

Imaging of Mucormycosis in COVID 19 patients

Neha Choudhary^{1*}, Vipasha Singh², Sunita³, Hemant Kumar Mishra⁴

¹Junior resident, Department of Radio Diagnosis, Mahatma Gandhi Medical College and Hospital Jaipur, Rajasthan, India

²Assistant professor, Head of Department of Radio Diagnosis, Jhalawar Medical College, Jhalawar, Rajasthan, India

³Junior resident, Department of Radio Diagnosis, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

⁴Professor, Department of Radio Diagnosis, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

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Abstract

Background: Rhino-orbito cerebral mucormycosis (ROCM) is an acute, fulminant, invasive fungal infection caused by saprophytic fungi seen in SARS CoV-2 patients. The objective of this study was to describe the imaging findings in patients with rhino orbital cerebral mucormycosis. **Materials and methods:** Study was done from 12 May 2021 to 5 July 2021. Total 48 patients were taken into the study with positive SARS CoV-2. Magnetic Resonance Imaging (MRI) images were analysed by using descriptive statistics analysis. **Results:** MR imaging of 48 patients showed predominant involvement of the ethmoid (77%) and maxillary (85%) sinuses. Extension to the orbit (35%) and face (43%) skull base (8%) and brain (4%). MRI showed T2 isointense to hypointense soft tissue thickening and heterogeneous post contrast enhancement as the main finding, bone erosion was seen in 35% or with rest of the patients showing extrasinus extension across grossly intact appearing bones on imaging. **Conclusion:** MRI shows a spectrum of findings in rhino orbito cerebral mucormycosis. Imaging plays a major role in assessing the extent of involvement and complications.

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Background

Coronavirus disease-19 is an infectious viral disease, it can be associated with other co-infections. The current second wave of the COVID-19 pandemic in India has seen a rise in the rhino-orbital mucormycosis. Rhino-orbital mucormycosis is an acute, fulminant, lethal opportunistic, invasive fungal infection caused by saprophytic fungi belonging to the genera *Mucor*, *Rhizopus* and *Absidia* that initially infect the paranasal sinuses and may frequently extend into the orbits and cerebral parenchyma. Uncontrolled diabetes mellitus and the extensive use of corticosteroids without proper blood sugar monitoring is also come out as important aggravating factor. Early diagnosis is necessary as medical and surgical intervention can reduce mortality and morbidity. Mucormycosis can be life threatening as it has a high mortality rate of over 50%. When limited involvement of the paranasal sinuses is present, survival rates are between 50% to 80%. However, mortality is greater than 80% when brain invasion has occurred. The clinical features in the early stages are typically with headache, fever, facial pain, nasal obstruction, nasal discharge and crusting. The disease progresses rapidly leading to cranial nerve palsies and features of CNS involvement within a period of a few hours to days.

Material and method

This is hospital based prospective observational study. Institutional ethics committee clearance was obtained prior to this study. We analyzed the clinical features, history of patients, associated comorbidities, location of mucormycosis disease, use of steroids and its outcome in patients with COVID-19 infection. MR PNS and brain imaging including axial, coronal and sagittal T1 weighted (TR/TE 644/6.6 ms), T2-weighted images (TR/TE 4000/80 ms) and fat suppressed post contrast T1 weighted images STIR images (TR/TE 4000/56ms), diffusion weighted images (TR/TE 5800/63 ms), ADC images (TR/TE 5760/63ms) were acquired. MRI imaging was performed using 3 T Siemens machine. Both T1- and T2-weighted images were obtained as well as T1-weighted images after intravenous injection of gadopentetate dimeglumine (0.1 mmol/kg). The MR signal intensity was compared with gray matter on the T1- and T2-weighted images. Gadolinium enhancement was graded from no to marked enhancement.

