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**Research Article**

# Institutional experience of mucormycosis over a period of 10 years - retrospective case series

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## ABSTRACT

**Background:** Mucormycosis is an invasive fungal infection seen in immunocompromised patients. Most common presentation is face or orbital pain, headache, lethargy, visual loss, proptosis, or palatal ulcer. Because of its angioinvasive properties, it can rapidly spread to intracranial tissues and orbit. It can lead to fatal complications such as blindness, intracranial infections, convulsions and even death. Aim of current study was to diagnose this condition; a high index of suspicion is required. Blackish crusts are characteristically seen and Potassium hydroxide (KOH) staining of these crusts can give a rapid diagnosis.
**Methods:** Study Design was retrospective review of the charts. We reviewed the charts between January 2001 and December 2010 and compiled together 60 cases of mucormycosis.
**Results:** The most common presentation was orbital cellulitis. Some patients presented with features of acute sinusitis. The most common cause of immunosuppression was diabetes mellitus. Patients were started on amphotericin. The prognosis was bad in 7 patients who lost vision and 8 patients died.
**Conclusion:** Diagnosis in the early stage needs a high degree of suspicion. The underlying illness, the time between the onset of the disease and the establishment of treatment, and the occurrence of cerebral ischemic events play a role in worse survival rates.

**Keywords:** Mucormycosis, Orbital cellulitis, Amphotericin, Diabetes mellitus

## INTRODUCTION

Mucormycosis is a group of destructive opportunistic mycosis caused by filamentous fungi of order mucorales. Mucormycosis is the 3rd most common invasive mycosis in order of importance after candidiasis and aspergillosis in hematological and Allogeneic Stem Cell Transplantation (ASCT) patients.[1]

These fungi will cause lethal infections in immune-compromised patients especially those with uncontrolled diabetes accompanied with keto-acidosis.[2]

Invasive mucormycosis is characterized by the rapid development of tissue necrosis due to vascular invasion and subsequent thrombosis. Disease may manifest as rhino-orbital-cerebral, pulmonary, cutaneous, gastrointestinal, or disseminated forms.[3] In this retrospective study we evaluated the clinical characteristics and treatment outcome for mucormycosis cases.

## METHODS

Charts of 60 patients with histopathologically confirmed diagnosis of mucormycosis treated at St. John's medical

college hospital, Bangalore, India from Jan 2001 - Feb 2010 were analyzed. Evaluation at presentation included a detailed history, otorhinolaryngological, ophthalmic and neurological examinations to assess the extent of the disease.

Initial investigations included complete blood counts, blood urea, serum creatinine, serum glucose, urine for ketone bodies and blood gas analysis. Diagnosis was made on histopathological examination and KOH preparation of biopsy specimens obtained from the nasal cavity and/or paranasal sinuses and the palate. An orbital Fine Needle Aspiration Cytological (FNAC) study was done in some patients when histopathological diagnosis from other sites was equivocal. Computerized tomographic scans of the paranasal sinuses, orbits and brain were obtained to assess the extent of disease.

Treatment with systemic Amphotericin B was started as soon as a diagnosis of mucor was established in all patients, along with treatment to stabilize the underlying metabolic derangement. After a test dose of 1 mg of amphotericin B in 100 ml of normal saline, 0.7 mg/kg/day of amphotericin B was given over 6 hours. The dose was increased by 25 mg/day on alternate days to a maximum of 100 mg/day and continued till a cumulative dose of 2.5-3 gm was reached.

Three distinct treatment groups were identified based on the nature of surgery that the patients underwent. Patients in treatment group 1 (TG-1) underwent sino-nasal debridement only. Some patients in this group who had orbital involvement also received intraorbital amphotericin B (1 mg/ml/dose retrobulbar injection once a day or through an irrigating cannula). Treatment group 2 (TG-2) consisted of sino-nasal debridement with orbital exenteration. Treatment group 3 (TG-3) received only medical treatment with intravenous amphotericin B as all these patients refused surgery. Adverse effects were overcome by pre medications, avoiding concomitant nephrotoxic drug, and by administering liposomal amphotericin.

## RESULTS

Sixty patients presented between January 2001 and December 2010; out of 60 patients, 33 were males and 27 were females. Distribution of age among genders is given in Table 1. The age group ranged between 20 to 73 years. The most common cause of immunosuppression was diabetes mellitus (43 cases). Diabetic ketoacidosis was the cause in 12 cases. Chronic renal failure accompanied with diabetes mellitus was underlying cause for mucormycosis in 5 patients. Most common presentation was orbital cellulitis. Symptom presentation is given in Figure 1. Some patients presented with features of acute sinusitis. Out of 60 patients 38 underwent debridement. 10 underwent orbital exenteration and 12 received periorbital ampho injection. Treatment assignment to patients is shown in Figure 2. 49 patients completed the course. 3 discharged against medical advice. 8 patients died. Hypokalemia was observed in 5 patients.

