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Original Research Article

Orbital involvement in COVID-19 associated mucormycosis

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ABSTRACT

Background: Mucormycosis is an opportunistic, potentially lethal, fungal infection predisposed by uncontrolled diabetes mellitus, immunosuppressive therapy, primary or secondary immunodeficiency, injudicious use of corticosteroids, hematological malignancies, hematological stem cell transplantation, solid organ malignancies, solid organ transplantation. Rhino-orbital mucormycosis is the commonest form of mucormycosis. This study was done to discuss the management strategies (orbital decompression/clearance, orbital exenteration, retrobulbar amphotericin B) in the treatment of orbital mucormycosis and its clinical outcomes.
Methods: A retrospective descriptive study was conducted between May 2021 and October 2021 at Bowring and Lady Curzon hospital, Shri Atal Bihari Vajpayee Medical College and Research Institute, Karnataka, India.181 patients with post-COVID RTPCR negative rhino-orbital mucormycosis were included in the study. Patients underwent endoscopic orbital clearance, orbital exenteration based on the extent of orbital involvement.
Results: 143 were males and 38 were females. 160 patients underwent orbital decompression and clearance of necrotic tissue. 21 patients underwent orbital exenteration. Final visual acuity of perception of light (PL) positive and above was achieved in 147 patients. 57/58 (98.27%) patients had improvement in extraocular movements post-surgery and resolution of diplopia after orbital decompression/clearance.
Conclusions: Endoscopic orbital clearance helps to reduce the need for orbital exenteration in PL negative patients. TRAmB as adjuvant helps in decreasing the ocular morbidity. Orbital exenteration is best avoided, when possible, to avoid cosmetic disfigurement and psychological trauma to the patient.

Keywords: Black fungus, COVID-19 associated mucormycosis, Rhinoorbital mucor

INTRODUCTION

Mucormycosis is a potentially lethal and angioinvasive disease with a propensity to affect the immunocompromised individuals like patients with uncontrolled diabetes, patients on chronic or high dose of corticosteroids or immunosuppressive drugs, hematological malignancy patients, and solid organ transplant.[1]

Infection from the paranasal sinuses reach the orbit from ethmoid or maxillary sinuses. Orbital involvement presents with different degrees of orbital cellulitis and may progress to affect brain (typically at the frontal lobes) through the orbital apex.[2]

Orbital exenteration is a radical procedure involving removal of all contents of the orbit. It has been the surgical standard of treatment for orbital mucormycosis, but causes

cosmetic disfigurement and has a profound impact on the patient's psyche. There are no clear-cut studies on indications for orbital exenteration.[3] In Orbital clearance only the affected areas of orbital fat and soft tissues are removed. Recent studies have demonstrated that exenteration may not be necessary in most cases of rhino-orbital mucormycosis.[4,5] Administration of amphotericin B via retrobulbar injection is recommended to improve signs of orbital involvement and subsequent complications. Retrobulbar injection of amphotericin B is recommended in patients with signs of optic nerve compression, including a progressive decrease in visual acuity and positive relative afferent pupillary defect.[6] This study was done to discuss the management strategies (orbital decompression/clearance, orbital exenteration, retrobulbar amphotericin B) in the treatment of orbital mucormycosis and its clinical outcomes.

METHODS

A retrospective descriptive (record based) study was conducted between May 2021 and December 2021 at Bowring and Lady Curzon hospital, Shri Atal Bihari Vajpayee Medical College and Research Institute, Karnataka, India. 181 patients with post-COVID (reverse transcriptase polymerase chain reaction (RTPCR) negative rhino-orbito-cerebral mucormycosis (ROCM) who were histopathologically and/or radiologically proven mucormycosis [European Organization for Research and Treatment of Cancer/Mycoses study group (EORTC/MSG group) criteria] and who underwent surgery were included in the study (Figure 1).[7] RTPCR positive ROCM patients were excluded from the study.

Figure 1: Orbital mucormycosis.

