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Localized surgical debridement for the management of orbital mucormycosis

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Purpose: To describe the role of localized debridement and instillation of amphotericin B for the management of orbital mucormycosis post COVID-19 infection with a view to avoid exenteration. **Methods:** The records of all patients with orbital mucormycosis post COVID-19 infection in the last 6 months from December 2020 to June 2021 were evaluated, and ten patients were identified who were successfully managed with localized debridement, that is, removing the fungal tissue and necrotic material and amphotericin B gel instillation locally. MRI scan was used to identify the area of fungal infiltration and presence of necrotic material. Early surgery in the form of transconjunctival orbitotomy was performed for disease in the infraorbital fissure area, and superior transcutaneous lid crease approach was employed for disease in the superomedial orbit or medial orbit. Most patients had lid edema, ptosis, and proptosis; this resolved with the medication. Systemic antifungals were given and the follow-up ranged from 1 to 5 months. **Results:** The 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. **Conclusion:** 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.

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Rhino-orbital mucormycosis has seen a great resurgence in the second wave of COVID-19 infection in India. Early diagnosis with aggressive medical and surgical management is the key to increase life salvage in this deadly infection.[1] Before the development of amphotericin B in 1955, mucormycosis was usually fatal, but in the present times, amphotericin B is the first line of medical therapy for this disease.[2] Cure with medical therapy alone is unlikely as the drug cannot reach the necrotic tissues.[2] Conventionally, intravenous amphotericin B along with orbital exenteration and extensive sinus debridement has been considered by many as the treatment of choice.[3]

Exenteration is a radical surgery with removal of the eyeball, periorbita, and all contents of the orbit. This procedure has long been the surgical standard, but it causes cosmetic disfigurement and has a profound impact on the patient's psyche. There are no clear-cut studies on when to perform orbital exenteration. Some recent studies have demonstrated that exenteration may not be necessary in most cases of rhino-orbital mucormycosis.[1,4] Newer medical and surgical techniques can help in eye salvage in these cases.[5-7] In this paper, we describe the role of localized debridement and instillation of amphotericin gel locally to get rid of the nidus of infection and ensure salvage of the eye and vision, with the objective of avoiding exenteration.

Methods

The medical records of the Ophthalmology and Infectious disease service of Deenanath Mangeshkar Hospital were reviewed for post COVID-19 infection cases confirmed to have rhino-orbital mucormycosis from December 2020 to June 2021; from these, cases who had undergone localized debridement without orbital exenteration were selected. A total of 10 patients were identified. All patients had undergone a detailed history and ophthalmic and otorhinolaryngologic evaluation to understand the extent of the disease. The details of all the patients are summarized in Table 1. Nasal endoscopy was done in every patient at presentation, and any suspicious crust or black necrotic tissue was sent for microbiology testing by calcofluor white stain. All patients underwent a detailed clinical evaluation, especially the blood glucose levels and the glycosylated hemoglobin levels. MRI scan of the orbits, sinuses, and screening of the brain with CT correlation was performed in every patient.

The surgical procedure was discussed with every patient. Where necessary, discussion of orbital exenteration as a treatment option was explained. The procedure of limited debridement was explained to the patients. An informed decision was made to preserve the eyeball, and none of the patients opted for orbital exenteration despite the theoretical chance of leaving residual fungal disease with limited debridement alone. Fungal tissue typically appears as hypointense on T2 imaging on MRI scan and may show peripheral enhancement. On post-contrast T1 fat suppression imaging, fungal elements are hypo-enhancing

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Table 1: Clinical features and outcome of cases undergoing localized surgical debridement

