ORIGINAL RESEARCH

Spectrum of MR Imaging Features of Rhino-Orbito- Cerebral Mucormycosis in COVID-19 Patients in Tertiary Care Hospital

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ABSTRACT

Background: Mucormycosis is amongst the most lethal form of zygomycosis occurring in post covid – 19 patients. The disease is seen almost exclusively in immunocompromised patients since normal phagocytic activity in immunocompetent hosts provides an adequate barrier against infection. Several cases of mucormycosis in people with COVID-19 have been reported world – wide, in particular from India. Rhino-orbito-cerebral mucormycosis is a life-threatening infection. The objective of this study was to study the radiological features of Rhino-Orbito-Cerebral Mucormycosis in Contrast Enhanced MRI Brain-Orbit-PNS in COVID-19 patients admitted in tertiary care hospital. **Materials and Methods:** The case records of patients with biopsy/culture proven invasive mucormycosis were reviewed. Contrast enhanced Magnetic Resonance Imaging (MRI) images were retrieved from the Picture Archiving and Communication System (PACS) and analyzed. **Results:** Contrast enhanced MR imaging of 64 patients were reviewed. In the majority of patients (47, 73.4%) pansinusitis was present. The combination of maxillary, ethmoid and sphenoid (10, 15.6%) was the second most common seen. Bilateral sinus involvement was more common (79.1%) than unilateral sinus involvement (20.9%). Bony erosions were most common seen in 37 cases (57.8%) followed by black turbinate sign which was seen in 28(43.7%) of cases. Loss of periantral fat is earliest sign of soft tissue involvement & was seen in maximum number of cases (75%). In our study extension to the orbit (48, 75%) and face (35, 55%) preceded involvement of the deep skull base (9, 14%) and brain parenchymal complications (17,26%). MRI showed T1 isointense to hyperintense, T2 isointense to mildly hypointense soft tissue thickening and heterogeneous post contrast enhancement as the main finding. MRI is quite helpful to assess early bony involvement, ocular & cerebral involvement. **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. Cerebral involvement was more common in uncontrolled diabetic patients.

Keywords: Mucormycosis, MRI, Rhino-Orbito- Cerebral, COVID-19.

BACKGROUND

Mucormycosis is amongst the most lethal form of zygomycosis occurring in post covid – 19 patients[1]. The disease is seen almost exclusively in immunocompromised patients since normal phagocytic activity in immunocompetent hosts provides an adequate barrier against infection [2]. Several cases of mucormycosis in people with COVID-19 have been reported world – wide, in particular from India [3]. Mucormycosis is an angio-invasive disease caused by mold fungi of the genus Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia of Order-Mucorales, Class-Zygomycetes. The Rhizopus Oryzae is the most common type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhino-orbito-cerebral (ROCM) form. Mode of contamination occurs through the inhalation of fungal spores [3].

An unholy trinity of diabetes, rampant use of

corticosteroid in a background of covid -19 appears to increase mucormycosis. The primary reason that appears to be facilitating Mucorales spores to germinate in people with COVID-19 is an ideal environment of low oxygen, high glucose (diabetes, new onset hyperglycemia, steroid- induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritin) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated or background comorbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators[3].

Clinical presentation is classified according to organ involvement. It can be rhino-orbito-cerebral, pulmonary, cutaneous, gastrointestinal or disseminated[4]. ROCM describes a fulminant infection of the nasal cavities, paranasal sinuses, neck spaces, orbits and intracranial structures caused by Mucorales species. We classify ROCM into 2 broad categories, based on anatomic involvement: sinonasal (nasal cavity and paranasal sinuses) and extra- sinus (deep neck, orbital and intracranial) involvement[5].

