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ENDOSCOPIC MANAGEMENT OF NASAL MUCORMYCOSIS WITH AMPHOTERICIN B

Otorhinolaryngology

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ABSTRACT

Objective: Mucormycosis is an aggressive fungal infection that may still cause fatal complications. However, the rarity of this disease has made optimal treatment a controversial issue. This study aimed to evaluate the use of Amphotericin B in the endoscopic management of nasal mucormycosis. **Subjects And Methods:** 101 Patients with infection limited to the nose and sinuses coming to the Department of ENT, Maharaja Yashwantrao Holkar Hospital, Indore, were selected. Patients underwent endoscopic debridement of all necrotic tissue; cottonoid pledgets soaked in amphotericin B solution were then placed in the nasal cavity. Subsequently, long-term antifungal therapy was administered. **Results:** The overall survival rate was 95 percent (96 cases); survival rates in the diabetic and systemic complication groups were 41 and 20 percent, respectively. Apart from predisposing factors, orbital and maxillary sinus involvement also significantly correlated with patient outcome. **Conclusion:** Topical use of amphotericin B combined with endoscopic surgical debridement, followed by intravenous amphotericin B treatment, may constitute acceptable management for selected patients, with less morbidity than conventional treatments.

KEYWORDS

INTRODUCTION

Mucormycosis is an aggressive fungal infection which may cause fatal complications in immunocompromised and diabetic patients. [1,2] This fungus is angioinvasive and causes thrombosis of vessels, with consequent black necrosis of nasal and sinus tissue.[3] Despite tremendous progress in the treatment of mucormycosis, it still has a high mortality rate especially in immunocompromised patients. However, conventional treatment can itself cause substantial morbidity. In the wake of second wave of COVID-19, an increased number of mucormycosis cases were reported known as COVID associated Mucormycosis.

Most authors recommended prompt surgical debridement and long-term antifungal therapy. Surgery is used to remove necrotic tissue, reduce the concentration of fungal spores and facilitate the effect of antifungal drugs. [4, 5] Reversal of predisposing factors is an indispensable part of treatment. [6,7,8]

Traditionally, some authors have recommended aggressive surgical resection of affected tissue.[9,10] However, following wide application of nasal endoscopy in sinus surgery, other authors have reported comparable results with frequent endoscopic debridement.[1,11,12] These authors have claimed that, in selected cases, this method has less morbidity, a better surgical field of vision, and comparable results.[2,11,13] However, the poor state of most infected patients results in high mortality rates regardless of treatment type. As a result, much research has been conducted in an attempt to improve treatment outcomes.

In this study, we evaluated patient outcomes following the use of topical amphotericin B during endoscopic management of rhinocerebral mucormycosis.

METHODS:

STUDY SUBJECTS

101 Consecutive patients referred to the ENT department of a tertiary referral centre of Central India MGM & MYH Hospital, Indore were recruited to the study between May 2021 and August 2021.

Inclusion Criteria

- We included patients in this study who were admitted under Mucor Unit (consisting of mainly 4 departments- ENT, Ophthalmology, Dental & Medicine) in Maharaja Yashwantrao Holkar Hospital , Indore, suffering from symptoms suggestive of mucormycosis.
- Patients both males and females were included in the study. Nasal endoscopy confirmed the presence of necrosis.
- All patients underwent computed tomography (CT) scanning (and magnetic resonance imaging in some cases) to determine the extent of infection. Additionally, biopsies of involved tissues were evaluated pathologically and biologically to establish a definitive diagnosis. However, in critical cases we did not wait for the results of analysis before commencing treatment.

Exclusion Criteria

We excluded from the study patients with central nervous system (CNS) involvement, extensive orbital involvement or palatal necrosis.

Ethical Approval

Detailed information about the study was provided for participants, and written, informed consent was obtained from each one.

