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Nasal Mucormycosis: Our experience with 24 cases

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ABSTRACT:

Background: Mucormycosis is a rare fungal infection affecting people with impaired immunity. The aim of this study is to shed light on the epidemiology, incidence, and outcome of patients with mucormycosis hospitalized at a tertiary care center in Pondicherry.

Methods: We conducted a retrospective chart review between January 2008 and January 2018. All patients with proven or probable mucormycosis were included.

Results: A total of 24 patients were included. Their median age was 49 years and the majority were males. Comorbidities included mainly hematologic malignancy and diabetes mellitus. A liposomal amphotericin B formulation alone or in combination with other antifungals was used as a first line agent in all patients.

Conclusion: The incidence of mucormycosis has significantly increased over the past 10 years at our institution, most likely due to increased risk factors.

KEYWORDS: amphotericin B, debridement, invasive fungal infection, mucormycosis, mycoses, rhinocerebral mucormycosis, zygomycosis

ABBREVIATIONS

EORTC – European Organization for Research and Treatment of Cancer
MSG – Mycoses Study Group

INTRODUCTION

Mucormycosis is a rare and serious invasive fungal disease caused by fungi of the class Mucormycetes [1]. Mucormycosis has been increasingly recognized as a cause of high morbidity and mortality in immunocompromised patients, especially in those with uncontrolled diabetes mellitus [2], hematologic malignancies [3] and patients on prolonged glucocorticoid treatment. Although there have been significant advances in imaging and laboratory techniques, the diagnosis of mucormycosis still remains a challenge as there is no circulating antigen detection test available, nor are there options of pathognomonic radiographic imaging. Therefore, diagnosis relies on clinical suspicion and direct visualization of the organisms from tissue biopsies and isolating the organism in cultures [4]. Since the data related to mucormycosis is scarce, we analyzed all recorded cases of mucormycosis in our tertiary care center over a period of 10 years to describe the burden, outcome, and management of patients with this rare disease.

MATERIAL AND METHOD

The study was carried out in a tertiary care center and was approved by the institutional review board. A 10-year retrospective chart review was conducted on medical records of patients with mucormycosis between January 2008 and January 2018. Medical records, laboratory data, imaging findings, and operative reports were reviewed for all cases. Cases without histopathological confirmation were excluded from the study. The patients were classified as having mucormycosis based on the revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group (EORTC/MSG) criteria [5].

RESULTS

The median age was 49 years, (range 37–80 years) with a male preponderance (male 15 and females 9). The underlying conditions included uncontrolled diabetes in 20 patients (83%), hematologic malignancy in 3 patients (13%), and 1 patient with renal transplant (4%) (Fig. 1.). Fifty percent of the patients had a nasal-only disease (n = 12), 12% had rhino-orbital disease (n = 3) and 38% had rhino-orbito-cerebral disease (n = 9). Eighty percent of the patients with rhino-orbital and rhino-orbito-cerebral disease presented with complete blindness and never recovered their vision. Twenty-one patients underwent surgical debridement, while the remaining 3 had extensive cerebral involvement and succumbed to the illness within a day of admission. Thirteen out of 21 patients who underwent surgery survived, and the remaining 8 patients died (Fig. 2.). The cause of death in the 8 patients included cavernous sinus thrombosis (n = 4), septicemia (n = 3) and amphotericin related toxicity in 1 patient. The overall mortality was 46% (n = 11). All patients were treated with liposomal amphotericin B at a dose of 4–7 mg/kg per day and were continued till 3–4 weeks.

