

Case Report

Occlusion of the Internal Carotid Artery due to Intracranial Fungal Infection

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In recent years the immunocompromised population has increased rapidly to include people with acquired immune deficiency syndrome (AIDS), drug abusers, and transplant patients. Accordingly, the incidence of intracranial fungal infection has increased. Our institution experienced 2 cases of internal carotid artery (ICA) occlusion due to invasion of the cavernous sinus by an intracranial fungal infection. The first case was a 60-year-old man who presented with headache, eye pain, conjunctival injection, right-sided diplopia, and blurred vision. Infected tissues within the frontal and ethmoid sinuses were removed via bifrontal craniotomy and endoscopic sinus surgery through the Caldwell Luc approach. The second case was a 63-year-old woman who developed right-sided facial pain after a tooth extraction. The infection was not controlled despite continuous use of anti-fungal agents, resulting in death from sepsis. We believe that when intracranial fungal infection is suspected in a patient with orbital symptoms and a focal neurologic deficit, immediate angiographic investigation of possible ICA occlusion is warranted. Aggressive treatment with antifungal agents is the only way to improve prognosis.

Key Words : Internal carotid artery occlusion · Fungal infection.

INTRODUCTION

In recent years the immunocompromised population has increased rapidly to include people with acquired immune deficiency syndrome (AIDS), drug abusers, and transplant patients. Accordingly, the incidence of intracranial fungal infection has increased. The most common causative organisms of intracranial fungal infection are aspergillus species, followed by cryptococcus, mucormycosis, candida, cladosporium and dematiaceous fungi^{5,11,12}. Although rare, several cases of intracranial fungal infections have been reported that involved invasion of the cavernous sinus⁸. Intracranial fungal infection is caused by the extension of a localized nasal infection, infection of the paranasal sinuses, or direct infection of intracranial cavities. Though exceedingly rare, cavernous sinus invasion has been reported from direct infection as well as from invasion by adjacent vessels¹⁴. Cavernous sinus infection is accompanied by severe complications such as intracerebral hemorrhage, subarachnoid hemorrhage, and cerebral infarction due to internal carotid artery (ICA) occlusion^{1,3,8,9}.

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Our center experienced 2 cases of ICA occlusion due to cavernous sinus invasion by intracranial fungal infections. We report these cases here along with a review of the relevant literature.

CASE REPORT

Case 1

A 60-year-old man visited our clinic with a 7-day history of headache, eye pain, conjunctival injection, right-sided diplopia, and blurred vision. The patient was medicated due to poorly-controlled insulin-dependent diabetes mellitus. Initial brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) revealed no parenchymal lesion or vascular lesion other than a small lacunar infarction (Fig. 1A, B). Under the diagnostic impression of diabetic ischemic 3rd and 6th nerve palsies with sinusitis, steroid treatment was begun. After 2 months, the patient returned with aggravation of the previous symptoms. Laboratory investigation showed a white blood cell (WBC) count of 11,890/mm³, C-reactive protein (CRP) of 6.2 mg/dL, blood glucose of 225 mg/dL, and erythrocyte sedimentation rate (ESR) of 53 mm/hour. He was admitted, and on hospital day 5 follow-up brain MRI and MRA revealed findings suggestive of invasive sinusitis in the frontal and anterior ethmoid sinuses and occlusion of the petrous and cavernous portions of the right ICA (Fig. 1C, D). Six-vessel cerebral angiography led to identification of occlusion of the right proximal ICA as well as the right anterior

circulation, supplied by the left anterior communicating artery (ACA) and the right posterior communicating artery (PCA) (Fig. 1E-H). The patient was treated with amphotericin B (50 mg/day) and steroids for 5 days; however, due to increased creatinine levels this was changed to liposomal amphotericin. Symptoms did not improve, so surgery was performed. The infected tissues were removed within the frontal and ethmoid sinuses via a bifrontal craniotomy and endoscopic sinus surgery through the Caldwell Luc approach. The pathologic diagnosis was mucormycosis. Postoperative computed tomography (CT) of the paranasal sinuses showed near-total removal of infected tissue. Follow-up angiography showed that still no contrast media filled the right ICA. Hemodynamics were maintained by multiple collateral vessels supplying the right anterior circulation. The patient's symptoms improved with persistent use of antifungal agents. At the present time, no notable neurologic deficits remain.

