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Successful treatment of rhino-orbital mucormycosis by a new combination therapy with liposomal amphotericin B and micafungin

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Abstract

Mucormycosis is a rapidly progressive fungal infection that usually occurs in patients with diabetes mellitus or in immunocompromised patients. Sinus involvement is the most common clinical presentation and the rates of mortality increase with the orbital extension. The treatment of mucormycosis includes aggressive surgical debridement and systemic antifungal therapy. Early diagnosis and prompt initiation of effective antifungal drugs are essential for successful outcome. However, the role of orbital exenteration for the case of orbital involvement remains controversial, and the drugs effective against mucormycosis are limited. We present a successfully treated case with rhino-orbital mucormycosis caused by *Rhizopus oryzae* in a diabetic and dialysis patient. The early diagnosis, surgical debridement and a new combination therapy with liposomal amphotericin B and micafungin were effective. This new combination antifungal therapy will be useful for the treatment of mucormycosis.

Keywords: Rhino-orbital mucormycosis; Liposomal amphotericin B; Micafungin; Rhizopus oryzae; Maxillary sinus

1. Introduction

Mucormycosis is a rapidly progressive and often fatal fungal infection caused by fungi of the order *Mucorales*. *Rhizopus*, *Rhizomucor* (*Mucor*), and *Apophysomyces* are the organisms most commonly isolated from clinical specimens [1]. Mucormycosis is classified according to the site of involvement as sinus, pulmonary, cutaneous, gastrointestinal, cerebral, kidney and general disseminated. Each of these entities is associated with specific host factors and outcomes. Sinus involvement is the most common clinical presentation and is frequently associated with diabetes mellitus or immunocompromised disease [2]. The diagnosis is confirmed histologically and culture is used to identify the specific species. Histologically, mucormycosis is characterized by fungal hyphal invasion into blood vessels with subsequent thrombosis and tissue ischemia [3]. Acidosis and hyperglycemia are ideal environments for fungal growth. *Rhizopus* spp. have the enzyme ketone reductase, and these conditions inhibit the host defense mechanisms [4]. The deferoxamine therapy for the treatment of aluminium or iron overload in dialysis patients is an additional predisposing factor, because the fungi can take up iron from the deferoxamine chelate for their growth [2].

The treatment of mucormycosis includes aggressive surgical debridement and systemic antifungal therapy. Early diagnosis and prompt initiation of effective antifungal drugs are essential for successful outcome. The prognosis is much better if the disease has not penetrated beyond the sinus prior to surgical debridement, but the rates of mortality increase with the orbital extension [5]. The effect of orbital

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exenteration for the case with orbital involvement remains controversial [6–8], and the antifungal drugs effective against mucormycosis are limited. Amphotericin B deoxycholate and its lipid formulations have been only used for the treatment of invasive mucormycosis. Recently, it has been reported that *R. oryzae*, the most common pathogen causing mucormycosis, expressed the target enzyme for antifungal drug, echinocandins, and that the combination therapy with liposomal amphotericin B and caspofungin, an echinocandin was synergistic and may be more effective for rhino-orbital-cerebral mucormycosis [4].

We present the successful treatment of a diabetic and dialysis patient with rhino-orbital mucormycosis caused by *R. oryzae* who was managed with early diagnosis, surgical debridement and a new combination antifungal therapy with liposomal amphotericin B and micafungin, an echinocandin. The clinical manifestations, radiologic and histopathological findings, and treatment of this rare lesion are discussed.

2. Case report

A 70-year old man presented to the Department of Otorhinolaryngology, Shiga University of Medical Science hospital with a two weeks history of post-traumatic acute maxillary sinusitis on the right side, characterized by purulent nasal discharge, progressive cheek pain and swelling. He had been treated with oral and intravenous antibiotics without improvement. His past history included insulin-dependent type 2 diabetes mellitus and chronic renal failure requiring hemodialysis. His blood sugar was 526 mg/dl, HbA1c 8.9%, white blood cell count 12600 cells/μl, and, C-reactive protein was 13.2 mg/l.