Observation

MRI provides better evaluation of soft tissue involvement and intracranial, perineural spread, vascular obstruction and skull base invasion but CT is better for bony involvement. Finding of plain T1, T2 and post contrast T1 images were documented. Due to iron and manganese in the fungal elements MRI demonstrates variable signal intensity. On post contrast MRI, the type of contrast enhancement and involvement of any extra sinus structures and fat stranding including orbit, face, pterygopalatine fossa, masticator space, parapharyngeal space, nasopharynx, oropharynx brain and cavernous sinus were noted. Fungal hyphae tend to involve nerves and vessel wall leading to perineural spread and cavernous sinus invasion. Any complications like vascular obstruction involving internal carotid arteries was noted on MRI.

*Correspondence

Dr. Neha Choudhary

Junior resident, Department of Radio Diagnosis, Mahatma Gandhi Medical College and Hospital Jaipur, Rajasthan, India

E-mail: choudharyneha652@gmail.com

Stranding in the retrobulbar fat was seen as orbital cellulitis . Involvement of internal carotid arter(I.C.A.) and cavernous sinus(C.S.) was seen as thickening with presence of abnormal surrounding soft tissue and non enhancement on post contrast scans. Patients with intracranial extension were looked for dural enhancement, presence of extradural collections, cerebritis, intracerebral abscess, and infarcts.

Our study group contained 48 patients out of which 32 were males and 16 females, ages ranging from 11 to 90 years, mean age was 50 years. Majority of patients were from 31 to 70 years in age group. 23 patients (47%) had a history of diabetes mellitus, 18 (37%) patients had a history of steroids used for treatment, 47 (98%) patients were covid 19 positive. The clinical features reported were headache, fever, facial pain, nasal obstruction, nasal discharge and crusting, cranial nerve palsies and features of CNS involvement are in decreasing order.

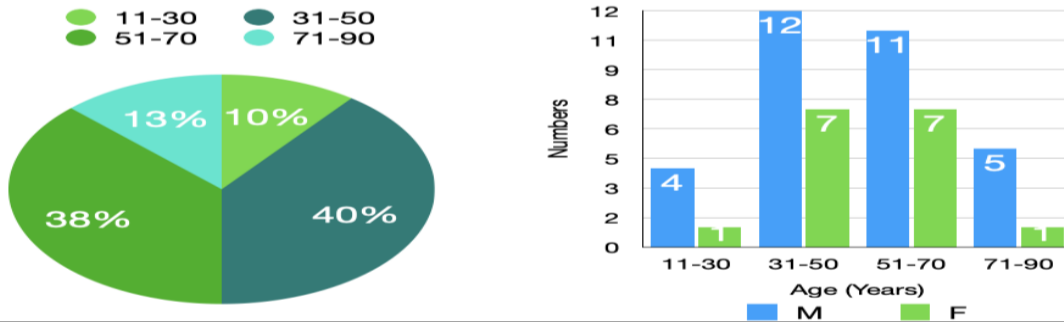


Fig 1: MR imaging features of ROCM

Sinonasal involvement

Normal paranasal sinuses are air-filled structures hypointense on all sequences because they are air-filled structures. The common imaging findings of ROCM are listed in the bar diagram. Opacification of the sinuses by soft tissue is seen in fungal sinusitis. Multiple sinus involvement is seen in most cases of ROCM. MRI imaging shows the contents of the sinuses have varying signal characteristics. The T2W signal intensity is determined by the extent of necrosis leads to hyperintensity and “the presence of iron and manganese (paramagnetic elements) within the fungal hyphae leads to hypointensity”[7]. On post contrast scans, the contents of the sinuses may show a variety of appearances ranging from: variable enhancing and nonenhancing areas, and complete central non enhancement with

or without a thin irregular rim of peripheral enhancement. “The diagnostic feature of post contrast T1W image is heterogeneous enhancement with absence of enhancement in the necrotic region because of thromboembolism in the small vessels and causing necrosis. The imaging pattern described by Taylor AM et al “[16] lesion described as “black turbinate sign” diagnostic of mucormycosis. The maxillary sinus was the most common paranasal sinus involved in our study (85%). In the majority of patients (81%) multiple sinuses were involved. The combination of maxillary, ethmoid and sphenoid was most frequently seen. In a few cases pan sinusitis was also seen (8%). Bilateral sinus involvement was more common than unilateral sinus involvement. Detail of the paranasal sinuses and nasal space involvement is given in bar diagram

