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Case Report

Fatal rhino-orbito-cerebral mucormycosis

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ABSTRACT

Rhinocerebral mucormycosis is a rare but often fatal invasive fungal infection. It is frequently encountered in immunocompromised hosts such as diabetes mellitus, AIDS, hematological malignancies receiving high-dose chemotherapy, and transplant patients. Rhinocerebral involvement is the most common form. A 62-year-old female patient who was admitted with complaints of redness, swelling, pain, elevated body temperature, closure of the left eye, and high fever was diagnosed with rhino-orbito-cerebral mucormycosis based on physical examination, radiological imaging, histopathological results, and tissue culture. The case of the patient who died despite repeated surgical debridement and antifungal therapy is presented to draw attention to the extremely fatal rhino-orbito-cerebral mucormycosis cases.

Keywords: Amphotericin B, diabetes mellitus, rhino-orbito-cerebral mucormycosis, sinusitis.

Mucormycosis is an opportunistic fungal infection that is pretty uncommon and often fatal. The main clinical forms are rhinocerebral, pulmonary, cutaneous, gastrointestinal, and disseminated.[1] While disseminated or pulmonary mucormycosis is more prevalent in immunocompromised patients, the rhino-orbito-cerebral form is more common in diabetics. Members of the *Mucoraceae* family, Rhizopus, Absidia, Mucor, and Rhizomucor, are the most common causative agents of mucormycosis.[2] These fungi are found all over the world and are most commonly found in soil, rotten fruits and vegetables, and moldy foods. Predisposing factors for mucormycosis include uncontrolled diabetes, lymphoma, leukemia, and long-term corticosteroid or immunosuppressive therapy. In most cases, transmission occurs through the inhalation of mold fungi that are common in nature. In healthy people, mold fungi spores are destroyed by phagocytes; however, in immunocompromised patients or those with phagocyte dysfunction, spores may invade the vascular endothelium and cause infection.[3,4] The etiological factors that cause mucormycosis are mostly found in the *Mucoraceae* family, with Rhizopus oryzae being the most common species. It is responsible for approximately 60% of mucormycosis cases and 90% of rhinocerebral form in humans.[3]

In this case report, we presented the case of a diabetic patient who was diagnosed with rhino-orbito-cerebral mucormycosis.

CASE REPORT

A 62-year-old female patient was admitted to the polyclinic with complaints of redness, swelling, pain, elevated body temperature, closure of the left eye, and high fever. The patient, who had been taking levofloxacin tablets for a week for sinusitis, had a sudden closure in her left eye yesterday. Cranial magnetic resonance (MR) imaging was performed on the patient who applied to the neurology outpatient clinic. Pansinusitis, pre- and post-septal cellulitis, diffuse contrast enhancement in the left optic nerve sheath were observed. Her medical history revealed that she had diabetes mellitus for 15 years and used insulin. The patient was conscious and cooperative during the physical examination; her blood pressure

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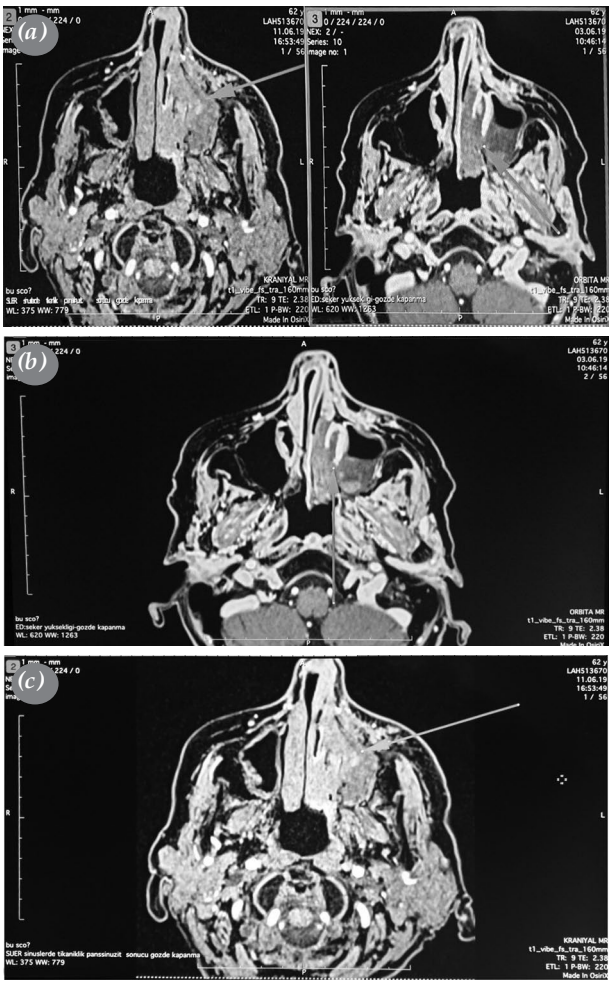

Figure 1. (a-c) Involvement of the right ethmoid sinus in paranasal sinus computed tomography.