Case 2

A 63-year-old woman visited our clinic with a 2-day history of right facial pain, headache and visual disturbances. On neurologic examination the patient had lancinating pain on the V2, V3 area. On ophthalmologic examination, there was decreased visual acuity in the right eye (OD/OS : 0.3/0.9). Laboratory investigation showed a WBC count of 5,990/mm³, CRP of 3.4 mg/dL, blood glucose of 104 mg/dL, and an ESR of 61 mm/hour. Cultures of sputum and blood were negative. Brain MRI and MRA showed a mass lesion involving the right nasal cavity and ethmoid sinus that extended into the right optic canal, the sphenoid sinus and the cavernous sinus (Fig. 2A, B). Transnasal endoscopic biopsy demonstrated aspergillosis.

Amphotericin B was administered for 4 days, but changed to ambisome due to side effects including vomiting and hypokalemia. After 21 days, the patient developed right-sided ptosis, optic neu-

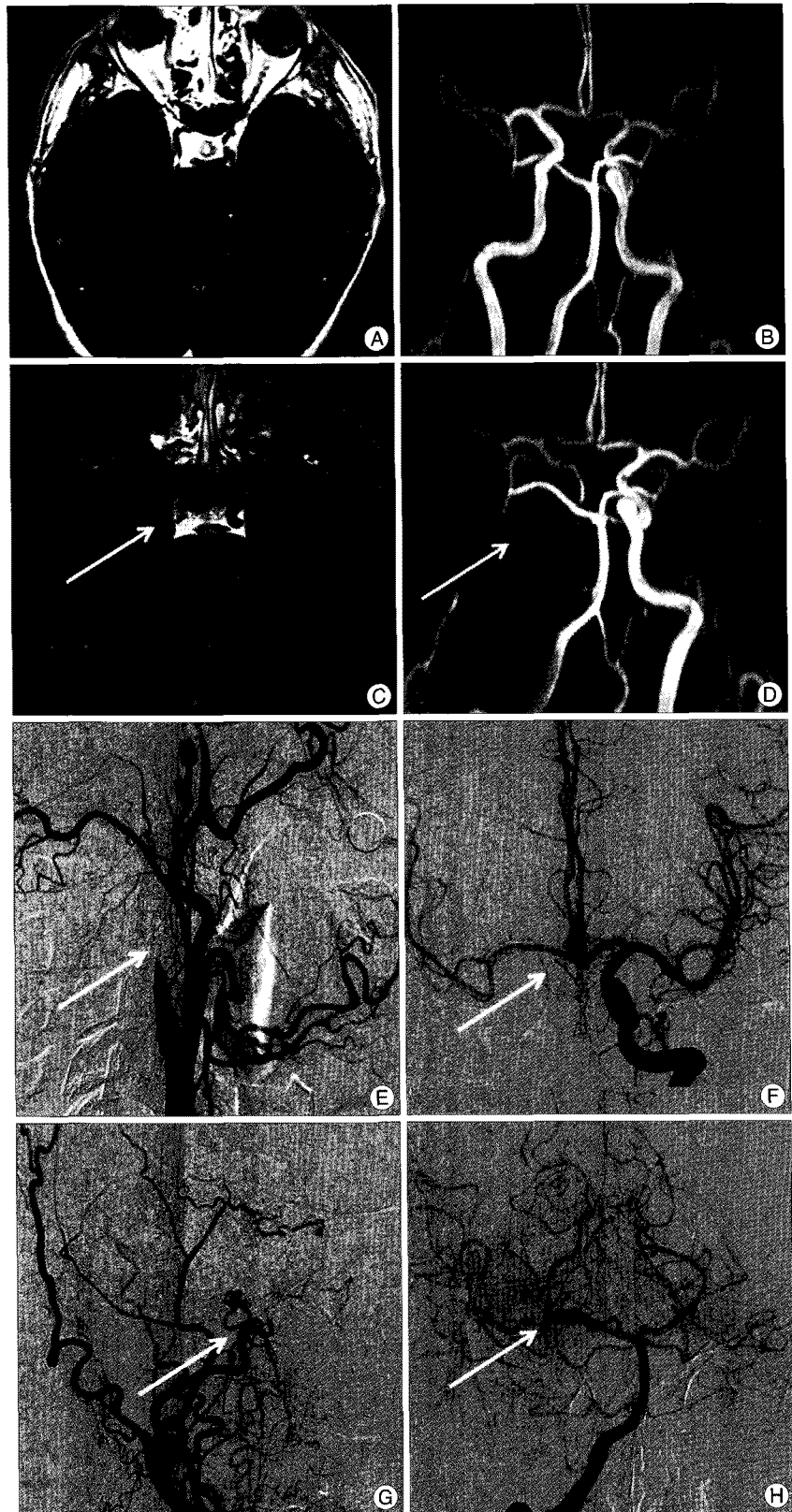


Fig. 1. Initial brain MRI and MRA reveal no parenchymal or vascular lesions other than a small lacunar infarction (A and B). Follow-up brain MRI and MRA show findings suggestive of invasive sinusitis in the frontal and anterior ethmoid sinuses and occlusion of the right ICA (C and D). Six-vessel cerebral angiography leads to identification of a right proximal ICA occlusion as well as the collaterals that supplies the right anterior circulation (left ACA, right external carotid artery, and right PCA) (E-H).

