

Massive Cerebral Infarction Due to Rhinocerebral Mucormycosis

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Rhinocerebral mucormycosis is rare, but fatal infection of the nasal cavity and sinuses. It can spread to the orbits and cranium within days, and prognosis is directly associated with length of time before diagnosis and treatment. Rhinocerebral mucormycosis can cause cerebral infarction via carotid artery occlusion. Therefore, neurosurgeon is paramount in making the proper management. We recently encountered a case of rhinocerebral mucormycosis with massive cerebral infarction. The clinical and radiological details of this case are presented here with a brief review of the literature.

KEY WORDS : Rhinocerebral mucormycosis · Cerebral infarction.

Introduction

Mucormycosis can be presented with various clinical manifestations including pulmonary, gastrointestinal, cutaneous and rhinocerebral symptoms. Rhinocerebral mucormycosis, the most common form of mucormycosis, is potentially lethal fungal infection characterized by rapid progression and high mortality⁷. Early detection and treatment is essential. Rhinocerebral mucormycosis can cause cavernous sinus or carotid artery thrombosis, resulting in cerebral infarction^{5,6}. To our knowledge, twenty five cases of rhinocerebral mucormycosis have been reported in Korean literatures^{8,12}. However, there is no report of massive cerebral infarction caused by carotid artery occlusion.

Here we describe a case of rhinocerebral mucormycosis with carotid artery occlusion, which resulted in very rapid and fatal clinical progress.

Case Report

A 70-year-old woman who had no previous history of a medical illness presented with three days blurred vision and facial swelling. She also complained of headache, proptosis, and facial numbness. On the day after admission (Day 1), her vital signs were stable but visual acuity was 0.06 and the optic

disc was slightly pale. Neurological examination revealed the right oculomotor nerve paralysis. Laboratory findings showed

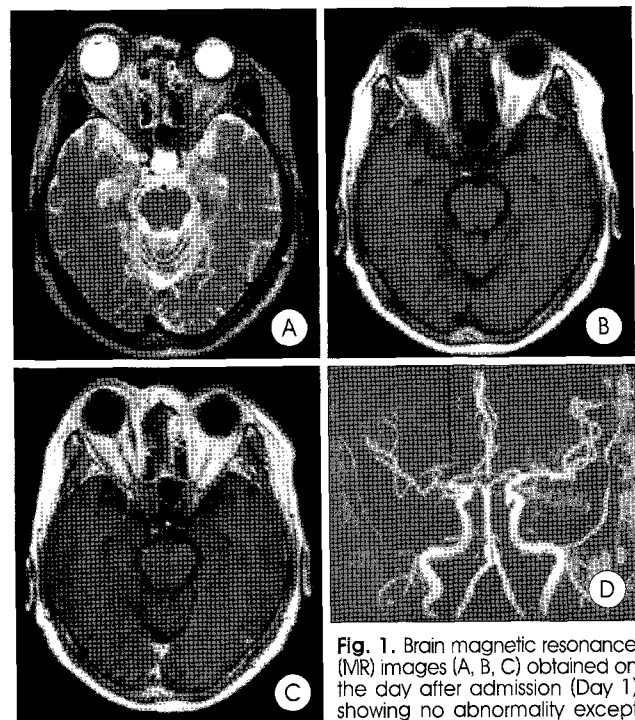


Fig. 1. Brain magnetic resonance (MR) images (A, B, C) obtained on the day after admission (Day 1) showing no abnormality except right periorbital swelling and paranasal sinusitis. MR angiography (D) shows no definite large arterial abnormality.

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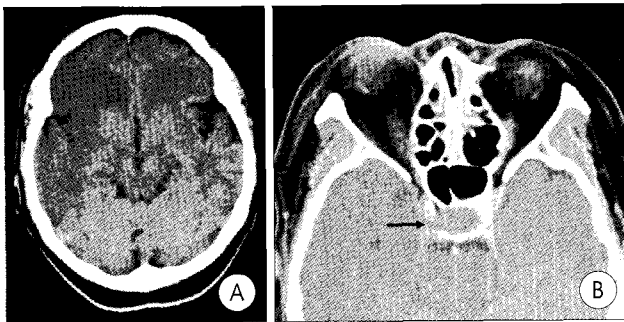


Fig. 2. Brain computed tomography(CT) scan (A) showing low density on the right frontal and temporal lobes. CT scan of the paranasal sinuses with enhancement (B) showing decreased enhancement in the right cavernous sinus (black arrow).

leukocytosis (20,000/ μ l with 90% neutrophils), elevated serum level of C-reactive protein (77mg/L) and erythrocyte sedimentation rate (34mm/hr), and hyperglycemia (475mg/dL).