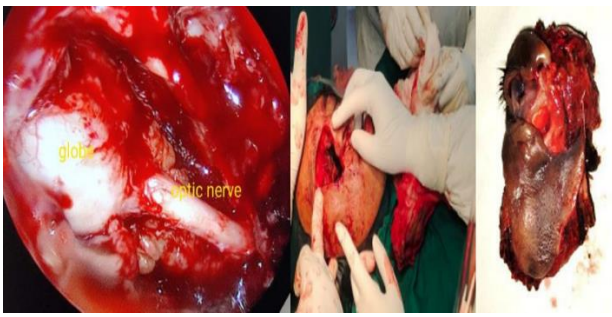

Figure 2: Orbital clearance, orbital exenteration and specimen.

After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria were enrolled in the study. Detailed ophthalmic examination was done for all patients to check for visual acuity, extraocular movements (EOM), fundus examination. All patients underwent contrast enhanced magnetic resonance imaging (CEMRI) with screening computerized tomography (CT) of nose, paranasal sinuses, orbit and brain. All patients underwent surgical debridement of involved paranasal sinuses and management of orbit was based on clinical, radiological examination findings.

Endoscopic orbital decompression/clearance

Nasal cavity was packed with cottonoids soaked in 4% lignocaine with adrenaline. After transnasal endoscopic debridement of sinuses, lamina papyracea is identified and removed. Medial and inferior longitudinal incisions were made in the periorbita to allow the orbital fat to herniate into the sinonasal cavity effectively decompressing the contents of the orbit. Orbital fat is teased with ball probe and recti muscles is examined for involvement. In patients with minimal orbital inflammation and in PL negative patients with minimal or no necrotic tissues in orbit (on intranasal endoscopy and radiological examination), orbital decompression/clearance was done. In PL negative patients and in patients with optic neuritis, optic nerve decompression was done.

Orbital exenteration

It is a radical removal of the orbital contents including the globe, periorbita, intraconal and retrobulbar structures (Figure 2). Indications for exenteration were extensive inflammation of orbital contents, corneal melt, globe rupture, orbital apex involvement and indentation of posterior wall of orbit on MRI; not done in cases with bilateral involvement.

Transcutaneous retrobulbar amphotericin B (TRAmB) was given in all cases who underwent orbital clearance. All patients received 14 days of intravenous liposomal amphotericin B (AMB) daily and 7 doses of TRAmB [3.5 mg of AMB injected retrobulbar with a 23G needle] every 48 hours.

The outcome measures used were improvement in visual acuity, extraocular movements, reduction in periorbital swelling. Data collected in the proforma was collated in MS Excel and analysed statistically using statistical package for the social sciences (SPSS) software version 24 and are presented in the form of graphs, percentages.

RESULTS

181 patients were included in the study. 143 (79%) were

male and 38 (21%) were female with age ranging from 12 to 78 years (Table 1). Patients with orbital involvement presented most commonly with eye pain followed by vision disturbances, eye swelling, drooping of eyelid, protrusion of eyeball (Figures 3 and 4). 160 patients underwent orbital decompression and clearance of necrotic tissue. 21 patients underwent orbital exenteration.

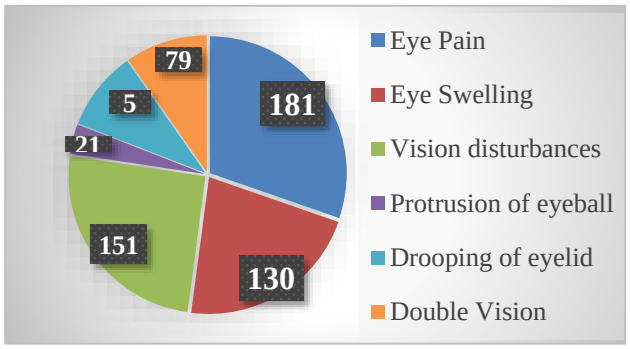

Figure 3: Symptoms of orbital mucormycosis.

