

MANAGEMENT OF COVID ASSOCIATED ORBITAL MUCORMYCOSIS IN TERTIARY CARE HOSPITAL

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ABSTRACT

Objectives: The aim of the study was to study epidemiological characteristics and management of orbital mucormycosis in cases of rhino-orbital mucormycosis in tertiary care hospital.

Methods: It is a retrospective study of 258 patients presenting to KGH, Visakhapatnam, over a duration of 3 months from June to August 2021. After taking detailed history regarding symptoms of mucormycosis, visual acuity was noted, slit lamp examination was done and necessary investigations such as microbiology, pathology specimens were sent and analyzed, imaging done, and management done accordingly.

Results: The majority of patients came with ENT-related symptoms were treated with endoscopic debridement, that is, 216 (84%), endoscopic debridement with orbital decompression of 23 (9%), transcutaneous retrobulbar amphotericin B of 21 (8%), orbital exenteration of 17 (6.5%), total and partial maxillectomy of 28 (10.8%), temporal lobe abscess drainage of 7 (2.7%), frontal lobe abscess drainage of (1.16%), frontal bone abscess drainage of 3 (1.16%), dural abscess drainage of 6 (2.3%), 15 (5.8) treated conservatively, and 30 (11.6%) death.

Conclusion: COVID-19 infection in presence of glycemic dysregulation predisposes to development of Rhino-orbital-cerebral mucormycosis. Strict glycemic control and judicious use of corticosteroids might help in decrease incidence of mucormycosis cases. Most of the patients presents with ENT-related symptoms if not treated early may spread to orbit and intracranial sites. Early treatment during early presentation might help prevent spreading orbital extension and intracranial extension.

Keywords: COVID-19 associated mucormycosis, Orbital mucormycosis, Diabetes mellitus in mucormycosis, Corticosteroids in mucormycosis, Management of mucormycosis

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INTRODUCTION

Mucormycosis is a devastating fungal infection caused by a group of mold called mucormycetes involving paranasal air sinuses, orbits, and intracranial sites. Unforeseen complication of COVID-19 pandemic associated with high morbidity and mortality.

Aim

The aim of the study was to study management of COVID-associated orbital mucormycosis in tertiary care hospital.

Study design

It is a retrospective study of 258 cases of diagnosed as Rhino-orbital-cerebral mucormycosis (ROCM) attending our hospital during the period of 3 months from June 2021 to August 2021. All these patients are diagnosed with past or active COVID-19 with symptoms of ROCM predominantly with ophthalmological symptomatology.

METHODS

A data collection sheet – age, sex, date of COVID-19 diagnosis with history, date of onset of ROCM symptoms, associated comorbidities, and clinical features of ROCM.

Symptoms

Severe headache, drooping of eyelids, defective vision, loss of extraocular movements, periorbital swelling, and protrusion of eyeball (Fig. 2) along with ENT-related symptoms.

Detailed ocular examination including visual acuity, anterior segment examination, proptosis, ptosis, extraocular movements, fundus examination, and other investigations done are X-ray orbits, computed tomography scan

of brain, orbits, contrast-enhanced magnetic resonance imaging, (Fig. 3) serum electrolytes, liver function tests, and kidney function tests.

ROCM was staged as per the proposed code – mucor guidelines by (National Centre of Biotechnology Information) (Fig. 1) [6].

Treatment

All patients were given tab Posaconazole 300 mg BD day 1300 mg OD from day 2. Those patients who are having predominant ocular symptoms (Stages 3 and 4) were given five doses of retrobulbar amphotericin B of 1 ml (3.5 mg/ml) on alternate days preceded by I/V amphotericin B for 3 days and I/V amphotericin B is continued for 2 weeks (5 mg/kg body weight).

Surgical management was done for those patients who are not responding for medical management and based on radiological findings such as endoscopic debridement, endoscopic debridement with orbital decompression, orbital exenteration, neurosurgical interventions such as frontal lobe abscess drainage, temporal lobe abscess, partial or total maxillectomy, and conservative treatment for patients with poor general condition and mild disease.

