Two Cases of Rhinocerebral Mucormycosis

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ABSTRACT

Mucormycosis is a rare opportunistic fungal infection. The most common infection site is the paranasal sinuses, although it can also occur in the lungs and skin. The fungus adheres to tissue membranes and forms thrombi, causing ischemia and hemorrhagic necrosis. Rhinocerebral mucormycosis can occur in the nose, but might rapidly spread to the orbit and intracranium. Therefore, prompt and aggressive treatment is required. However, because of its low incidence, few reported cases have focused on accompanying disease, proper treatment period, and disease progression. Herein, we report two cases of rhinocerebral mucormycosis with a brief literature review.

KEY WORD : Mucormycosis.

INTRODUCTION

Mucormycosis is a rare necrotizing infection caused by fungi within the class Zygomycetes, order Mucorales, and genera Rhizopus, Rhizomucor, Mucor, Absidia, Apophysomyces, Cunninghamella, Saksenaea, etc.1 Because it can be serious and rapidly fatal, early diagnosis and aggressive treatment are important.2 Mucormycosis usually affects immunocompromised patients with diabetes mellitus (DM) and neutropenia, but it can also occur in patients with no other medical history. Recently, as diagnostic and treatment methods have developed, more patients undergo immunosuppressive treatment, which is associated with the increasing incidence of mucormycosis.3 The main principle of treatment is aggressive surgical debridement and intravenous administration of an antifungal agent.4 Yet, because of its low incidence, few cases with consideration of accompanying disease, proper treatment period, disease progression, etc. have been reported. We herein report two cases of rhinocerebral mucormycosis with a brief literature review.

CASE REPORT

Case 1

A 66-year-old male patient was admitted for a 2-week history of nasal obstruction and pain. The patient was referred from a local clinic to our department for abnormal findings related to his nasal septum. The physical examination revealed necrotic changes of the nasal septum and part of the cartilage; thus, the patient was admitted to our department with suspicion of mucormycosis. He had no relevant past history with the exception of pulmonary tuberculosis, which had been diagnosed 7 years earlier and was reportedly fully treated. Initial computed tomography (CT) findings showed cartilage defects of the nasal septum, while the other parts of the nasal cavity and sinuses were relatively clear. Under general anesthesia, the patient underwent wide excision of the necrotic portion of the nasal septum and postoperative medicine (Amphotericin-B; Fungizone 1 mg/kg/day) including intravenous administration of and endonasal irrigation with a same agent for three months. Nine days later, an electrolyte imbalance due to acute kidney injury occurred, and the patient was referred to the Department of Infection Medicine. The surgery did not relieve the patient’s constant headache, and 18 days later, a mass on his forehead was observed. Fine-needle aspiration biopsy of the mass revealed purulent discharge, and magnetic resonance imaging
MRI findings were consistent with osteomyelitis accompanied by cellulitic change. We decided to refer the patient to the Neurosurgery Department and begin surgical management. The patient underwent craniectomy and cranioplasty, and the pathologic results of the resected specimen showed hyphae consistent with mucormycosis. On postoperative day 82, the operative wound of the nasal cavity and forehead was healing well and the patient was discharged. The patient is currently undergoing regular outpatient follow-up visits with no special complaints or recurrence.