57/58 (98.27%) patients had improvement in extraocular movements post-surgery and resolution of diplopia after endoscopic orbital clearance/decompression which was significant (Figures 5 and 6). All patients had mild increase in periorbital edema in the early postoperative period which resolved completely at the end of 1 month. Final visual acuity of PL+ and above was achieved in 147 patients. 13 patients who were PL- at the time of admission and who did not have necrotic tissues in orbit (in intraoperative endoscopy and on imaging) did not have any improvement in vision post-surgery. 14 (7.73%) patients succumbed to the disease in the postoperative follow-up.

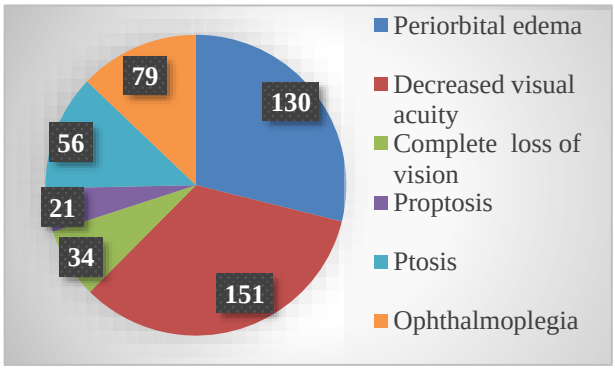

Figure 4: Signs of orbital mucormycosis.

Figure 5: (a) Pre-operative and (b) post-operative picture of right rhino-orbital mucormycosis.

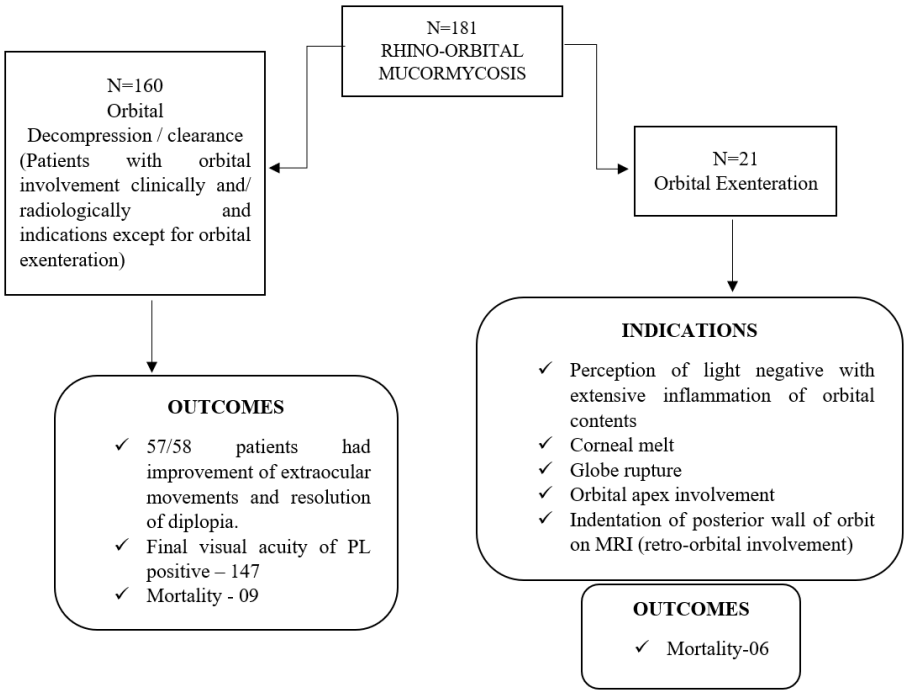

Figure 6: Management of orbital mucormycosis and its clinical outcome.

Table 1: Demographic profile of the patients.

Variables	N
Total number of patients	181
Age group (years)	12-78
Median age (years)	45
Sex (%)	Male- 143 (79)
	Female- 38 (21)
Past history of COVID-19 infection (%)	181 (100) patients

DISCUSSION

Rhino-orbito-cerebral mucormycosis is the commonest form of mucormycosis. The ethmoid sinus is an important route of infection, since mucormycosis may invade through the thin lamina papyracea and enter into the orbit and its contents. The organisms may extend to the orbital apex posteriorly, leading to orbital apex syndrome. Involvement of optic nerve can lead to visual disturbances. Involvement of the superior orbital fissure and its contents, such as cranial nerves III, IV, and VI, and branches of V1 and V2, may cause diplopia, ophthalmoplegia, and sensory loss to the corresponding areas of the face and cornea. The fungus will gain access to the cavernous sinus and to the brain parenchyma, causing vascular thrombosis and infarction from the orbital apex.[8] Patients with orbital involvement present with eye pain, periorbital swelling, visual disturbances, diplopia, proptosis and ptosis.