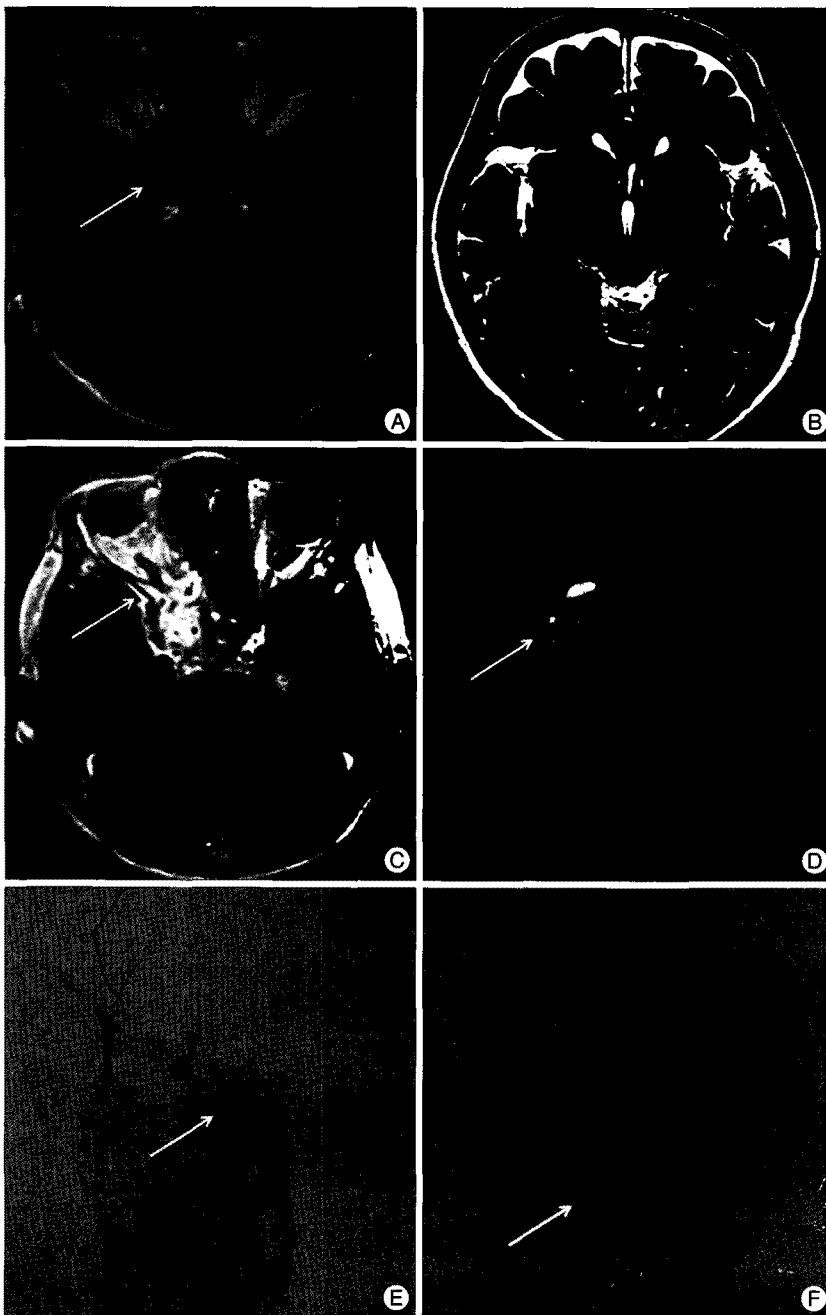


Fig. 2. Initial brain MRI and MRA show a mass lesion involving the right nasal cavity and ethmoid sinus. The lesion extends into the right optic canal, the sphenoid sinus and the cavernous sinus (A and B). Follow-up brain MRI shows an acute to subacute infarct of the right basal ganglia (C and D). Cerebral angiography shows complete occlusion of the right cavernous ICA and the left meningeal collateral circulation from the ACA and the right PCA cortical branches that supply the right cerebral hemisphere (E and F). MRA : magnetic resonance angiography, ICA : internal carotid artery, ACA : anterior communicating artery, PCA : posterior communicating artery.

ropathy, and third and sixth cranial nerve palsies. Caspofungin 1,700 mg (50 mg/day) was administered, as intracranial fungal infection with cavernous sinus invasion was suspected. Endoscopic surgery was performed due to the lack of improvement in symptoms. After the surgery, antifungal medication was continuously administered. Three months following the surgery, the patient experienced sudden-onset left-sided weakness. On

cerebral infarction. Very rare cases have shown ICA occlusion and secondary abscess formation^{4,7,10,13}.

