

Rapidly Progressive Rhino-orbito-cerebral Mucormycosis Complicated with Unilateral Internal Carotid Artery Occlusion: A Case Report

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Rhinocerebral mucormycosis is an acute fulminant opportunistic fungal infection usually seen in diabetic or immunocompromised patients. The fungi that cause mucormycosis inoculate the nasal mucosa and may spread to the paranasal sinuses, orbit, and brain. Our patient initially presented with mild ethmoid sinusitis. At that time, brain MRI and contrast-enhanced MR angiography were grossly normal. However, aggravation of sinusitis with extension to the right orbit and anterior cranial fossa rapidly developed within two months. Moreover, an occlusion of the right internal carotid artery was combined. We report a case of a pathologically-proven rhino-orbital-cerebral mucormycosis with serial follow-up imaging for over one year.

Key Words : Mucormycosis; Carotid artery, Internal; Fungal sinusitis

Mucormycosis is a fungal infection, caused by the pathogenic genera *Absidia*, *Mucor*, *Rhizomucor*, and *Rhizopus* of the family Mucoraceae [1, 2]. Mucoraceae are saprophytic fungi and frequently found in soil, residue plants, spoiled food, and upper respiratory tract of healthy people [2]. These fungi are nonpathogenic in normal hosts, but infections typically develop in patients with diabetes mellitus or immune deficiency. Such infections are often manifested as rhinocerebral,

pulmonary, cutaneous, gastrointestinal, and systemic in form. Rhinocerebral mucormycosis is the most common form of the disease [2–4].

The exact pathogenesis and pathways of spread of rhinocerebral mucormycosis are not clearly known. It is generally believed that fungi initially inoculate the nasal mucosa, spreading to the paranasal sinuses, orbit, and finally the intracranial fossa [3]. When spores are converted into hyphae, they become invasive and may spread through the sinuses into the brain and orbits [3–6]. Mucormycosis typically presents as an acute fulminant infection, but a chronic form of the disease exists [5]. Isolated central nervous system infection and invasive rhinocerebral mucormycosis in immunocompetent patients have been reported [1, 6].

We describe the imaging findings of a rhino-orbital-cerebral mucormycosis in a diabetic patient that was rapidly progressive within two months, causing a unilateral internal carotid artery (ICA) occlusion. The patient initially presented with a small lesion confined to the ethmoid sinus, but serial follow-up imaging studies showed a rapid progression of the lesion with orbital and intracranial extension, subsequently result-

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ing in a unilateral ICA occlusion.

CASE REPORT

A 61-year-old man was admitted to our hospital for the first time with a headache. Initial magnetic resonance imaging (MRI) of the brain showed no intracranial abnormality except mild ethmoid sinusitis. An initial contrast-enhanced MR angiography (MRA)

of the carotid and brain are grossly normal. In addition, an initial brain CT scan obtained at that time showed mild sinusitis confined to the anterior ethmoid sinus, and mild mucosal thickenings of both maxillary sinuses.

After the patient had been discharged from our hospital, he was readmitted approximately two months later because of diplopia of the right eye for 3 days. He has a history of recurrent sinusitis. In addition, he has

