Original Article

Estimation of the pattern of ocular manifestations, risk factors, and imaging of rhino-orbital-cerebral mucormycosis in COVID-19 patients

Rajwinder Kaur[1], Grace Budhiraja[2], Upasana Bhumbla[3], Manjot Kaur[4], Vandana Sharma[1], Priyanka Gupta[1], Ritesh Singla[1], Akashdeep Goel[1], Ekta Gupta[1], Priyanka Dahiya[1]

[1]Department of Ophthalmology, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India, [2]Department of ENT, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India, [3]Department of Microbiology, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India, [4]Department of Radiodiagnosis, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India

Abstract

Purpose: To estimate the pattern of ocular manifestations, as observed clinically and radiologically, and associated risk factors in cases of coronavirus disease 2019 (COVID-19)-related rhino-orbital cerebral mucormycosis (ROCM) during the second wave at presentation to the hospital in northern India. **Materials and Methods:** A total of 35 patients of ROCM associated with active cases of COVID-19 or recovered cases of COVID-19 presenting to the Ophthalmology outpatient department or admitted in the COVID ward of the hospital with clinical features suggestive of ROCM. They were confirmed as mucormycosis on KOH and fungal cultures of nasal scrapings and histopathology of debrided tissue. This is an ambispective study with retrospective medical records review for COVID-19 analysis and prospective assessment of ROCM-associated COVID-19 during the second outbreak of the COVID-19 pandemic. **Results:** The total patients included were 35, which ranged in the age group of 52.91+/- 11.93 years, and the male-to-female ratio was 24:11. The duration between the first positive COVID report and onset of COVID-19-associated ROCM was 9.46+/-11.63 days. The majority (82.9%; n-29) either were diabetics or had high blood glucose levels during the recent COVID-19 infection. 45.7% of patients gave a history of steroid therapy. The most common ocular clinical features were ptosis (80%) and loss of vision 48.7%, respectively. There was diffuse involvement of sinuses in 18 cases (51.4%). Staging based on magnetic resonance imaging scans showed that 7 (20%) had stage II, 20 (57.1%) had stage III, and 28.7% had stage IV disease. Ten patients had varied intracranial extension ranging from meningitis and cavernous sinus thrombophlebitis/thrombosis to brain abscess. **Conclusions:** COVID-associated ROCM was very rapidly spreading and more destructive. Ptosis and loss of vision related to third nerve involvement and CRAO, respectively, were alarming signs and bad prognostic indicators to the patient. Intracranial involvement and CRAO were poor prognostic features in this type of mucormycosis.

Keywords: COVID-19, manifestation, ocular, rhino-orbital cerebral mycosis

Address for correspondence: Dr. Rajwinder Kaur, Department of Ophthalmology, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India.
E-mail: rajujerry26@gmail.com

Received: 05-07-2024 **Revised:** 12-08-2024
Accepted: 26-08-2024 **Published:** 13-01-2025

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_1161_24

Introduction

It was a real challenge to the healthcare system of India to manage the tsunami of the second wave of coronavirus disease 2019 (COVID-19) pandemic in 2021. India found itself

How to cite this article: Kaur R, Budhiraja G, Bhumbla U, Kaur M, Sharma V, Gupta P, *et al*. Estimation of the pattern of ocular manifestations, risk factors, and imaging of rhino-orbital-cerebral mucormycosis in COVID-19 patients. J Family Med Prim Care 2025;14:259-67.

derelict with acute dearth of antifungal drugs, amphotericin B injection, ventilators, and oxygen cylinders. The country was struggling to control COVID-19-associated morbidity and was caught unaware by public health emergency of mucormycosis, commonly labeled as 'black fungus,' a rare but potentially lethal fungal infection. Mucormycosis is caused by the mucoromycetes, a class of moulds, in which Rhizopus and Mucor are the most common species.[1] However, this upsurge of mucormycosis coinfections in both active and recovering COVID-19 cases was a matter of concern worldwide. The main reason of this surge was an ideal environment provided to mucor by low immunity, hypoxia, hyperglycemia, nonjudicious use of steroids, metabolic acidosis, diabetic ketoacidosis, hematological malignancies, bone marrow/solid organ transplantation, state of iron overload, and immunosuppression secondary to disease/drugs. Uncontrolled diabetes is considered a significantly critical risk factor.[2,3]

Rhino-orbital cerebral mucormycosis (ROCM) is a fulminant opportunistic fungal infection in which the olfactory system and brain get infection with aerosolized spores from the Mucorales genus of fungus, which mainly includes Rhizopus, Mucor Apophysomyces, Lichtheimia, and rarely Cunninghamella. The spores first invade the nasal cavity, causing local tissue necrosis and often leading to mild symptoms such as nasal stuffiness and blood-stained nasal discharge, and sequentially spread to other sinuses, primarily maxillary and ethmoidal sinuses, both orbits, the cavernous sinuses, the meninges, and ultimately the brain, being angioinvasive in nature.[4] ROCM has an overall survival rate of only 60%.[5] Therefore, adequate and timely intervention is the most important factor in the management of this dreadful disease. Management of ROCM is typically a combined teamwork by multidisciplinary departments, mainly otolaryngologists, ophthalmologists, endocrinologists, infectious disease specialists, maxillofacial surgeons, neurologists, and radiologists. Hence, High index of suspicionalong with radiological investigations such as computed tomography (CT) and magnetic resonance imaging (MRI) play a fundamental role in determining the extent of the disease spread and planning the surgical management.