On magnetic resonance(MR) images obtained on Day 1, no definitive abnormal lesion except right periorbital swelling was observed (Fig. 1). Infusion of the intravenous antibiotics was started empirically because laboratory findings strongly suggested an acute infectious disease. However, the medical condition of patient worsened to drowsy mentality, left hemiparesis, and left blurred vision on Day 3. Brain computed tomography(CT) with enhancement on Day 3 demonstrated low density on the right frontotemporal lobe and decreased enhancement in the right cavernous sinus (Fig. 2). On Day 4, the patient's mentality deteriorated to deep stupor. Multiple facial skin lesions such as grayish discoloration, an epidermal ulcer and eschar were observed (Fig. 3).

We performed a biopsy at the epidermal ulcer on face. CT scan and MR images obtained on Day 4 revealed the massive infarction on the right cerebral hemisphere and occlusion of the right internal carotid artery(ICA) (Fig. 4). Regardless of our effort for treatment, the patient's condition became worse. On Day 9, the patient died due to overwhelming sepsis.

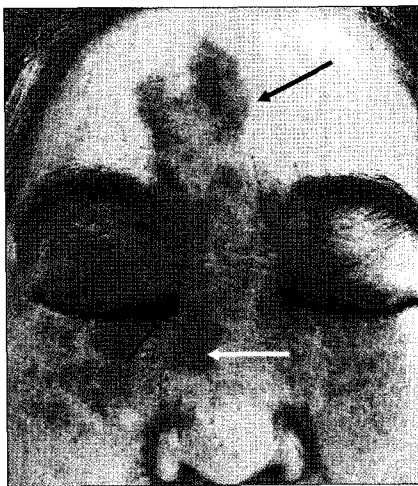


Fig. 3. Photograph showing multiple skin lesions : grayish discoloration (black arrow), an ulcer (white arrow) and eschar (red arrow).

Microscopic examination of the specimen demonstrated intravascular hyphae and confirmed the diagnosis of mucormycosis on three days after the patient's death (Fig. 5).

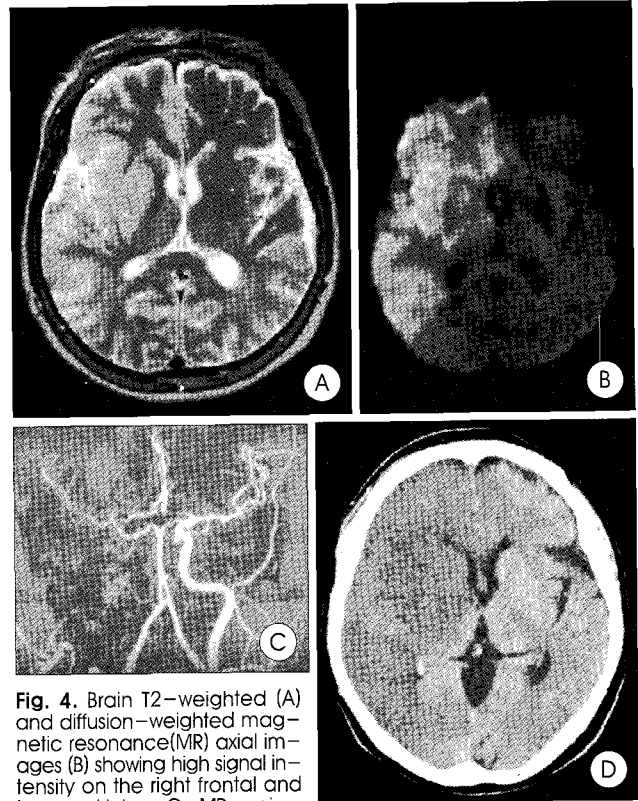


Fig. 4. Brain T2-weighted (A) and diffusion-weighted magnetic resonance(MR) axial images (B) showing high signal intensity on the right frontal and temporal lobes. On MR angiography (C), there is no signal intensity of the right internal carotid artery and poor visualization of right middle cerebral artery. Brain computed tomography (D) showing diffuse low density on the right cerebral hemisphere.

