstract

This is the first report of a carotid aneurysm that developed from a cavernous carotid artery contiguous with a prolactinoma during medical treatment of the prolactinoma, which gradually grew larger while the tumor regressed. A 78-year-old woman presented with headache and neurological symptoms indicating the involvement of cranial nerves in the cavernous sinus. Gadolinium-enhanced T1-weighted magnetic resonance imaging on admission revealed an abnormal right cavernous sinus, with an approximately 17 mm mass extending into the right cavernous portion of the internal carotid artery, and was contiguous with the intracavernous carotid artery. She was diagnosed with pituitary apoplexy due to a prolactinoma and started cabergoline treatment. After medical treatment, a carotid aneurysm emerged. The aneurysm continued to grow and reached a maximum diameter of 10.4 mm at 81 months after the initiation of treatment. The patient underwent endovascular coil embolization, following which the aneurysm regressed. Association between a prolactinoma and the development of a contiguous aneurysm remains undetermined. However, this is an odd phenomenon, and to the best of our knowledge, this is the first reported case of the development of an aneurysm that was associated with a pituitary tumor.

Keywords: intracranial aneurysm, cabergoline, prolactinoma, endovascular procedure

Introduction

Many studies have reported the association of a pituitary adenoma (PA) and an intracranial aneurysm (IA), and these studies have shown the incidence of PA with IA to be 0.5–7.4%.[1–5] Some authors have reported that the incidence of IA was higher in patients with pituitary tumors than that in the general population, but whether PAs contributed to IA formation remains unclear. There are several reports regarding cases of PA coexisting with an adjacent IA.[6–11] However, since transsphenoidal surgery is the preferred method for the treatment of symptomatic intrasellar PAs, very few cases have been reported about changes in the size of pituitary tumors and IAs after medical treatment. There are only two cases of growth hormone (GH)-secreting PA with a coexisting aneurysm that enlarged during medical treatment.[12,13] To the best of our knowledge, this is the first case of a carotid aneurysm that developed in a cavernous carotid artery and was contiguous with a prolactinoma. The aneurysm finally grew to 10.4 mm as the prolactinoma responded to treatment; hence, the patient underwent endovascular coil embolization.

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Case Report

History and examination

A 78-year-old woman with a history of angina, diabetes, hypertension, and hypothyroidism suddenly developed pain on the right side of her face and right lower rear molar. Four days later, she could not consume food due to right facial pain. She