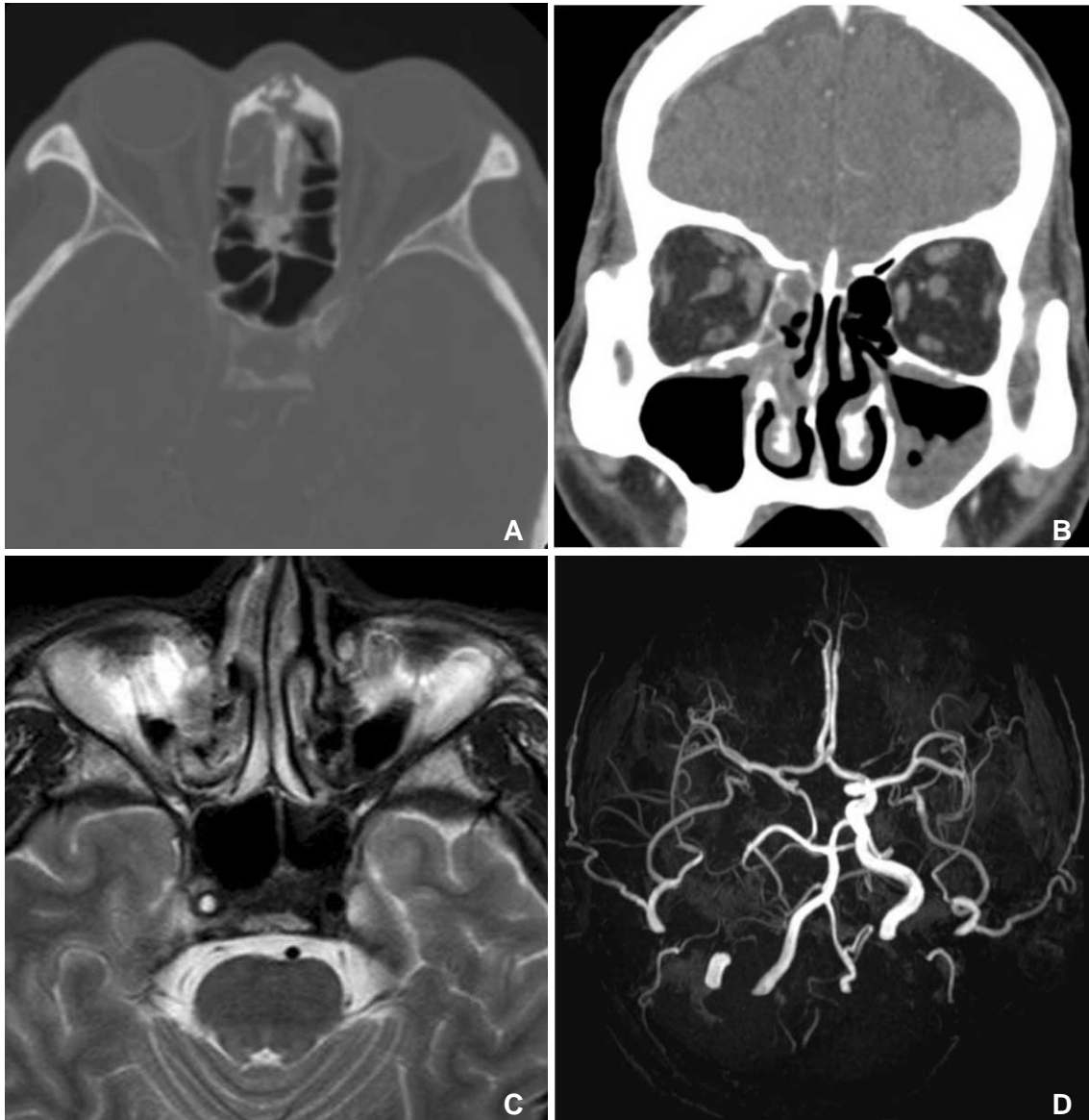


Fig. 1. A. Axial CT images on bone window setting show bone destruction of the frontal bone adjacent to the frontal sinus, anterior ethmoid sinus wall, and cribriform plate with opacification of the frontal and ethmoid sinuses.
B. Coronal CT image on the soft tissue window setting shows fluid or soft tissue density lesion in the left maxillary and right anterior ethmoid sinuses, with extension of the inflammation into the superomedial portion of the right orbit, between the superior rectus and medial rectus muscles and no evidence of involvement of the optic nerve.
C. T2-weighted images demonstrate heterogeneous high signal intensity in the ethmoid sinus. Note also the lack of a flow void with high signal intensity in the carvenous portion of the right internal carotid artery.
D. Time-of-flight MR angiography shows occlusion of the right internal carotid artery (ICA). Continued

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Fig. 1. E. Right common carotid angiography shows occlusion of the right proximal ICA at cervical segment. **F.** Postoperative follow-up brain MRI obtained at 6 months after the operation. No signal void of the right cavernous ICA is suggestive of a right ICA occlusion. Note also the bulging contour of the right cavernous sinus, probably resulting from thrombophlebitis.

been taking diabetes mellitus and hypertension medication for 4 years. A right-eye examination revealed proptosis and restricted extraocular motility in both lateral and medial directions. The visual acuity and fundus of both eyes were completely normal. His blood sugar level was 120 mg/dL and other lab findings, such as complete blood count and urine analysis, were within normal levels. CT scan of the paranasal sinuses revealed frontal, ethmoid, and left maxillary sinusitis with associated bone destruction of the frontal bone, anterior ethmoid sinus wall, and cribriform plate. Inflammation of the right orbit was also noted (Fig. 1A, B). These findings were compatible with invasive fungal sinusitis. MRI of the paranasal sinuses showed heterogeneous enhancing lesions in the above-mentioned paranasal sinuses with extension of the inflammation into the right orbit and anterior intracranial fossa (Fig. 1C). The lesions were isointense or slightly hypointense on T1-weighted MR image (T1WI), and mostly hyperintense on T2-weighted MR image (T2WI). In addition, loss of signal void in the petrous and cavernous portion of the right ICA was noted with high signal intensity on both T1WI and T2WI. A three-dimensional time-of-flight (3D TOF) MRA of the carotid and brain (Fig. 1D) showed occlusion or severe stenosis of the right proximal ICA at the level of the carotid bifurcation. Conventional cerebral angiography (Fig. 1E) showed occlusion of the cervical segment of the right ICA with no distal flow. However, collateral circulation from the contralateral

carotid artery through the anterior communicating artery was effective.