Age (years)	Sex	Systemic status	Orbital findings	Sinus involved	MRI findings	Surgical management	Outcome	Follow-up
34	M	Old pancreatitis	Left chemosis, diplopia, abduction -1, proptosis	Left maxillary	Left orbital soft tissue in infratemporal region, inferomedial orbit involvement	Fess with inferior orbital clearance	Complete resolution, no ophthalmoplegia	4 months
50	F	Diabetes, hypertension	Right proptosis, ptosis, lid edema	Right maxillary, ethmoid	Right orbital erosion of floor and medial wall, soft tissue in infraorbital fossa up to pterygopalatine fossa touching the lateral wall of cavernous sinus	Fess with inferior orbital clearance, medial orbital wall removal endoscopically	Complete resolution, no proptosis	4 months
36	M	None	Right cheek heaviness and pain inferior orbit rim	Right frontal, ethmoid, maxillary	Right orbit erosion of floor and medial wall, soft tissue in infraorbital fossa up to pterygopalatine fossa	Fess with inferior orbital clearance, medial endoscopic clearance	Complete resolution	5 months
51	F	Diabetes	Right eyelid edema, vertical diplopia	Right maxillary, ethmoid, sphenoid	Right orbit infraorbital fossa pterygopalatine fossa up to foramen rotundum	Fess with inferior orbital clearance	No diplopia	5 months
46	F	Diabetes	Left eyelid swelling, headache,	Bilateral ethmoid, sphenoid, frontal	Left orbit erosion of medial wall and floor, soft tissue seen, muscle enhancement, left infraorbital fossa	Fess with inferior orbital clearance	No diplopia	5 months
44	M	None	Left eyelid edema, ptosis, proptosis, sixth nerve palsy	Bilateral ethmoid, left maxillary, sphenoid	Superomedial mass extraconal in left orbit, fat stranding, muscle enhancement	Fess with superior orbital clearance	Ptosis mild, sixth nerve palsy resolved	5 months
50	F	Diabetes	Right lid edema, ptosis, proptosis, sixth nerve palsy	Right ethmoid and sphenoid	Right orbital soft tissue in floor and medial wall, fat stranding, orbital apex involved	Fess with medial orbitotomy, inferior orbitotomy	Complete resolution	5 months
45	M	Diabetes	Left eyelid edema, ptosis, proptosis, ophthalmoplegia	Bilateral ethmoid, sphenoid	Soft tissue medial and inferior wall of left orbit extraconal location	Fess with medial and inferior orbitotomy	Partial resolution of ophthalmoplegia	5 months
59	F	Diabetes, Hypertension	Right ptosis, hemifacial pain	Bilateral maxillary, right frontal, right ethmoid	Thinning medial wall and floor right orbit, soft tissue in floor and medial wall	Inferior orbitotomy	Eye resolved, Dead - cardiac arrest (after 1 month)	1 month
56	M	Diabetes	Right side face tenderness, swelling lower lid	Right Maxillary ethmoid	Erosion of floor of right orbit, soft tissue infraorbital fossa, pterygopalatine fossa, up to the apex of cavernous sinus	Fess with inferior orbital clearance	Resolved no deficit	5 months

and inflammation in the orbit is seen as fat stranding. Based on the radiologic assessment (on MRI scan) of the presence of fungal infection in the orbit, we performed localized debridement and removal of all necrotic tissue. The soft tissue was typically in the superomedial quadrant or medial part of the orbit or along the infraorbital fissure. A lid crease incision for the superomedial and medial location and an inferior transconjunctival incision for the inferior orbit, followed by opening the periorbita to reach the infraorbital fissure, were adopted to reach the nidus of infection. All clinically involved fungal tissue or necrotic tissue was removed. Lipid-based amphotericin B gel 0.1% w/w was injected at the site of debridement with a 5-cc syringe and an 18-G 1.5-inch needle.

All patients received systemic amphotericin B once the diagnosis of mucormycosis was established based on microbiologic evaluation of the nasal endoscopy material by calcofluor white for mucor hyphae, for a period of 3 weeks. After a test dose of 1 mg of amphotericin B, 5 mg/kg/day was administered over 6 hours in all the patients in 5% dextrose infusion. Renal functions were monitored regularly for rise in serum creatinine. Following this, step-down therapy with oral posaconazole 300 mg per day was prescribed for a period of 3 months. Evaluation of the patients was performed to monitor clinical improvement, and MRI scan was performed in all patients at an interval of 3 weeks after the debridement.

