Rhinocerebrocutaneous mucormycosis caused by *Mucor* species: A rare causation

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ABSTRACT

Rhinocerebral mucormycosis is the most common form of mucormycosis occurring commonly in patients of diabetic ketoacidosis. Fungi of the order *Mucorales* belong to six families, among whom *Rhizopus* is the most common, while *Mucor* is a rare cause. We report a 45-year-old female with uncontrolled diabetes mellitus diagnosed to have rhinocerebrocutaneous mucormycosis caused by *Mucor* species. The diagnosis was confirmed on histology and culture. A high-index of suspicion is required for early diagnosis and timely initiation of therapy to optimize the outcome. Our patient succumbed to her infection.

Key words: *Mucor* species, mucormycosis, uncontrolled diabetes

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INTRODUCTION

Mucormycosis represents a group of life-threatening infections caused by fungi of the order *Mucorales*. It is highly invasive and rapidly progressive resulting in high rates of morbidity and mortality. Rhinocerebral mucormycosis is most commonly associated with diabetes and immunosuppressive states. The initial symptoms are nonspecific. The infected tissue appears to be normal during the early stage of infection and progresses through the erythematous phase before the onset of violaceous discoloration and finally a black necrotic eschar.

CASE REPORT

A 45-year-old married woman presented with complaints of rapidly spreading black lesion near the right side of the nose. Patient denied history of foul smell and purulent discharge from the nose. There was no history of trauma, headache, pain in the eye, or seizures. She was a diagnosed case of diabetes mellitus on irregular treatment with oral hypoglycemic drugs and insulin therapy since four years. There was a history of previous hospitalization on three occassions for diabetic ketoacidosis. At the time of admission, patient was conscious and oriented to time, place and person. She was afebrile and had no significant lymphadenopathy. Mucocutaneous examination revealed a single, well-defined, erythematous, edematous plaque with black necrotic central eschar measuring 5 cm × 3 cm involving the right side of the nose, nasolabial fold, and malar region [Figure 1]. On oral examination black necrotic eschar measuring 2 cm × 2 cm involving the right side of hard palate was seen [Figure 2]. Nasal mucosa revealed right middle turbinate hypertrophy. Systemic examination including central nervous system was normal. Based on the clinical examination findings, a differential diagnosis of mucormycosis and aspergillosis was considered. The fasting blood glucose was 120 mg/dl and hemoglobin A1c was 15%, representing very poor diabetic control. The patient was seronegative for HIV and hepatitis B surface antigen. All other hematological and biochemical investigations were within normal limits. Examination of the tissue smear on 10% KOH mount revealed aseptate right angled hyphae. Fungal culture with Sabouraud's dextrose agar at 37°C showed cotton wool like colonies of *Mucor* species [Figure 3]. Lactophenol cotton blue preparation showed mature sporangia of *Mucor* species [Figure 4]. Histopathology was suggestive of mucormycosis. The organism appeared as eosinophilic, thick-walled aseptate hyphae with neutrophilic infiltrates; a few of them appeared hollow on cross-section in the dermis and subcutaneous tissue [Figure 5]. Tissue Gomorri's methenamine silver (GMS) stain revealed dark brown colored hyphae suggestive of mucormycosis [Figure 6]. Chest