The patient underwent endoscopic sinus surgery with an excision of infected mucosa using a right Caldwell Luc approach. The pathologic examination of the surgical specimen revealed broad, nonseptated hyphae morphologically consistent with mucormycosis. The organisms were easily visible with hematoxylin-eosin, periodic acid-schiff, and special Gomori's methenamine silver stain. The definitive diagnosis of rhinocerebral mucormycosis was made on histopathologic examination. Antifungal therapy using amphotericin B was started.

Thereafter, we reviewed two postoperative MRI scans obtained 6 months and 14 months later. The most interesting point in our case was that serial follow-up MRI still revealed a loss of the signal void of the right cavernous ICA and bulging of the right cavernous sinus (Fig. 1F). These findings can be interpreted as a thrombophlebitis with occlusion or severe stenosis of the ICA. The patient took long-term medication after the operation for over one year, and his initial presenting symptoms improved. The patient did not present the major symptoms consistent with thrombophlebitis and occlusion of the right ICA because he had good angiographic collateral circulation from the contralateral carotid artery, although surgery and postoperative medication management were also effective to some extent.

DISCUSSION

Rhino-orbito-cerebral mucormycosis is classically presented as a fulminant opportunistic infection in diabetic or immunocompromised patients. The common presenting symptoms and signs are headache, fever, sinusitis, facial swelling, and unilateral orbital apex syndrome. Convulsion, changes in consciousness, coma, and stroke may occur [2, 3, 5, 6]. The infection arising from the nasal area or paranasal sinuses may spread to the orbit or intracranially destroy the adjacent bone and soft tissue. The pathologic explanation of this invasion pathway is that the fungus has a propensity for growing along the walls of blood vessels [3, 7]. Mucormycosis may spread intracranially from the paranasal sinuses along perivascular channels, or through the cribriform plate into the anterior cranial fossa. Intracranial dissemination is associated with increased mortality [2].

CT findings of sinonasal mucormycosis include soft-tissue opacification with hyperdense material, nodular mucosal thickening, and an absence of fluid levels in the maxillary, ethmoid, frontal, and sphenoid sinuses, in decreasing order of incidence [5, 6]. Other CT features include bone change of a sinus wall, a focal mass with increased density in the sinus, and infiltration of adjacent soft tissue or bone destruction [8]. The sinus contents have a variety of MR signal characteristics, including T2 hyperintensity or marked hypointensity on all sequences, possibly due to the presence of iron and manganese in the fungal elements. For rhino-orbito-cerebral mucormycosis, thickening and lateral displacement of the medial rectus muscle are characteristic of orbital invasion from the disease in the ethmoid sinuses. A lack of enhancement of the superior ophthalmic vein or ophthalmic artery and internal carotid artery may be seen, and this is related to vasculitis and thrombosis. Intracranial findings include infarcts related to vascular thrombosis, mycotic emboli, and frontal lobe abscesses [5].

Our case was initially presented as a mild sinusitis confined to the anterior ethmoid sinus. Subsequently, in a short period of two months, the lesion rapidly progressed from the sinus with a direct extension to the right orbit and involvement of the right ICA. Follow-up neuroimaging studies with MRI, MRA, and conventional angiography showed occlusion of the right proximal ICA at the carotid bifurcation level. Bone destruction of the frontal bone, anterior ethmoid sinus wall, and cribriform plate was also noted. The rapid

progression of the lesion with total occlusion of unilateral ICA is a rare presentation of rhino-orbito-cerebral mucormycosis. Although some cases have previously been reported, to the best of our knowledge, those case reports of rhinocerebral mucormycosis with complication of ICA occlusion did not display various images, including CT, MRI, MRA, and conventional angiography, as much as we did in our report.

It is necessary to observe the finding that most of the cases in which intracranial extension was seen on imaging studies were clearly symptomatic. In this instance, rapid progression of the rhino-orbito-cerebral mucormycosis arising from a mild ethmoid sinusitis was compatible with a clinical course of the patient, because the initial symptoms were non-specific, but diplopia was newly developed within just two months. Finally, our case is thought to be unique and informative in that for the cerebral involvement of mucormycosis, ICA occlusion can rapidly develop, but its recovery may be not occur shortly. In addition, the patient's presenting symptoms were relatively mild regardless of unilateral ICA occlusion. This may be due to a combination of surgery, long-term medication, and good collateral circulation.

To conclude, rhino-orbito-cerebral mucormycosis is a rapidly progressive infection and may cause ICA occlusion in a short time, especially if the involvement of the cavernous sinus is present. ICA occlusion by cerebral invasion of mucormycosis may not recover well regardless of active treatment. Radiologists should raise the suspicion of mucormycosis as a cause of invasive fungal sinusitis in the clinical setting of diabetes mellitus, even if mucosal thickening is seen in the wall of the paranasal sinuses.

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