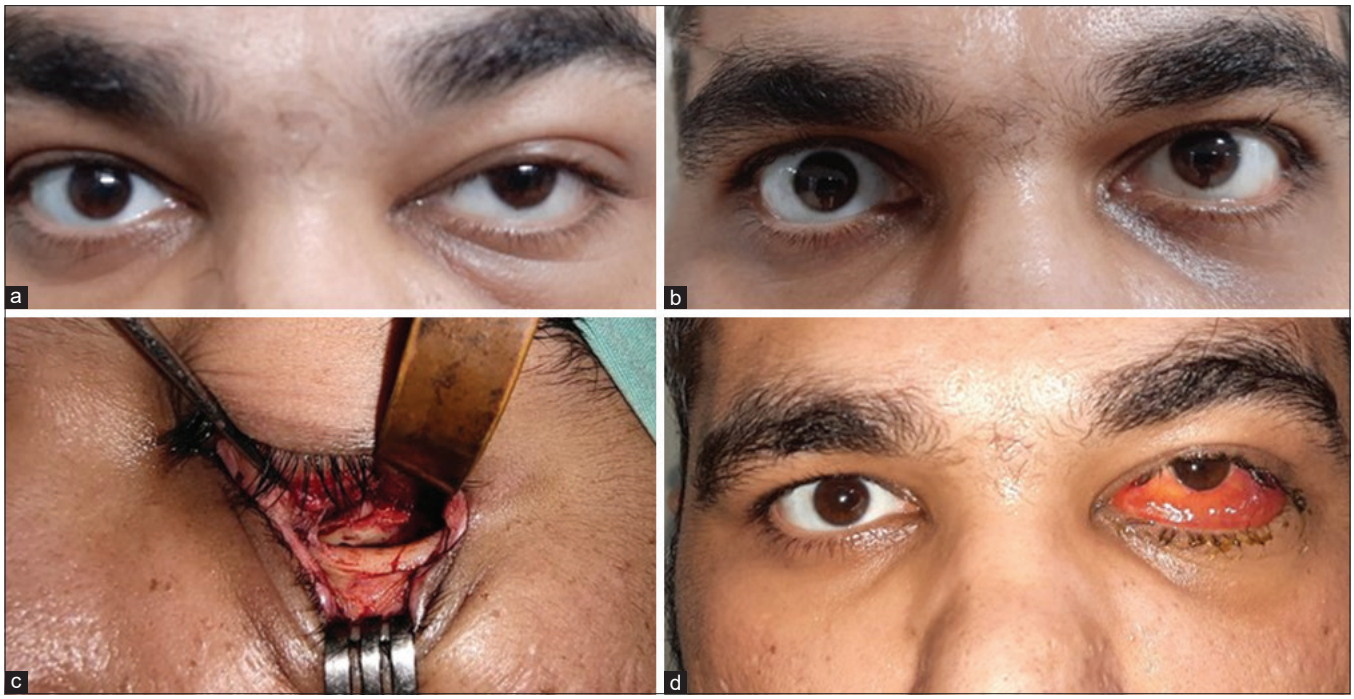

Figure 1: (a) A 34-year-old male presented post FESS elsewhere with left rhino-orbital mucormycosis with left eyelid edema, mild proptosis, and ptosis. Fungal soft tissue was noted in the MRI in the infraorbital fissure. (b) Post localized orbital clearance and amphotericin B instillation, his signs and symptoms improved (1-month post-surgery). (c) Transconjunctival inferior orbitotomy was done, elevating the periorbita to reach the inferior orbital fissure region. (d) Post surgery and instillation of amphotericin B, he developed chemosis and yellowish discoloration, which resolved in a week

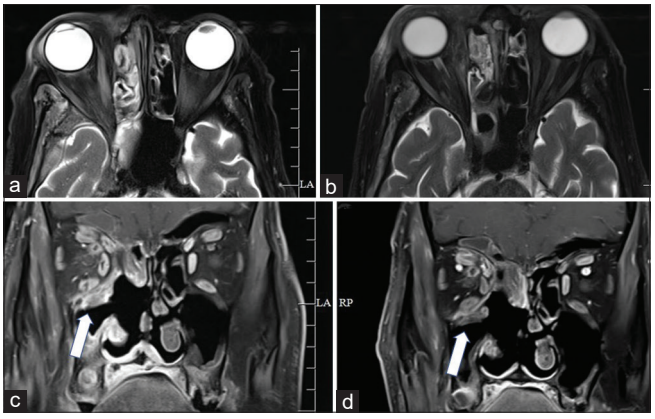

Figure 2: MRI images of the patient from Fig. 1. (a) Axial STIR T2 images. Right paranasal sinuses show T2 dark areas representing fungus and edema in the right infratemporal fossa. (b) Post treatment, significant regression in paranasal sinus disease, medial rectus edema subsided, and right orbital fat stranding regressed. (c) Coronal post-contrast T1 fat-saturation images: right orbital fat stranding with enhancing soft tissue in the infraorbital fissure (arrow). (d) Post treatment, right orbital fat stranding and soft tissue in the inferior aspect shows significant regression (arrow)

Results

Ten patients had undergone limited orbital debridement in this series of which there 5 were male and 5 were female, with age ranging from 34 to 59 years [Table 1].