RESULTS

Out of all 258 patients, males were 196 (76%) and females 62 (24%). Coming to age distribution, 2 (0.7%) patients were <30 years of age, 58 (22.4%) were 30–40 years of age, 72 (28%) were 41–50 years, 66 (25%) were 51–60 years, and 60 (22.4%) were >60 years of age. Fifty-five (21.3%) patients were with active COVID-19 with 5–10 days interval and 203 (78.7%) patients who are post-COVID with 20–35 days interval. Among these 258 patients, 201 (78%) were known



Fig. 1: (a) Complete ptosis of the right eye, (b) Ptosis, proptosis, and chemosis of the right eye, and (c) Panophthalmitis with melting of anterior segment

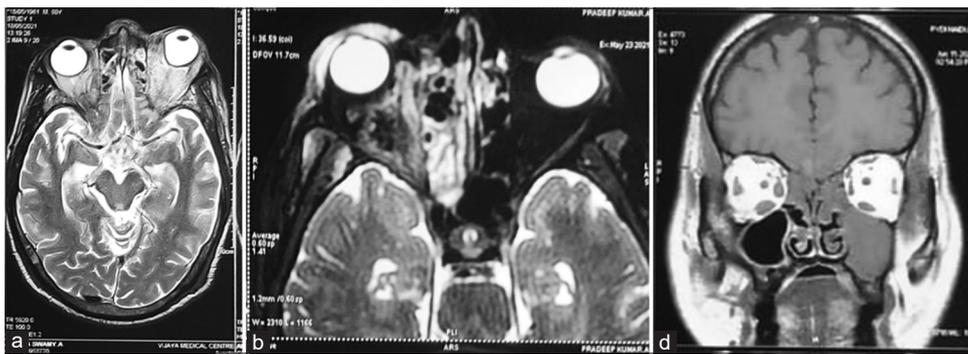


Fig. 2: (a) Contrast-enhanced magnetic resonance imaging (CE MRI) axial section showing tenting of the globe, (b) CE MRI axial section showing hypointense collection in myofascial space, and (c) MRI coronal section showing bulky right and inferior recti muscles

Table 1: Presenting signs and symptoms of rhino-orbital-cerebral mucormycosis (n=258) and their frequency of occurrence

Symptoms	n
Headache	250
Nasal obstruction	193
Facial swelling	134
Black/bloodstained nasal discharge	12
Hemifacial pain	90
Proptosis	51
Ptosis	78
Total ophthalmoplegia	25
Dental pain	13
Loosening of teeth	11

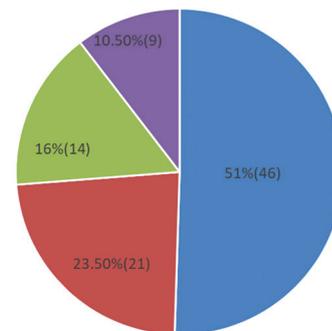
Table 2: ROCM staging

Stage of disease	n (258)	n (%)
Stage 1	0	0
Stage 2	128	50
Stage 3	90	35
Stage 4	40	15

Table 3: Occurrence of mucormycosis in diabetics and other comorbidities

Comorbidities	n=90	%
Known diabetic	67	75
Newly diagnosed	14	15
Other comorbidities	6	6
No risk factors	3	4

occurrence of mucormycosis with corticosteroid usage



■ oral steroids ■ I/V Methyl prednisolone ■ I/V Dexamethasone ■ no corticosteroids

diabetic, 47 (18%) were newly diagnosed, 5 (2%) were with other comorbidities, and 5 (2%) were with no risk factors. Among these 258 patients, 115 (46%) patients had usage of oral corticosteroids, 56 (22%) patients had used I/V methylprednisolone, 60 (21%) patients used I/V dexamethasone, and 27 (11%) patients were with no usage of corticosteroids. The presenting symptoms with frequency of

occurrence is given in table 1, the patients with ROCM staging in table 2, the occurrence of mucormycosis in patients with comorbidities in table 3, the interventions done in patients with mucormycosis in table 4.