Procedure And Medical Treatment

- Based on findings from endoscopy and imaging, all patients underwent functional endoscopic sinus surgery (FESS) after normal anesthetic workup.
- During endoscopic sinus debridement, all necrotic tissue was removed down to the level of viable tissue. In addition, involved sinuses were opened wherever necessary to facilitate drainage of fungal elements. Any suspicious tissue specimen was sent for Histopathological examination.
- After the completion of surgery and achievement of haemostasis, cottonoid pledgets soaked in amphotericin B solution and betadine solution were placed in the nasal cavity for 48 hrs. After 48 hrs, pack was removed and suctioning was done.
- The process of Nasal endoscopy with amphotericin gel insertion was done on 4th and 6th postoperative day.
- All patients were also treated with intravenous amphotericin B (1 mg/kg/day), receiving at least 3 g of the drug, in addition to reversal of predisposing factors.

PATIENT VARIABLES AND FOLLOW-UP PERIOD

We evaluated patient's demographic data and their results for complete nasal endoscopy and CT scanning. Each patient's clinical presentation and predisposing factors were assessed. Biochemical indices and treatment complications were obtained from patients' medical records. After surgical debridement, all patients were followed up for at least six months to detect recurrence. Post-operative nasal endoscopy was conducted, under local anesthesia, in order to remove crusts and to examine the nasal and sinus cavities for recurrence, until healing was complete. Any patients with recurrence underwent repeated endoscopic surgery.

91 patients who had diabetes mellitus, 76 patients were insulin-

dependent and 15 patient had an episode of diabetic ketoacidosis 1 month earlier precipitated by steroid therapy. Strict diabetic control was instituted with frequent monitoring of blood glucose levels and insulin therapy.

RESULTS

During the study period, 101 patients were recruited to the study.

Of the original 101 patients, 46 (45.5 per cent) were female and 55 (54.4 per cent) male, with a mean age of 49 years (range, 18–80 years).

The most common predisposing factor in this series was diabetes mellitus. Only one of the diabetic patients had ketoacidosis at the time of mucormycosis diagnosis.

The most common clinical presentation was cheek anaesthesia followed by nasal obstruction.

All patients underwent CT scanning and nasal endoscopy. According to imaging and nasal endoscopy, 41 (40.5 per cent) patients had bilateral involvement, 15 (58.3 per cent) had unilateral left involvement and 25 (41.6 per cent) had unilateral right involvement.

Medical treatment was commenced before surgery in 79 patients, and after surgery in the remainder. Recurrence was detected in 6 patients. The mean duration of treatment was 36 days.

The overall patient survival rate was 95 percent (96 patients). 6 (5.9 per cent) patients died. By comparison, the patients who were excluded from the main series and received conventional treatment had a survival rate of only 37.5 per cent (three patients).

The time delay between diagnosis and treatment did not correlate with survival and prognosis. Of the different sites of involvement, only maxillary sinus involvement showed a significant relationship with poor prognosis. The extent of necrosis seen on pre-operative diagnostic nasal endoscopy did not correlate with survival. However, there was a significant difference between the survival rates of diabetic patients (70.58 per cent) and patients with malignant disease (40 per cent)

DISCUSSION

Mucormycosis is a fulminant and often lethal infection caused by an opportunistic fungus of the Phycomycetes family. Usually, affected patients are those with poorly controlled diabetes with ketoacidosis or immunocompromised as a consequence of cytotoxic drugs, burns, hematologic malignancies, end-stage renal diseases, or administration of immunosuppressive medications after organ transplantation.[14] It presents in a rapidly aggressive manner with headaches, fever, nasal obstruction, rhinorrhea, and black, necrotic, intranasal crustae. Progression can lead to ophthalmic or nervous symptoms and death. [17] Local infection follows the inhalation of aerosolized spores that may deposit in the nasal mucosa and spread into the neighbor structures. Once the sinus tract is involved, the fungus appears to invade the arteries, proliferating within the internal elastic lamina, and then penetrating the endothelium producing thrombosis, infarction, hemorrhage and extensive tissue necrosis.[18]

It is recommended to do aggressive surgical debridement and long-term antifungal treatment. [5,10,13] Of various recent treatment proposals, the direct introduction of amphotericin B to the sinus cavity in order to reduce the density of fungal spores is a good option. Because of the adverse renal and hepatic effects of amphotericin B (which can cause serious complications), some researchers have used it topically in form of gel and solution during treatment. [13,19]