Most patients presented with lid edema (10), diplopia (5), ptosis (5), and proptosis (5). Vision with correction ranged from 6/6 to 6/12 in the affected orbit. The most common site of sinus involvement was ethmoid (9) followed by maxillary sinus (6). Involvement of the infraorbital fossa was seen in 9 patients and superomedial location of soft tissue indicative of fungus was noted in one patient. Depending on the location, orbitotomy was performed, fungal tissue cleared, and amphotericin B gel was instilled. Post injection, there was lid edema, conjunctival chemosis, and mild yellow discoloration of the conjunctiva in three patients who had undergone inferior orbital clearance. This resolved within 7 days. Follow-up ranged from 1 to

Figure 3: (a) A 51-year-old lady presented with right eye proptosis, lid edema, chemosis, and vertical diplopia. Inferior orbital fissure disease was noted. (b) Following inferior orbital clearance and injection of amphotericin B, there was complete resolution of the disease. (c) A 46-year-old lady presented with lower lid edema, conjunctival chemosis, and proptosis of her left eye. (d) Post orbital clearance in the inferior orbital fissure region with instillation of amphotericin B, her symptoms and signs resolved

5 months post intervention. Vision was stable and did not deteriorate in any patient. One patient had residual ptosis and one had only partial resolution of the ophthalmoplegia. All were alive and well, except one patient who expired due to cardiac arrest. Some representative cases are depicted in Figs. 1–3.

Discussion

Before the discovery of amphotericin B, the only modality of management of rhino-orbital mucormycosis was radical surgery including debridement of the sinuses and nasal cavity, along with orbital exenteration.[2] Amphotericin B was first extracted from *Streptococcus nodosum* in the year 1955 by Gold *et al.*, and Harris reported it as a cure for mucormycosis in the same year.[8] The most significant side effect of this drug is nephrotoxicity, which decreased with the development of a more effective and less toxic form: the liposomal amphotericin B in 1991.[9] This form increased the therapeutic index 20-fold with less kidney penetration and more intracellular delivery.[10] The liposomal form allows higher cumulative dosing with less toxicity.[10] However, the vaso-occlusive nature of the fungus makes it difficult for the drug to reach the site of infection. Thus, direct treatment of the debrided tissues with local application of amphotericin B has been suggested.[6]

The primary reason for performing an orbital exenteration is to prevent intracranial extension.[2] The fungal infection can spread via the orbital apex to the brain.[2] In addition, when there is an expanding lesion in the orbital apex, it can lead to orbital apex syndrome. In orbital apex syndrome, there is involvement of the third (oculomotor) nerve, fourth (trochlear) nerve, sixth (abducens) nerve, ophthalmic branch of the fifth (trigeminal) nerve, and the second (optic) nerve. Mechanical compression, ischemia, or vasculitis can occur in orbital apex syndrome; this can give rise to ptosis, ophthalmoplegia, optic neuropathy, loss of corneal sensation, and facial numbness.[11] If there is orbital apex syndrome, the diagnosis and cause should be established fast and treatment should be initiated as soon as possible. There is no clear consensus on when exenteration is indicated. Hargrove *et al.* studied 113 published articles with 292 cases of orbital mucormycosis to determine the indications for exenteration and reported that there is no standard consensus on when exenteration may benefit a mucormycosis patient.[12]

In our patients, we used a multimodal therapy combining both intensive medical therapy and surgical support with the main purpose of avoiding exenteration. Amphotericin B, being fungicidal, is an effective therapy for mucormycosis. Systemic amphotericin B was given to every patient. Surgical debridement helps in removing necrotic material and facilitates drug penetration. Orbital exenteration is not necessary in most cases of rhino-orbital mucormycosis, and early disease can be managed effectively without exenteration.[1,4,13] In our patients, we identified the focus of infection using MRI scan and effectively cleared the tissue by using a transconjunctival approach for the inferior orbit and floor, and a transcutaneous upper lid crease approach for disease of the superomedial orbit. The disease can spread to the orbital apex from the superior orbit and from the infraorbital fissure to the pterygopalatine fossa and subsequently enter the middle cranial fossa. Necrotic tissue can easily be cleared at these sites; we instilled amphotericin gel at the site of debridement. Local application of amphotericin B is more effective when applied at the site of infection as compared to intravenous administration. Even nasal irrigation of amphotericin B has been successful.[2] In addition, transcutaneous retrobulbar amphotericin B injections have been successful in avoiding exenteration.[6,13-15] We encountered inflammation in three cases with mild lid edema and conjunctival chemosis post the intervention, but this completely resolved within seven days.

Conclusion

Orbital exenteration may not be needed in less aggressive presentations of mucormycosis. Orbital exenteration is best avoided, when possible, to avoid cosmetic disfigurement and psychological trauma to the patient. Performing good sinus clearance of the disease, instituting systemic antifungals early, along with localized debridement and application of amphotericin B gel to the site of debridement, can help in salvaging the vision and the eye in most cases.

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Conflicts of interest

There are no conflicts of interest.

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