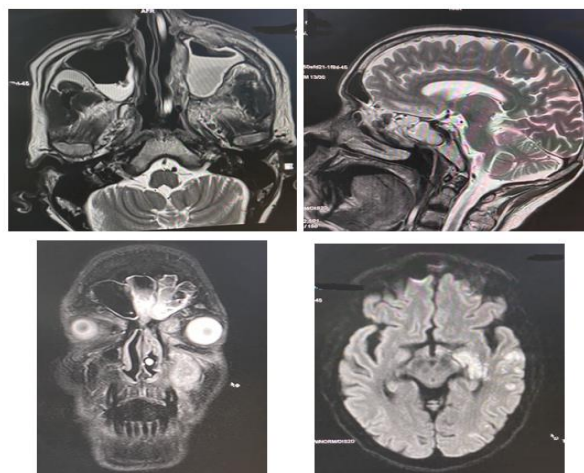
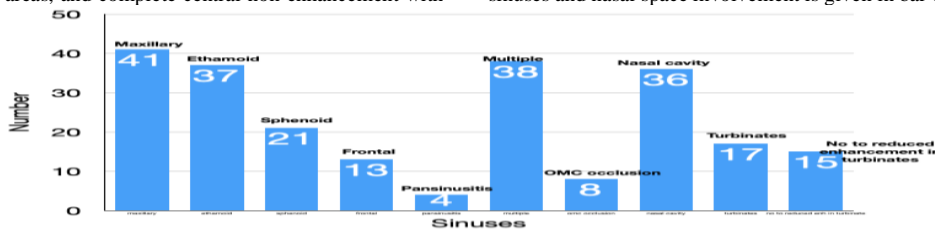


Fig 2:Sinonasal involvement

Case no 8,-T2w axial shows pansinusitis with bony destruction of left maxilla with soft tissue extension, post GD shows cellulitis with optic neuritis,DWI axial sections showing multiple focal acute infarcts in left MCA territories , left watershed zones, internal capsule. On MRI, the lesions were isointense/hypointense and hyperintense on T1W images in all cases. On T2W images rhino orbito cerebral lesions were seen as (a) T2 isointense to mildly hypointense soft tissue lesions in 16 cases (33%) (b) T2 heterogeneous soft tissue lesions in 32 cases (66%)

