INTRODUCTION

The ubiquitous fungi of the order Mucorales, which are commensals of healthy nasal mucosa but produce fulminant infection in an immunosuppressed host, are the source of the opportunistic, possibly fatal infection known as mucormycosis. [1]

The most typical manifestation of mucormycosis is the rhino-orbito-cerebral type (ROCM), with other manifestations include pulmonary, cutaneous, gastrointestinal, and disseminated forms. [2]
The second COVID-19 pandemic that struck India between March and July 2021 saw an enormous rise in ROCM cases, prompting the country to proclaim an epidemic of this once-rare disease. In light of this link, the name COVID associated mucormycosis (CAM) was developed.\[1\]

According to a review of the literature, 81% of CAM cases were reported from India. Preexisting uncontrolled diabetes, a diabetogenic state brought on by COVID-19, immune dysregulation manifested as an elevated immature neutrophil count, a deficient innate immune system, decreased CD4 and CD8 cell counts, elevated ferritin levels, and the inappropriate use of steroids to treat COVID pneumonia are just a few of the plausible explanations. Other likely culprits include the widespread use of supplements that contain zinc and iron, industrial oxygen, and tainted oxygen humidifiers.

**Clinical characteristics, epidemiology, and etiopathogenesis of CAM**

The fungal spores are inhaled into the nasopharynx following which tissue invasion, thrombosis and necrosis progress from the nose to paranasal sinuses, orbit and brain. According to recent literature, middle-aged guys are primarily affected by the disease, and the majority of them present within 0–14 days after a COVID-19 positive test.

Nasal stuffiness, bad odour, epistaxis, black nasal discharge, nasal mucosal discoloration or eschar, loosening of teeth, face pain or swelling, paresthesia, and sinonasal and perisinus involvement are some of the clinical signs.

Proptosis, ptosis, rapid loss of vision, and diplopia are common symptoms of orbital illness. Patients may experience headache, altered sensorium, paralysis, cranial nerve palsy, and focal seizures if the infection has reached the brain.

**Pathways of spread**

Direct tissue invasion is the main method of mucormycosis transmission. It may spread across anatomical areas by breaking through natural bony flaws, through natural channels like the nasolacrimal ducts, lymphatics, and neurovascular bundles, or by breaking through bone degradation. [Image 1] summarises the anatomical pathways implicated in the progression of ROCM. A thorough evaluation of the disease's extent requires careful attention to each of these anatomical locations on MRI.

**Diagnosis**

- Although histology and fungi culture are used to make the conclusive diagnosis of mucormycosis, imaging plays a crucial role in making an early diagnosis, early identification of complications, and follow up of the patient.
- The imaging modality of choice to identify early extrasinus expansion, particularly intracranial illness in the context of CAM, is MRI due to its fine soft tissue contrast resolution.
- Compared to CT, MRI offers superior sensitivity for detecting all cerebral complications of CAM, with the exception of cortical bone involvement.

**MATERIALS AND METHODS**

**Source of Data**

The main source of data for study will be COVID 19 RTPCR positive patients who have undergone MRI PNS, ORBITS and BRAIN as part of screening in department of Radio diagnosis, Narayana Medical College, Nellore.

**Method of Collection of Data (including sampling procedure if any):**

The study was carried out in the Department of Radio diagnosis at Narayana medical college and hospital over a period of 4 months (March 2021-July 2021).

**Inclusion Criteria**

1. Patients who are COVID 19 RTPCR positive admitted in ICU
2. Patients who are COVID 19 RTPCR positive and treated with steroids.
3. Patients who are COVID 19 RTPCR positive and having comorbidities such as T2DM,HTN,CKD
4. Patients who are COVID 19 RTPCR positive and using immunosuppressant drugs

**Exclusion Criteria**

1. Pregnant mothers
2. Patients who are claustrophobic.

**Equipment and Technique Used**

- Once a patient met the study’s inclusion criteria, he or she would be subjected to MRI evaluation after obtaining their consent.
- All subjects underwent MRI PNS, orbits and brain by GE 3 tesla discovery 750W MRI machine.

An emergency kit to manage adverse reactions due to contrast was made available if necessary.
Technique of Examination
All subjects were screened before entering MRI gantry for ferromagnetic objects, implants, pacemakers, aneurysmal clips etc. Subjects were examined in supine position after proper positioning and immobilization of head. The standard head coil was used for the scan.