A preliminary study was thus designed to document the clinical and radiological features along with laboratory confirmation in this disease. It was created in such a way so as to gain an insight into early diagnosis of COVID-19-associated mucormycosis (CA-ROCM), with an effort to save the vision and life of the patient. This ambispective observational study was undertaken with the aim to estimate the pattern of ocular manifestations and imaging of ROCM in COVID-19 patients.

Materials and Methods

This was an ambispective study with retrospective medical records review for COVID-19 analysis and prospective assessments of ROCM-associated with COVID-19 during the second outbreak of the COVID-19 pandemic, which was conducted among patients presenting to our hospital. All the patients with ROCM managed or comanaged between April 1, 2021 to September 30, 2021 were included. The study was conducted in the Department of Ophthalmology, Otorhinolaryngology and Radiodiagnosis and Lab Medicine after the approval of Research and Ethics Committee.

Inclusion criteria: Active cases of COVID-19 or recovered cases of COVID-19 presenting to Ophthalmology OPD or admitted in the COVID ward of the hospital with clinical features suggestive of ROCM with a confirmed diagnosis of a mucormycosis on KOH and fungal cultures of nasal scrapings and histopathology of debrided tissue were included in the study. Figure 1 Spectrum of microbiological investigations

Exclusion criteria: Patients with clinical and radiological findings suspected of ROCM or acute sinusitis/cellulitis with no history of COVID infection and subjects proven to be negative for mucormycosis on KOH and fungal culture of nasal scrapings and histopathology of debrided tissue were excluded.

Proven ROCM was defined as clinical-radiological features along with microbiological confirmation on direct microscopy and culture with special stain or molecular diagnostics. Sen M[6] proposed a staging system based on clinico-radiological findings and results of nasal endoscopy to determine the extent and severity of ROCM. It divides ROCM in four stages: Stage I (disease limited to nasal mucosa), Stage II (involving paranasal sinuses), Stage III (involving the orbit), and Stage IV (CNS involvement). (3a): Nasolacrimal duct, medial orbit, and vision

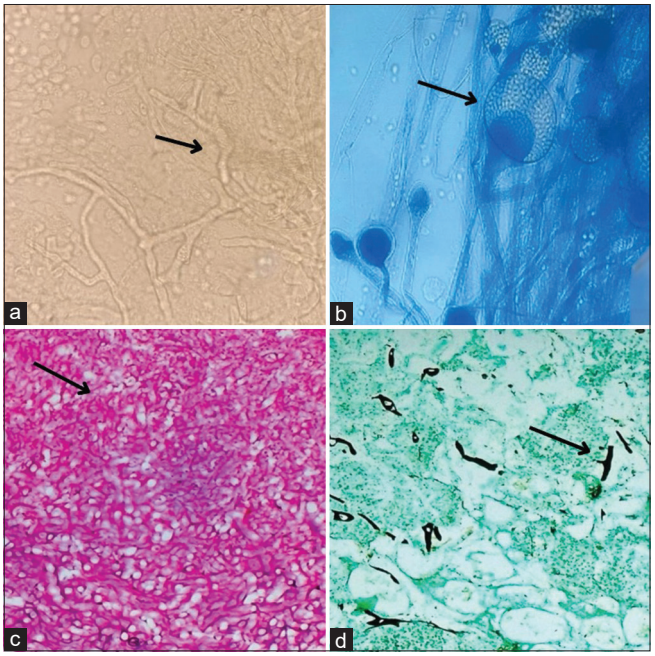

Figure 1: Spectrum of microbiological investigations: (a) KOH-broad aseptate hyphae (shown with black arrow); (b) Lactophenol cotton blue stain shows columella plus broad sporangiophore (shown with black arrow); (c) Hematoxylin and eosin stain shows broad septate hyphae (shown with black arrow), and (d) GMS stain shows broad hyphae (shown with black arrow)

unaffected. (3b): Diffuse orbital involvement (>1 quadrant or >2 structures), vision unaffected. (3c): Cental retinal artery or ophthalmic artery occlusion or involvement of superior ophthalmic vein thrombosis; superior orbital fissure, inferior orbital fissure, orbital apex, and loss of vision. (3d) Bilateral orbital involvement.