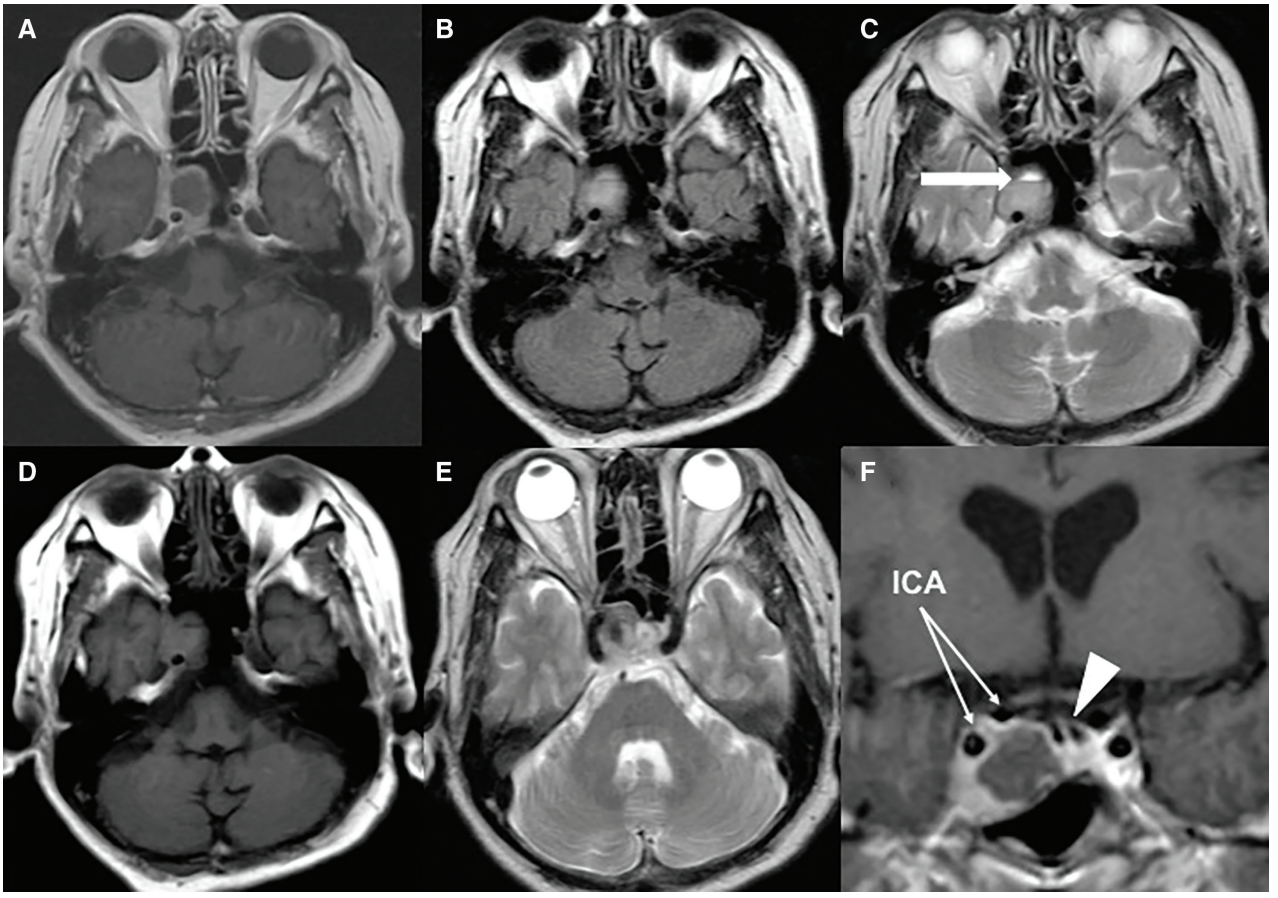

Fig. 1 MRI findings at the time of admission. T1-weighted sequence with gadolinium enhancement reveals a cystic mass in the right cavernous sinus (A). Fluid-attenuated inversion recovery (B), T2-weighted image (C), and T1-weighted image (D). T2-weighted image (C) shows the fluid–fluid level (arrow), and T2-weighted image (E) sequence reveals a lesion with a high-signal intensity in the left cavernous sinus. The prolactinoma is adjacent to the right cavernous sinus portion of the ICA on the T1-weighted sequence with gadolinium enhancement (F). The pituitary stalk is displaced by the compression of tumor (arrowhead). MRI: magnetic resonance imaging, ICA: internal carotid artery.

also had right side ptosis. Gadolinium-enhanced T1-weighted magnetic resonance imaging (MRI) on admission revealed an abnormal right cavernous sinus, with an approximately 17 mm mass extending into the right cavernous portion of the internal carotid artery (ICA) and extending below the intracavernous ICA into the inferior cavernous sinus compartment (Knosp–Steiner classification grade 3B) (Fig. 1A–1D).[14,15] A high-intensity lesion on the left side of the mass, which seemed to be a hemorrhage, was detected with T2-weighted imaging (Fig. 1E), and the hemorrhage also led to the formation of a fluid–fluid level (Fig. 1C). Since a confirmed diagnosis of an aneurysm could not be made based on these findings, an angiography was performed; however, it failed to identify any specific abnormalities around the ICA (Fig. 2A and 2B). Biochemical investigations revealed prolactin, 585 (6.1–30.5) ng/ml; adrenocorticotropic hormone, 17 (7.2–63.3) pg/ml; GH, 0.64 (0.28–1.64) ng/ml; somatomedin, 228 (55–170) ng/mL; follicle-stimulating hormone, 2.3 (2.0–16.7) mIU/ml; luteinizing hormone, 0.2 mIU/ml (<0.2); and thyroid-stimulating hormone, 1.99 (0.3–4.3) μIU/ml.