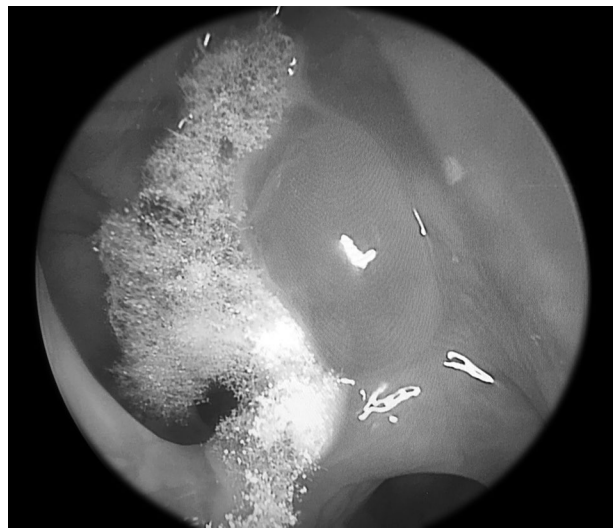

Figure 2. The appearance of fungi in the right ethmoid sinus.

was 120/80 mmHg, her fever was 38.3°C, and she had redness, edema, and ptosis in her left eye. Piperacillin-tazobactam 3×1 gr intravenous (IV), vancomycin 2×1 gr IV was started in the patient with leukocytes 20,400 mm^3, hemoglobin 13.3 g/dL, creatinine 0.67 mg/dL, ALT 27 U/L, CRP 247 mg/L, and erythrocyte sedimentation rate 107 mm/h. Meropenem was started on the fifth day of hospitalization due to a decrease in hemoglobin. The neurologist evaluated the patient who developed headache and vision loss on the ninth day of hospitalization. There was total ophthalmoparesis in the left eye, no light reflex, and left nasolabial groove faint. A written informed consent was obtained from the patient.

Cranial and orbital MRI were performed on the patient. Inflammation and edema in soft tissues adjacent to the maxillary sinus and around the pterygoid muscles at the major level of the left sphenoid bone, osteomyelitis secondary to sinusitis of the left sphenoid bone, involvement in soft-tissues around the orbital region on the left, total in the right frontal sinus, partial in the left frontal sinus, almost the entire in both ethmoid sinuses, more pronounced in the left maxillary sinus, mucosal thickenings forming partial loss of aeration in the left sphenoid sinus were detected. The patient underwent surgery after being evaluated by otorhinolaryngology. Sinuses were cleared, and necrotic tissues were removed. Samples were taken for pathology and microbiology. In the patient who had fungal hyphae observed during surgery, 5 mg/kg/day amphotericin B was started. The pathology result was invasive fungal sinusitis due to Mucor. In the follow-up, the CRP level was 31.9 mg/L, the leukocyte count was 10,200 mm^3, the ALT was 10 U/L, and the erythrocyte sedimentation rate was 92 mm/hour. After her general condition deteriorated, the patient was referred to the upper service. Ten days later, it was learned that the patient had died.

DISCUSSION

Mucormycosis is a rapidly progressive, fatal, and opportunistic infection caused by fungi of the class Zygomycetes. Rhino-orbito-cerebral mucormycosis is more common in diabetics; rhinocerebral, pulmonary, or diffuse