A detailed data collection sheet was formulated for complete information from the hospital records, which included demographic profiles, date of onset of symptoms, clinical features, associated comorbidities, treatment received for COVID-19, nasal endoscopy findings, microbiological, pathological and radiological details, and management for ROCM. We also analyzed the records of computed tomography scans/MRI of the brain, paranasal sinuses (PNSs), and orbit findings.

Results

Demographic data and risk factor data are shown in Table 1. In the present study, 35 patients were included; 24 were male and 11 were female. The age ranged from 52.91+/- 11.93 years, and the male-to-female ratio was 24:11. The duration between the first positive COVID report and onset of COVID-associated ROCM (CA-ROCM) was 9.46+/-11.63 days. Thirteen patients were under home care, 18 patients were hospitalized, and four patients gave history of recent fever. History of treatment of COVID was present in 31 (88.57%). History of steroid use was present in 16 patients (45.7%). The mean duration of treatment (steroid) in days was 11.25 days. The majority of the patients (82.9%) either were diabetics (DM) or developed uncontrolled blood glucose levels during the recent COVID-19 infection. Other comorbidities found were asthma (n-5), HCV (n-4), HBsAg (n-1), and hypertension (HTN) in three patients. RT-PCR for Covid -19 was positive in 17 patients (48.6%) and negative in 18 (51.4%). The mean days of onset of mucormycosis was 8.75 days.

Pattern of clinical presentation: Clinically, it was noted that unilateral involvement was more common; the right orbit was involved in 17 cases (48%) and the left orbit was involved in 14 cases (40%), while bilateral orbital involvement was present in one case. Primary symptoms were nasal block (n-9), nasal discharge (n-8;), orbital and facial pain (n-19), orbital/facial edema (n-18), facial discoloration (n-2), diplopia (n-10), proptosis (n-16), and loss of vision (n-18). Primary signs were nasal ulcer/eschar (n-13), nasal discharge (n-7, periocular/facial edema (n-18), periocular/facial discoloration (n-2), periocular hypoesthesia (n-9), ptosis (n-16), diplopia (n-4), proptosis (n-16), and loss of vision (n-18). Light perception was negative in 18 (51.4%); and vision was better than 20/100 in 17 patients (48%). Among the 18 patients with vision loss, the cause was found to be unilateral central retinal artery occlusion in 16 patients and optic nerve compression in one patient. Exposure keratitis was present in one case due to seventh nerve involvement. There was complete ophthalmoplegia in 17 patients (37.1%) secondary to orbital apex syndrome. Axial proptosis was seen in the majority of the patients. Figure 1 shows the common ocular spectrum of presentation to the hospital. Figure 2 shows the spectrum of clinical presentation.

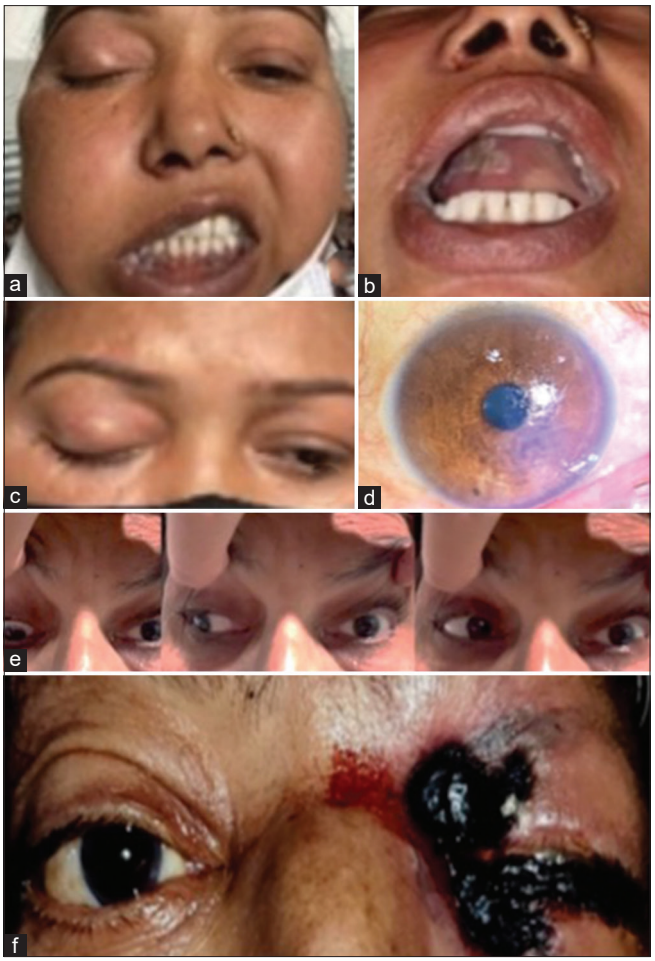

Figure 2: Spectrum of clinical presentation: (a) Bilateral severe ptosis (RE > LE) with facial edema, (b) palatal eschar, (c) complete ptosis of the right upper lid, (d) young male with corneal involvement, (e) bilateral complete ophthalmoplegia, and (f) cutaneous involvement affecting left eye upper and lower lids including medial canthus

