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Original Research Article

Role of orbital exenteration in management of rhino-orbito-cerebral mucormycosis (ROCM) - A prospective analytical study

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ABSTRACT

Mucormycosis is an uncommon, opportunistic fungal infection. The most crucial decision in the management of rhino-orbital mucormycosis is when to advise exenteration. This study aims at understanding the pattern of cases which progressed and had extensive involvement of the entire orbital cavity with mild intra cranial extension requiring exenteration as life salvage measure in the setting of epidemic of mucormycosis in a pandemic of COVID – 19. Patients suspected or diagnosed with invasive orbital mucormycosis visiting our hospital were admitted and included in the study. CT PNS with orbit were done for all patients and MRI brain with orbit were done in patients in whom intracranial spread and involvement of optic nerve were present. Patients were started on liposomal intravenous amphotericin B (5mg/kg/day) and intraorbital amphotericin B injection when indicated and closely monitored for clinical progression. All patients were taken up for FESS and if positive for mucormycosis on histopathological examination. In cases wherever exenteration was indicated, after confirming that there was no perception of light and obtaining informed consent with psychiatric counselling patient was taken up for orbital exenteration. Lid sparing exenteration was the method of choice. A total of 41 patients out of 696(5.89%) underwent exenteration out of which 21(51.2%) were right sided and 20(48.8%) were left sided. 12 patients (29.2%) of those who had undergone exenteration did not have a history of being tested positive/ been symptomatic for COVID 19. 1 patient (2.4%) was not diabetic. All patients (100%) had sinonasal involvement (Involvement of one or more paranasal sinuses) with involvement of orbital cavity to different degrees. 4 out of 41(9.75%) patients had deteriorated and required ICU care. 1 patient succumbed to death (2.4%) due to multiple comorbidities. On histopathological examination of exenteration specimen, 2(4.87%) patients turned out to be negative for mucormycosis. In 32(78.04%) of them the socket healed well while 5(12.1%) had slough who required 2 or more sittings of sloughectomy. As mucor is angio invasive rapidly progressive highly fatal infection close monitoring for invasion into structures like apex of orbit and intra cranial spread is essential for timely intervention and decision to perform exenteration. This is crucial for arrest of progress and life salvage.

1. Introduction

The literature fails to provide a broad base of information to decide on the indication of exenteration in daily practice.

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Moreover, with the sudden surge and exponential rise in the number of post COVID – 19 mucormycosis, decision making regarding the procedure of exenteration was more challenging as it causes disfigurement which poses psychological threat to the patient. The decision for exenteration often depends on the judgement of the treating ophthalmologist. This study aims at understanding the patterns of cases which progressed to involve the entire orbital cavity and CNS requiring exenteration as life saving measure in the setting of epidemic of mucormycosis in a pandemic of COVID – 19. Aim of this study was to (1): Understand the indications of orbital exenteration in patients with rhino-orbito-cerebral mucormycosis, (2): Analyze the outcomes and prognosis of patients undergoing orbital exenteration for invasive mucormycosis.