Imaging Protocol
The following MRI sequences will be taken covering from teeth to top of frontal sinus in axial plane and from nasal cartilage to pons in coronal plane:
- T1 weighted,
- T2 weighted,
- T2 fat saturated,
- FLAIR (Fluid attenuation inversion recovery),
- T1 post contrast,
- T1 post contrast fat saturated,
- DWI and SWI sequences will be obtained.

RESULTS
The research population comprised of 200 patients who were COVID 19 RTPCR positive at Narayana medical college, Nellore between March 2021 & July 2021. All patients had MRI screening of PNS, orbit and brain in accordance with the procedure, & data were recorded. Out of screened population 50 patients were found to have rhinoorbital cerebral mucormycosis.

Demographics
Our study group comprised 50 mucor patients with ages ranging from 20 to 72 years (mean =46 years). Out of which 30(60%) were male and 20(40%) were female. The majority of patients (77%) were aged over 40 years, with those aged 42–61 years (57%) being most affected. 35 patients (70%) had a history of uncontrolled diabetes, 15 patients (15%) had other risk factors like post-organ transplant patient, on immunosuppressive drugs and IV drug abuse.

Orbital Mucormycosis

Figure 1: Orbital l disease in ROCM. Axial FLAIR (a) showing mucosal thickening in the left nasal cavity extending into left orbit with obliteration of retrobulbar fat causing proptosis. Coronal T2 weighted(b) image showing involvement of superior oblique, medial rectus, inferior rectus, intraconal and extraconal compartments.

Figure 2: Orbital disease in ROCM Axial T2FS(a), FLAIR (b), TIFS pre contrast (c), TIFS post contrast (d) showing right pre septal involvement of orbit in orbital mucor.

Figure 3: Orbital disease in ROCM Coronal T2w(a), Sagittal T2w (b) showing mild bulky optic nerve with heterogenous signal intensity suggestive of optic neuritis

Paranasal Involvement

Figure 4: Sinonasal disease in ROCM Axial T2w(a-c), TIFS pre contrast(d,f), post contrast(e,g) showing mucosal thickening and heterogenous enhancement of right ethmoidal, maxillary and frontal sinuses with adjacent soft tissue changes

Figure 5: Axial TIFS pre contrast (a), post contrast(b) images of brain showing mild bulky, heterogenous enhancing right temporalis muscle
Cerebral Mucormycosis

Table 1: showing anatomical involvement. (predominant)

<table>
<thead>
<tr>
<th>Structure of involvement</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNS and nasal cavity</td>
<td>21</td>
<td>42</td>
</tr>
<tr>
<td>Orbit</td>
<td>19</td>
<td>38</td>
</tr>
<tr>
<td>CNS</td>
<td>10</td>
<td>20</td>
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A fungus of the order Mucorales causes the severe opportunistic fungal infection known as Mucormycosis. India is currently dealing with a massive increase in Coronavirus disease-related mucormycosis (COVID-19). Those who are immunologically or metabolically weakened, such as patients who have recently contracted COVID-19 infection, can experience a rapid progression of this fungal illness. The most crucial elements that affect prognosis in the therapy of mucormycosis are early suspicion, quick diagnosis, and beginning of treatment.[4] The mainstay of treatment for patients with rhino-orbital-cerebral mucormycosis (ROCM) is imaging.[5]

Out of 200 COVID RTPCR positive MRI screened patients, 50 patients found to have imaging features suggestive of ROCM. Irrespective of clinical symptoms and signs, MRI imaging gives exquisite detail about the extent of involvement, disease spread, prognostication which helps further in treatment planning.[6]

Imaging manifestations varied among 50 individuals with 21 patients showing the involvement of PNS and nasal cavity, 19 patients showing the involvement of orbits, 10 patients showing the involvement of central nervous system.[7-10]

Table 2: representing anatomical involvement of rhinal mucormycosis

<table>
<thead>
<tr>
<th>Paranasal sinus involved</th>
<th>No of patients (n=21)</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Ethmoidal sinuses</td>
<td>10</td>
<td>47</td>
</tr>
<tr>
<td>Maxillary sinuses</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Frontal sinuses</td>
<td>3</td>
<td>14.5</td>
</tr>
<tr>
<td>Sphenoid sinuses</td>
<td>5</td>
<td>24</td>
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Table 3: representing anatomical involvement of orbital mucormycosis