**Table 1: Age and gender distribution of patients presented with mucormycosis.**

| Age group | Male | Female |
|---|---|---|
| 20-30 | 1 | 0 |
| 30-40 | 4 | 7 |
| 40-50 | 7 | 8 |
| 50-60 | 17 | 10 |
| 60-70 | 4 | 2 |

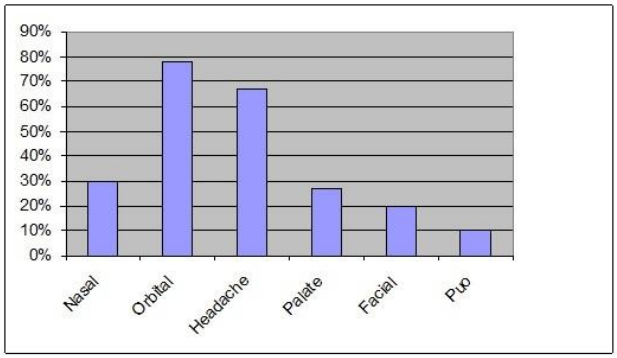


**Figure 1: Presentation of symptoms in patients with mucormycosis.**

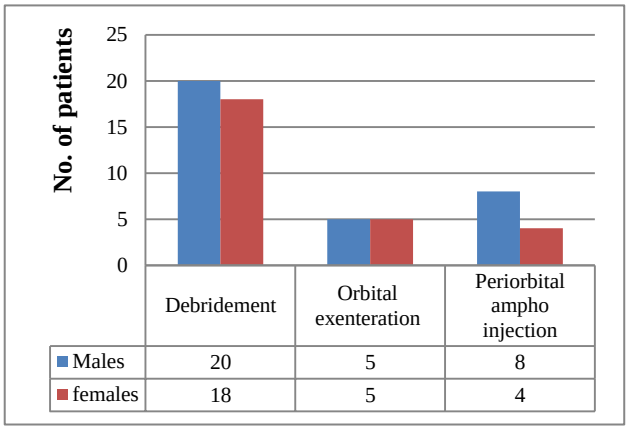


**Figure 2: Treatment for patients with mucormycosis.**

## DISCUSSION

The agents of mucormycosis (zygomycosis) normally reside in the environment. The abundant airborne sporangiospores may be inhaled or contaminate wounds or burns of patients with predisposing conditions such as diabetes or immunosuppression or trauma, and cause a spectrum of diseases.[4]

The clinical manifestations of mucormycosis are divided into at least six syndromes: rhino-cerebral, pulmonary, cutaneous, gastrointestinal, central nervous system and miscellaneous (bone, kidney, heart, or mediastinum.[5] The

entry point of mucorales is the upper aerodigestive tract (nasal mucosa or digestive tract). The invasive form has high affinity for the arteries and grows along the internal elastic lamina, eventually penetrating the endothelium and cause thrombosis, stroke and extensive tissue necrosis.[6]

Risk factors for the development of mucormycosis include DM with or without ketoacidosis, neutropenia, protein-calorie malnutrition, and iron overload with or without the use of deferoxamine.[2]

There are two predisposing factors for the disease: metabolic acidosis and a deficit in the function of neutrophils and monocytes. In this sense, in patients suffering from diabetic ketoacidosis, the fungal infection is favoured, since the mucorales have a system of acetone-reductase that facilitates their growth in media rich in glucose with acid pH. The pathogenesis of this disease is arterial invasion by the fungi themselves, causing thrombosis and tissue infarction.[6]

Clinically rhino-orbito-cerebral mucor mycosis can be described as acute fulminating infection. Patients are usually present with nasal discharge, orbital cellulitis, facial pain, headache, fever, ophthalmoplegia, ptosis and proptosis.[7] However, facial nerve paralysis is relatively uncommon and can be found in approximately 11%-22% of patients with rhino cerebral mucormycosis. In earlier reported cases facial nerve involvement was due to intra cranial involvement or due to middle ear invasion. In the recent cases reported it was found to be due to suppurative parotitis or other parotid lesions but rarely as a result of parotid involvement due to mucormycosis.[6]

In few patients we observed the involvement of parotid gland with mucormycosis that was proven by aspiration of fluid from the gland and found positive for fungal stains and culture. As a result of gland involvement facial nerve paralysis occurred. This occurrence is very rarely reported in a case of mucormycosis. The facial nerve paralysis improved after commencement of amphotericin B and patient recovered from the paralysis (from grade IV to grade I) by the time he discontinued the treatment due to rapidly rising serum creatinine levels and chest complaints.

The prognosis depends on the extent of infection, underlying diseases and the establishment of an early treatment. Liposomal amphotericin B is the medical treatment of choice, coupled with an adequate surgical debridement of devitalized areas and the correction of the underlying metabolic and immune factors. Kidney function must also be controlled in order to prevent blood urea nitrogen and creatinine exceeding 50 and 3 mg/dl, respectively. If this happens, the dose should be decreased until kidney function recovers.[6]

In our case we started the patients on amphotericin B conventional treatment due to the constraints of affordability. Patients improved considerably after the commencement of treatment. The therapy was discontinued due to rapidly rising creatinine levels and chest complaints.

The underlying illness, the time between the onset of the disease and the establishment of treatment, and the occurrence of cerebral ischemic events play a role in worse survival rates.[6] Factors favouring rapid recovery in our patients were early diagnosis and prompt commencement of treatment.

## CONCLUSION

In conclusion mucormycosis is a potentially aggressive and sometimes fatal fungal infection.

Diagnosis in the early stage needs a high degree of suspicion. The management following a diagnostic biopsy includes rapid correction of the underlying metabolic and immunological derangements, intravenous amphotericin B and surgical clearance of all infected nasal and sinus tissue. If headache, facial pain, ophthalmic signs and facial nerve paralysis as well as signs of parotitis, develop in patients with DM or in those in an immuno compromised state, rhino orbito-cerebral mucormycosis should be cautiously considered, and antifungal treatment should be started as early as possible after diagnosis.

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