Based on the extremely elevated prolactin concentration (585 ng/mL), she was diagnosed with pituitary apoplexy caused by a prolactinoma that had probably invaded the cavernous sinus. Treatment was initiated using cabergoline, 0.25 mg/week, and the prolactinoma appeared to respond, as indicated by reduced serum prolactin concentration (95.4 ng/mL), after approximately 3 weeks of treatment. Afterward, the patient's prolactin concentration progressively decreased, and the prolactin concentration was 3.2 ng/mL at 30 months (Fig. 3A and 3B), 2.6 ng/mL at 56 months (Fig. 3D and 3E), and 34.5 ng/mL at

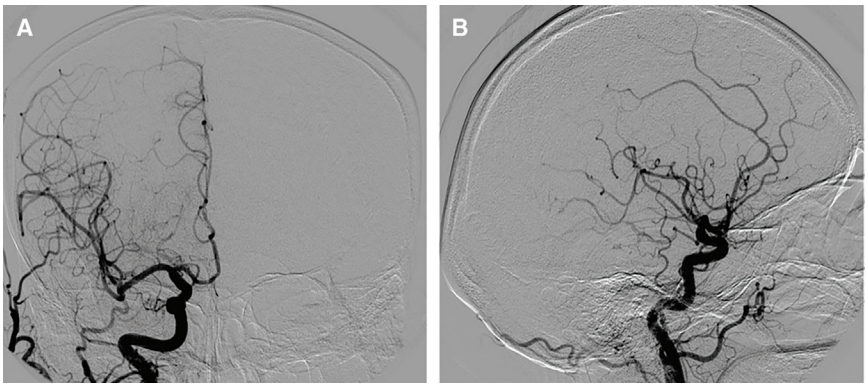

Fig. 2 Angiography findings at the time of admission. Anterior–posterior (A) and lateral (B) views of right common carotid artery (ICA) angiography at the time of admission reveals no aneurysm in the cavernous portion of the ICA. ICA: internal carotid artery.

81 months (Fig. 3G and 3H) after the commencement of cabergoline treatment. The tumor also decreased in size from 18.7 mm × 15.1 mm × 17.4 mm on admission (Fig. 1A and 1F) to 9.2 mm × 8.1 mm × 6.1 mm at 81 months after the commencement of medical therapy (Fig. 3G and 3H). Her symptoms disappeared as the tumor reduced in size. However, approximately 30 months after the initiation of treatment, a brain MRI revealed a newly formed aneurysm in the cavernous segment of the right ICA (aneurysm maximum diameter: 1.8 mm) (Fig. 3C). The aneurysm continued to grow and reached a maximum diameter of 3.0 mm at 56 months and 10.4 mm at 81 months after the commencement of treatment (Fig. 3F and 3I). The patient then underwent endovascular coil embolization, following which the aneurysm disappeared (Fig. 4). Five years after embolization and cabergoline treatment, the patient continues to be symptom free and the tumor has not recurred. However, the aneurysm became recanalized, and the patient is still being followed up closely.

Discussion

The association between IAs and PAs has been reported in many studies. Pant et al.[16] designed a study to evaluate such an association in a large series of 467 PA cases. An aneurysm was more frequently seen with increasing age, and the age distribution resembled that of aneurysms in the general population. Although the combination of an aneurysm and a PA was most frequently seen in patients with nonfunctioning adenomas and was least frequent in cases of prolactinomas, Pant et al. concluded that this association was due to age. Furthermore, they observed no association between IA and PA, and between hormone secretion and the invasive nature of the tumor since there were no cases of intrasellar aneurysms or aneurysms that were directly in contact with an adenoma. However, some authors reported that the incidence of cerebral aneurysms in patients with PAs was higher than in the general population.[3–5,17,18] Additionally, IAs are observed more frequently in GH-producing PAs.[3,12,19,20] Oh et al.[21] retrospectively analyzed 800 patients who underwent transsphenoidal surgery for PA and 3850 control patients from the general population. They also concluded that the prevalence of IA was higher in patients with PA compared to that in age-matched controls using comparison analysis. However, they pointed out that the coexistence of IA and pituitary tumors tends to be biased toward increased incidence, because the vascular anatomy around the PAs is more likely to be checked in detail in patients with PAs.

