

Ocular outcome of post-Covid rhino-orbital mucormycosis after one year

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Abstract

Introduction: Mucormycosis is a potentially lethal, angioinvasive fungal infection predisposed by poor immune function. During second wave of COVID 19 infection we had to also face rhino-orbital-cerebral Mucormycosis (ROCM). Patients with orbital involvement had a higher mortality than those with sinus only disease.² We aimed to study the ocular outcome, at the end of one year, of the post covid rhino-orbital Mucormycosis (ROM) patients

Aims: To study the ocular outcome of post COVID rhino-orbital mucormycosis (ROM) at the end of one year.

Methods and Materials: Hospital based retrospective cohort study was conducted in 79 post COVID ROM patients. The patients were followed up at the end of one year. Comparison between previous records and current findings were tabulated and outcome parameters were analyzed.

Results: Out of 79 ROM patients, 50 (63.29%) patients were followed up. Among them 60%(24 patients) who had no ocular involvement during active ROM were found to be normal at the end of one year. 17.1 %(6 patients) had residual effects, these patients underwent CDI/ FESS with TRAMB. Two patients underwent orbital Exenteration and had healthy sockets with no complications at the end of one year.

Conclusion: 24(60%) Mucormycosis patients with no orbital and ocular findings who were followed up at the end of one year were found to be normal. Whereas 35(44.3%) mucormycosis patients with ocular findings who underwent CDI/FESS with TRAMB among them 6(17%) mucormycosis patients were found to have residual effects like complete ophthalmoplegia, ptosis, lagophthalmos, exposure keratopathy, optic atrophy even at the end of one year. This states that patients with orbital involvement had ocular morbidity inspite of timely management.

Keywords: Orbital Mucormycosis, Post - Covid, TRAMB, CDI/FESS, ROM

Introduction

Mucormycosis is a potentially lethal, angioinvasive fungal infection predisposed by diabetes mellitus, corticosteroids and immunosuppressive drugs, primary or secondary immunodeficiency, haematological malignancies, haematological stem cell transplantation, solid organ malignancies, solid organ transplantation, etc.¹

During the second wave of COVID 19 infection we had to face another hassle of the formerly obscure, but notoriously fatal disease, rhino-orbito-cerebral mucormycosis (ROCM). Patients with orbital involvement had a higher mortality than those with sinus only disease.²

Mucormycosis induces vascular thrombosis, resulting in poor penetration of systemic antifungal. The most widely accepted therapy includes parenteral antifungal therapy and surgical debridement of sinuses.³ Options for the orbit include transcutaneous retrobulbar injection of amphotericin B (TRAMB), conservative debridement with irrigation (CDI), and orbital Exenteration.⁵

We aim to study the ocular outcome, at the end of one year, of the post COVID rhino-orbital mucormycosis (ROM) patients, who were treated with parenteral amphotericin B, TRAMB, CDI, functional endoscopic sinus surgery (FESS) and orbital Exenteration.

The scarcity of literature in this subject prompted us to undergo a thorough analysis of the long-term follow-up of these post COVID recovered ROM patients.

Aims and objectives of the study

To study the ocular outcome of post COVID rhino-orbital Mucormycosis (ROM) at the end of one year.

Materials and methods

A retrospective cohort study was conducted in 79 patients diagnosed with rhino-orbital mucormycosis. Prior approval from Institutional Ethical Committee was obtained for conducting the study. Duration of study was 3 months.

Inclusion criteria

- Patients with rhino-orbital-mucormycosis (ROM) post COVID

Exclusion criteria

- Patients who did not give consent.
- Patients with no history of Covid infection
- Patients who were lost to follow up.

Retrospective analysis of data of 79 post covid ROM patients was carried out. The patients were then asked to come for follow up at the end of 1 year. After taking

written informed consent, detailed ophthalmological examination was done. Uncorrected & best corrected visual acuity was recorded for each patient using Snellen’s chart, a slit lamp examination of anterior segment was performed, intraocular pressure was measured using non-contact tonometry, fundoscopic examination was done with indirect ophthalmoscope using 20D lens. Based on the examination findings, appropriate treatment was initiated. Comparison between previous records and current findings were tabulated and outcomes were analyzed.

Statistical methods

Categorical data were represented in the form of frequency and percentage.

Results

Data was collected for 79 patients with rhino-orbital mucormycosis. Among them, 40 patients (50.63%) had no ocular findings. The different treatment modalities patients with ocular findings received were CDI/ FESS with TRAMB and orbital Exenteration. 35(44.3%) underwent CDI/ FESS with TRAMB and 2 (2.53%) underwent orbital Exenteration (Table 1).

Follow-up was done at the end of 1 year. Among 79 patients, 50 (92.59%) patients were followed up. 3(5.5%) patients were lost to follow up and 1(1.85%) patient died later due to cerebrovascular ischemic attack (Table 2).6 (17.1%) patients out of 50 patients which were followed up had residual effects. These patients underwent CDI/ FESS with TRAMB (Table 3).