MRI is superior than CT in detecting early invasion of mucormycosis, owing to its increased slice orientation as well as superior anatomic resolution. The ability to depict cross-sectional anatomy and pathology with better tissue characterization and even without administering intravenous gadolinium-based contrast agent is a distinct advantage of MRI over CT scanning. Contrast administration is useful in differentiation of viable from a dead necrotic tissue in sinusitis with an added advantage of differentiating abscess from phlegmon in orbit and intracranial extensions. MRI has the highest accuracy in the detection of cavernous sinus involvement and perineural spread, which are uncommon but serious complications of fungus sinusitis. DWI is helpful in detecting optic nerve infarction and plays a crucial role in differentiating orbital cellulitis from orbital abscess as it is the critical finding, which can alter management from medical to surgical[1]. Imaging helps in assessing the extent of disease, identification of complications like ICA thrombosis and is indispensable for surgical planning. MRI proved to be very useful in detection of complications like orbital cellulitis, cavernous sinus thrombosis and ICA thrombosis[2]. The goal of this study is to systematically review MR imaging spectrum of Rhino-Orbito-Cerebral Mucormycosis in Covid-19 patients.

MATERIALS AND METHODS

The case records of patients with culture and histological evidence of acute invasive rhino-orbito-cerebral mucormycosis were retrospectively evaluated for relevant clinical data. Contrast enhanced Magnetic Resonance Imaging (MRI) images and reports were retrieved from the Picture Archiving and Communication system (PACS) (Meddiff. Pvt. Ltd) from the Institution. MRI scans were performed on 1.5 Tesla MR Scanners (Philips MultiVa) using a 16 Channel neurovascular coil (NV) -16 coil. Multiplanar, multiecho MRI of paranasal sinuses with orbits and brain were performed with the set protocol as per table 1 & table 2.

RESULTS

A total of 64 patients with rhinocerebral mucormycosis are having preoperative contrast MRI imaging and histopathology confirmation were identified.

Demographic and clinical findings

Our study group comprised of 44 males and 20 females with ages ranging from 30 to 75 years (mean age = 53 years). The majority of patients (93.7%) were aged over 40 years. Thirty-nine patients (60.9%) had a history of uncontrolled diabetes, two patients (3%) had a predisposing immunocompromised status.

The clinical symptoms reported in our series were headache (56, 88%), nasal discharge (44,69%), facial swelling (44,69% patients), facial pain (42, 65%), decreased vision (39, 61%), fever (9, 14%), and epistaxis (5, 9%). Seven patients (11%) presented with multiple cranial nerve palsy (Table 3).

Imaging findings

A. Sinonasal involvement

In the majority of patients (47, 73.4%) pansinusitis was present. The combination of maxillary, ethmoid and sphenoid (10, 15.6%) was second most commonly seen. Bilateral sinus involvement was more common (79.1%) than unilateral sinus involvement (20.9%). The sinuses involved in mucormycosis are detailed in Table 4.

B. Bone involvement

Bony erosions appear as permeative destruction involving the sinus walls and the contiguous bony structures. Mycotic microvascular involvement of nasal mucosa leads to infarction of surrounding tissue, which is non-enhancing on post-contrast T1-weighted images. Infarcted tissue shows diffusion restriction on DWI images. This devitalized and necrotic sinonasal mucosa with complete non-enhancement on MR imaging represents “the black turbinate” sign (Figure 1) This represents earliest imaging finding of nasal mucormycosis on MR imaging[6].

In our study Bony erosions were most common and seen in 37 cases (57.8%) followed by black turbinate sign which was seen in 28 (43.7%) of cases. Other findings were remodeling/thinning seen in 18 cases (28%) and Irregular bone destruction seen in 6 (9.3%). Isolated marrow involvement was seen in 2 cases (3%). Bone involvement is detailed in Table 5.

C. Soft Tissue Involvement

Loss of periantral fat is earliest sign of soft tissue involvement & was seen in maximum number of cases in our study (Table 6). Extension of mucormycosis beyond the sinus can be seen without

any bone destruction as it tends to spread along vascular channels and nerves.[7] Spread of mucormycosis from nasal cavity along either posterior nasal nerves or the sphenopalatine artery justifies the involvement of sphenopalatine foramen and ipsilateral pterygopalatine fossa.

