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Role of orbital exenteration in rhino-orbital-cerebral mucormycosis: Orbital exenteration in mucor “A BOON or A BANE”

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Abstract---Purpose–Mucormycosis is an uncommon, rapidly progressive, commonly fatal, opportunistic serious fungal infection. The high mortality rate highlights the importance of early detection and treatment. The purpose of this study to determine the outcome of orbital exenteration in Rhino-orbital-cerebral mucormycosis(ROCM) patients. Methods and materials–This study includes all proven ROCM patients who had undergone orbital exenteration based on SION Scoring system from 1st may 2021 to 30 June 2021 in MYH hospital, Indore. Those patients were reviewed and the outcome of orbital exenteration was analysed. Results- Total 29 ROCM patients were

underwent for orbital exenteration based on SION Scoring system. 19(65.5 %)out of 29 patients had intracranial extension and 10 (34.480%) did not have intracranial extension.Out of 29, 6 (20.68%) patients had succumbed to death within 10 days of orbital exenteration was having bilateral orbital involvement with intracranial extension.23(79.34%) patients have favorable outcome with regular follow up. Conclusion- Survival of mucormycosis patients depends on the their good glycemc control,immune status, laterality of the orbital involvement and early detection of intracranial extension of the disease.With prompt medical (high dose intravenous amphotericin B) and early aggressive surgical intervention involving FESS and orbital exenteration can prevent intracranial extension and may improve survival rate .Intracranial extension of the disease has invariably been associated with high mortality.Bilateral orbital involvement with intracranial extension has poor prognosis.Early orbital exenteration alone has no benefit in long term survival.

Keywords---ROCM, TRAMB, orbital exenteration, intracranial extension, SION scoring.

Introduction

Rhino-orbital-cerebral mucormycosis (ROCM) is a life-threatening infection associated with high morbidity and mortality. ^(1,2) Opportunistic fungi, belonging to the order Mucorales, are responsible for this rapidly progressing fatal infection.^(3,4) The high mortality rate highlights the importance of early detection and treatment. The infection consists of angioinvasion by the fungal hyphae, vascular thrombosis, and tissue necrosis ⁽⁵⁾. The clinical hallmark is tissue necrosis manifested as a necrotic lesion, eschar, or black discharge in the nasal or oral cavity. There is growing evidence to show that COVID-19 infection increases the risk of a patient acquiring secondary fungal infections ⁽⁶⁻⁸⁾ This puts such patients at a high risk to develop ROCM. Exenteration may improve the prognosis but the indications of doing so remain unclear. Exenteration of orbits is both radical and disfiguring procedure. For the surgeons, exenteration represents the final attempt at cure. For the patients, the thought of sacrificing a prominent part of face is not comforting.

Method

This retrospective observation study done on proven mucormycosis patients who presented at our tertiary care center from 1st may 2021 to 30 June 2021.

Inclusion criteria

All proven ROCM patients who had total ophthalmoplegia and SION score more than 23, medically and neurologically fit for orbital exenteration and gave consent for orbital exenteration had been included in this study.

Patients records were analysed and the following data recorded: Age, sex, histological diagnosis, radiological findings, dental and ENT interventions, presence of recurrence, long term outcomes and cause of death. Any patient who had symptoms and signs and has history of recently (< 6 weeks) treated covid 19, uncontrolled diabetes mellitus, use of systemic corticosteroids, tocilizumab, mechanical ventilation, supplemented oxygen were considered as possible ROCM. When clinical signs and symptoms were supported by diagnostic nasal endoscopy findings, contrast enhanced MRI, CT scan -probable ROCM. Clinico-radiological findings coupled with microbiological confirmation on microscopy, culture or histopathology with special stains proves ROCM as diagnosis. Patients with MRI findings showing orbital extension and with ocular examination within normal limits were treated with liposomal TRAMB in 3-5 days interval. Orbital Exenteration planned in patients showing signs of progressive disease like ptosis, fixed dilated pupil with vision loss, total ophthalmoplegia, periorbital pain, altered mental status and palatal necrosis with MRI showing retinal artery thrombosis, orbital apex necrosis and extensive intraorbital extension. SION SCORING system was applied on this patient. Score more than 23 considered for orbital exenteration and less than 23 score treated with the TRAMB.

