

Ocular manifestations of Rhino-orbital mucormycosis in COVID 19 patients in a tertiary care hospital

¹Ramapriyadharshini J, ²Ilango K, ³Vijay prasad R, ⁴Rajavel MSPS, ⁵Maheswaran S

¹Assistant professor, ²Professor, ³Assistant professor, ⁴Assistant professor, ⁵Associate Professor
^{1,2}Department of Ophthalmology, ^{3,4,5}Department of Otorhinolaryngology
Velammal medical college and research institute, Madurai, Tamilnadu, India

Abstract:

Introduction:

Rhino-orbital mucormycosis is a debilitating invasive fungal disease. Mucormycosis is relatively a rare disease affecting only severely immunocompromised patients. This disease has now become a notifiable health disease after covid pandemic leading to mortality and debilitating morbidity. In rhino-orbital cerebral mucormycosis, sinus and nasopharynx are affected first which then rapidly spreads to involve orbit and brain if not treated aggressively at the earliest. The aim of the study is to discuss the various ocular manifestations of mucor and also to highlight the unique features of covid related mucormycosis from endemic mucormycosis.

METHODS

This is a retrospective review of 50 cases presented in our institute between the period of march 2021 to february 2022.

Results:

All patients acquired mucor either during covid illness or within 6 weeks of COVID recovery. All patients had poor diabetic control and steroid intake during covid illness as the important predisposing factor. Ocular manifestations in the form of preseptal cellulitis, orbital cellulitis, orbital apex syndrome, central retinal artery occlusion were the common initial presentation. The primary focus of orbital spread is from direct orbital floor erosion from maxillary sinus rather than from ethmoidal sinus highlighting peculiar presentation of covid related mucormycosis from endemic mucor.

Conclusion:

Covid related mucormycosis has a fulminant course and high mortality risk. Diagnosis during the early stages of covid related mucor is challenging as many patients had atypical initial presentation like central retinal artery occlusion, proptosis even before nasal symptoms. The unique features of Covid related mucormycosis were very rapid progression to orbit within 2 days and different primary source of orbital spread, directly through orbital floor invasion from maxillary sinus unlike Endemic Mucormycosis. Early diagnosis with high index of suspicion and aggressive surgical and appropriate antifungal treatment can only save the patients from visual morbidity and mortality.

Keywords: Rhino orbital mucormycosis, covid related mucormycosis, orbital cellulitis, ocular manifestations of mucor, retrobulbar amphotericin, exenteration.

Introduction:

Rhino-orbital mucormycosis is a rare aggressive opportunistic invasive fungal infection. This disease affecting immunocompromised individuals has emerged as an epidemic outbreak after covid pandemic [1-4]. Nasopharynx and sinus are affected first which is followed by rapid progression to orbit and brain [5-7]. Ocular manifestation in the form of proptosis is the most common initial presentation. Intracranial spread will be devastating and rapid leading to fatal outcome. This organism has a predilection to invade and occlude vascular lumen leading to necrotizing vasculitis and characteristic black eschar formation [5-7]. Mortality ranges from 24 to 49 %. It may reach 80 % if there is a intracranial spread [8-10]. In this retrospective study we have observed different ocular manifestations as well as unique ocular features of covid related mucormycosis from endemic mucormycosis.

Methods:

Detailed retrospective study of 50 patients with covid related rhino-orbital mucormycosis who were diagnosed and treated at velammal medical college hospital and research institute, after confirmed histological and radiological evidence of mucormycosis were included in the study. Detailed retrospective analysis of all patients including presenting illness, onset, progression of ocular symptoms like defective vision, restriction of ocular movements, pain, protrusion of eyeballs, then covid vaccination status, other factors like uncontrolled diabetes, prolonged steroid intake, Post organ transplant recipients were noted. This is followed by detailed review of radiological imaging, biopsy reports, and medical and surgical management details. All those patients had underwent functional endoscopic sinus surgery, some patients with extensive maxillary sinus involvement underwent Caldwell approach in addition to endoscopic debridement. Ocular examination including visual acuity, anterior and posterior segment examination were recorded in detail. Ocular manifestations in the form of proptosis, preseptal cellulitis, orbital cellulitis, orbital apex involvement, central retinal artery occlusion, exposure keratitis secondary to facial nerve palsy, other ocular manifestations and unique features of covid related mucor were observed.