D. Orbital involvement

Neuro-ophthalmic involvement of fungal sinusitis develops due to progressive fungal invasion & thin lamina papyracea and valveless ethmoidal veins[8]. Both pre- and postseptal cellulitis can be seen in patients with mucormycosis. On imaging, pre-septal cellulitis is limited to the soft tissue anterior to the orbital septum. In contrast, postseptal cellulitis involves the contents of orbit putting optic nerve at risk. Radiologically, postseptal cellulitis typically shows diffuse soft tissue stranding posterior to orbital septum and varied degree of proptosis. In cases of severe proptosis, posterior globe shows tenting demonstrating the "guitar pick" sign (Figure 2)[9]. DWI is helpful in detecting optic nerve infarction (Figure 3) and plays a crucial role in differentiating orbital cellulitis from orbital abscess as it is the critical finding, which can alter management from medical to surgical. Involvement of orbital structures in our study are as detailed in Table 7.

E. Intracranial involvement: Intracranial involvement in our study is detailed in Table 8.

- **Cavernous sinus involvement-** Involvement of orbit is an alarming imaging feature to look for involvement of cavernous sinus. Enhancing soft tissue in orbital apex and cavernous sinus indicates cavernous sinus involvement on imaging. In addition, adjacent ethmoid sinus involvement with bulky and lateral displacement of medial rectus can be seen[10]. Changes in signal intensity, size and contour of cavernous sinus and increased dural enhancement along the lateral border of cavernous sinus (Figure 4) indicate cavernous sinus thrombophlebitis.
- **Angioinvasion:** Extensive involvement of vessels with resultant thrombosis (Figure 12) and tissue necrosis is the pathological hallmark feature of mucormycosis[11]. Mucormycosis may show diffuse arterial wall involvement leading to vasculitis or may directly invade into the vessel forming a mucorthrombus (Figure 5).
- **Perineural invasion:** Perineural invasion is another possible mechanism of central nervous system extension of mucormycosis. Perineural invasion was considered unusual but contrast-enhanced MRI studies have documented perineural invasion via the trigeminal nerve[12]. On MRI, perineural spread appears as a thick sheet of enhancing tissue along the involved cranial nerve or its branch in addition to loss of normal fat pad adjacent to a foramen.
- **Brain parenchymal & meningeal involvement:** Furthermore devastating complication of mucormycosis is parenchymal involvement, which occurs by invasion through superior orbital fissure, cribriform plate, angioinvasion and perineural route[13]. As consequence of hematogenous spread of mucormycosis causing vasculitis and inflammation of the meninges leads to meningitis. Involvement of brain parenchyma is suggestive of cerebritis and is the precursor of abscess formation (Fig 6). Untreated cases of cerebritis can lead to cerebral abscess formation. DWI sequence is more specific for fungal abscess, which shows restricting wall and intracavitary projections while sparing the core of the lesion[14]. Patterns of intracranial spread are detailed in Table 9.

Table 1: Pre-contrast

Axial	T1, T2, Flair T2, FFE (GRE), DWI,
Coronal	T1FS
Sagittal	T1, T2, STIR
3D	T2, T2FS, T2 3D DRIVE

Table 2: Post-Contrast

Axial	T1FS
Coronal	T1FS
Sagittal	T1FS, T1 3D TFE

Table 3: Clinical feature

Clinical features	(Number, Percentage)
Headache	56 (88%)
Nasal discharge	44 (69%)
Facial swelling	44 (69%)
Facial pain	42 (65%)
Decreased vision	39 (61%)
Fever	9 (14%)

Epistaxis	5 (9%)
Multiple cranial nerve palsy	7 (11%)

Table 4: Sinuses involved.