Proposed Staging of Rhino-Orbito-Cerebral Mucormycosis (ROCM)				
Staging of Rhino-Orbito-Cerebral Mucormycosis	Symptoms	Signs	Primary Assessment	Confirmation of Diagnosis
Stage 1: Involvement of the nasal mucosa 1a: Limited to the middle turbinate 1b: Involvement of the inferior turbinate or ostium of the nasolacrimal duct 1c: Involvement of the nasal septum 1d: Bilateral nasal mucosal involvement	Nasal stuffiness, nasal discharge, foul smell, epistaxis	Foul-smelling sticky mucoid or black-tinged, or granular or haemorrhagic nasal discharge, nasal mucosal inflammation, erythema, violaceous or blue discoloration, pale ulcer, anaesthesia, ischemia, eschar	Diagnostic nasal endoscopy, Contrast-enhanced MRI (preferred) or CT-scan	Deep nasal swab or endoscopy-guided nasal swab or nasal mucosal biopsy for direct microscopy, culture and molecular diagnostics; nasal mucosal biopsy for rapid histopathology with special stains
Stage 2: Involvement of paranasal sinuses 2a: One sinus 2b: Two ipsilateral sinuses 2c: > Two ipsilateral sinuses and/or palate/oral cavity 2d: Bilateral paranasal sinus involvement or involvement of the zygoma or mandible	Symptoms in Stage 1 + facial pain, facial edema, dental pain, systemic symptoms (malaise, fever)	Signs in Stage 1 + unilateral or bilateral, localized or diffuse facial edema, edema localized over the sinuses, localized sinus tenderness	Diagnostic nasal endoscopy, Contrast-enhanced MRI (preferred) or CT-scan	Same as Stage 1 + sinus biopsy for direct microscopy, culture and molecular diagnostics and rapid histopathology
Stage 3: Involvement of the orbit 3a: Nasolacrimal duct, medial orbit, vision unaffected 3b: Diffuse orbital involvement (>1 quadrant or >2 structures), vision unaffected 3c: Central retinal artery or ophthalmic artery occlusion or superior ophthalmic vein thrombosis; involvement of the superior orbital fissure, inferior orbital fissure, orbital apex, loss of vision 3d: Bilateral orbital involvement	Symptoms in Stage 1 and 2 + pain in the eye, proptosis, ptosis, diplopia, loss of vision, infraorbital and facial V1 V2 nerve anesthesia	Signs in Stage 1 and 2 + conjunctival chemosis, isolated ocular motility restriction, ptosis, proptosis, infraorbital nerve anesthesia, central retinal artery occlusion, features of ophthalmic artery occlusion and superior ophthalmic vein thrombosis. V1 and V2 nerve anesthesia, and features of III, IV and VI nerve palsy indicating orbital apex/superior orbital fissure involvement.	Diagnostic nasal endoscopy, Contrast-enhanced MRI (preferred) or CT-scan	Same as Stage 2 + orbital biopsy if indicated and if feasible (if the disease is predominantly orbital) for direct microscopy, culture and molecular diagnostics and rapid histopathology
Stage 4: Involvement of the CNS 4a: Focal or partial cavernous sinus involvement and/or involvement of the cribriform plate 4b: Diffuse cavernous sinus involvement and/or cavernous sinus thrombosis 4c: Involvement beyond the cavernous sinus, involvement of the skull base, internal carotid artery occlusion, brain infarction 4d: Multifocal or diffuse CNS disease	Symptoms in Stage 1 to 3 + bilateral proptosis, paralysis, altered consciousness, focal seizures	Signs in Stage 1-3 (some features overlap with Stage 3) + V1 and V2 nerve anesthesia, ptosis, and features of III, IV and VI nerve palsy indicate cavernous sinus involvement. Bilaterality of these signs with contralateral orbital edema with no clinico-radiological evidence of paranasal sinus or orbital involvement on the contralateral side indicate cavernous sinus thrombosis. Hemiparesis, altered consciousness and focal seizures indicate brain invasion and infarction.	Diagnostic endoscopy, Contrast-enhanced CT Scan, MRI (preferred)	Same as Stage 3