Investigations done during initial presentation were blood glucose, urine routine and ketones, complete blood count, urea, creatine, KOH and histopathological evaluation of biopsy specimens, computed tomogram of Para nasal sinus, orbit and brain. The most common CT PNS (paranasal sinus) MRI PNS with orbit image finding was sino-orbital invasive fungal infection with orbital floor erosion.

Management was initiated as soon as the KOH reports confirmed the diagnosis. Aggressive surgical debridement with endoscopic sinus surgery and intravenous liposomal amphotericin B was given in a dose of 3 – 5 mg per kg per day in 500 ml 5% dextrose along with adequate prehydration with normal saline for a period of 4 weeks. A cumulative dose of 2- 3 grams of liposomal amphotericin B were given. If there is an ocular involvement in the form of preseptal and orbital cellulitis, in addition to the above treatment the patient also received transcutaneous retro bulbar amphotericin B (TRAMB) in the dose of 3.5mg/dl. The injections were repeated after 2-3 days if there is no clinical improvement in the form of worsening of proptosis and ophthalmoplegia . Those patients with orbital apex involvement with no vision potential underwent exenteration after ruling out intracranial spread and orbital rehabilitation prosthesis were suggested later.

Results:

The mean age of presentation was 45 – 65 years "Table 1", "chart 1". 42 patients were males. 8 patients were females."Table 2". All cases had unilateral involvement. All patients with rhino-orbital mucormycosis either had active covid disease or within six weeks of post covid recovery. Uncontrolled diabetes was the most important predisposing factor in all patients. All 50 patients had history of steroid intake during the course of covid disease suggesting the possible contributing role of steroids in causing mucormycosis. Only 5 patients received one dose of covid vaccination, Other 45 patients did not get covid vaccination. Those patients who had one dose of covid vaccination presented with preseptal cellulitis only, has shown marked improvement after first dose of TRAMB compared to remaining 45 patients. Onset and progression of the symptoms were found to be acute and rapid within a period of 2 days which contributes to ocular manifestation as initial presentation unlike nasal symptoms in endemic mucormycosis. As per the imaging findings primary focus of fungal infection to the orbit is from the maxillary sinus through direct orbital floor erosion in covid related mucormycosis and not from ethmoid sinus which is the common mode of spread in endemic mucormycosis.

All 50 patients underwent functional endoscopic sinus surgery which is followed by intravenous liposomal amphotericin B for primary sinus involvement. Of which 25 patients underwent combined FESS with caldwell luc maxillary sinus clearance for extensive sinus disease with orbital floor involvement. Of the 50 patients with invasive fungal sinusitis, 32 patients presented with preseptal cellulitis, 14 patients presented with orbital cellulitis with features of defective vision, marked proptosis, chemosis, ophthalmoplegia, with or without pupil involvement due to compressive optic neuropathy"Fig.1". Among orbital cellulitis patients, one patient had exposure keratitis. Two patients presented with central retinal artery occlusion, 2 patients presented with orbital apex syndrome"Fig.2", "Table 3", "chart 2". All 46 patients who presented with preseptal cellulitis and orbital cellulitis were given TRAMB(transcutaneous Retrobulbar Liposomal amphotericin). Among which 11 patients were given second dose of TRAMB after 3 days of first dose. In all 32 patients who received TRAMB, further post septal spread was prevented there by preventing the need for mutilating exenteration procedure. 2 patients presented with CRAO as initial presentation didn't regain their vision as they have presented after golden hour and also subsequently lost their life due to covid related respiratory compromise. One patient presented with exposure keratitis secondary to facial nerve palsy due to skull base involvement of the disease was treated with topical antibiotics, cycloplegics and lubricants recovered well. Among 50 patients, 2 patients underwent exenteration for extensive orbital involvement with orbital apex extension in order to prevent intracranial spread."Table 4", "Chart 3", "Fig.3". Strict diabetic control and covid vaccination has definite role in disease prevention.

CONCLUSION:

From our study, we could observe that covid related mucormycosis has many unusual ocular manifestations in the form of central retinal artery occlusion, exposure keratitis in addition to proptosis secondary to preseptal cellulitis, orbital cellulitis and orbital apex syndrome. Ocular manifestations were the initial presenting symptom in all patient due to acute onset and rapid progression of covid related mucor within a period of 2 to 3 days. In endemic mucormycosis, presenting symptom used to be nasal stuffiness, facial pain followed by ocular symptom after a period of 4 to 7 days. Steroid intake during covid illness has definite contributing role. Those patients even with one covid vaccination had a rapid recovery than those without any vaccination. Another peculiar distinguishing feature of this covid related mucor observed was orbital involvement occurred secondary to orbital floor (maxillary roof) erosion from maxillary sinus whereas generally orbital involvement spreads from ethmoidal sinus. To conclude, this devastating and debilitating covid related mucor has many atypical and unique features which cost the life and vision of the patients with various ocular manifestations if not intervened earliest.