Sinuses involved	No. of cases (Percentage)
Maxillary + Ethmoid	3 (4.6%)
Maxillary + Ethmoid +sphenoid	10 (15.6%)
Frontal + maxillary +Ethmoid	4 (6.2%)
Pansinusitis	47 (73.4 %)

Table 5: Bones involved in mucormycosis infection

Bones involved in mucormycosis infection	No. of cases (Percentage)
Black Turbinate	28 (43.7%)
Isolated marrow involvement	2 (3%)
Erosion	37 (57.8%)
Remodeling/Thinning	18 (28%)
Irregular bone destruction	6 (9.3%)

Table 6: Soft Tissue Involvement

Soft Tissue Involvement	No. of cases (Percentage)
Loss of Periantral fat	48 (75%)
Pterygomaxillary Fissures/Pterygopalatine fossa /Sphenopalatine Foramen involvement	9 (14%)
Pre maxillary soft tissue	47 (73%)
Masticator/ Infratemporal fossa	45 (70%)
Palate	16 (25%)
Oral Cavity	5 (8%)

Table 7: Orbital Involvement

Orbital Involvement	
Involved structure	**No. of cases (Percentage)**
Preseptal	39 (60.9%)
Post septal	39 (60.9%)
Proptosis	21 (32.8%)
Guitar pick sign	1 (1.5%)
Optic nerve ischemia	9 (14%)
Frank Abscess	2 (3.1%)
Intra Conal (I)	2 (3.1%)
Extraconal (E)	9 (14%)
Combined(I+E)	30 (46.8%)

Table 8: Intracranial involvement in mucormycosis infection

Intracranial involvement in mucormycosis infection	
Involved structure	**No. of cases (Percentage)**
Cavernous Sinuses	
With thrombosis	2 (3.1%)
Without thrombosis	2 (3.1%)
Angioinvasion	
Partial ICA thrombosis	1 (1.5%).
Complete ICA thrombosis	1 (1.5%).
Perineural	0
Parenchymal involvement	
Infarct	7 (10.9%),
Meningitis	2 (3.1%)
Abscess /Cerebritis	1 (1.5%).
Extradural collection	1 (1.5%).

Table 9: Pattern of Intracranial Spread

Pattern of Intracranial Spread	
Pathway	**No. of cases (Percentage)**
Via Superior Orbital Fissure	6 (9.3%)
Via Cribriform Plate /Medial orbital wall	29 (45.3%)
Via Angio Invasion	5 (7.8%)
Via Perineural	0

Figure 1: Coronal T1 post contrast image showing area of non-enhancing mucosa which stands out against the normal enhancing mucosa representing black turbinate sign.

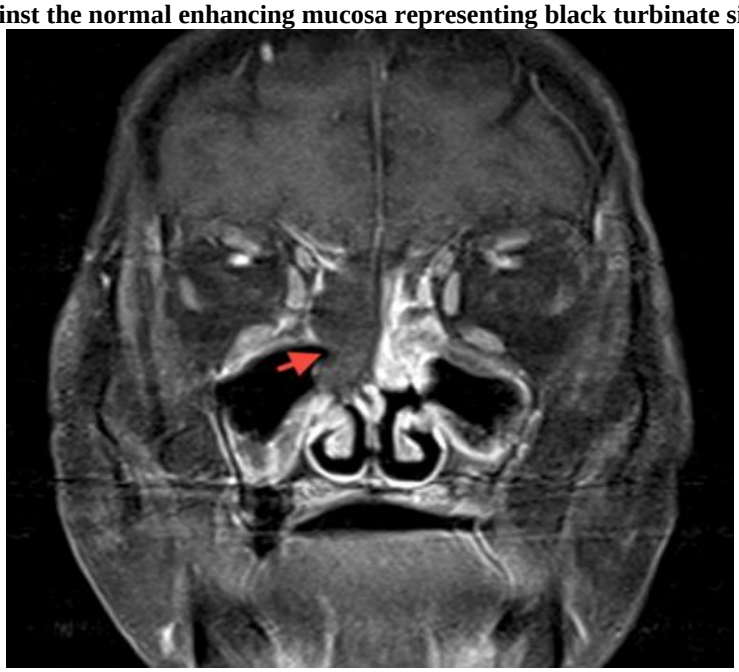


Figure 2: Axial T2 image showing left proptosis & posterior globe shows tenting demonstrating the "guitar pick" sign