Pattern of Imaging features: We recorded that involvement of right-sided sinuses (n-13; 37.1%) was more than left (n-10; 28.6%). Bilateral sinuses were involved in ten patients (28.57%). Diffuse involvement of sinuses was seen in 16 patients (45%) and maxillary sinus involvement in 19 patients (54.3%), followed by ethmoid sinuses. Ten patients (28.57%) developed intracranial involvement in the form of partial (n-1) or complete cavernous sinus thrombosis (n-2) and thrombosis of the internal carotid artery (n-6); intracerebral abscess was found in four cases in the anteromedial part of the temporal lobe, acute infarct in two cases in the bilateral basi-frontal region, and superior ophthalmic vein thrombosis was seen in one case.

All ten patients with intracranial involvement with PL negative vision in the involved eye underwent orbital exenteration. Twenty-five patients (71.4%) did not have any intracranial involvement, but a few of them showed early signs of ROCM on

Table 1: Demographic data, risk factors, clinical presentation, and radiological presentation

	Frequency	Percentage
Gender		
M	24	68.6%
F	11	31.4%
History of Diabetes		
Yes	29	82.9%
No	6	17.1
Maximum severity of covid during the course of treatment		
Home care, ambulatory	11	31.4%
Home care, needed assistance	2	5.7%
Hosptialized, no oxygen	3	8.6%
Hospitalized, oxygen - mask/prongs	11	31.4%
Hospitalized, oxygen - on-invasive	2	5.7%
Hosptialized, ventilator	2	5.7%
No covid (Undiagnosed fever)	4	11.4%
TREATMENT OF COVID		
Yes	23	65.7%
No	12	34.3%
Route of admnistration of steroids		
IVMP	7	20%
Dexamethasone	6	17.1%
Hydrocortisone	3	8.6%
None	19	54.3%
Duration of treatment (steroid) in days		
5	0	Mean-11.25
5-10	12	
11-15	4	
>15	29	
Comorbidities		
Asthma	5	14.7%
HCV+	4	5.7%
HBsAg+	1	2.9%
Hypertension	3	8.6%
RTPCR		
Positive	17	48.6%
Negative	18	51.4%
Days of onset of mucormycosis		
<5	16	Mean-8.75
6-10	5	
11-15	6	
>16	8	
Ophthalmoplegia		
Partial III	8	22.9%
Complete III	3	8.6%
VI	0	0%
III + VI	4	11.4%
III + IV + VI	15	37.1%
NO	7	20%
Other cranial nerve involvement		
Trigeminal	15	42.9%
Facial	1	2.9%
Both	2	5.7%
No	13	37.14%
Proptosis		
Axial	15	42.9%
Abaxial	1	2.9%
No	19	54.3%
Vision		
PL negative	17	48.6%
<20/200	0	0%
>20/100	17	48.6%

Contd...

Table 1: Contd...

	Frequency	Percentage
Cause of Vision Loss in PL negative		
Normal vision	16	45.7%
CRAO	16	45.7%
ON compression	1	2.9%
Exposure Keratopathy	1	2.9%
Primary management		
IV Amphoteracin -B	9	51.4%
Oral Posconazole	35	100%
Only FESS	6	17.1%
FESS + Exentration	18	51.4%
FESS + maxillectomy	4	8.5%
TRAMB	7	20%
Final outcome		
Alive with regression	17	48.6%
Alive with stable residual	7	20%%
Alive with progression	4	11.4%
Dead	4	11,4%
Confirmation on radiology and extent of involvement		
Nose only	0	0
Nose + PNS	8	22.8%
Nose + PNS + ORBIT	17	48.6%
Nose + PNS + ORBIT + CST	3	8.5%
Nose + PNS + ORBIT + CST + Brain	7	20%
Laterality of PNS		
Right	13	37.1%
Left	10	28.6%
Bilateral	12	34.3%
PNS involvement depending on predominant location		
Ethmoid	12	34.3%
Maxillary	14	40%
Sphenoid	9	25.7%
Diffuse	13	37.14%
Laterality of orbit		
Right	17	48.6%
Left	14	40%
Bilateral	1	2.9%
No involvement	3	8.6%
Orbital involvement predominant location		
Medial orbit	12	34.3%
Superior wall	0	0
Inferior wall	5	14.2%
Apex	10	28.5%
Diffuse	8	22.8%
None	0	0
Laterality of CNS		
Right	3	8.5%
Left	5	14.3%
Bilateral	2	5.7%
No involvement	25	71.4%
CNS involvement depending on predominant location		
Partial CST	1	2.9%
Complete CST	2	2.9%
ICA thrombosis/Infarction	6	17.1%
Abscess	4	11.1%
Temporal lobe infarct	2	2.9%
Skull base-basifrontal	2	2.9%
Diffuse	1	2.9%
No CNS involvement	25	71.4%

Contd...