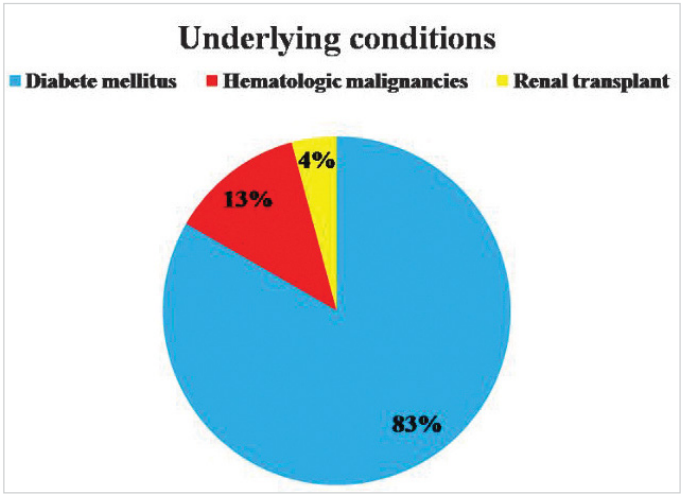

Fig. 1. Distribution of underlying condition in patients with mucormycosis (n = 24).

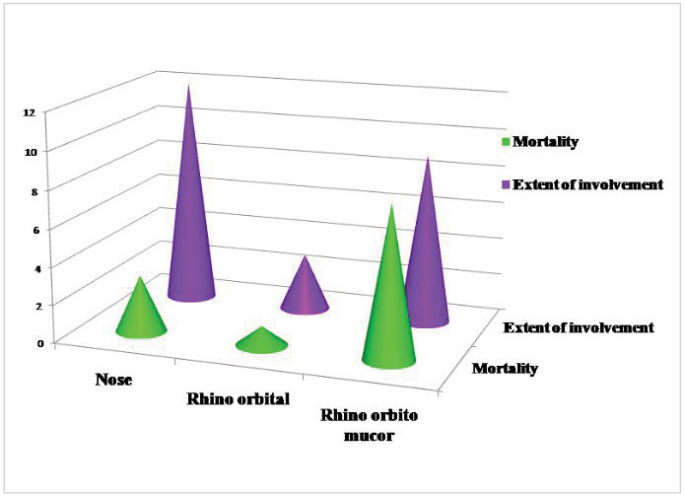

Fig. 2. Extent of mucormycosis and associated mortality.

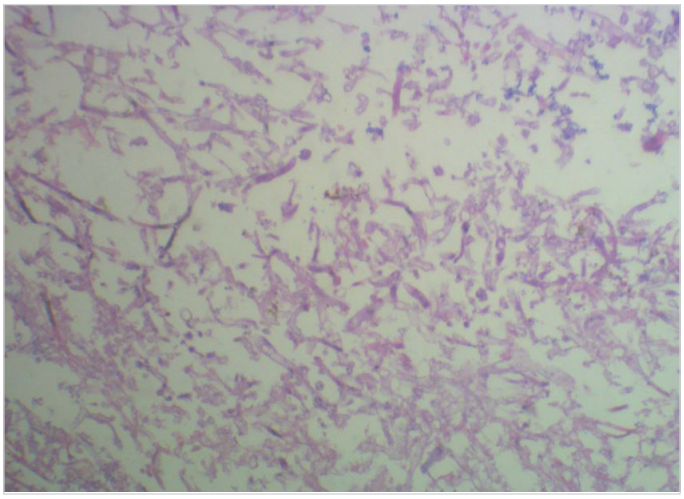

Fig. 3. Histopathological picture showing broad-angled aseptate hyphae and necrotic tissue suggestive of mucormycosis.

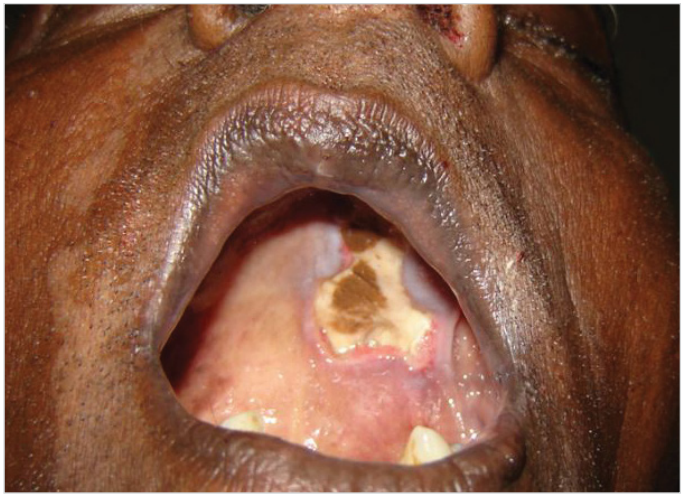

Fig. 4. Patient presenting with palatal erosion due to mucormycosis.

