

Neurological Manifestations of Post Covid Rhino Orbito Cerebral Mucormycosis – An Institutional Experience

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Received: 22-06-2023 Revised: 11-07-2023 / Accepted: 15-08-2023

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Conflict of interest: Nil

Abstract

Introduction: An epidemic of Mucorales was reported following the second wave of COVID 19 in India, and intracranial extension of the same was one of the most dreadful complications. The present study was done to analyze the demographic data and provide an overview of the diverse clinico-radiological presentations of post covid ROCM.

Materials and Methods: We systematically reviewed 30 patients diagnosed with post covid Rhino orbito cerebral mucormycosis admitted at our hospital during MAY 2021 to JULY 2021. Data pertaining to demographic variables, clinico-radiological features were analysed using percentage of total cases.

Results: A total of 30 patients with rhino orbito cerebral mucormycosis were enrolled in the study. The majority of subjects were males. The most common age group affected was 41-50 years. History of preexisting diabetes mellitus was recorded in 15 (67.35%) patients. Most common presenting symptom was facial pain (77%), followed by drooping of eyelid and proptosis (73%) with 63% of the patients developing double vision. Diminution of vision was seen in 40 % of the patients. Focal deficits were seen in 7 patients. Altered sensorium was seen in 4 of them. Seizures were documented in two patients.

Conclusion: High index of suspicion with thorough knowledge of varied clinico-radiological presentations of rhino orbito cerebral mucormycosis is necessary for prompt initiation of treatment and thereby aiding in reduction of morbidity and mortality.

Keywords: COVID-19, Mucormycosis, Cavernous Sinus Internal Carotid Artery, Brain MRI Mucormycosis.

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Introduction

Mucormycosis denotes an acute or subacute rapidly progressing infections caused by the angioinvasive fungi in the order of Mucorales. The fungus is unique to cause devastating disease in patients with poorly controlled diabetes mellitus and immunocompromised patients and often causes significant morbidity and mortality. The commonest clinical manifestation is rhino-orbital cerebral mucormycosis (ROCM).

The Leading International Fungal Education (LIFE) portal estimates the annual global prevalence of mucormycosis approximately as 10,000 cases when Indian data is not included. When included it becomes 910,000 cases annually.[1] The burden in India is particularly high, and is estimated to be 70 times greater than

the expected global prevalence. Rhinocerebral mucormycosis is initiated with inhalation of spores into the paranasal sinuses and the invasion of blood vessels in the tissue. Involvement of the central nervous system by direct extension from infected paranasal sinuses or hematogenous dissemination from the lungs. Despite advances in imaging and the availability of novel drugs, cerebral mucormycosis continues to be associated with high rates of death and disability.

The rate of progression from sinusitis to invasive disease may be rapid (i.e., within a few days), but is highly variable. Ptosis, painful proptosis, abscess of eyelids, and corneal numbness with edema are signs of extension into the orbit. Evidence of ophthalmoplegia (internal as well as external) with

the latter being partial or complete, afferent pupillary abnormalities, fixed pupils, nystagmus, and a loss of vision secondary to fungal invasion or retinal artery occlusion can occur. Superior orbital fissure syndrome and superior ophthalmic vein thrombosis have been known to occur. A painless orbital apex syndrome has also been well described. Cranial nerve palsies with varying involvement of II, III, IV, V, VI, and VII nerves are common. Cerebral edema may lead to coma, and vascular occlusion (internal carotid artery thrombosis, pseudoaneurysm, in rare cases, carotid cavernous fistula) progresses to cerebral infarcts. Cavernous sinus thrombosis with loss of vision is believed to be a characteristic feature of mucormycosis where cavernous sinus thrombosis without loss of vision is observed in bacterial infections. Invasion of brain parenchyma, leads to cerebritis and abscesses. Hemiparesis, altered consciousness and focal seizures signal brain invasion and infarction. Spread across the clivus to the basal meninges and the basilar artery may lead to thrombosis or rupture with subarachnoid haemorrhage.