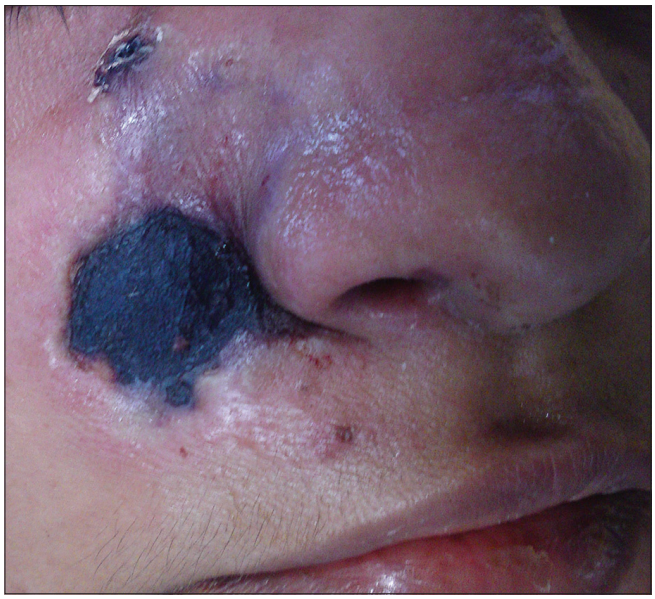

Figure 1: A single well-defined black necrotic eschar measuring 5 cm × 3 cm over the right maxillary region

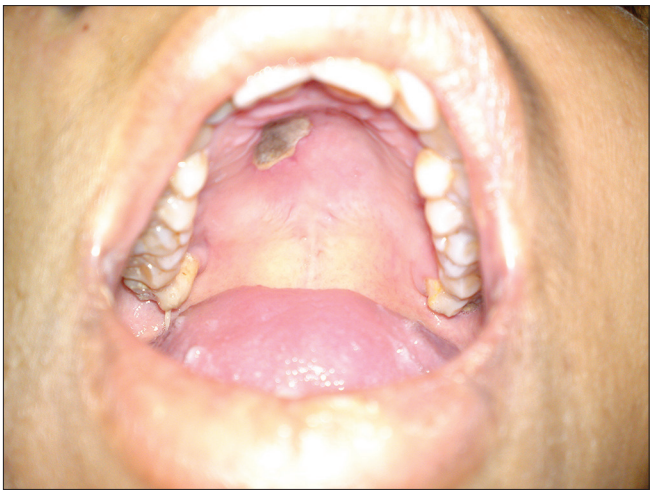

Figure 2: A single well-defined black necrotic eschar with slough on the hard palate

Figure 3: Sabouraud's dextrose agar showed cotton wool like colonies of Mucor

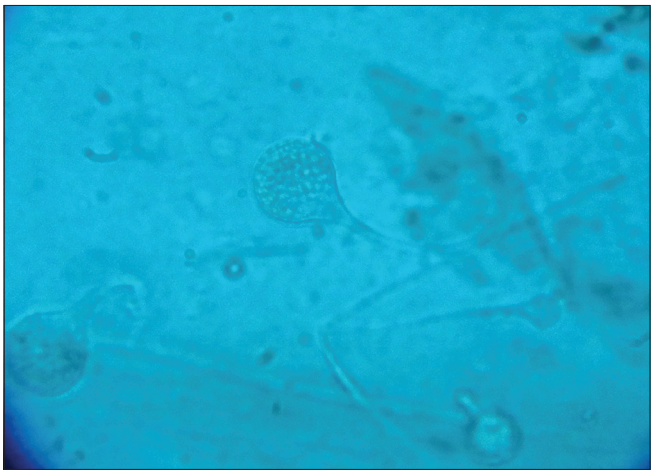

Figure 4: Lactophenol cotton blue preparation showed mature sporangia of Mucor species

radiograph was normal. Magnetic resonance imaging of the brain showed mild edema of the extraocular muscles in the medial aspect with increased soft tissue thickness over the right orbital region. There was evidence of mucosal thickening in the right maxillary, frontal, sphenoid sinuses, and ethmoidal air cells suggestive of sinusitis. There was minimal mucosal thickening and subcutaneous edema involving the right maxillary sinus [Figure 7]. Tablet voriconazole 200 mg twice daily for 5 days was started by the consulting physician, but showed no improvement; injection liposomal amphotericin-B was started at an initial dose 0.5 mg/kg/day, accelerated upto 5 mg/kg/day. However, the patient succumbed possibly because of rapid systemic progression of the infection.