Case 2
A 76-year-old female patient was referred from a local clinic to our department for a 10-day history of facial and periorbital swelling. She was on medication for hypertension and DM. She had been diagnosed with pulmonary tuberculosis 40 years ago and had reportedly fully recovered. Physical examination revealed that both malar areas were injected, and necrotic changes were present on the left septal mucosa. CT on the day of admission showed a soft tissue density in both sinuses and cellulitic change in the right maxillary sinus.
malar area. Because of the patient’s age, uncontrolled DM, and electrolyte imbalance, surgical treatment was performed with local anesthesia. After opening the maxillary, ethmoidal, and sphenoidal sinuses, we removed discharge and debrided tissue from all sinuses and widely excised the necrotic tissues from the septum, both inferior turbinates, and both maxillary sinuses. The pathologic report of the specimen revealed hyphae consistent with mucormycosis. On postoperative day 6, despite surgical excision, necrotic tissues remained spread throughout the nasal cavity, and her electrolyte imbalance became aggravated. Therefore, under consultation with the Department of Infection Medicine on postoperative day 7, we changed the treatment to liposomal amphotericin B (Fungizone 50 mg/VI, 1 mg/kg/day) treatment to liposomal amphotericin B (Ambisome 50 mg/VI, 1 mg/kg/day). Acute kidney injury occurred, and the patient was transferred to the Department of Infection Medicine on postoperative day. Her general condition became aggravated with time; she developed a deeply somnolent mental state and required ICU care. From the day of admission, the patient complained of continuing diarrhea and hematochezia. A biopsy with a rectal endoscopy revealed a diagnosis of rectal cancer (adenoma). On postoperative day 67, the patient was discharged to her local hometown clinic and subsequently died.

**DISCUSSION**

Mucormycosis is a rare opportunistic infection and represents the third most common angio-invasive fungal infection after candidiasis and aspergillosis. The paranasal sinuses are the most commonly involved site, although it can also occur in the lungs, skin, and other areas. Inhaled fungal hyphae penetrate tissues, causing thrombosis and tissue ischemia. The majority of patients with mucormycosis reportedly have uncontrolled DM. However, recent studies have shown increases in the numbers of infected patients with leukemia, lymphoma, renal failure, organ transplants, nutritional deficiency, HIV, etc. In addition, according to a number of case reports, chronic sinusitis and long-term use of systemic steroids can be underlying factors of mucormycosis infection. The infection can present as a headache, facial tenderness, fever, periorbital swelling, ophthalmoplegia, facial cellulitis, ptosis, proptosis, facial weakness, and even as mental changes, which can be fatal. It usually takes several days to progress, but in some cases, it can rapidly manifest rapidly in a matter of hours. Diagnosis begins with a thorough physical examination. The infected site shows typical black eschars, which may subsequently ulcerate or perforate. In cases of ulcers of the palate, malignant diseases such as Wegner’s granulomatosis, neurosyphilis, tuberculosis, lymphoma, squamous cell carcinoma, and minor salivary gland tumors should be excluded, which requires a biopsy. The diagnosis of mucormycosis can be made by detecting aseptate, right-angled branching hyphae through direct microscopy or histopathological examination. In addition, CT and MRI are essential for identification of intracranial or bone extension. Primary treatment is wide excision of the necrotic portion and a systemic intravenous antifungal agent. Local treatment with an amphotericin mixed solution spray can be performed. Because mucormycosis can rapidly extend to the surrounding tissues, including the orbit, early and aggressive surgery should be carried out. Because the necrotic portion can block the passage of the antifungal agent, all necrotic portions should be thoroughly removed. The standard for wide excision is removal of tissues until bleeding occurs at the bone and soft tissues. In the past, ethmoidectomy with sphenoidotomy, frontal sinusotomy, and maxillectomy were usually performed as surgical treatments. However, the recent surgical trend has been towards diagnosis and necrotic debridement under endoscopy.

In the 1960s, when amphotericin had not yet been developed, mucormycosis was considered to be fatal.
amphotericin B is bacteriostatic rather than bactericidal, a longer administration time is required; therefore, it is important to correct the underlying medical conditions. To resolve the renal toxicity associated with amphotericin B, a liposomal formulation of amphotericin has recently been widely used, and is known to be released to the kidney by enhancing migration of amphotericin to phagocytes.

Although surgical timing is not a critical factor, it is typical to start treatment with an antifungal agent and proceed to surgery within 1 week after the diagnosis. In addition, because mucormycosis limited to the nose and paranasal sinuses is known to have a better prognosis, it is important to start aggressive treatment before the central nervous system becomes involved. In our cases, one patient recovered completely whereas the other patient died, which is thought to have arisen from the differences in the patients’ medical and general conditions.

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REFERENCES