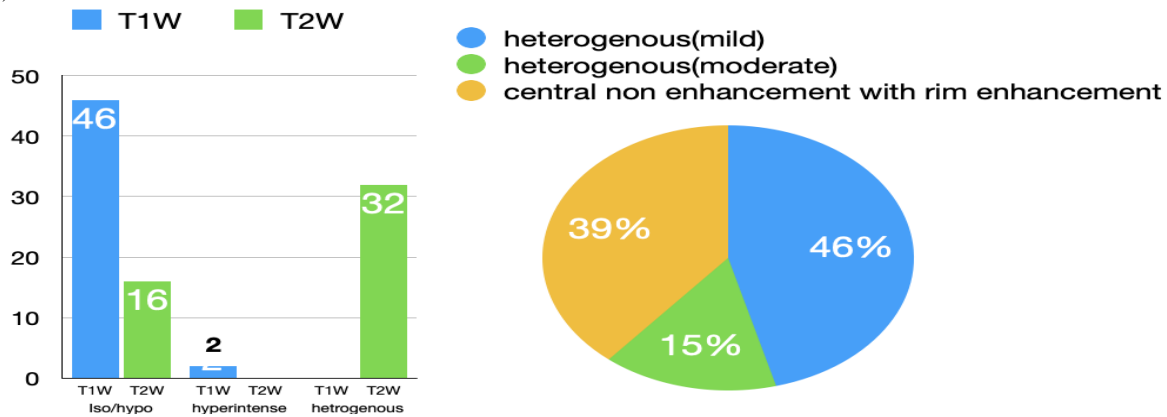


Fig 3: MRI imaging finding

Extra Sinus extension

The most common site of extra sinus involvement was face (43%) and orbit(35%), followed by osseous erosion, pterygopalatine fossa, orbital apex, masticator space,, skull base, cavernous