Before going for orbital exenteration, medical fitness was taken and neurosurgery fitness for patients with intracranial extension were taken. The number of patients with total ophthalmoplegia, not improving on TRAMB was 115. SION SCORING system was applied on these patients. Based on the scoring system, it was observed that those patients who crossed a score of 23 were the eligible candidates for orbital exenteration. 48 out of 115 total ophthalmoplegic patients crossed the score of 23, out of which only 34 were fit for surgery. Remaining 14 patients were not fit for surgery due to deranged hematological findings or poor general condition. 5 out of 34 patients had not given consent for orbital exenteration.

SION SCORING SYSTEM devised by a team of experienced otorhinolaryngologists and ophthalmologist from prior experience in managing mucormycosis .

Table 1 Clinical symptoms

	0	2	3
Vision	Normal or same as prior to other symptoms	Decreased vision after developing other symptoms	Total blindness
Pupil	Normal	RAPD	Fixed
Ocular motility	Normal	Extra-ocular muscle palsy/Diplopia	Fixed eyeball
Proptosis	Absent	-	Present
Intracranial spread	Normal	Headache, projectile vomiting, confusion	Altered consciousness, Pulsatile Exophthalmos, coma

Table 2 Ophthalmology**Fundus changes Points**

Normal	0
Cotton wool spots	1
Congested tortuous retinal blood vessels	2
Optic disc oedema	2
Central retinal vein occlusion	2
Central retinal artery occlusion	2
Retinal detachment	2
Choroidal folds	2
Optic disc pallor	2
Total	15

Table 3 Imaging

Orbital involvement by the disease (globe/muscles/fat)	3
Intracranial spread/superior orbital fissure/ inferior orbital fissure involvement	3
Optic neuritis	3
Sphenoid sinus involvement	2
Frontal sinus involvement	1
Ethmoidal sinus involvement	1
Infra-temporal fossa involvement	1
Maxillary sinus involvement	1

Result

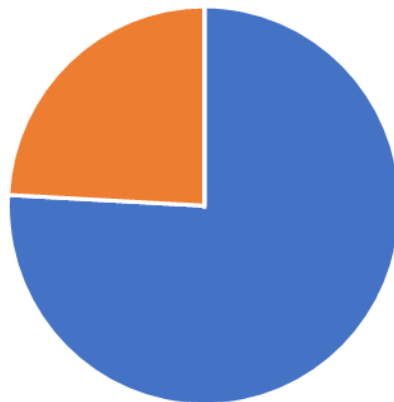
29 patients were underwent orbital exenteration has been included in this study. Out of 29, 5 (17.24%) patients were female and 24 (82.75%) were male. 4 (13.79%) were below 40 year of age, 25 (86.20%) were above 40 year of age. All patients had history of covid-19 disease and had taken steroid. All had Hb1ac > 9%. 7 (24.13%) patients had bilateral orbital involvement. 23 (79.31%) patients had intracranial extension. 6 (20.69%) patients had succumbed to death within 10 days of orbital exenteration. All of these patients had bilateral orbital involvement with intracranial extension and 23 (79.31%) patients have survived and have regular follow up.

Intracranial extension in MRI brain contrast	No. of patients	%
Acute brain infarct	8	34.78%
Cavernous sinus thrombosis	6	26.08%
Cerebral abscess	4	17.39%

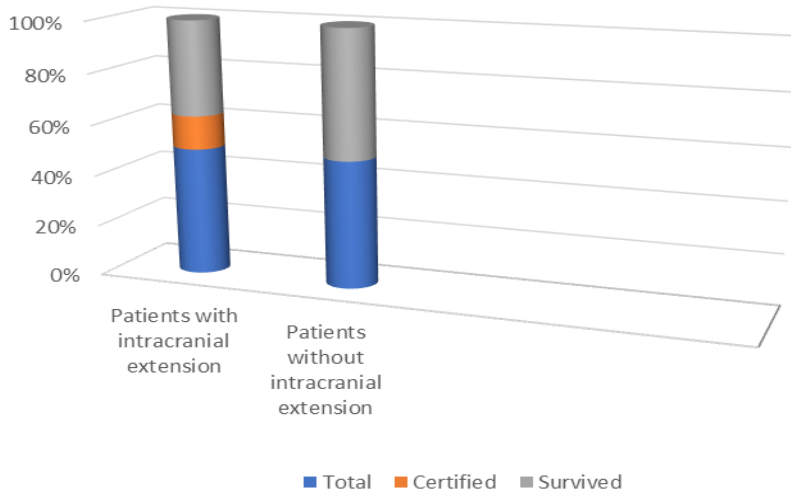
Intracerebral hemorrhage	3	13%
MCA thrombosis	2	9%