Table 1: Contd...

	Frequency	Percentage
Stage of ROCM at diagnosis[6]		
2C	2	5.7%
2D	5	14.3%
3A	4	11.1%
3B	2	5.7%
3C	16	45.7%
3D	1	2.9%
4A	1	2.9%
4B	1	2.9%
4C	4	11.1%
4D	4	11.9%

CE-MRI, which were later planned for maxillectomy along with orbital exenteration. The typical pattern of "*guitar pick sign*", that is, posterior globe tenting, was seen in one case. The signal intensities on T1- and T2-weighted MR showed heterogeneous or hypotense signals along with enhancing and nonenhancing areas on contrast imaging. The signs of early orbital infection are retro-orbital fat stranding and edema of extraocular muscle (best seen in saturated T1W sequence). The optic nerve thickening and perineural enhancement with high signal intensity on diffusion-weighted imaging are indicative of optic nerve invasion. Isolated optic nerve involvement is suggestive of spread of infection through branches of the ophthalmic artery and is an indication for early exenteration. Figure 3 shows the spectrum of imaging.

Sinus surgery along with maxillectomy with exenteration of the globe was done in 18 cases (51.4%), and sinus debridement with maxillectomy was done in the rest of the cases along with amphotericin wash. Transcutaneous Amphotericin B (TRAMB) was given in seven cases with minimal orbital involvement (20%). In our study, 18 patients had ophthalmoplegia associated with complete loss of vision and negative perception of light. All these patients were immunocompromised, were suffering from diabetes mellitus, presented late in our center, and underwent exenteration in initial stage or at a later stage. Four patients died; these were among those with cerebral involvement.

Discussion

Mucormycosis is more common in developing countries like India with a prevalence of 0.14 per 1000 population.[3] The prevalence of mucormycosis among hospitalized COVID-19 patients was doubled at 0.27% in comparison with previous year. The mean age of patients was 52.91+/- 11.93 years, with a preponderance of men, which comprised 68.6% of the study subjects. This has been consistent with prior published series. Males are at a greater risk of developing severe COVID-19 infections due to outdoor exposure to mucor, which is endemic in India.

Risk factors. In developing countries like India, diabetes is the most critical and affirmative risk factor for mucormycosis. It was found in 54% to 75% of patients with mucormycosis.[3] In our cohort, the majority (82.9%) either were diabetics or had developed uncontrolled blood glucose levels during the recent COVID-19 infection. De novo or unchecked diabetic mellitus was the most common culprit for the sudden upsurge of mucor.[3] Various studies reported uncontrolled diabetes as the most common comorbidity (86.7% associated with mucormycosis).[6-11] Prabhakar *et al.*[12] reported 88% of the patients had diabetes at the time of infection. The percentage of patients who required oxygen was 37.4%; it was found closer to that of Prabhakar study (41%). 45.7% gave a history of steroid intake in some form. Immunocompromised state, hematological malignant conditions, uncontrolled diabetes mellitus, and steroid therapy during COVID-19 put these patients at risk for mucormycosis.[6,11,12] History of recent steroid administration, oxygen therapy, and prolonged hospital stay during active COVID-19 were common risk factors in our cohort. A systematic review of cases by Singh *et al.*[13] revealed a history of steroid use in 76.3% of COVID-19-associated mucormycosis cases, though in our cohort, immunocompromised status was found in ten cases. In our study, other comorbidities found were asthma (n-5), HCV (n-4), HBsAg (n-1), and hypertension (HTN) in three patients. In 25 patients (71.4%), lymphopenia (86%) was present It has been shown as the main risk factor, associated with mucormycosis in hematological disorders.[14] Thus, both COVID-19 and its treatment in the form of steroids make patients vulnerable to opportunistic mucor infection.

Imaging

Progressive and rapid intracranial spread of mucormycosis is an emergency to deal with. It forms the cornerstone of early diagnosis and timely management in patients with clinically suspected ROCM cases. In such patients, clinical suspicion with proper knowledge of imaging to detect earliest evidence of ROCM, empirical antifungal therapy can be started even before confirmed diagnosis by microbiology or histopathology, which would thus be a lifesaving decision. Mucormycosis predominantly spreads by direct invasion to the surrounding tissues. It may invade anatomic spaces by bone destruction and by creeping across natural orifices/natural pathways like nasolacrimal ducts, lymphatics, and neurovascular bundles. ROCM spreads through the following pathways: (a) direct spread from ethmoid sinus and maxillary sinus toward the orbit or intracranial compartment; (b) through pterygopalatine fossa where nasal pathology may gain

