



CLINICAL PRESENTATIONS, DIAGNOSIS AND TREATMENT OF RHINO-ORBITAL-CEREBRAL MUCORMYCOSIS (ROCM)-A CLINICAL STUDY

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ABSTRACT **AIM:** To document and analyse clinical presentation, staging and possible interventions for clinical detection and management of ROCM.

METHODS: In a retrospective analysis, 40 cases of ROCM were identified from June 2021 to August 2021 in Government General Hospital, Government Regional Eye Hospital, Kurnool medical college, Kurnool, Andhrapradesh. All the ROCM cases were diagnosed clinically and confirmed by microbiological and/or histopathological examination. The relevant demographic data, clinical, ophthalmic manifestations, medical treatments, and surgical interventions were recorded and analyzed.

RESULTS: The mean age of the patients was 48.95 years (age range: 40 - 60 years); 70% of the patients were males and 30% were females. Diabetes mellitus was noted in 75% (30/40) of the cases. The most common clinical feature was orbital pain with or without headache 77.5% (31) followed by 65% (26) patients had ophthalmoplegia, 62.5% (25) eyelid swelling, 52.5% (21) diminution of vision, 47.5% (19) nasal block/discharge, 47.5% (19) ptosis, 40% (16) proptosis, 15% (6) loosening of teeth. Most of the patients were in stage 3 (42.5%) maxillary sinuses were the most frequently involved site (66.7%) followed by the ethmoid sinus. Intravenous Liposomal Amphotericin B (LAMB) was given for 2 to 4 days followed by surgical debridement was done in the treatment of 82.5% of the cases, Retrobulbar amphotericin B (75%) and orbital exenteration (27.5%) of the cases. A neurosurgical intervention like craniotomy with frontal lobe abscess excision, temporal lobe abscess excision was done in 17.5% of the cases. Histopathologically proven cases were 65%.

CONCLUSION: The incidence of mucormycosis is more in patients recovering from Covid-19, probably because of the immunocompromised state induced by the virus, use of steroids and associated co-morbidities like diabetes, chronic renal failure etc. Diabetes mellitus is considered to be the main predisposing factor for ROCM. To prevent and reduce the mortality rate of this acute disease, early diagnosis and early intervention is recommended.

KEYWORDS : Diabetes, rhino-orbital-cerebral mucormycosis, ROCM, orbital pain.

INTRODUCTION

Mucormycosis is an opportunistic fungal infection caused by fungi of the order Mucorales, the most common is *Rhizopus oryzae*, which is responsible for this rapidly progressing fatal infection. Immunocompromised patients, particularly those with uncontrolled diabetes, are known to be susceptible to mucormycosis. The most commonest form of presentation is rhino-orbital-cerebral mucormycosis (ROCM). The fungi colonise and infect the nasal mucosa first, followed by the sinus, then spreading to neighbouring anatomical sites such as the orbit, cavernous sinus, and brain after inhaling fungal spores found in the environment. The infection causes vascular thrombosis and tissue necrosis due to the invasion of fungal hyphae into blood vessels. The clinical hallmark of ROCM is tissue necrosis which manifested as a necrotic lesion, eschar, or black discoloration in nasal or oral cavity.

COVID-19 infection raises the incidence of subsequent fungal infections, putting patients at a higher risk of developing ROCM. In the current study, we reviewed the confirmed cases of ROCM and assessed the patient demographic characteristic, underlying disease, clinical manifestations and management.

MATERIALS AND METHODS

This is retrospective observational study of 40 patients who were included in the study after obtaining informed consent. Demographic parameters such as age, gender and co-morbidities were noted. A detailed history was taken from the patient, and all the patients were subjected to clinical examination, radiological assessment in the form of Magnetic Resonance Imaging (MRI) with gadolinium (GAD) contrast-enhanced brain with nose, paranasal sinus and orbit, diagnostic nasal endoscopy, endoscopy guided nasal smears/biopsy for microscopic examination using Potassium hydroxide (KOH)/histopathological examination, and ophthalmological evaluation. All patients were treated with either one or a combination of surgical interventions namely, Functional endoscopic sinus surgery

(FESS)/sinus debridement and/or maxillectomy and orbital exenteration with adjuvant Intravenous Liposomal Amphotericin-B infusion.