According to a review of the literatures, factors that enhance the rate of treatment success are early diagnosis, early radical debridement, drainage, early decision of ocular exenteration (especially for those with visual loss), appropriate parenteral and local amphotericin B treatment, management of underlying

brain MRI, acute to subacute infarctions of the right basal ganglia and the right frontal and parietal subcortical white matter were noted (Fig. 2C, D). Cerebral angiography showed complete occlusion of the right cavernous ICA as well as the leptomeningeal collateral circulation from the ACA and the right PCA cortical branches that supply the right cerebral hemisphere (Fig. 2E, F). Despite persistent antifungal treatment, the infection was not controlled. The patient died due to sepsis one month after beginning treatment.

DISCUSSION

In 1943, Gregory et al.⁶ reported 3 cases of rhino-orbito-cerebral mucormycosis in patients with uncontrolled diabetes mellitus who suffered from unilateral orbital cellulitis, complete ophthalmoplegia, and cerebral tissue invasion. Since then, Baker et al.² proposed the term rhinocerebral mucormycosis. A diagnosis of intracranial mucormycosis can be made based on histological findings that include broad, pleomorphic hyphae that vary in caliber with branches that are predominantly at right angles. The diagnosis of aspergillosis can be made when H&E staining reveals branching and nonseptate hyphae with subsequent speciation on fungus culture.

Intracranial fungal infection can be caused by the extension of a localized nasal infection, infection of the paranasal sinuses, cavernous sinus invasion, or direct infection of the brain parenchyma. Infection can invade adjacent blood vessels, including the retinal artery, ophthalmic artery and ICA, causing complications such as intracranial infection, systemic embolism, intracerebral hemorrhage, subarachnoid hemorrhage and

ing medical conditions, and hyperbaric oxygen therapy. Early treatment prevents infarct development. It is essential for the patient's prognosis to confirm the presence of a vascular lesion by angiography.

In the first case, early aggressive treatment with antifungals combined with near-total mass removal, in addition to the patient's well-developed collateral circulation, prevented cerebral infarction and ensured an excellent clinical outcome. In this case, the angiographic findings of cavernous sinus invasion and ICA occlusion were essential. On the other hand, in the second case, aggressive management was not pursued. When hemiparesis by intravascular thrombosis occurred, even proper antiplatelet and heparin therapies were not carried out. For patients with ICA occlusion and a well-developed collateral circulation, aggressive treatment will contribute to a successful outcome.

CONCLUSION

When intracranial fungal infection is suspected, immediate angiographic investigation of the possibility of cerebral vasculopathy or ICA occlusion must be considered. Aggressive treatment, including surgery and antifungal agents, most likely enhances prognosis.

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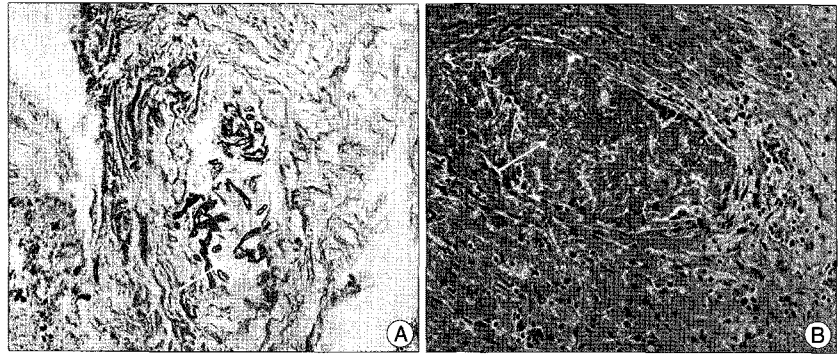


Fig. 3. A : Broad, pleomorphic hyphae that vary in caliber and branch predominantly at right angles are disseminated throughout. Acute and chronic inflammatory cell infiltration is also seen (H&E, $\times 400$). B : Fungal hyphae with acute angle branching are impacted in the paranasal sinus soft tissue. Surrounding chronic inflammatory cell infiltration is also seen (H&E, $\times 400$).