sinus, brain and internal carotid artery. Further details of extrasinus extension including the type of involvement is given in bar diagram

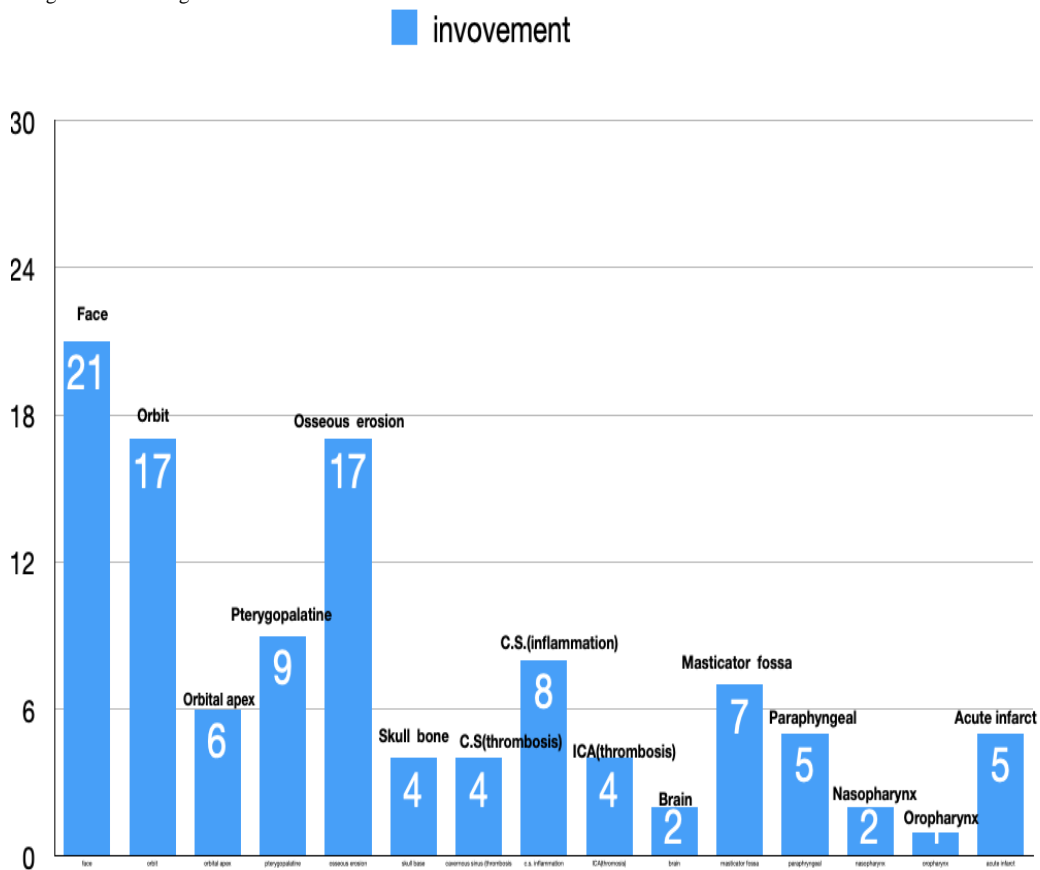
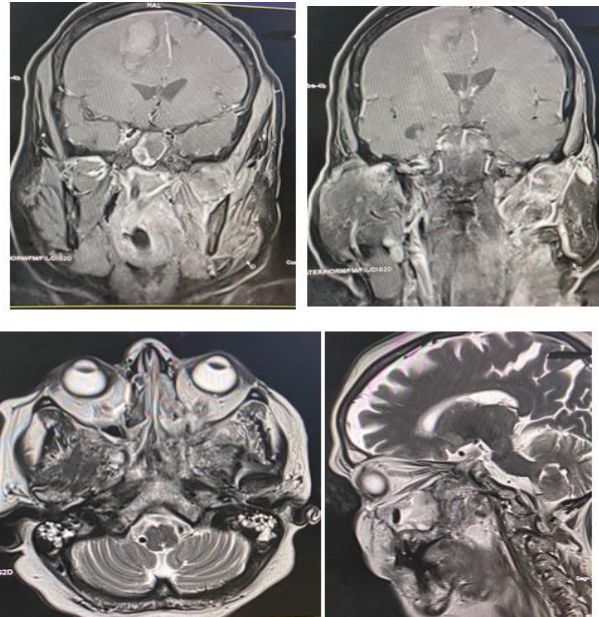
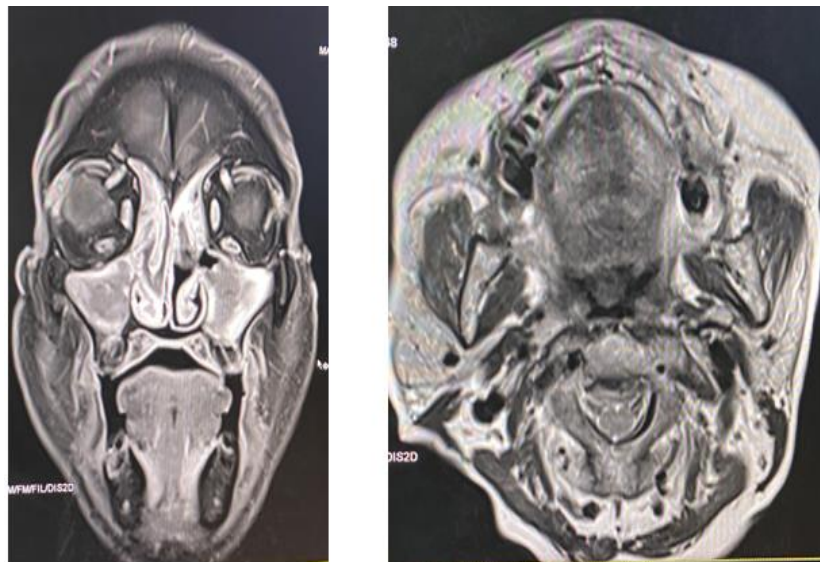