Two cases similar to our case have been reported, and they involved GH-secreting pituitary tumors. Hori et al.[12] reported a case of enlargement of an aneurysm that was contiguous with a GH-secreting PA as a result of tumor regression due to bromocriptine therapy. Khachatryan et al.[13] also reported that shrinkage of a GH-secreting PA after medical treatment was associated with enlargement of the aneurysm that was embedded within the tumor. Regarding the association between hormones and PAs, it has been hypothesized that an elevated level of GH and insulin-like growth factor-1 induce the formation of an IA due to arteriosclerosis, degenerative modifications, and collagen change in the arterial wall.[4,5] However, in our case, the IA increased as the prolactinoma regressed, so the development of the IA was unlikely to be affected by hormonal effects alone. Apart from the effects of endocrine hormones,

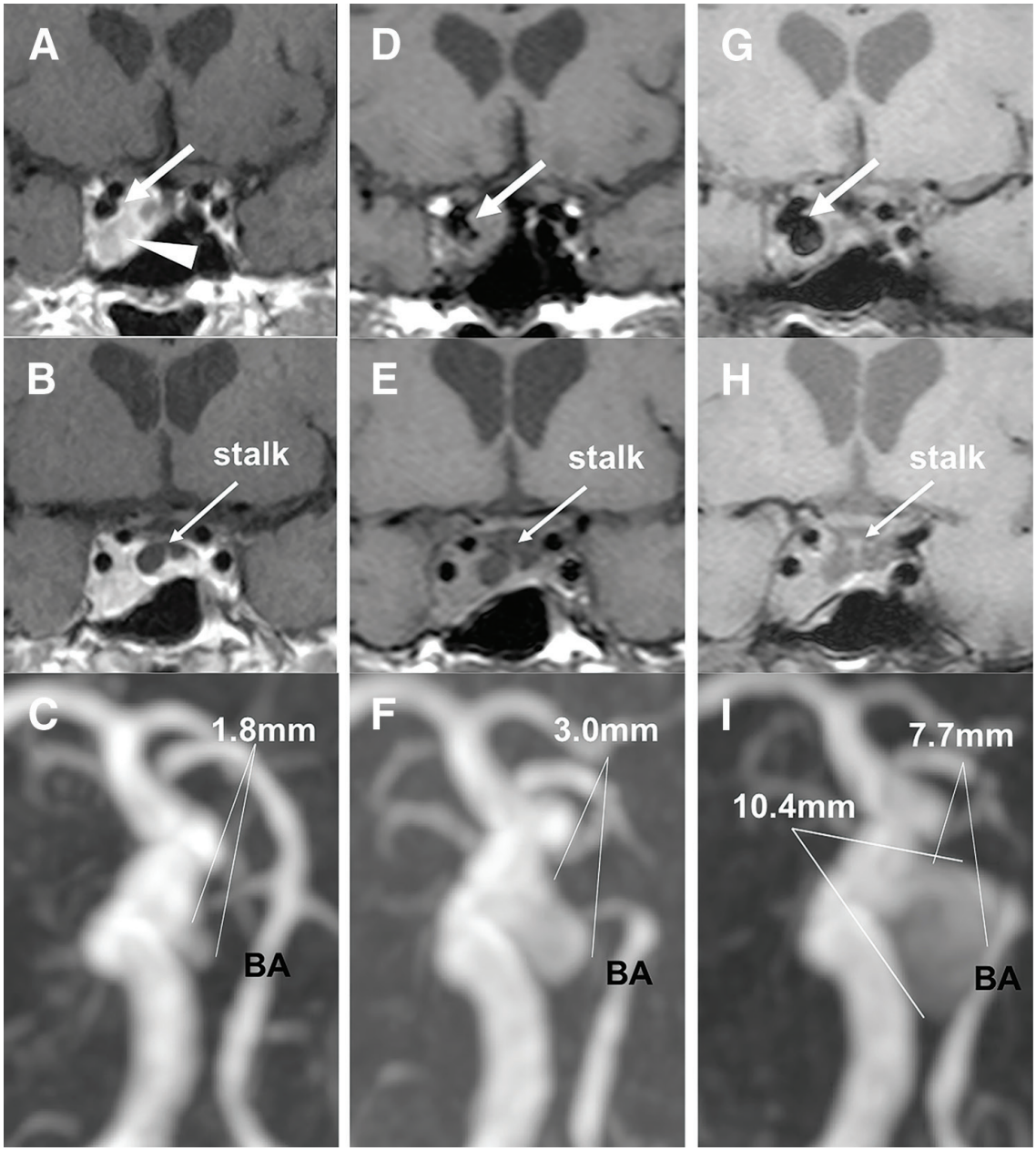

Fig. 3 Coronal MRI and MRA findings. Coronal T1-weighted sequence with GE images (A and B) and MRA (C) 30 months after cabergoline treatment of the prolactinoma. T1-weighted sequence with GE (A) reveals that the prolactinoma (arrowhead) extended to the lateral side of the ICA and is contiguous with the aneurysm (arrow). The coronal T1-weighted magnetic resonance images (D and E) and MRA images (F) 56 months after the initial treatment. Coronal fat suppression T1-weighted magnetic resonance images (G and H) and MRA images (I) 81 months after the initial treatment. A new aneurysm emerged in the cavernous portion of the right ICA (arrow) and has grown larger during the treatment of the prolactinoma (C, F, and I). MRI: magnetic resonance imaging, MRA: magnetic resonance angiography, GE: gadolinium enhancement, ICA: internal carotid artery, BA: basilar artery.