Endoscopic examination of the right nasal cavity revealed black necrotic tissues in the lateral wall and inferior turbinate with abundant purulent secretion. Computed tomography (CT) scan demonstrated soft-tissue lesion in the right maxillary sinus with minimally displaced fractures of the posterior-lateral wall of maxillary sinus and the inferior wall of the orbit (Fig. 1a). These fractures were caused by the facial trauma when he fell down at one month ago. The patient was given intravenous antibiotic therapy with meropenem, and the repeated antral punctures and irrigation of the maxillary sinus. He also required insulin administration and the blood sugar level was maintained at a 120–230 mg/dl level. The culture of maxillary sinus secretion was identified as *R. oryzae* (Fig. 1b). A repeated CT scan at 14 days after the first examination revealed progressive

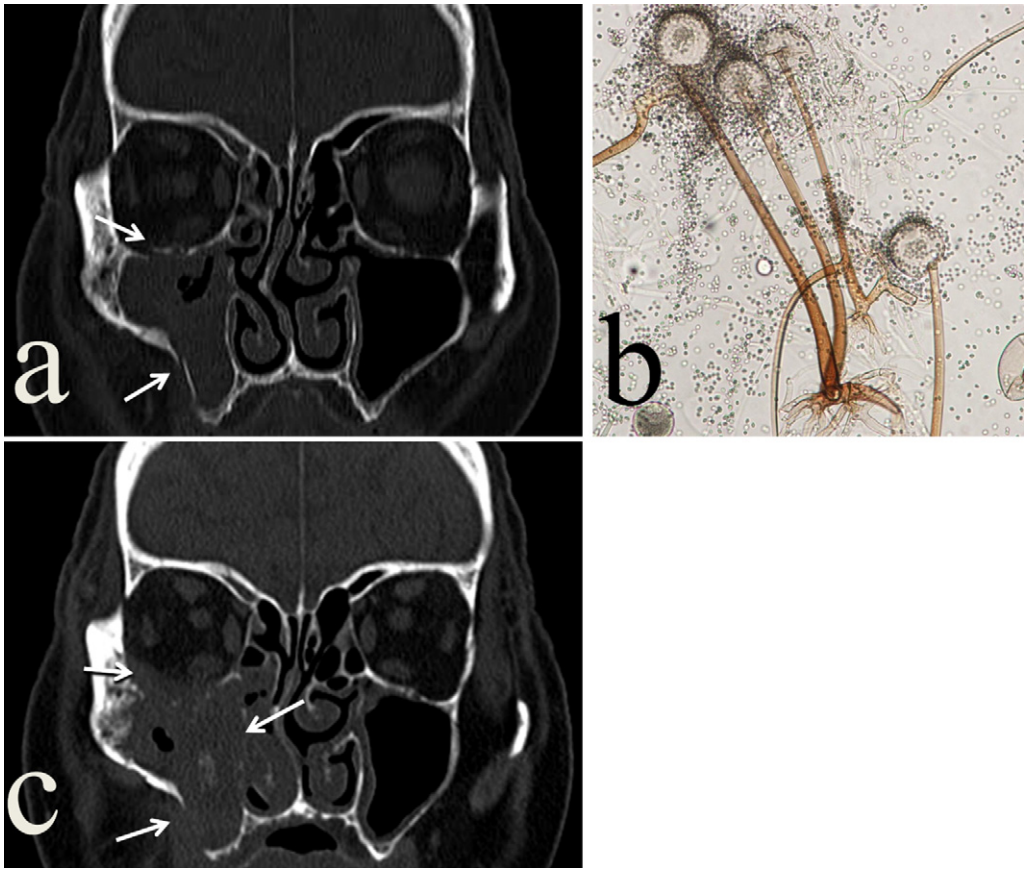

Fig. 1. (a) Coronal CT scan on the day of admission showing soft-tissue lesion in the right maxillary sinus with minimally displaced fractures of the posterior-lateral wall of maxillary sinus and the inferior wall of orbit (arrows). (b) Microscopic view of *R. oryzae* in culture, showing rhizoids, sporangia, and sporangiophores arised from the rhizoids. The sporangia had columellas, and the spores were ovoid (no staining). (c) Coronal CT scan on the 14th day after the admission showing progressive bone destruction of the right maxillary sinus with direct extension into the orbit (arrows).