All patients underwent urgent endonasal endoscopic debridement wherever needed under general anesthesia. Clearance of maxillary, ethmoidal, frontal and sphenoidal sinuses if they were involved. Necrosed remnants of inferior and middle turbinates were removed. Debridement was done till healthy bleeding tissue was encountered. All patients postoperatively continued on Liposomal Amphotericin B in renal corrected dosages for two-three weeks. Apart of correction of underlying predisposing condition, regular endoscopic nasal toilet were performed to remove crusting and to examine sinus cavities for recurrence until healing occurred. Follow up nasal endoscopy reveals well healed mucosal lined nasal and sinus cavities with no evidence of mucormycosis. Another advantage of endoscopic debridement is ease in further endoscopic examination, cleaning of crusts and residual disease, thus preventing recurrences. All patients were kept under stringent follow up with weekly rigid nasal endoscopy for first four weeks and then, and once a month for 6 months thereafter.[20]

Our patients' overall survival rate was approximately 93 per cent, which was acceptable considering the non-diabetic patients in our series.[4,7,8,21] Moreover, in comparison with the results of conventional mucormycosis treatment at our centre, this survival rate represented a positive improvement.[22] Considering the lower incidence of post-operative complications following endoscopic treatment, and the comparable findings reported by the present study and similar reports, we would recommend our treatment modality in selected cases.[2,11,23]

Maxillary sinus involvement was associated with a significantly poor prognosis.

Reviewing our patient's causes of death revealed complications associated with extensive mucormycosis involvement. Of the former, CNS involvement can be considered a fatal complication.[3,7,8]

Some reports have considered a treatment delay of more than 6 days to represent an indicator of poor prognosis. [8] However, a mean delay of 16.6 ± 7.7 days had no significant relationship with survival in our series. It would appear that reversal of predisposing factors and commencement of antifungal therapy are more effective than early surgery in improving patient prognosis.[13]

The most important prognostic factors in our study were patient's predisposing conditions. Our diabetic patients had a significantly better prognosis than our patients with patients with systemic complications. Blood glucose level can be considered an important factor in defining treatment outcome. Ketoacidosis is considered to be a risk factor for poor prognosis, the small number of patients with this complication in our series caused no significant difference. [10]

- Defining the best treatment method is difficult, due to the condition's rarity
- This study assessed topical amphotericin B plus endoscopic surgical debridement, followed by intravenous amphotericin B, in 101 patients
- Survival rates were 93 per cent overall, and 71 per cent in diabetic cases and 40 per cent in other complicated cases.

Based on the above findings, the treatment modalities used in our series can be considered an effective method, with acceptable complications. This conclusion is in agreement with other studies.[13]

CONCLUSION

Mucormycosis is a rare condition which can still be fatal. A combination of endoscopic surgical debridement plus topical amphotericin B usage, followed by intravenous amphotericin B therapy, is acceptable in the management of selected patients, and has less morbidity compared with conventional treatment. Early detection of sinonasal mucormycosis in immunocompromised patients enables prompt aggressive treatment. Powered endoscopic debridement is efficient and feasible, leading to excellent local control and which ultimately led to reduced morbidity and mortality. The early the surgical intervention is offered in the form of endoscopic sinus clearance the better are the results in controlling the disease progression. The aggressive control of immune compromise status along with surgery and 4 weeks of amphotericin B drug can improve the mortality rates in such patients.

Total dosage for liposomal amphotericin B ranged from 2.5 to 5.5 g.

Tables:

Table I: Patients' Predisposing Factors

FACTOR	N	%
Diabetes	68	67.3
Other complications	11	10.8
COVID 19	32	31.6

Table II: Patients' Clinical Presentation

Symptom	N	%
Nasal obstruction	83	82.1
Nasal discharge	22	21.7
Headache	65	64.3

Cheek anesthesia	90	89.1
Periorbital oedema	76	75.2

Table III: Side Of Involvement

Side of involvement	Number of pts involved	%
Left nasal involvement	15	14.8
Right nasal involvement	25	24.7
Bilateral nasal involvement	41	40.5

Table IV: Results Of Imaging And Diagnostic Nasal Endoscopy

Parameter	Value
Septal involvement (pts. (n %))	86 (85.1)
Middle turbinate involvement	81(80.1)
Involvement beyond septum & turbinate (pts. (n (%))	54(53.4)