2. Materials and Methods

1. Consecutive patients suspected or diagnosed with invasive mucormycosis were admitted and included in the study.
2. In history whether diabetic if so the control of their diabetic status, Covid 19 infection, treatment with steroids and oxygen administration were elicited.
3. Thorough clinical examination including visual acuity, extraocular movement evaluation& pupillary assessment were done to quantify and stage the disease clinically.
4. Indirect ophthalmoscopy was performed to rule out central retinal artery occlusion, disc edema, etc.
5. CT PNS with ORBIT was performed in all patients under evaluation.
6. MRI Brain with orbit was done in patients in whom intracranial spread like involvement of cavernous sinus or cavernous sinus thrombosis, brain abscess, leptomeningeal spread and also optic nerve involvement.
7. Management was carried out by guidelines in coordination with other departments like ENT, Internal medicine, Diabetology, Nephrology and neurology.
8. Intravenous liposomal amphotericin B (5mg/kg/day) was initiated for all patients in correct dosage with duration according to the protocol
9. Indication for starting intra-orbital amphotericin B (1ml of 3-5mg/ml) was clinical/ radiological involvement of orbital contents (Stage 3 or worse; Guidelines for the Diagnosis, Staging and Management of Rhino-Orbito-Cerebral Mucormycosis)
10. A minimum of 3 doses of RB and a maximum of 5 to 7 doses (initial 3 doses on consecutive days followed by weekly intervals) were given and closely monitored to look for clinical progression
11. All Patients were taken up for FESS surgery. If positive for mucormycosis on histopathological examination, vision of no perception of light was confirmed and informed consent obtained from patient and attenders.
12. Current indications for exenteration in ROCM includes
    (a) Stage 3c or worse as proposed in staging by Honavar et al
    (b) Non salvageable globe
    (c) Significant proptosis with fulminant orbital involvement and rapidly progressive disease
    (d) Necrosis and associated thrombosing vasculitis
    (e) Unilateral cases and failure to respond to conservative therapy (worsening or no improvement within 72 hours)
13. Patient was referred to departments of medicine, diabetology and anesthesia for fitness and also provided psychiatric counselling, to all patients who were taken up for orbital exenteration.
14. Lid sparing exenteration was the method of choice
    (a) Under general anaesthesia and sterile aseptic precaution, a four-quadrant block with bicarbonate fortified lignocaine was given. Incision crease was marked 2mm above and below the lid margin after taking stay sutures for easy manipulation of globe.
    (b) Blunt dissection was done up till periosteum on all slides after severing the medial and lateral canthal tendons.
    (c) Periosteum was elevated from underlying bone in all quadrants and bleeding was arrested with cautery as required.
    (d) Globe removed en masse after severing the optic nerve.
    (e) Residual debris removed and thorough wash with amphotericin and socket packed with sterile gauze soaked in betadine and lids sutured with 4-0 silk (Figure 5) Postoperatively patients were closely followed. Slough, if present was removed on regular basis and daily dressings changed.
    (f) Once the patients whose socket was healthy, dry and no recurrence were fitted with stuck on prosthesis in coordination with department of OMFS.

3. Results

A total of 41 patients out of 696 (5.89%) required exenteration. Of these 28 were males (68.2%) and 13 were females (31.8%) (Figure 1a). 21 (51.2%) were right sided and 20 were (48.8%) left sided exenterations (Figure 1b). 3 (7.3%) cases had asymmetrical bilateral involvement, only the worse was taken up for exenteration. 9 (21.9%) were 31-40 years, 12(29.2%) from 41 – 50 years, 14(34.1%) from 51 to 60 years and 6 (14.6%) were above 60 years (Figure 2).

12 patients (29.2%) of those who underwent exenteration did not have a history of COVID 19 (Figure 3). 1 (2.4%) out of 41 was nondiabetic. All (100%) patients had sinonasal involvement (involvement of one or more paranasal sinuses) with involvement of orbital cavity to different degrees. 4 (9.75%) patients had cavernous sinus involvement on imaging. 4 out of 41 (9.75%) were planned for repeat FESS with orbital exenteration in a single sitting owing to risk of multiple episodes of general anesthesia. Post operatively general condition of 4 out of 41 (9.75%) had deteriorated and required ICU care. 1 death (2.4%) was documented due to multiple comorbidities in postoperative period (Figure 4). On histopathological examination, 2 (4.87%) turned out to be negative for mucormycosis. 32 (78.04%) of them had good healing of socket while 5 (12.1%) required two more sittings of sloughectomy. Of 41m 34 patients (82.9%) were stable and discharged as on 30/10/2021 while remaining 7 (17.04%) are under observation.

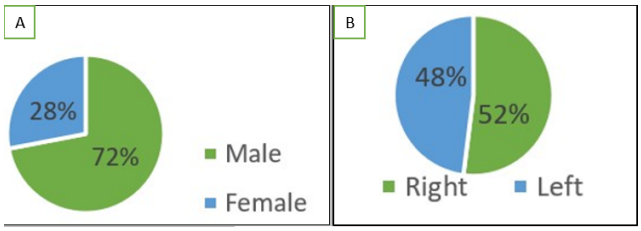

Fig. 1: a: Gender distribution; **b:** Laterality.