A high degree of suspicion is a must and any delay in diagnosis with the subsequent delay in initiation of IV amphotericin can worsen morbidity and mortality. Delay from diagnosis to treatment for more than 6 days is associated with poor survival.[2] The morbidity and mortality in rhino-orbital cerebral mucormycosis is determined by the reversibility of underlying risk factors, the time of initiation of IV Amphotericin and the time of initiation of surgical debridement. A delay in any of the above measures could affect survival.[3,4,5,6] The current survival of patients without brain involvement can be up to 50%-80% but the survival drops to 20% with brain involvement. An epidemic of Mucorales was reported following the second wave of COVID 19 in India, and intracranial extension of the same was one of the most dreadful complications. In this study we took the opportunity to study the varied neurological manifestations of post covid ROCM, which may aid in early recognition and thereby early initiation of treatment.

Materials and Methods

It is a hospital based prospective observational study on cases presenting with ROCM to our tertiary care from May to July 2021. Ethical approval for the study was sought from the institutional Ethics Committee. Informed written consent was taken from patients. Patients aged

more than 18 years with provisional diagnosis of rhino orbito cerebral mucormycosis by mandatory presence of neurological manifestations and radiological findings either computed tomography [CT] scan or magnetic resonance imaging [MRI] with fungal evidence on either KOH mount, culture or histopathological examination of the biopsy samples were included. Confirmed diagnosis of cerebral involvement by any one of the two:

1. CT scan - irregular low-density areas inside the cerebral parenchyma.
2. MRI - low T1-weighted imaging signals and high T2-weighted imaging signals.

While recruiting the subjects, the diagnosis of mucormycosis and its cerebral extension was confirmed, signs and symptoms, microbiological examination, blood investigations, and radiological examinations were recorded. A detailed history, complete ophthalmic, oto-rhino-laryngeal and neurological examination was done at presentation. History of COVID-19, past or concurrent, including diagnostic test for COVID-19 was recorded. History of any comorbid ailments and its treatment was recorded. Imaging studies included magnetic resonance imaging (MRI) or CT scan of orbits, brain, and paranasal sinuses with or without contrast.

Statistical Analysis

The data was analyzed using Microsoft Excel. Data pertaining to demographic variables, clinico-radiological features were analysed using percentage of total cases.

Results

A total of 30 patients with rhino orbito cerebral mucormycosis were enrolled in the study. The majority of subjects were males (n=22; 73%). The age of the subjects ranged from 20 to 60 years. The most common age group affected was 41-50 years (n=12;40%). A previous positive history of COVID-19 was elicited in 25 (83%) of the patients; with confirmed COVID-19 illness in only 20 patients. Two patients were concurrently positive for SARS-CoV-2. History of preexisting diabetes mellitus was recorded in 15 (67.35%) patients. Comorbidities other than diabetes were present in 8 patients and included mainly hypertension. Coronary artery disease was present in three and chronic kidney disease was present in one patient. Table 1 depicts the demographic profile and distribution of various risk factors among all the study patients.

Table 1: Demographic Profile and Risk Factors

	Number (n)	Percentage (%)
Gender - Male	22	73

Female	08	27
Age –		
21-30 yrs	02	7
31-40 yrs	09	30
41-50 yrs	12	40
51-60 yrs	07	23
Comorbidities –		
DM	15	50
HTN	06	20
CKD	01	3
CAD	03	10
Post Covid Status	22	73

Most common presenting symptom was facial pain (77%), followed by drooping of eyelid and proptosis (73%) with 63% of the patients developing double vision. Diminution of vision was seen in 40 % of the patients. Focal deficits were seen in 7 patients. Altered sensorium was seen in 4 of them. Seizures were documented in two patients. Table.2 demonstrates the clinical presentation.

Table 2: Clinical Profile of the patients

Clinical Symptoms	Number (n)	Percentage (%)
Headache	18	60%
Facial pain	23	77%
Ptosis/Proptosis	22	73%
Diminision of vision	12	40%
Double vision	19	63%
Facial numbness	15	50%
Facial weakness	14	47%
Dysarthria	6	20%
Dysphagia	4	13%
Focal weakness	7	23%
Altered sensorium	4	13%
Seizure	3	10%



Figure 1: Bilateral orbital involvement with ptosis and cheek eschar



Figure 2: Left cheek eschar with left orbital involvement

On radiological assessment, 22 (73%) patients demonstrated orbital infiltration with five patients (17%) having bilateral involvement. 8 (27%) developed cavernous sinus infiltration, 6 (20%) cases developed internal carotid artery infiltration, three of them had infarcts and nineteen patients (63%) developed cerebral abscesses.