Table 1: Treatment modality distribution table

	Total	Deaths during active disease
Mucor patients with no ocular findings	40 (50.63%)	13
Mucor patients who underwent CDI/ FESS with TRAMB	35(44.3%)	10
Mucor patients who underwent Exenteration	2(2.53%)	0
Mucor patients who were referred to higher centre	2 (2.53%)	2
Total	79	25

Table 2: Follow up at the end of one year

Follow up at the end of one year			
	Patients who had no ocular findings 24 out of 40 were followed up (60%)	Patients with CDI/ FESS with TRAMB 24 out of 35 were followed up (68.5%)	Patients who underwent Exenteration 2 out of 2 were followed up (100%)
Normal	24(60%)	18(51.4%)	Both had healthy sockets with no complications
Residual effect	-	6(17.1%)	

Table 3: Comparison of ocular findings during mucor and at the end of one year

	BCVA During mucormycosis	Ocular findings during mucormycosis	BCVA during follow up	Residual effect seen with CDI/ FESS with TRAMB patients during follow up
Patient 1 - RE	6/60, 6/36	<ul style="list-style-type: none"> RE orbital cellulitis Complete Ophthalmoplegia Proptosis 	CFCF, 6/36	<ul style="list-style-type: none"> Cicatricial ectropion of lower lid Exposure keratopathy Fungal corneal ulcer with hypopyon
Patient 2 - LE	6/12,6/36	<ul style="list-style-type: none"> Complete Ophthalmoplegia Chemosis Mid dilated fixed pupil Proptosis Lagophthalmos 	6/12,6/18	<ul style="list-style-type: none"> Lagophthalmos Epithelial stippling Ectropion with punctal eversion
Patient 3 - RE	3/60,6/12	<ul style="list-style-type: none"> Complete Ophthalmoplegia Chemosis Mid dilated fixed pupil Complete ptosis Central retinal artery occlusion 	HM+,6/12	<ul style="list-style-type: none"> Complete Ophthalmoplegia Ptosis Optic atrophy
Patient 4 - BE	PL-,PL-	<ul style="list-style-type: none"> Complete Ophthalmoplegia Complete Ptosis Mid dilated and fixed pupil Occipital cortex infarct 	PL-,PL-	<ul style="list-style-type: none"> Complete Ophthalmoplegia Ptosis Mid dilated and fixed pupil Occipital cortex infarct
Patient 5 - LE	6/12,1/60	<ul style="list-style-type: none"> Complete ptosis PDR with HRC Complete Ophthalmoplegia Complete Ptosis Mid dilated and fixed pupil 	6/12,PL-	<ul style="list-style-type: none"> Ophthalmoplegia Ptosis Consecutive optic atrophy PDR with tractional retinal detachment involving macula
Patient 6 - LE	6/24, 1/60	<ul style="list-style-type: none"> Complete Ophthalmoplegia Chemosis Mid dilated fixed pupil Proptosis Complete ptosis Central retinal artery occlusion 	6/24, PL-	<ul style="list-style-type: none"> Optic atrophy Ophthalmoplegia Complete Ptosis

Discussion

Mucormycosis is the third most common invasive fungal infections following candidiasis and aspergillosis ⁷. Mucormycosis is a lethal infection that could present as a local or systemic disease, with high degree of morbidity and mortality. One of the most common forms of mucormycosis is rhino-orbito-cerebral mucormycosis. ^{8, 9} Localized pain, blepharoptosis, proptosis, chemosis, multiple cranial nerve palsies, ophthalmoplegia, headache, and sudden vision loss are the most common

ocular signs and symptoms.⁷Sudden loss of vision may occur due to central retinal artery occlusion, ophthalmic artery occlusion, thrombosis of posterior ciliary arteries, infarction of the intraorbital part of optic nerve, or direct fungal invasion of the intracranial part of the optic nerve or optic chiasm.¹³ Rarely, it can also present as a painless orbital apex syndrome.¹⁴ From the orbit, the infection can spread to the brain through cribriform plate of ethmoid bone and orbital apex. Invasion of the cavernous sinus and cavernous part of carotid artery can lead to occlusion of the carotid arteries, infarctions in cerebral cortex, intracranial aneurysm/haemorrhage, fungal meningitis, mycotic intracranial abscess and eventually death.¹⁵

Predisposing factors for this disease include diabetes mellitus, corticosteroids and immunosuppressive drugs, primary or secondary immunodeficiency, haematological malignancies and haematological stem cell transplantation, solid organ malignancies and solid organ transplantation.⁵

The increasing incidence of ROM in the setting of COVID-19 has become a matter of concern. These patients are more prone to ROM due to the associated Comorbidities (e.g., diabetes mellitus, chronic obstructive pulmonary disease), need for oxygen administration, and immunocompromised conditions (e.g., corticosteroid therapy, ventilation, intensive care unit stay).⁵

The studies for pathogenesis of the infection show that there are alterations in cell-mediated immunity, such as chemotaxis, phagocytosis and cytokine secretion in diabetics. Thus T-cells (CD4+ and CD8+) that produce cytokines such as interleukin (IL) 4, IL-10, IL-17 and interferon-gamma (IFN- γ) and damage the fungal hyphae lack in such patients leading to pre-disposition to

infection.¹⁶ Also procoagulant state and vasoconstriction lead to ischaemia and hence necrosis of the tissues. Mucormycosis also induces vascular thrombosis, resulting in poor penetration of systemic antifungals.