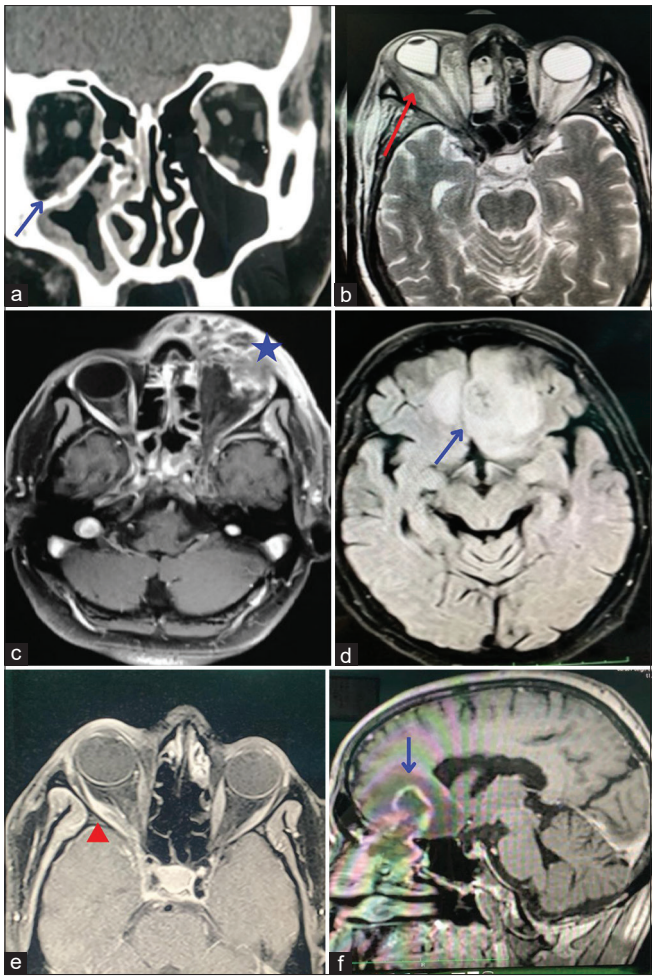

Figure 3: Spectrum of imaging pattern: (a) CT coronal scan shows thickening of right inferior rectus along with fluid and right maxillary sinusitis (shown with blue arrow); (b) T2 MRI orbit axial scan shows right eye proptosis with stretching of optic nerve in right orbit, which in turn deformed the posterior globe into a characteristic "*Guitar Pick*" shape (shown with red arrow); (c) FLAIR axial MRI image showing left eye periorbital and preseptal swelling with proptosis and retroorbital fat stranding (shown with blue star). Image shows T2 hyperintense signals in bilateral sphenoid and ethmoid sinuses; (d) FLAIR axial image showing vasogenic edema in the bilateral frontal lobe with abscess in the left frontal lobe (shown with blue arrow); (e) post-contrast T1 W image showing right orbital proptosis with thickened and hypoenhancing medial and lateral recti muscle (shown with red triangle) and bulky cavernous sinus with narrowing of flow void of right internal carotid artery, suggestive of partial thrombosis; (f) postcontrast T1W sagittal image showing peripherally enhancing abscess with vasogenic edema in the left frontal lobe extending from the left ethmoid sinus (shown with blue arrow)

access into infratemporal fossa and cavernous sinus; (c) through sphenoid sinus, which may spread to cavernous sinus, brain, and skull base; (d) through maxillary sinus infection, which can spread into facial and retro-antral soft tissue and finally may involve nasolacrimal duct; and (e) through the apex of the orbit and cavernous sinus; intraorbital disease gains access to the cranium.

An early characteristic imaging feature of invasive fungal sinus infection on postcontrast T1W images is the absence of enhancement in areas that normally enhance. The angioinvasive nature of the fungus causes microthrombosis and tissue necrosis in the affected regions, resulting in the lack of enhancement of nasal *turbinate* on MR imaging, known as the "*Black Turbinate sign*". The recognition of this sign may play a major role in early diagnosis of ROCM.[15,16]

Paranasal sinus

It usually starts with thickening of the turbinates, followed by paranasal involvement seen radiologically as hypodense mucosal thickening of the sinus mucosa. Various studies have shown involvement of maxillary sinus and ethmoid sinus frequently.[2,6,17-19] This finding coincides with our study, where maxillary sinus and ethmoid sinus were found to be more commonly involved. Foci of erosion along with destruction were seen in the walls of all sinuses in our series, including the maxillary, ethmoidal, frontal, and sphenoidal sinuses. Hard palate was involved in four cases; this was a deciding factor for maxillectomy in such cases. Thus, it is essential to evaluate the bony structures in suspected cases, where CT scan images have an edge over MRI. The modality of choice is contrast-enhanced MRI for better soft tissue resolution and characterization with cross-sectional anatomy and pathology. Contrast administration helps in identifying nonviable necrotic tissue.[20]

Orbit and extension surrounding area: Local spread to masticator space and infratemporal fossa results in facial edema and hypoesthesia. Maximum patients turned up to the department of ophthalmology with alarming signals when they had sudden vision loss (CRAO), ptosis (third nerve involvement), facial pain, facial edema, and ophthalmoplegia. Bilateral involvement, CRAO, total ophthalmoplegia, and CNS involvement were bad prognostic signs. On the basis of clinical and radiological findings, orbital mucormycosis can be divided as mild or limited orbital disease and moderate to severe orbital mucormycosis.