Table 1: Age distribution of cases

AGE	NO.OF CASES
45 -55 yrs	10
55-65 yrs	40

Table 2: Gender distribution of cases

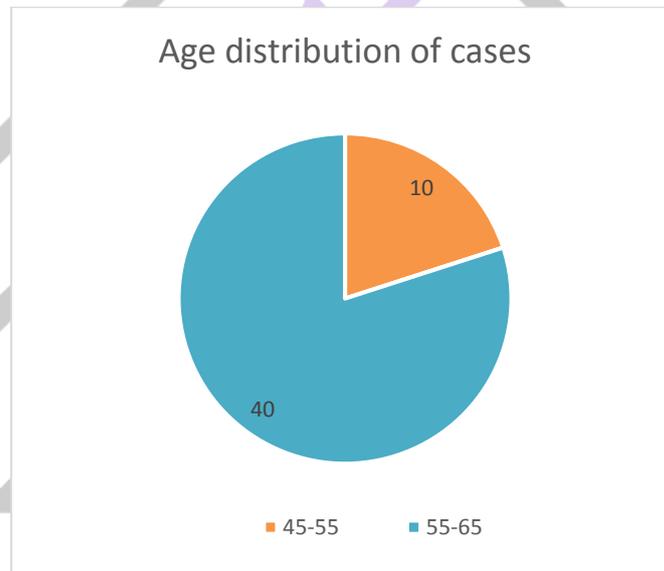
GENDER	NO.OF CASES
MALE	42
FEMALE	8

Table 3: various ocular manifestations among cases

OCULAR MANIFESTATION	No.of cases
Preseptal cellulitis	32
Orbital cellulitis	13
Exposure keratitis	1
Central retinal arteryocclusion	2
Orbital apex involvement	2

Table 4: Different treatment modalities for rhinorbital mucormycosis

Mode of management	No. Of cases
Endoscopic debridement only	25
Endoscopic debridement with Caldwell luc approach	25
Inj. Retrobulbar liposomal amphotericin b	46
Exenteration	2
Intravenous amphotericin B	50