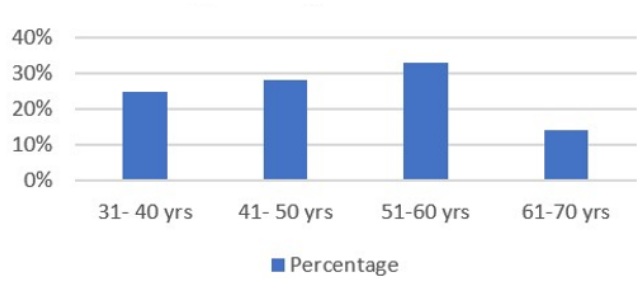

Fig. 2: Age distribution.

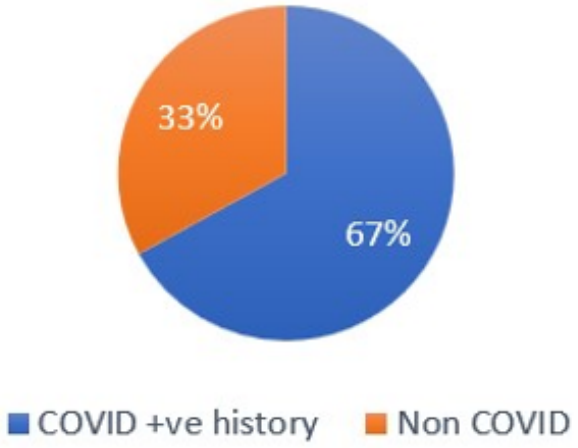

Fig. 3: COVID 19 status.

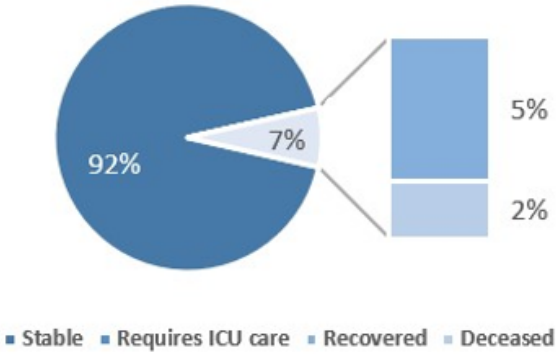

Fig. 4: Post-operative course.

Fig. 5:

4. Discussion

Piromchai et al[1] observed that more than 70% of the mortalities occurred within the subgroup of patients who exhibited symptoms of the disease within 14 days before admission. Hence, ROCM management requires an urgent individualized multidisciplinary, multimodal approach including combination of appropriate systemic antifungal treatment, surgical debridement of necrotic tissues and correction of underlying conditions like hyperglycemia and acidosis etc.

Though aggressive focal control is recommended as mainstay of controlling the invasive process,[2] some cases exhibit malignant course not contained by this modality. Only 5% requiring orbital exenteration in our study explains this effective multimodal approach.

Though both sides being affected almost equally by the disease (51.2% vs 48.8%), there is barely any predilection in laterality of disease. Due to the morbidity associated with bilateral disease with extensive intracranial extension, no bilateral exenteration was done.

In our study, highest incidence of working age group (51.1% between 30 to 50 years) and males being predominantly more affected (68.2% males vs 31.8% females) lays emphasis on the socio-economic burden

associated with prolonged hospital stay and a protracted recovery period and also cosmetic & psychological impact on the patient.

COVID-19 infection, its treatment, resultant immunosuppression, and associated comorbidities had made patients vulnerable to opportunistic infections including mucormycosis[3] and rapid progression due to worsening of the disease process requiring exenteration. 12% patients did not have a positive history of previous COVID-19 infection could be explained by having had asymptomatic infection gone unnoticed. One patient was nondiabetic but was positive for COVID 19 and was treated with steroids suggesting the role of steroid administration in contributing the disease etiology due to immunosuppression.