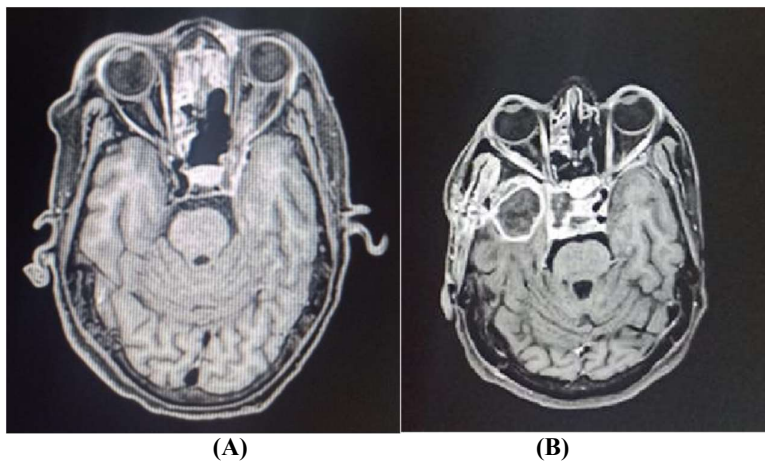


Figure 3:

- A. MRI Brain Axial view showing involvement of left cavernous sinus and causing encasement of left internal carotid artery with mildly reduced caliber of left ICA.
- B. Post contrast MRI Brain Axial section showing right temporal abscess with post contrast enhancement with involvement of right cavernous sinus with mildly reduced caliber of right ICA.

Discussion

The clinical manifestations of mucormycosis are protean ranging from trivial symptoms and signs of local infection pertaining to invasive mucormycosis of various internal organs. The manifestations of rhiniorbital cerebral mucormycosis includes orbital cellulitis (OC) and orbital periostitis (OP), orbital apex syndrome (OAS), superior orbital fissure syndrome (SOFS), cavernous sinus syndrome (CSS) and rhino cerebral mucormycosis (RCM).

Male gender predominance, similar to that reported in other studies is seen in our study also. Twentytwo patients (73%) had a positive

association with SARS-CoV-2 infection, similar to that in the studies done by M. A. Najafi et al.[7], Patel et al.[8] Song et al[9] studied the association between Covid-19 and invasive fungal sinusitis in April 2020, and concluded that a large number of patients affected by or recovered from Covid-19 are at increased risk of developing invasive fungal diseases, and gave a management algorithm for such cases. Diabetes was present in 50% of our patients, comparatively less when compared to the study by S Pandey et al[10] and similar to the study done by Yadav et al.[11] In our study, facial pain was the most common symptom (77%), suggesting that sinus invasion was commonly present in most of them. In a similar study done by Yadav et al

facial pain/ swelling was the most common symptom, while headache being the most common symptom in the study done by Patel et al. Facial pain followed by headache was the most common symptom in the study done by A Sekaran et al.[12] Proptosis/ptosis was present in 73 % of our patients suggesting progressive spread to the orbit. This was in accordance to the proposed staging of ROCM by Honavar.[13]

Diminution of vision was seen in 40% of the patients, similar to that seen in the studies done by Yadav et al, Patel et al, Dubey et al.[14] Acute visual loss is another ominous sign of ROCM.[15] Reduction in visual acuity in cases with mucormycosis is explainable on the basis of infarctions in blood vessels supplying the retina or optic nerve, compression on the nerve along its course within the cavernous sinus, or direct infection and necrosis.[16,17]

Cavernous sinus involvement was seen radiologically in 27% of the patients and among them there is evidence of thrombosis involving the long segment of the left internal carotid artery in 20%. Despite internal carotid artery occlusion, there was clinical or radiological signs of stroke in only 10%. The presence of good collateral blood supply via the circle of willis appears to protect against the occurrence of cerebral ischemia. Cerebral abscess was noticed in 63% of the patients, which is high compared to other studies but was comparable to the study done by Markala et al.[18] Location of the abscess was basifrontal in 10 patients, basitemporal in 7 patients and parietal in 2 patients. Brain parenchyma invasion by deadly fungus was characterized by predominant involvement of frontal and temporal lobe, hypothesized to be due to close proximity which facilitates contiguous invasion of fungus from frontal sinus and cavernous sinus respectively.

Conclusion

High index of suspicion with thorough knowledge of varied clinico-radiological presentations of rhino orbito cerebral mucormycosis is necessary for prompt initiation of treatment.

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