**Chart 1:** Age distribution of cases

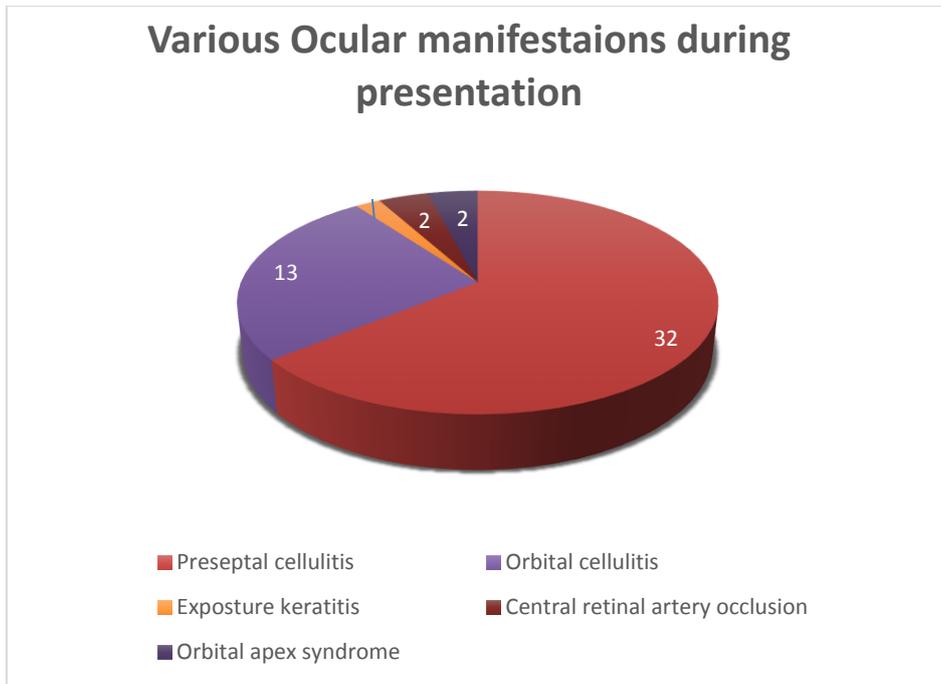


Chart 2: Various ocular manifestations of Mucormycosis

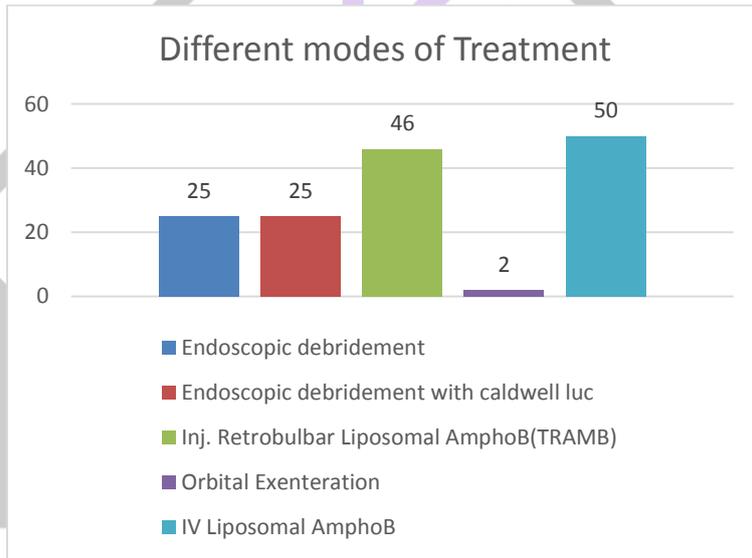


Chart 3: Different treatment modalities for rhinorbital mucormycosis



Figure.1 Mucor patient showing right orbital cellulitis.



Figure.2 Mucor patient with left eye proptosis with orbital apex involvement.



Figure.3 Picture showing left eye Post orbital exenteration status.

REFERENCES:

- [1] Ms S, Menezes VH, Vv S, Am B. Institutional experience of mucormycosis over a period of 10 years - retrospective case series. *International Journal of Advances in Medicine*. 2017 Feb 11;1(2):141–4.
- [2] Rootman J. *Diseases of the Orbit: A Multidisciplinary Approach*. Lippincott Williams & Wilkins; 2003. 654 p.
- [3] Prakash MVS, Kumar PA, Umamaheswari TG, Harivanzan V. The clinical pattern of orbital mucormycosis in a tertiary eye care hospital. *TNOA Journal of Ophthalmic Science and Research*. 2020 Jan 1;58(1):14.
- [4] Sarkar S, Gokhale T, Choudhury SS, Deb AK. COVID-19 and orbital mucormycosis. *Indian Journal of Ophthalmology*. 2021 Apr;69(4):1002–4.
- [5] Pal S, Agarwall R, Sharma K, Jain V, Mishra P. Fungal infections of the orbit: The present scenario in a developing country. *IP International Journal of Ocular Oncology and Oculoplasty*. 2021 Apr 28; 7:49–54.
- [6] Kalin-Hajdu E, Hirabayashi KE, Vagefi MR, Kersten RC. Invasive fungal sinusitis: treatment of the orbit. *Curr Opin Ophthalmol*. 2017 Sep;28(5):522–33.
- [7] Pearls in the Diagnosis and Management of Rhino-Orbito-Cerebral-Mucormycosis [Internet]. [cited 2022 Mar 27]. Available from: <https://www.eophtha.com/posts/pearls-in-the-diagnosis-and-management-of-rhino-orbito-cerebral-mucormycosis>
- [8] Alsubaie MA, Alghamdi SA, Alghamdi SA, Abdelaal AM, Satti MB. Rhino-Orbital-Cerebral Mucormycosis Causing Orbital Apex Syndrome and Blindness. *JCDR [Internet]*. 2018 [cited 2022 Mar 27]; Available from: http://jcdr.net/article_fulltext.asp?issn=0973-709x&year=2018&volume=12&issue=4&page=ND01&issn=0973-709x&id=11389

- [9] Colon-Acevedo B, Kumar J, Richard MJ, Woodward JA. The Role of Adjunctive Therapies in the Management of Invasive Sino-Orbital Infection. *Ophthalmic Plast Reconstr Surg.* 2015 Oct;31(5):401–5.
- [10] Ashraf DC, Idowu OO, Hirabayashi KE, Kalin-Hajdu E, Grob SR, Winn BJ, et al. Outcomes of a Modified Treatment Ladder Algorithm Using Retrobulbar Amphotericin B for Invasive Fungal Rhino-Orbital Sinusitis. *Am J Ophthalmol.* 2021 Jun 9; 237:299–309.