several mechanisms of aneurysm formation associated with PAs have been proposed, such as local circulatory stress, mechanical effects, and direct invasion.[20,22] Oh et al.[21] demonstrated that cavernous sinus invasion of a pituitary tumor into the ICA was correlated with the incidence of IA; however, hormone type and sex were not found to be associated factors using multivariate analysis. In our present case, a prolactinoma was contiguous with the intracavernous carotid artery before medical

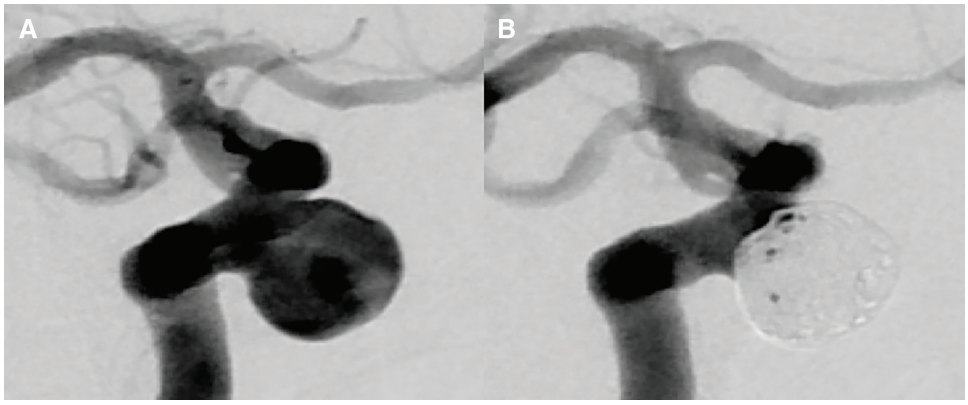

Fig. 4 Angiography findings before and after embolization of the right ICA. The aneurysm's diameter was 10.4 mm before embolization (A); after coil embolization, blood flow through the aneurysm was almost completely eliminated (B). ICA: internal carotid artery.

treatment. Based on these hypotheses, the aneurysm may have been influenced by physical effects of the prolactinoma, such as stretching and compression of the artery; therefore, the wall of the cavernous portion of the ICA was invaded and weakened by it.[9,10] The weakened arterial wall and blood flow caused a new small aneurysm, and the traction force produced by the regression contributed to its enlargement.[22]

However, a clear association between PA and IA remains undetermined, so whether these hypotheses contributed to the development of the IA in our case is not clear.

This is the first report of a case of a carotid aneurysm that emerged from the cavernous carotid artery that was contiguous with a prolactinoma during medical treatment, which then gradually grew larger as the tumor regressed. Whether the prolactinoma contributed to the development of the IA is unclear; however, we have presented this odd phenomenon and where the development of an aneurysm was associated with a pituitary tumor.

Conflicts of Interest Disclosure

All authors have no conflicts of interest.

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