Diagnosis is usually based on identifying organisms in tissue by histopathology, culture, KOH preparation and molecular tests.¹⁰The most widely accepted treatment approach is parenteral antifungal therapy along with surgical debridement of sinuses, which should be started early after diagnosis. For orbital mucormycosis, orbital exenteration, conservative debridement with irrigation (CDI), and more recently, transcutaneous retrobulbar injection of amphotericin B (TRAMB) are the available treatment options.

Here, we report the one year follow up of 79 patients with ROM treated with TRAMB in conjunction with systemic antifungals or CDI with FESS or orbital exenteration to evaluate the long-term ocular outcome.

Out of 79 patients, 50(63.29%) were males and 29(36.70%) were females. Among them, 40 (50.63%) patients had no ocular findings. The different treatment modalities patients with ocular findings received were CDI/ FESS with TRAMB and orbital Exenteration. 35(44.3%) underwent CDI/ FESS with TRAMB and 2 (2.53%) underwent orbital exenteration.

25(31.64%) patients succumbed to the disease during the active stage of infection and one patient died 6 months later due to a cerebrovascular ischemic attack.

Out of 50 patients who were followed up, 24(60%) of the patients who had no ocular involvement during active mucormycosis were found to be normal at the end of one year. Out of 35(44.3%) patients who underwent CDI/ FESS with TRAMB, 18 (51.4%) patients were found to be normal and 6 (17.1%) patients had residual effects at the end of one year.

Out of the two patients who underwent orbital Exenteration, both were found to be having healthy sockets and no associated complications at the end of one year. The residual effects seen in the patients were as follows:

- Patient -1 had BCVA of 6/60 in the right eye during mucormycosis and ocular findings RE orbital cellulitis, complete ophthalmoplegia and proptosis The present ocular findings of the same patient were cicatricial ectropion of lower lid, exposure keratopathy, fungal corneal ulcer with hypopyon and the KOH staining revealed aseptate fungal hyphae suggestive of reinfection of cornea and the vision worsened to counting fingers close to face. Which infers that inspite of timely management redundant fungi was found in ocular tissue.
- Patient -2 had BCVA of 6/36 in the left eye during mucormycosis and ocular findings were lagophthalmos, chemosis, proptosis, periorbital oedema and complete ophthalmoplegia The present ocular findings of the same patient were lagophthalmos, epithelial stippling and ectropion with punctal eversion with BCVA of 6/18.
- Patient -3 had BCVA of 3/60 in the right eye during mucormycosis and ocular findings like complete ptosis, dilated non-reactive pupil, lid oedema and CRAO and complete ophthalmoplegia. The present ocular findings of the same patient were complete ophthalmoplegia, complete ptosis and the CRAO progressed to optic atrophy worsening the vision of the patient to hand movements only.
- Patient - 4 had Vision of no perception of light in both eyes. During mucormycosis ocular findings were LE complete ophthalmoplegia, complete ptosis, exposure keratopathy, RAPD, proptosis and patient

had developed occipital cortex infarct during active mucormycosis. The present ocular findings were complete ophthalmoplegia, complete ptosis in left eye and no perception of light in both eyes.

- Patient -5 had BCVA of 1/60 in the left eye during mucormycosis had ocular findings like complete ophthalmoplegia complete ptosis, mid-dilated non-reactive pupil, fundus findings showed CRAO, PDR with HRC and the present ocular findings of the same patient were complete ophthalmoplegia, complete ptosis, optic atrophy and tractional retinal detachment involving macula. The vision of the patient worsened to no perception of light in left eye.
- Patient -6 had BCVA of 1/60 in the left eye during mucormycosis had ocular findings like complete ophthalmoplegia, complete ptosis, mid-dilated non-reactive pupil and CRAO. The present ocular findings of the same patient were complete ophthalmoplegia, complete ptosis and optic atrophy with worsening in the vision to no perception of light.

Literature search revealed no similar studies done in terms of long term follow up of ocular outcome of mucormycosis patients.

Although orbital exenteration was a life-saving procedure, cosmetically the results were poor.

Hence, we can conclude that CDI with TRAMB are globe-saving alternatives in the treatment of rhino-orbital mucormycosis that show significant resolution in signs and symptoms and also play a major role in halting the intracranial progression of the disease in early stages.

Conclusion

24(60%) Mucormycosis patients with no orbital and ocular findings who were followed up at the end of one year were found to be normal. Whereas 35(44.3%)

mucormycosis patients with ocular findings who underwent CDI/FESS with TRAMB among them 6(17%) Mucormycosis patients were found to have residual effects like complete ophthalmoplegia, ptosis, lagophthalmos, exposure keratopathy, optic atrophy even at the end of one year. This states that patients with orbital involvement had ocular morbidity inspite of timely management.

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