All patients having sinonasal and orbital involvement in CT scan and 3 patients demonstrating cavernous sinus thrombosis in MRI Brain points out the invaluable role of different modalities of radiological imaging in management of ROCM. In clinical practice, role of MRI has been complementary to CT and has been crucial in evaluating intracranial (acute brain infarcts, cavernous thrombosis) and intra-orbital (diplopia, sudden loss of vision) complications. Use of IV contrast has proven useful in disease extending beyond sinuses (orbital apex, skull base, brain) but has to be weighed against the drawbacks of contrast induced nephropathy in addition to Amphotericin induced in such patients.

The standard guidelines for orbital exenteration in treating ROCM is not available in literature.[4–6] Several guidelines have been proposed by different scientific bodies to aid in decision-making for exenteration. Hanover SG[7] proposed management algorithm for ROCM in the setting of COVID-19, according to it orbital exenteration is recommended for extensive orbital involvement (central retinal artery or ophthalmic artery occlusion, superior ophthalmic vein thrombosis, orbital apex involvement, loss of vision and bilateral involvement), limited CNS involvement (focal or diffuse cavernous sinus involvement or thrombosis) and in case of extensive CNS involvement (involvement beyond cavernous sinus, skull base involvement, brain infarction or diffuse CNS involvement) if general systemic condition of patient permits surgery. In our study all patients had extensive orbital involvement with or without minimal CNS involvement were eligible for exenteration. Sing VP et al.[8] suggested that orbital exenteration should be individualized based on retinal artery involvement, aggressiveness of the disease, underlying debilitating diseases, response of antifungal chemotherapy and visual status. Levinsen et al.[9] recommended aggressive orbital exenteration when dealing a case of ROCM with orbital apex syndrome, peribulbar or facial necrosis with or without cranial nerve involvement. In our study 3 (7.3%) patients had orbital apex syndrome with progression and required exenteration. Shah K et al[10] proposed "Sion hospital scoring system" to solve dilemma associated with orbital exenteration in ROCM.

There are multiple ways of approaching the procedure including lid sparing exenteration, extended enucleation and endoscopic orbital exenteration.[11] In our study, lid sparing exenteration was preferred due to its better cosmetic outcomes with rapid healing and earlier fitting of prosthesis.[12]

Post-operative course of most patients in our study was uneventful. 4(9.75%) patients with multiple comorbidities required ICU care and ventilator support as advised by anesthetist. This emphasizes the need for multidisciplinary approach and prior planning to avoid life threatening complications in the immediate post-operative period. 1(2.4%) patient had succumbed to the anesthesia – related complications post operatively.

The histopathological examination of exenteration specimen was tested negative for mucormycosis in 2 of 41 (4.81%) cases and was documented to be inflammatory pathology inspite of the FESS specimen showing positivity for mucor. This could be due to more anterior locations of disease spread in orbital cavity or inadequate sampling techniques missing out on areas of involvement.

Postoperatively, 5 (12.19%) patients required slough removal with toileting of orbital cavity with amphotericin suggestive of continuing disease process despite careful removal of residual necrotic debris. This suggests the role of meticulous post-operative care of both general condition and wound site. All 5 (12.19%) patients socket healed completely before being discharged.

More than 75% patients completed their course of treatment and discharged after obtaining clearance from various departments and have been insisted to be on regular follow up for planning for fitting of orbital prosthesis.

5. Conclusion

Mucormycosis involves orbit and other ocular structures. Ophthalmologist may be the first to see the patient with this highly morbid condition. It is important this should be considered as one of the differential diagnosis lists as delay in establishing diagnosis and initiating therapy could prove fatal. Aggressive medical and surgical management is most essential and require multi-disciplinary approach. Management should be coordinated and planned among the various multidisciplinary services and in-depth discussion with patient and family regarding prognosis are essential in good patient care. No standard guidelines currently exist to guide physician on when exenteration may benefit mucormycosis patients. Further studies are required to determine which variable indicate the extent of disease and which variables may predict the progression with or without exenteration. Being disabled does not mean unabled but differently abled.

6. Source of Funding

None.

7. Conflict of Interest

None.

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