DISCUSSION

Mucormycosis represents a group of life-threatening infections caused by fungi of the order *Mucorales*. Recent reclassification has abolished the class zygomycetes and placed the order *Mucorales* in the subphylum mucormycotina. *Mucorales* are saprophytic fungi characterized by broad, nonseptate, thick-walled hyphae found in the environment, particularly grow in soil, decaying wood and vegetable matter.[1,2] The infections caused by the *Mucorales* are most accurately referred to as mucormycoses.

Fungi of the order *Mucorales* belong to six families, all of which can cause mucormycosis. Among them, *Rhizopus oryzae* is the most common cause of infection. Other species of the *Mucoraceae* family that cause a similar spectrum of infections include *Rhizopus microsporus*, *Rhizomucor pusillus*, *Mycocladus corymbifer*, *Apophysomyces elegans*, and *Mucor* species, which despite its name is a rare cause of mucormycosis.[3]

Mucormycosis is manifested as rhinocerebral, pulmonary, gastrointestinal, cutaneous and disseminated type. Rhinocerebral form is the most common form and is fulminant in immunocompromised patients like those with diabetic

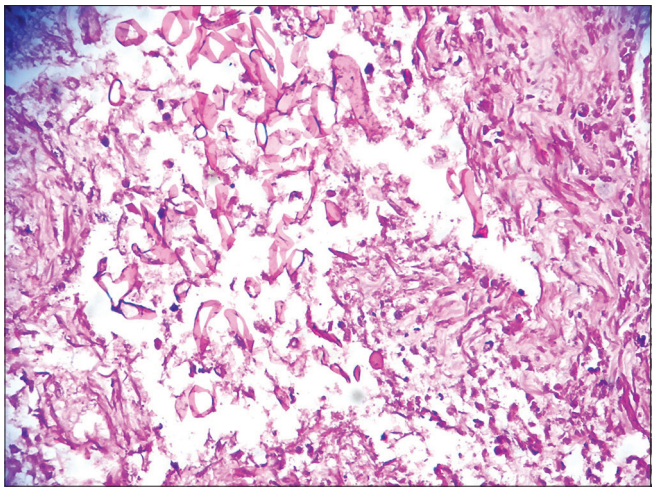

Figure 5: Eosinophilic, thick-walled aseptate hyphae with neutrophils, few of them appear hollow on cross section (H and E, ×40)

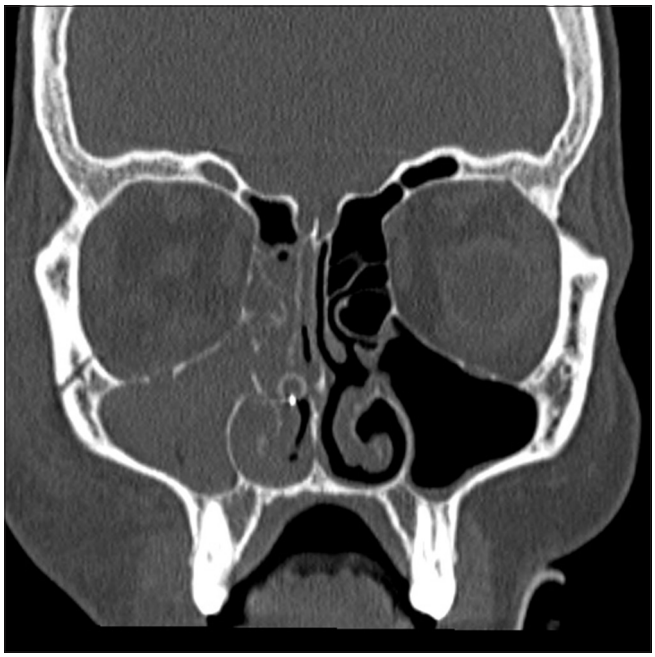

Figure 7: Magnetic resonance imaging of brain showed mild edema of extra ocular muscles in the medial aspect with increased soft tissue thickness in the orbital region over the right side. There was evidence of mucosal thickening in the right maxillary, frontal, sphenoid sinuses and ethmoidal air cells suggestive of sinusitis. There was minimal mucosal thickening and subcutaneous edema of the right maxillary sinus

ketoacidosis. The most commonly found genera in human diseases are *Rhizopus*, *Mucor*, and *Rhizomucor*. *Rhizopus arrhizus* is one of the most common species isolated from patients in a 10-year study of mucormycosis in India.[4]