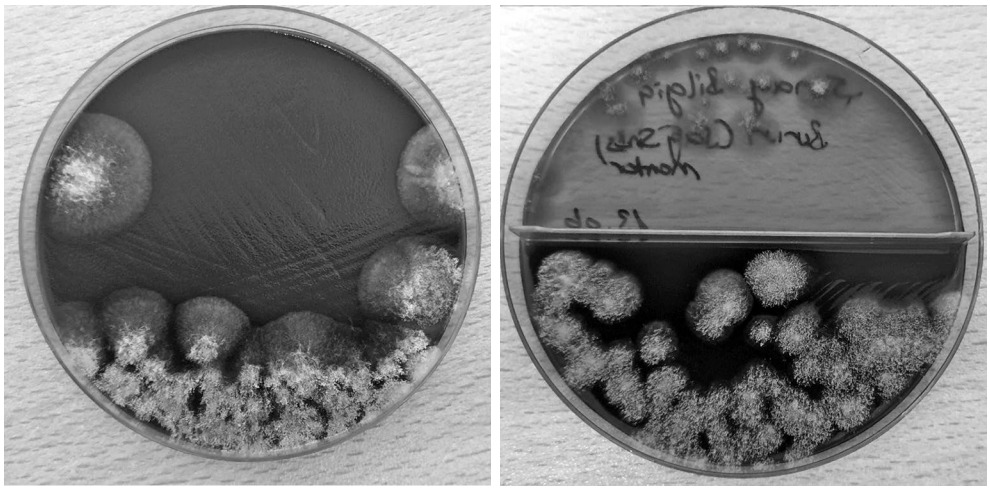

Figure 3. Colony of Mucor fungi grown on Petri dish from the patient.

mucormycosis is more common in patients with leukemia or neutropenia due to bone marrow transplantation; and the gastrointestinal form is more common in patients with protein-calorie malnutrition.[5] Diabetes is the most common predisposing factor (60-80%).[6-8] The increased prevalence of mucormycosis in diabetic patients is due to a decrease in the iron-binding capacity of transferrin, which allows fungi to grow faster by easily utilizing the iron in the serum. Furthermore, in ketoacidosis, fungal growth accelerates, and as the fungus multiplies, it causes vascular invasion, which increases ischemia and thus acidosis, creating a vicious cycle.[9]

Rhinocerebral mucormycosis begins with necrosis of the palate or sinuses. Necrosis spreads to the orbit and brain tissues. Spread occurs either directly as a result of necrosis or indirectly as a result of embolism from surrounding vessels.[10] Patients are commonly admitted with headaches and facial pain, fever, and soft tissue swelling due to cellulitis. Our patient was admitted with complaints of redness, swelling, pain, elevated body temperature, left eye closure, and a high fever; based on these findings, she was diagnosed with orbital cellulitis.

Since mucormycosis is an aggressive infection that spreads mostly from the paranasal sinuses to the orbital or cranial region, radiological imaging is essential in the diagnosis. It creates an appearance in computed tomography that can be seen in different densities filling the sinuses. The spread of the sinuses to adjacent structures is an important finding in distinguishing it from bacterial sinusitis. It can infiltrate the fat plane of the premaxillary and buccal area, as well as the pterygopalatine fossa, infratemporal fossa, and masticator space. It creates a hypointense signal because the hyphae show a very low signal structure on T1- and T2-weighted images in the sinus on MR images. In contrast-enhanced images, the Mucor focus does not show significant contrast enhancement, whereas significant contrast enhancement due to diffuse infiltration is observed along its periphery. When it invades the cavernous sinuses, it infiltrates the cranial nerve and internal carotid arteries, causing complications with a high mortality rate.

For a definitive diagnosis, a deep biopsy specimen from suspected nasal and/or oral mucosal lesions should be obtained. Mucormycosis is diagnosed by histopathological and microbiological examination of fresh tissue samples, the appearance of randomly hyphal branching without a septum, and macroscopic and microscopic examination of colonies grown on Sabouraud dextrose agar (SDA) medium.[11] Mold growth in the nasal tissue culture and histopathological examination of the biopsy specimen resulted in the definitive diagnosis in our case.

Medical and surgical treatment should be applied in combination to treat mucormycosis.

One of the most important factors determining treatment success is the correction or control of the underlying disease. Amphotericin B is the most commonly used drug in systemic antifungal therapy.[12] Because conventional amphotericin B has more side effects and inability to pass the blood-brain barrier, liposomal forms are preferred. Liposomal forms are the first choice in treatment because they have fewer side effects, better transition to the brain parenchyma, and can be used at higher doses.[13] In our patient, blood sugar regulation was achieved and liposomal amphotericin B treatment began. Simultaneous surgical debridements were also performed. The disease, however, could not be controlled despite multiple surgical debridements and concurrent antifungal treatment, and the patient died.

In conclusion, early diagnosis and control of the predisposing factor are critical in rhino-orbito-cerebral mucormycosis, which is extremely fatal. Treatment for mucormycosis requires more than just effective antifungal therapy. Appropriate surgical treatment can help to significantly reduce mortality. In order to treat mucormycosis successfully, aggressive early surgical debridement of infected tissue is necessary.

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