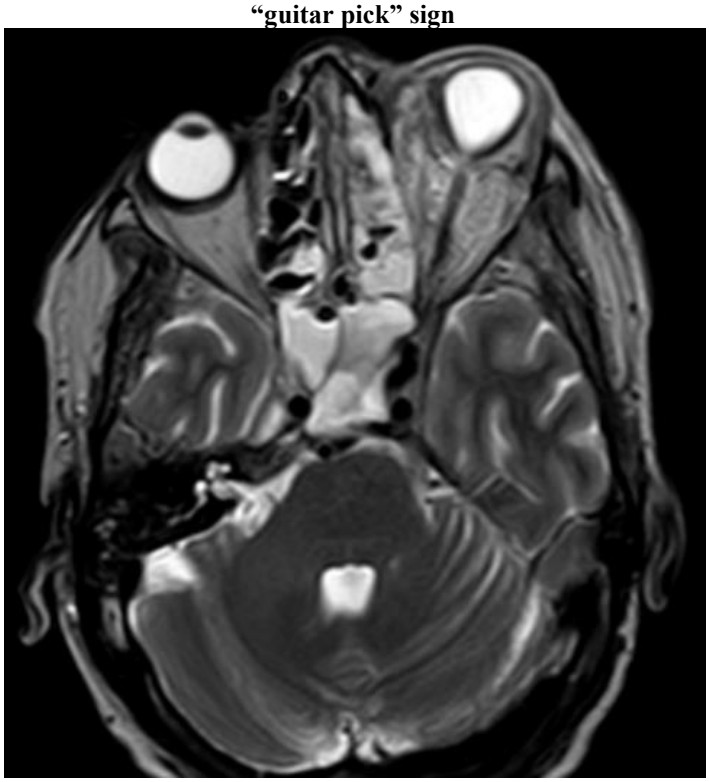


Figure 3: DWI images showing diffusion restriction along left optic nerve in a case of mucormycosis suggestive of optic nerve infarction

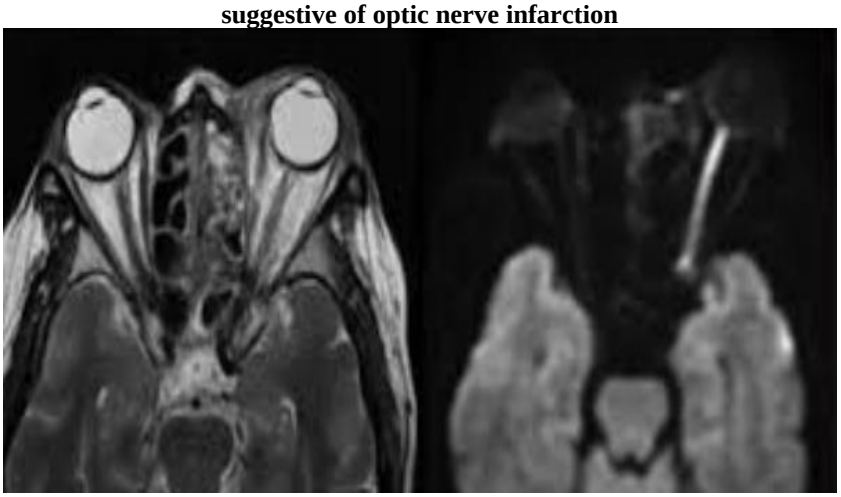


Figure 4: Axial T1 FS contrast images show non enhancing left cavernous sinus suggestive of thrombosis.