According to the literature review, mucormycosis caused by *Mucor* species is rare.[1] There were 361 cases reported by Espinel–Ingroff *et al*., 156 of which were identified (129 *Mucorales* and 27 *Entomophthorales*). Among them, *Rhizopus* spp. was the most frequent (95 cases) followed by *Mucor* spp. (19 cases).[5]

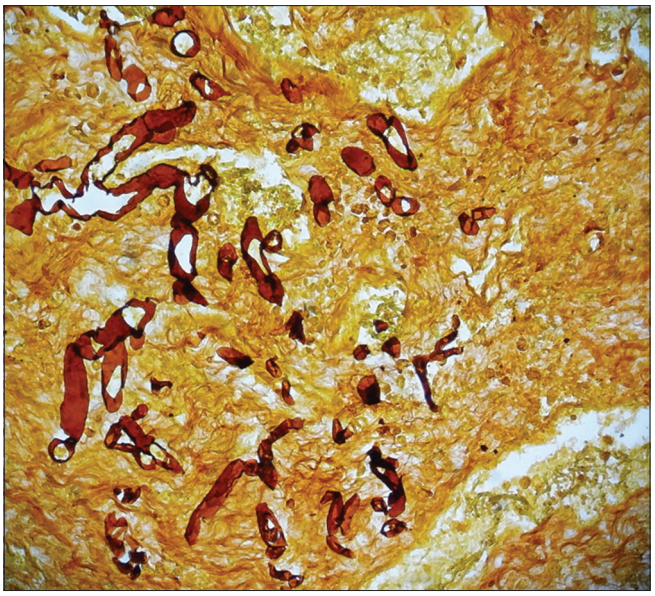

Figure 6: Similar section of tissue showed prominent fungal hyphae with special stain (GMS, ×40)

Rhinocerebral mucormycosis is a fulminant infection of the nasal mucosa that quickly spreads to contiguous structures such as palate, paranasal sinuses, orbit, face and brain.[5] In our patient, it presented as black necrotic eschar involving right side of the nose, malar area, nasolabial fold, nasal mucosa, and hard palate.

Mucormycosis is ubiquitous in nature. Light microscopy shows hyphae that are broad and nonseptate. When the spores are converted into hyphae, they invade and spread through the paranasal sinuses into the brain and orbit. Extension of these hyphae along blood vessels is followed by invasion and thrombosis.[6-8] It has a high mortality rate of 20-100%. The portal of entry is the nasal mucosa. Thereafter the fungal hyphae spread through the paranasal sinuses and into the blood stream and rapidly spread to other organs, leading to death. In the blood vessels, hyphae forms thrombi which reduce vascularity to the tissues and form a necrotic eschar.[8-11]

There is a close histopathological resemblance between the fungal hyphae of mucormycosis and aspergillosis, the main difference being hyphae of *Mucor* are nonseptate and branch at right angles whereas the hyphae of *Aspergillus* are septate, smaller and branching at more acute angles.[12] In our case, the characteristic fungal morphology of mucormycosis was identified on hematoxylin and eosin stain and confirmed by GMS stain. In addition, fungal culture also grew *Mucor* species.

Our patient was a case of uncontrolled diabetes mellitus since four years, and presented with a necrotic plaque extending from right maxillary region to the hard palate. The diagnosis of mucormycosis was based on clinical examination, fungal culture and histopathology. Management included surgical

resection of the eschar, and amphotericin B (0.5-5 mg/kg/day intravenous) along with diabetic control measures. Despite these medications, the patient died of infection within a span of 15 days.

CONCLUSION

It is important to rule out mucormycosis in diabetic patients, as early diagnosis and treatment can reduce the morbidity and mortality. Delay in management often leads to a fatal outcome. A combination of surgical debridement with amphotericin B remains the mainstay of treatment.

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