Radiological imaging of orbit helps to know the extent of involvement of mucormycosis. Early orbital invasion shows soft tissue infiltration and edema of the retroorbital fat around the extraocular muscles on fat-saturated T2W sequences. As orbital invasion most commonly occurs through the medial orbital wall, inflammatory tissue necrosis or abscess formation may be seen along the medial aspect of the orbit with lateral displacement and edema of the medial rectus muscle. Sudden vision loss can occur due to central retinal artery or ophthalmic artery occlusion, optic nerve infarction, or direct infiltration of the optic nerve.[9] Optic nerve infarction will be seen as high-signal intensity on diffusion-weighted imaging.[10] Direct invasion of the optic nerve will cause increased caliber of the nerve with signal intensity changes within it. Isolated optic nerve involvement suggests spread of infection through branches of the ophthalmic artery, which is an indication for initiation of aggressive treatment.[11] Diffuse orbital infection can present with severe proptosis and tenting of the globe.[12]

In a retrospective multicentric study conducted by Sen et al in 2021, 2826 patients were included in the study. Orbit was involved in 72% of patients, with stage 3c forming the bulk (27%). Overall treatment included intravenous amphotericin B in 73%, functional endoscopic sinus surgery (FESS)/paranasal sinus (PNS) debridement in 56%, orbital exenteration in 15%, and both FESS/PNS debridement and orbital exenteration in 17%. Intraorbital injection of amphotericin B was administered in 22%. At final follow-up, mortality was 14%. Disease stage >3b had poorer prognosis. Paranasal sinus debridement and orbital exenteration reduced the mortality rate from 52% to 39% in patients with stage 4 disease with intracranial extension ($p<0.05$).[13]

Murthy et al conducted a study in 2020 on role of localized surgical debridement for the management of orbital mucormycosis. Debridement was done in 10 patients by transconjunctival orbitotomy and superior transcutaneous lid crease approach. Ptosis, proptosis, and lid edema subsided in all, except in one patient who had residual ptosis and in one who had residual ophthalmoplegia. Vision deficit did not occur in any patient. All patients were successfully discharged on oral antifungal medication. Localized clearance of the fungal tissue and the necrotic material is a good option to avoid exenteration in cases of orbital mucormycosis, avoiding disfigurement and mental trauma to the patient.[14]

Based on clinical symptoms, signs and imaging findings, we did orbital decompression by removing lamina papyracea and incising periorbita allowing fat to prolapse. Extent of debridement of contents of orbit was individualized for each case based on imaging and intraoperative findings. When globe was intact, orbital clearance was done by removing the lamina papyracea and necrotic tissue within the orbit. Transcutaneous retrobulbar amphotericin B (TRAmB) was given in all cases who underwent orbital clearance. TRAmB added as an adjuvant in patients whose orbital involvement had been detected early, to minimize vision loss. It is a safe and effective treatment modality which reduces the ocular morbidity associated with post-COVID ROCM patients. Furthermore, TRAmB along with orbital clearance avoids patients from undergoing disfiguring and debulking procedures like exenteration.

Limitations

Need for longer follow-up duration post-surgery is required to establish the importance of early treatment and its outcome.

CONCLUSION

Early recognition of symptoms, adequate clearance of the disease and systemic antifungals can help in salvaging the vision and the eye in most cases. TRAmB as adjuvant helps in decreasing the ocular morbidity. Endoscopic orbital clearance helps to reduce the need for orbital exenteration in PL negative patients. Orbital exenteration is best avoided, when possible, to avoid cosmetic disfigurement and psychological trauma to the patient.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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