Demographic distribution, clinical manifestations, staging, treatment was noted.

RESULTS

Table 1: Co-Morbidities

CO-MORBIDITIES	NUMBER	PERCENTAGE
DIABETES	30	75
HYPERTENSION	19	47.5
RENAL DISEASE	10	25
HEPATITIS B/HEPATITIS C	3	7.5
BRONCHIAL ASTHMA	2	5
OBSESITY	2	5
NEUROFIBROMATOSIS	1	2.5

Chart 1: Presenting Symptoms

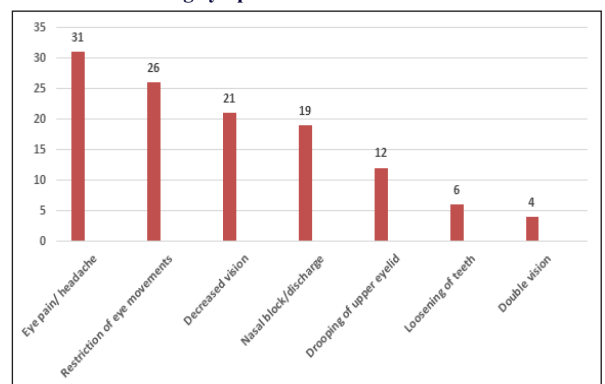


Table 2: Ophthalmic Findings

VISUAL ACUITY OF INVOLVED EYE	NUMBER	PERCENTAGE
No perception of light	11	27.5
Only perception of light	2	5
CF-CF to CF -3mts	9	22.5
CF -3mts to CF-6mts	18	45
ANTERIOR SEGMENT FINDINGS OF INVOLVED EYE		
Periorbital edema	25	62.5
Ptosis	19	47.5
Proptosis	16	40
Conjunctival chemosis	10	25
RAPD	6	15
FUNDUS FINDINGS OF INVOLVED EYE		
Normal Fundus	28	70
Optic disc edema	6	15
CRAO	4	10
Optic disc pallor	2	5
Attenuated blood vessels		

Chart 2: Staging Of Rocm

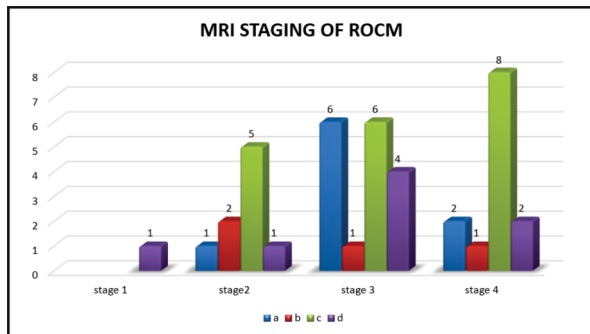
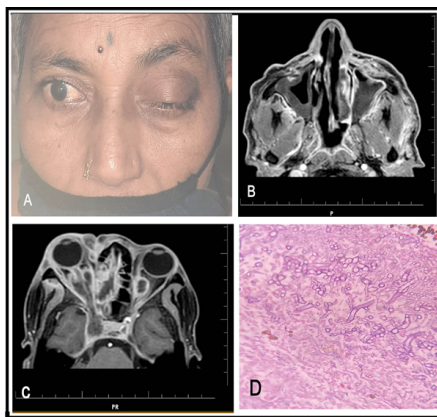


Figure 1



(A) The clinical picture shows complete ptosis of the left eye. (B) Post-contrast T1W Axial MRI image showing non-enhancement of inferior turbinate suggestive of a Black turbinate sign. (C) Post-contrast T1W Axial MRI image showing heterogeneous enhancement involving right side ethmoidal sinus, bilateral orbital apex, extending up to cavernous sinus on the right side and meningeal enhancement also noted on the right side. (D) 40×40 H and E Microscopy section studied showed extensive areas of necrosis with broad aseptate hyphae along with sporangia and spores features consistent with Mucormycosis.