Extension of infection in masticator space and infratemporal fossa was also common in our study, which corelated with studies of Agrawal *et al.*[21] and Yadav *et al.*[22] In these cases, muscles of mastication appear bulky with heterogeneous enhancement. Stranding of intraconal or extraconal fat along with the presence of abnormal T2 hypointense soft tissue was seen with varying degrees of enhancement with or without bulky nonenhancing recti muscles. Medial rectus and inferior rectus muscle were involved most often, as shown by various others studies too.[12,23,24] In our study also, the spread of infection occurred through bony erosion from ethmoid and maxillary sinuses. Orbital apex involvement indicated disease severity and extension of infection into cavernous sinus.

Sino-nasal mucormycosis was treated with systemic liposomal amphotericin B (5 mg/kg/day) in 100 mL of 5% dextrose along with debridement. Rhino-orbital mucormycosis patients were treated with transcutaneous retrobulbar amphotericin-B (TRAMB) (1 mL of 3.5 mg/mL) (n-7) and orbital decompression. In cerebral involvement, neurosurgical

drainage was done in one case. Systemic amphotericin-B or posaconazole was given for 2–8 weeks based on disease severity. Patients with clinical improvement were discharged and advised oral posaconazole 300 mg/day BD on the first day and once a day for 6 weeks. All included patients were followed up for a minimum period of 1 month after discharge. Death occurred in 11.4% (two in stage 4C and two in stage 4) patients.

Orbital exenteration is always associated with oculofacial disfigurement and psychological distress. Although orbital exenteration is a lifesaving procedure, unfortunately, indications for doing exenteration remain unclear.[25] The standard guideline for orbital exenteration in treating ROCM is not available in the literature. Singh VP *et al.*[26-28] suggested that orbital exenteration should be individualized based on retinal artery involvement, aggressiveness of the disease, underlying debilitating diseases, response of antifungal chemotherapy, and visual status.[28] Levinsen *et al.*[29] recommended aggressive orbital exenteration when dealing a case of ROCM with orbital apex syndrome and peribulbar or facial necrosis with or without cranial nerve involvement.

Conclusion

CA-ROCM was much more aggressive in its course where rapid orbital and cerebral involvement was seen with CA-ROCM. Early involvement of extraocular muscles, bilaterality, frozen globe, and vision loss had poor prognosis. A high index of suspicion is necessary to halt this aggressive monster at the earliest. Due to the angioinvasive course, the intraorbital compartment should be thoroughly reviewed even in the absence of bony erosions. The immune system of the patient plays a significant role in combatting mucormycosis with a multispeciality approach. Lymphopenia was another factor favorable to the fungus along with diabetes and the injudicious use of steroids.

Ethics approval and consent to participate

Taken.