Gender	No. of patients
Male	24(82.75%)
Female	5(17.24%)

Age	No. of patients
Below 40 year	4 (13.79%)
Above 40 year	25 (86.20%)



■ unilateral orbital involvement ■ bilateral orbital involvement ■ ■





Patient with intra cranial spread, right orbital exenteration done



Patient with intracranial spread, right orbital exenteration done Patient certified on post exenteration day 12 due to pontine hemorrhage



Patient was planned for exenteration but improved with early ENT debridement and consecutive 9 liposomal TRAMB

Discussion

The family Mucoraceae includes the three genera *Rhizopus*, *Rhizomucor* (*Mucor*), and *Absidia*, which are considered to be the most common fungi responsible for mucormycosis^(9,10) The fungi undergo spore formation, and inhalation of the airborne spores provides them access to the human oral and nasal mucosa.⁽¹¹⁾

Angioinvasion by the hyphae causes endothelial damage that results in a fibrin reaction and the development of mucor thrombus, which occlude the arteries and lead to ischemia, infarction, and consequent formation of the black necrotic eschar of the skin and mucosa that is characteristic of mucormycosis. Tissue biopsy is necessary to confirm the diagnosis.⁽¹²⁾ Mucormycosis is presumed when nonseptate hyphae with right angle branching are seen on the histopathology and is diagnosed by culture of the involved tissues. The fungus can be seen with H&E, periodic acid-Schiff, and Gomori's methenamine silver staining. In our patients, all three staining procedures readily showed the fungus. Examination must include CT scan or MRI. The key for a successful treatment is high suspicion and early diagnosis⁽¹³⁾ the status of the underlying immunocompromising state and the timing of institution of adequate medical therapy, especially within 72 hours of disease onset, are of prime importance in ensuring a good outcome.

Hargrove et al. searched the literature for 113 published articles with 292 cases of orbital mucormycosis in determining the indications for orbital exenteration and reported that no standard of care currently exists to guide physicians on when exenteration may benefit mucormycosis patients⁽¹⁴⁾ Maureen M Roden et al study reviewed 929 mucormycosis cases and found the survival rate to be 61 percent in cases treated only with amphotericin B, 57 percent in those treated only with surgery, and 70 percent in those treated with both surgery and amphotericin B.⁽¹⁵⁾

Kashkoui et al in their series found that survival was not significantly different in patients with or without exenteration, however, a significantly longer duration of symptom to death was observed in patients with exenteration indicating that performing exenteration may delay the time of death.⁽¹⁶⁾

Conclusion

Mucormycosis is associated with many diagnostic and therapeutic challenges. The use of multiple treatment modalities including aggressive surgical debridement, intravenous liposomal amphotericin B, intraorbital regular amphotericin B may allow complete resolution of orbital mucormycosis and spare the patient from the blindness and disfigurement associated with exenteration. Do not rush for exenteration as there is a lack of standard data as to when exenteration benefits a mucormycosis patient. The objective of orbital exenteration is to remove fungal infections showing signs of spread to the orbit. Survival of mucormycosis patients depends on their good glycemic control, immune status, laterality of the orbital involvement and early detection of intracranial extension of the disease. With prompt medical (high dose i.v. amphotericin B) and early aggressive surgical intervention involving FESS and orbital exenteration can prevent intracranial extension and may improve survival rate. Intracranial extension of the disease has invariably been associated with high mortality. Bilateral orbital involvement with intracranial extension has poor prognosis. Early orbital exenteration alone has no benefit in long term survival.

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