Fig. 3: Proposed staging of rhino-orbito-cerebral mucormycosis with clinical symptoms and signs evaluation and diagnosis

Among 258 cases, 90 patients (35%) were presented with ophthalmic complaints. In those 90 patients, 65 (72%) were male and 25 (28%) were female, 6 (7%) patients were 30–40 years of age, 20 (23%) were 41–50 years of age, 27 (30%) were 51–60 years of age, and 36 (40%) were >60 years of age. Most commonly right eye was involved 64 (75%) and left side of 21 (24%) patients, 5 (1%) bilaterally involved.

Interventions

There are patients who received >1 procedure at the same time or later depending on severity and location of the disease.

DISCUSSION

Mucormycosis has been known to be associated with immune compromised individuals [7] such as uncontrolled diabetes mellitus

[5], iron overload, major trauma, prolong eduse of corticosteroids [4], and IV drug abuse. The vulnerability of COVID-19 patients to mucormycosis has been attributed to presence of diabetes and use of immunosuppressive therapy. In our study, we found that males with 40–60 years of age group are more affected with orbital mucormycosis in post-COVID period with 30–40 days interval between being COVID-19 positive and onset of mucormycosis symptoms.

According to Aurora *et al.* [1], the median age of affliction of CA-ROCM patients has been reported as 44.5, 51.9, 52, and 55 years with male predilection of 60%, 71%, 66%, and 79%, respectively. 5–7, 15.89% of patients have history of corticosteroid usage during COVID-19 treatment period and 96% are with history of known diabetes and newly diagnosed, 2% with other comorbidities in their study.

Table 4: Interventions

Interventions done	N
Endoscopic sinus debridement	216
Endoscopic sinus debridement with orbital decompression	23
Retro orbital amphoterecin B	21
Orbital exenteration	17
Neurosurgical interventions	19
Total or partial maxillectomy	28
Conservative	15
Death	30

In a multicentric Indian study [2], comprising of 2826 COVID-19 associated-ROCM patients from both waves, 2194 cases were diabetic.

In another retrospective Indian study [3], on COVID-19 associated-ROCM exclusively during the second wave, from April 01, 2021, to June 01, 2021, out of the 70 cases, 49 cases were diabetic.

In our study, ptosis is most common ocular sign which has similarities with other study which was done by Aurora *et al.* In our study, 17 patients did not show any response to medical treatment and hence required orbital exenteration.

CONCLUSION

COVID-19 infection in the presence of glycemic dysregulation predisposes to development of ROCM. Strict glycemic control and judicious use of corticosteroids might help in decrease incidence of mucormycosis cases. Most of the patients presents with ENT-related symptoms if not treated early may spread to orbit and intracranial sites. Early treatment during early presentation might help prevent spreading orbital extension and intracranial extension.

AUTHORS CONTRIBUTION

Vejendla Bhavya Sri Sai, Postgraduate in department of Ophthalmology, Government Regional Eye Hospital, Visakhapatnam, advised the patients who are diagnosed with mucormycosis to undergo the investigations that are required for the study and collecting the information of reports, analyzing them, thereby framing the final outcome of the study, along with the other authors.

Kattoju Padmavathi, Assistant professor in Department of Ophthalmology, Government Regional Eye Hospital, Visakhapatnam, aided in diagnosis of patients with mucormycosis and compiling the reports of the patients thereby achieving the final outcome of the study.

CONFLICTS OF INTERESTS

The authors declared no conflicts of interest.

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