Sd = Standard Deviation; Pts. = Patients

Table V: Patients' Causes Of Death

Cause	N	%
Cardiopulmonary complications	2	1.9
CNS complications	3	2.9
Sepsis	1	0.9

Table VI : Results Of Disease Status

Disease status	Number of patients (n)	%
History of COVID19 without diabetes	24	31.3
History of COVID 19 with diabetes	60	75.2
History of non-COVID 19 with diabetes	11	10.8
No history of COVID 19 or diabetes	6	6.9

Table VII : Prognosis Of Patients

Prognosis	Number of patients (n)	%
Cured	94	93
Recurrence	5	4.9
Death	2	1.9

Figures:

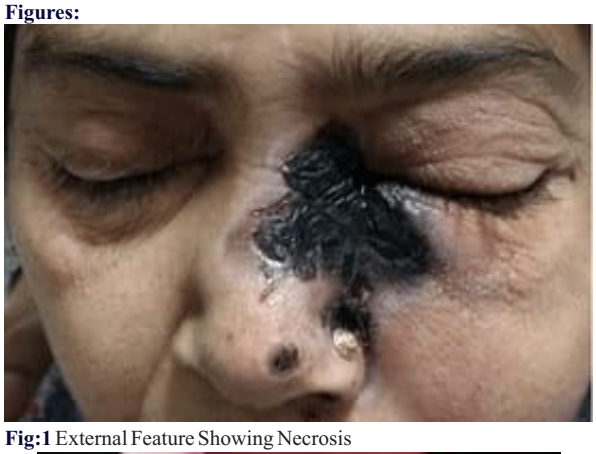

Fig:1 External Feature Showing Necrosis

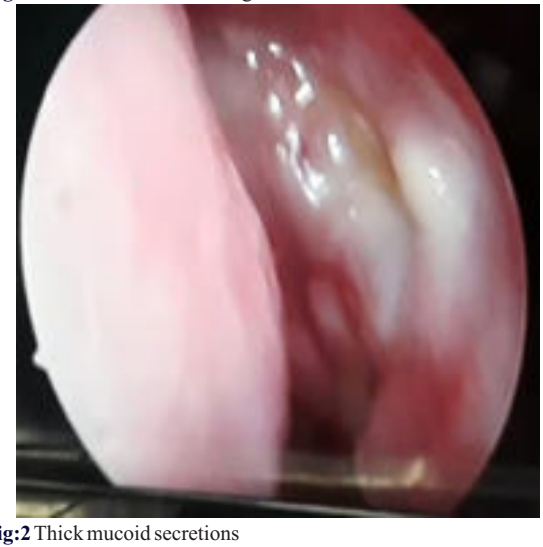

Fig:2 Thick mucoid secretions

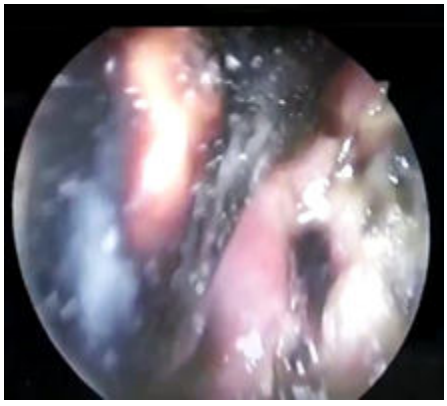

Fig:3 Showing Extensive Necrosis Inside Right Nasal Cavity

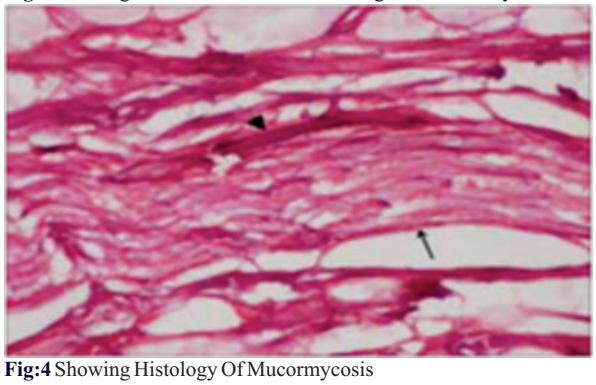

Fig:4 Showing Histology Of Mucormycosis

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