Consent for publication

Taken

Availability of data and materials

Yes

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: A clinical and diagnostic perspective from China. Mycopathologia 2020;31:1–8.
2. Joshi AR, Muthe MM, Patankar SH, Athawale A, Achhapalia Y. CT and MRI findings of invasive mucormycosis in the setting of COVID-19: Experience from a single center in India. AJR Am J Roentgenol 2021;217:1431–2.
3. Prakash H, Chakrabarti A. Epidemiology of mucormycosis in India. Microorganisms 2021;9:523.
4. Farmakiotis D, Kontoyiannis DP. Mucormycoses. Infect Dis Clin North Am 2016;30:143–63.
5. Vaughan C, Bartolo A, Vallabh N, Leong SC. A meta-analysis of survival factors in rhino-orbital-cerebral mucormycosis: has anything changed in the past 20 years. Clin Otolaryngol 2018;43:1454–64.
6. Sen M, Honavar SG, Bansal R, Sengupta S, Rao R, Kim U, *et al.* Epidemiology, clinical profile, management, and outcome of COVID-19-associated rhino-orbital-cerebral mucormycosis in 2826 patients in India – Collaborative OPAI-IJO study on mucormycosis in COVID-19 (COSMIC) Report 1. Indian J Ophthalmol 2021;69:1670-92.
7. Yohai RA, Bullock JD, Aziz AA, Markert RJ. Survival factors in rhino-orbital-cerebral mucormycosis: Major review. Surv Ophthalmol 1994;39:3–22.
8. Abdollahi A, Shokohi T, Amirrajab N, Poormosa R. Clinical features, diagnosis, and outcomes of rhino-orbito-cerebral Mucormycosis - A retrospective analysis. Curr Med Mycol 2016;2:15–23.
9. Vaezi A, Moazeni M, Rahimi MT, de Hoog S, Badali H. Mucormycosis in Iran: A systematic review. Mycoses 2016;59:402–15.
10. Prakash H, Ghosh AK, Rudramurthy SM, Singh P, Xess I, Savio J, *et al.* A prospective multicenter study on mucormycosis in India: Epidemiology, diagnosis, and treatment. Med Mycol 2019;57:395–402.
11. Verma V, Sarkar D, Moharana B, Singh P, Noyadu R, Sharma B. Study of rhino-orbital-cerebral mucormycosis and its correlates during COVID-19 pandemic in a tertiary eye care institute of central India. Indian J Ophthalmol 2023;71:3669-76.
12. Prabhakar A, Bansal S, Vyas S, Bhatia V, Kumar A, Patro S, *et al.* Clinicoradiological profile of COVID-19-associated rhino-orbital cerebral mucormycosis with a focus on computed tomography: A clinical case series and review. Am J Trop Med Hyg 2023;109:600-7.
13. Singh A, Singh R, Joshi S, Misra A. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes Metab Syndr 2021;15:102146.
14. Klimko NN, Khostelidi SN, Volkova AG, Popova MO, Bogomolova TS, Zuborovskaya LS, *et al.* Mucormycosis in haematological patients: Case report and results of prospective study in Saint Petersburg, Russia. Mycoses 2014;57(Suppl 3):91–6.
15. Safder S, Carpenter JS, Roberts TD, Bailey N. The "Black Turbinate"sign: An early MR imaging finding of nasal mucormycosis. AJNR Am J Neuroradiol 2010;31:771–4.
16. Taylor AM, Vasan K, Wong EH, Singh N, Smith M, Riffat F, *et al.* Black turbinate sign: MRI finding in acute invasive fungal sinusitis. Otolaryngol Case Rep 2020;17:100222.
17. Sarkar S, Gokhale T, Choudhury SS, Deb AK. COVID-19 and orbital mucormycosis. Indian J Ophthalmol 2021;69:1002-4.
18. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. Cureus 2020;12:e10726. doi: 10.7759/cureus.10726.
19. John TM, Jacob CN, Kontoyiannis DP. When uncontrolled

diabetes mellitus and severe COVID-19 converge: The perfect storm for mucormycosis. J Fungi (Basel) 2021;7:298.

20. Sreshta K, Dave TV, Varma DR, Nair AG, Bothra N, Naik MN, *et al.* Magnetic resonance imaging in rhino-orbital-cerebral mucormycosis. Indian J Ophthalmol 2021;69:1915-27.
21. Agrawal A, Dixit Y, Yonati V, Nigam P, Kheti P. Imaging of COVID-19-associated rhino-orbital-cerebral mucormycosis: Imaging analysis of 120 patients. Egypt J Otolaryngol 2022;38:154.
22. Yadav T, Tiwari S, Gupta A, Garg PK, Khera PS, Rajagopal R, *et al.* Magnetic resonance imaging in coronavirus disease-2019 associated rhino-orbital-cerebral mucormycosis (CA-ROCM)-imaging analysis of 50 consecutive patients. Curr Probl Diagn Radiol 2022;51:112–20.
23. Dubey S, Mukherjee D, Sarkar P, Mukhopadhyay P, Barman D, Bandopadhyay M, *et al.* COVID-19 associated rhino-orbital-cerebral mucormycosis: An observational study from Eastern India, with special emphasis on neurological spectrum. Diabetes Metab Syndr 2021;15:102267.
24. Honavar SG. Rhino-orbito-cerebral mucormycosis-Guidelines for diagnosis, staging and management. Indian J Ophthalmol 2021;69:1361–5.
25. Plowes Hernández O, Prado Calleros HM, Soberón Marmissolle Daguerre GS, Sadek González A. Rhino orbito-cerebral mucormycosis. Management strategies to avoid or limit intracraneal affection and improve survival. Acta Otolaryngol Esp 2015;66:348–52. English, Spanish.
26. Hargrove RN, Wesley RE, Klippenstein KA, Fleming JC, Haik BG. Indications for orbital exenteration in mucormycosis. Ophthalmic Plast Reconstr Surg 2006;22:286–91.
27. Colon-Acevedo B, Kumar J, Richard MJ, Woodward JA. The role of adjunctive therapies in the management of invasive sinoorbital infection. Ophthalmic Plast Reconstr Surg 2015;31:401–5.
28. Singh VP, Bansal C, Kaintura M. Sinonasal mucormycosis: A to Z. Indian J Otolaryngol Head Neck Surg 2019;71(S3):1962–71.
29. Levinsen M, Kiilgaard JF, Thomsen C, Heegaard S, Nissen KR. Medical and surgical treatment of rhino-orbital-cerebral mucormycosis in a child with leukemia. Am J Ophthalmol Case Rep 2021;22:101092.