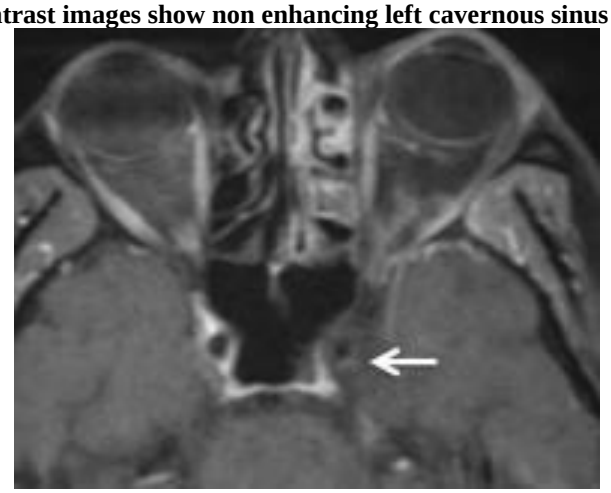


Figure 5: A,B showing Acute infarct in left frontoparietal region. C showing loss of T2 flow void in left ICA. D MRA brain showing non visualisation of left ICA & MCA.

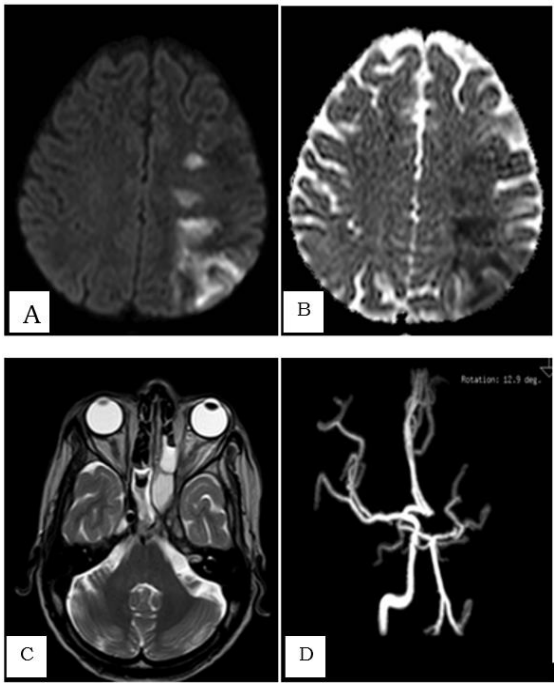
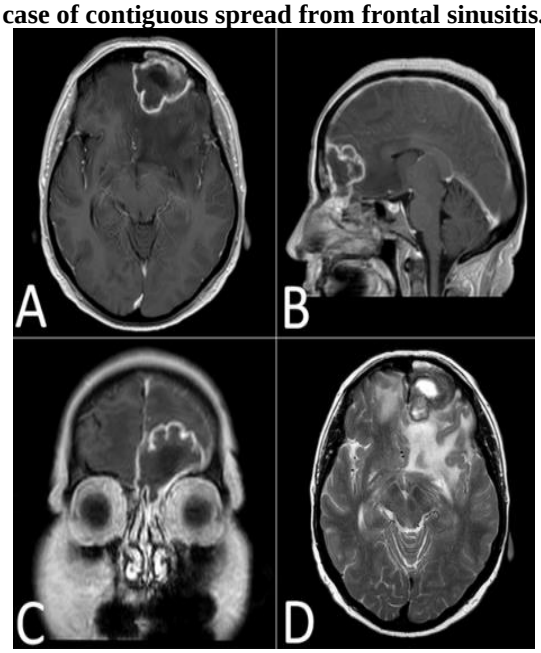


Figure 6: A, B, C, D images showing peripheral ring enhancing brain abscess with adjacent edema in a case of contiguous spread from frontal sinusitis.



CONCLUSION

Based on our study, MR imaging of rhino-orbito-cerebral mucormycosis shows heterogeneous variable T2W signal intensity and variable enhancement patterns. In our study group, patients tended to chiefly present in the advanced stages of the disease with extensive extra sinus involvement. MRI is an invaluable tool which is complementary to clinical evaluation in assessing the extent of disease and diagnosis of complications. Cerebral involvement was more common in uncontrolled diabetic patients.

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