Fig 4: Extra Sinus extension



Case no 30 :- T1w image shows extension of inflammation in bilateral face, left infra temporal space, & involvement of cavernous segment of ICA, hematoma seen in right frontal lobe and edema of optic chiasma.

Case no35 :- T2W image shows involvement of muscles of mastication, nasopharynx oropharynx and palate



Case no 46:- T1W image shows sinusitis, mucosal thickening in bilateral nasal cavities and bilateral osteomeatal complex occlusion

Case no 44:-T2W image shows altered signal intensity within maxillary alveolus and hard palate

Discussion

Mucormycosis is an angiotropic invasive fungal infection having a high tendency to damage the elastic lamina of vessels. It can involve different body organs but the rhinocerebral form is the most common type. The infection is usually after inhalation of the spores of the Phycomycetes fungi, “which is ubiquitous , most commonly belonging to the genera Mucor, Rhizopus and Absidia”[6]. These fungal spores are freely seen in soil, air, skin, body orifices, manure, spoiled food, and dust. The pterygopalatine fossa is believed to be the largest reservoir.

“In immunocompromised patients as well as patients with poorly controlled diabetes mellitus with diabetic ketoacidosis, and irrational use of steroids, these organisms can become pathogenic. Immunocompromised states include organ transplantation,

hematologic malignancies, chronic corticosteroid treatment and haemochromatosis”[6].

“From paranasal sinuses disease spread to orbit by destroying the wall of sinuses and through nasolacrimal duct and to the brain via destroying the superior orbital wall and cribriform plate orbital vessels or orbital apex with involvement of cavernous sinuses and meninges”[3,8,12,15].

Nerve dysfunction and thrombosis are the result of direct invasion. The involvement of blood vessels, bone, cartilage, nerves, perineural areas, and meninges are quite common.

The tissue necrosis at the palate leads to palatine eschars and the nasal turbinates destruction. Erosion of bones by spread of infection from sinuses were seen, which subsequently pierce into the orbital structures, and via a retro-orbital route spreading to the brain.

Infection spreading to the frontal lobes could also happen via the ethmoid sinuses, and to the nearby cavernous sinus results in cranial nerve palsies via sphenoid sinuses. Consequences of this leads to vascular occlusion, extensive thrombosis of the cavernous sinus, jugular veins, carotid artery and infarction, as well as dissemination to the brain parenchyma.

The clinical features are headache, fever, facial pain, nasal obstruction, nasal discharge and crusting, orbital apex syndrome with blurred vision. The disease progresses rapidly leading to cranial nerve palsies and features of CNS involvement within a period of a few hours to days. "In rhino orbito cerebral mucormycosis visual loss is earlier as compare to bacterial cavernous sinus thrombosis which favour the diagnosis of ROCM" [5].

Previous study by Mnif et al. and Herrera et al. shown that the disease causes orbital and aggressive sinonasal changes on imaging." [4,11] and study of Mohindra et al. had shown that vascular complications such as ischemia, thrombosis and invasion of cavernous sinus can detect by MRI" [14]. Appearance of cavernous sinus involvement hypo intense on T1 and T2 with inhomogeneous post contrast enhancement according to Razek and Castillo" [16]

In Our study of 48 mucormycosis patients. Sinonasal involvement was the initial presentation in patients, which later spread to the orbits, face, masticator space, pterygopalatine fossa, hard palate, maxillary alveolus, zygomatic process, Parapharyngeal space, nasopharynx, oropharynx skull base and intracranial extension to involve the cavernous sinus, internal carotid artery and cerebral hemispheres. MRI of the sinuses and orbits showed iso to hypointense and heterogeneous patterns noted, heterogeneous appearance on T2 had been seen in most cases.

Post contrast images showed heterogeneity with variable enhancing and non enhancing areas and complete central non enhancement of the lesion with or without thin irregular rim of peripheral enhancement. Especially, T2W signals or patterns of enhancement are variable and these patterns are not reliable markers for invasive fungal infection. Special attention to often subtle extra-sinus extension in the form of fat stranding and altered fat including orbit, retromaxillary, premaxillary, face, pterygopalatine fossa, masticator space, parapharyngeal space, nasopharynx, oropharynx is more important to suggest the diagnosis of invasive fungal infection on imaging [5,10].

Skull base and bone involvement are usually seen in late or chronic mucormycosis, however some patients with acute disease also show the bone involvement" [9,13]. The affected bones showed erosion, irregular lytic lesions, sclerosis, expansion. Many of the patients in our study showed early bone involvement as destructive bony changes in the acute phase of disease.

Conclusion

Based on our study, imaging of rhino orbito cerebral mucormycosis shows heterogeneous variable T2W signal intensity, different enhancement patterns and involvement of different sinuses, orbit and brain. In our study group patients are likely present in different stages of the disease, showing sinonasal, extensive extra sinus involvement and chiefly patients were immunocompromised and SARS CoV-2 positive patients. MRI is an irreplaceable tool which is complementary in assessing the extension and complications of disease.

There is no area of conflict regarding this study

Conflict of Interest: Nil Source of support: Nil

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