Discussion

Mucormycosis is a fungal infection occurring in diabetic or immunosuppressed patients and rapidly invades the nasal sinuses, orbits and cranium. It is mainly caused by zygomycetes such as the general rhizopus, mucor and absidia. Of these fungi, the rhizopus arrhizus and rhizopus oryzae are responsible for 95% cases of mucormycosis^{10,11}. These organisms are found in the soil, bread and fruit, and have been cultured from the oral and nasal mucosa of healthy people⁷. The most common risk factor is poorly controlled diabetes mellitus, which is associated with 60~80% cases^{7,11}. In our case, the patient was an undiagnosed diabetic person. Mucormycosis also can be found in patients with leukemias, renal disease, immunosuppression or transplantation, malnutrition, and in patients receiving deferoxamine treatment¹¹.

The most common early physical signs of rhinocerebral mucormycosis are facial edema and multiple cranial nerve palsies³. The patients may also complain of ptosis, proptosis, visual loss, complete ophthalmoplegia, and anhidrosis etc. These abnormalities are often consistent with orbital apex or superior orbital fissure syndrome. Patients with mucormycosis may or may not present with a fever and are often drowsy or obtunded



Fig. 5. Photomicrographs showing intravascular hyphae (black arrows). These clues confirm the diagnosis of mucormycosis (H-E stain $\times 200$ (A), $\times 400$ (B)).

on presentation.

Rhino cerebral mucormycosis develops in three stages¹⁾. In the first stage, there is local nasal mucosal and sinus infection with nasal stuffiness, discharge, local pain, and headache. Necrotic lesions of the nasal mucosa, turbinate, and hard palate also can be seen. In the second stage, there is advanced orbital involvement occurred by either direct extension through the sinuses or extension through the blood vessels, resulting in the orbital apex and superior orbital syndrome. Corneal anesthesia, conjunctival hemorrhage, exophthalmos, complete ophthalmoplegia, fixed dilated pupils and blindness can be manifested in this stage. In the third stage, cerebral involvement with spread of infection through superior orbital fissure or the cribriform plate causing a cavernous sinus and ICA thrombosis results in cerebral infarction or brain tissue necrosis^{5,6)}.

Mucorals hyphae have a predilection for growth into arteries, lymphatics, and nerves. Vascular invasion of the hyphae produces a fibrin reaction and the development of mucor thrombi, which occlude vessels, producing ischemia and infarction. This infarction produces the characteristic black, necrotic eschars in the nasal and oral cavities and on the face of the

patients. Vascular occlusion also produces local tissue acidosis that is ideal for fungal growth and protects the spread of intravenously infused antifungal agents. Mucorales can cause cavernous sinus or carotid artery thrombosis via direct extension through the ethmoid bone or orbital vessels in just a few days.

The diagnosis of rhino cerebral mucormycosis is made by observing the characteristic hyphae on biopsy of necrotic ulcers²⁾. Sampling discharge or blood is not sufficient for diagnosis because invasion of the tissue must be demonstrated. CT of the head may reveal nodular thickening of the sinus mucosa, sinus wall obstruction and intraorbital involvement. MR imaging is more clearly defining the extent of intracranial extension. Regions of intracerebral inflammation are usually hyperintense on T2-weighted MR images.

Treatment of rhino cerebral mucormycosis includes early diagnosis, correction of underlying conditions, early and radical surgical debridement and intravenous amphotericin B. Other adjunctive medical therapies are aggressive management of acidosis, minimization of immunosuppression in transplantation patients, and hyperbaric oxygen therapy^{4,9,13)}.

The survival rate of rhino cerebral mucormycosis is directly associated with the time of diagnosis. But even with early diagnosis and aggressive management, the prognosis of rhino cerebral mucormycosis remains poor. The mortality rate is approximately 20%. When the carotid artery becomes involved, this percentage rises to approximately 50%¹¹⁾. Findings indicating poor prognosis include intracranial involvement (hemiplegia and hemiparesis), bilateral sinus infection, facial necrosis, nasal deformity, and deferoxamine therapy⁹⁾.

Conclusion

Rhino cerebral mucormycosis is rare lethal fungal disease. If it involves the carotid artery, the mortality rate rises abruptly. Early diagnosis is essential to achieve a good treatment results. We propose that if an immunocompromised patient whose laboratory findings strongly suggest an infectious disease with complaint of sudden loss of visual acuity or symptoms of orbital apex syndrome, the administration of antifungal agent must be included in the first line treatment tools.

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