DISCUSSION

Mucormycosis of the nose and paranasal sinuses is an uncommon disease and is associated with high mortality rates. Its prevalence in India is estimated to be 0.14 per 1,000 population [6]. A large multicentre study conducted in India showed a comparatively higher incidence of mucormycosis in India at that time compared to Southern India [6]. Mucorales are opportunist pathogens and infect immunocompromised individuals. The most common organism in India are Rhizopus oryzae. However, Apophysomyces elegans and Saksenia vasoformis can infect healthy individuals following trauma [7]. It is worth noting that there has been an increase in infection with Rhizopus microporus which is more resistant to Amphotericin B compared to other Mucorales [6]. Histological presence of broad, ribbon-like aseptate hyphae, 10 to 20 µ across, with broad-angled branching, helps in the presumptive diagnosis of mucormycosis [4] (Fig. 3.). The diagnosis of mucormycosis in the present study was based on light microscopy or histopathology of the tissue for the visualization of characteristics of hyphae. Molecular typing and culture of fungus was not employed for diagnosis. As such, definitive causative fungi could not be identified in the present series. Mucormycosis is commonly found in immunocompromised states. Various mechanisms of pathogenesis have been described which includes impaired chemotaxis and phagocytosis, and increased expression of GRP-78 protein in diabetics which promotes angio-invasion [7]. The most common underlying condition in this series was diabetes followed by hematologic malignancy. This is in contrast to studies in the west where underlying hematologic malignancies account for the majority of cases [6–8]. This may be attributed to the high incidence of diabetes among the Indian population and a lack of awareness regarding the importance of glycemic control among the major cities of the Indian population [9]. Patients with diabetes and ketoacidosis are at an increased risk since low serum pH decreases the phagocytic activity of macrophages and neutrophils and naso-orbital mucormycosis usually present with nonspecific symptoms like fever (approx. 71%), and rhinorrhea (57%). Ocular pain, visual loss, proptosis and facial edema, when present, suggest advanced disease. Isolated involvement of the maxillary sinus presenting with palatal and alveolar necrosis is also known to occur [10] (Fig. 4.). The characteristic blackish eschar is a hallmark sign but is present only in 40–50% of cases. Cerebral involvement is a bad prognostic sign and carries a high mortality of 65–80% [11];

this was also seen in our study, in which 7 out of 9 patients with cerebral involvement succumbed to the illness. Beside the rhino-orbito-cerebral involvement, mucormycosis can cause isolated involvement of the lungs, gastrointestinal tract and the kidneys. Isolated nasal or naso-orbital mucormycosis has relatively better outcome due to early presentation, surgical debridement and an early administration of antifungals as the treatment of choice which significantly improves the outcome in these patients [12]. In our series, 60% of the patients who underwent surgical debridement survived. If patients do not improve within 48 hours then the possibility of drug resistance, inadequate debridement, deranged metabolic conditions like blood sugars or electrolytes, sepsis and possible co-infection with other organisms should be considered [13, 14]. Limitations of the study are the relatively small sample size. Therefore, multivariate analysis was not performed and no correlation between the outcome, duration of symptoms, the extent of involvement and type of antifungal therapy was made. The difference in survival might be affected by multiple confounders and might reflect the fact that sicker patients could not be operated and lower doses of drugs were given. Another limitation is the lack of fungal cultures. However, the presence of characteristic broad aseptate hyphae with broad-angled branching is usually sufficient for diagnosis.

CONCLUSION

Mucormycosis is a rare disease mostly affecting immunocompromised patients. Despite advances in medical therapy and laboratory procedures, mucormycosis remains associated with high mortality and morbidity. Cerebral involvement is a poor prognostic sign and carries significant mortality. Physicians must keep a high index of suspicion for this disease, especially in patients at risk as early diagnosis and treatment improve outcomes.

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