Treatment 3 :

TREATMENT	NO.OF PATIENTS	PERCENT AGE
IV LAMB followed by oral posaconazole	40	100
Endoscopic sinus debridement	33	82.5
Total or partial maxillectomy	7	17.5
Retrobulbar liposomal Amphotericin -B	30	75
Orbital exenteration	11	27.5
Neurosurgical intervention	7	17.5
Conservative treatment with poor general condition	6	15

DISCUSSION

Mucormycosis is known to be associated with severe neutropenia, uncontrolled diabetes mellitus, iron overload, chronic renal failure, longterm use of corticosteroid therapy. The vulnerability of COVID-19 patients to mucormycosis is more because of the presence of diabetes.

In our study 40 patients were taken, the maximum number of patients(25) were seen in the 40 - 60 years age group. The next most affected age group were greater than 60 years age group and less than forty years age group with 9 patients (23%) and 6 (15%) respectively. In our study, out of 40 patients 28 were males, 12 were females. Diabetes mellitus was shown to be the most common risk factor for ROCM in our study. 75% of cases were diabetes. In our study, the most common clinical feature was orbital pain with or without headache (77.5%). All of the patients had diagnostic nasal endoscopy, which revealed thickening of the mucosa in the affected area.

Microbiological Examination of specimen with KOH mount revealed wide-angled, broad aseptate hyphae suggestive of Mucor spp. in 70% (28) patients and culture shows Mucor spp in 55% (22) patients. The definite diagnosis is made after histopathological evaluation of biopsy specimens from the affected area. Histological evaluation is considered more sensitive than culture. In our study, histopathologically proven cases were 26 (65%). Imaging is very important and useful for assessing the extent of disease. The infection spread to the intracranial and orbital area can be evaluated by magnetic resonance imaging (MRI). In our study, most of the patients were in stage 3 (42.5%). The main approaches to the treatment of Rhino-orbital-cerebral mucormycosis include management of hyperglycemia and acidosis, systemic antifungal therapy with Intravenous Liposomal Amphotericin B, and immediate aggressive surgical resection of the involved area.

Curative surgical procedures, both endoscopic and open techniques, are utilized to debride the whole necrotic tissues. Because vascular thrombosis causes inadequate drug delivery to the infection site, medical treatment alone is ineffective. Early diagnosis and initiation of proper treatment are important for successful eradication of the infection and patient survival. Prognosis is directly associated with a time interval before diagnosis and treatment. Teamwork, with the involvement of ENT surgeons, Ophthalmologists, General physicians, Neurologist, Neurosurgeon, Endocrinologists and dental specialists are critical in the management of ROCM patients.

CONCLUSION

To conclude, the prevalence of diabetes in developing countries, the most common risk factor for ROCM, which leads to an increase in the incidence of ROCM. Strict glycemic control and judicious use of corticosteroids might help to decrease the incidence of mucormycosis cases. The majority of individuals who report with ENT-related symptoms should be treated as soon as possible to prevent the disease from spreading to orbit and intracranial sites. Most early intervention during nasal presentation might help to prevent spreading to neighbouring tissues

REFERENCES

- Prabhu RM, Patel R. Mucormycosis and entomophthoromycosis: a review of the clinical manifestations, diagnosis and treatment. Clin Microbiol Infect. 2004; 10(Suppl 1):31-47.
- Lanternier F, Lortholary O. Zygomycosis and diabetes mellitus. Clin Microbiol Infect. 2009; 15(5):21-5.
- Honavar SG. Code mucor: guidelines for the diagnosis, staging and management of rhino-orbito-cerebral mucormycosis in the setting of COVID-19. Indian J Ophthalmol. 2021;69(6):1361-1365. doi:10.4103/ijjo.IJO_1165_211
- Hatice Sebila Do'kmetas, a, Ercan Canbay b, Sarper Yilmaz c, Nazif Elaldi d, Ays, en Topalkara e, Ibrahim Oztoprak f, Esin Yildiz g. Diabetic ketoacidosis and rhino-orbital mucormycosis. Diabetes research and clinical practice 2002;32:139-142.
- Honavar SG. Rhino-orbito-cerebral mucormycosis- Guidelines for diagnosis, staging, and management. Indian J Ophthalmol 2021;69:XX-XX.