<table>
<thead>
<tr>
<th>Orbital structure involved</th>
<th>No of patients (n=19)</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Pre septal</td>
<td>3</td>
<td>15.7</td>
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<tr>
<td>Ocular globe</td>
<td>1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Intraconal</td>
<td>3</td>
<td>15.7</td>
</tr>
<tr>
<td>Extraconal</td>
<td>5</td>
<td>26.3</td>
</tr>
<tr>
<td>EOM</td>
<td>2</td>
<td>10.5</td>
</tr>
<tr>
<td>Optic nerve</td>
<td>6</td>
<td>31.5</td>
</tr>
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</table>

Table 4: representing anatomical involvement of cerebral mucormycosis

<table>
<thead>
<tr>
<th>Structure involved</th>
<th>No of patients (n=10)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral parenchyma</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>Cavernous sinus</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Meninges</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Extra axial collection</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Internal carotid artery</td>
<td>2</td>
<td>20</td>
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DISCUSSION

Different sinus contents produce different MRI signal characteristics. The amount of necrosis (which causes T2 hyperintensity) and the presence of paramagnetic elements like iron and manganese within the fungal hyphae cause T2 weighted hypointense signal. The sinus contents may appear in a variety of ways on postcontrast scans, including: 1. intense homogenous enhancement; 2. varied enhancing and nonenhancing zones; and 3. total core nonenhancement with or without a thin irregular rim of peripheral enhancement.

On postcontrast T1W images, invasive fungal sinusitis is characterised by the absence of enhancement in areas that ought to enhance. This is due to fungus angioinvasive nature, which causes tissue necrosis and microthrombosis in the affected areas. The necrotic eschar detected on clinical or rhinoscopic examination is represented by this look, known as the “Black Turbanite sign,” on imaging. Early ROCM diagnosis may be aided by seeing this symptom.

Orbital Involvement: Most common extra sinus involved structure in ROCM is orbit followed by face. Other sites of involvement include the masticator space, palate, skull base, pterygopalatine fossa, retroantral soft tissue etc. Pathways of least resistance, such as the lamina papyracea, nasolacrimal duct, ethmoid foramina, and perforations of the medial orbital walls by vascular channels, are frequently used by mucormycosis to invade the orbit. Rarely, when there is aggressive course, the loss of the orbits’ bone walls might allow an infection to migrate from the maxillary sinus via the orbital floor.

Imaging Findings

- Early orbital infection manifests as edema of the retroorbital fat around the extraocular muscles and soft tissue involvement.
- The retroorbital fat infiltration is best seen on fat-saturated T2W sequences. Inflammatory tissue or
abscess formation may be visible along the medial aspect of the orbit due to the frequent invasion of the orbit through the medial wall, as well as lateral displacement and edoema of the medial rectus muscle.

- Possible involvement of the optic nerve. Central retinal artery or ophthalmic artery occlusion, optic nerve infarction, or direct invasion of the optic nerve can all cause sudden onset of blindness. In diffusion-weighted imaging, optic nerve infarction is indicated by a high signal intensity of the nerve.

- Increased nerve diameter and alterations in signal strength can result from direct invasion of the optic nerve. Isolated optic nerve involvement means infection may have spread through ophthalmic artery branches, which is a sign that aggressive treatment should be started.

- Severe proptosis and globe tenting are symptoms of diffuse orbital infection. Even though it is uncommon, the involvement of the globe may be seen as an improvement and enhancement of the ocular coatings.

- Orbital apex involvement: Orbital apex syndrome may be caused by increasing soft tissue at the orbital apex that extends into the optic canal and superior orbital fissure. Suspicion of a fungal origin must be raised when sinusitis imaging abnormalities are linked to orbital apex syndrome.

- The superior orbital fissure can allow an infection to travel from the orbital apex posteriorly into the cavernous sinus, and the inferior orbital fissure can go through the pterygopalatine fossa and into the infratemporal fossa.

**CNS involvement**

Through continuous spread and, less frequently, bone invasion, infection spread from the sinuses to the brain. Brain abscesses and cerebritis are caused by the direct extension of mucus from the nasal cavity and paranasal sinuses to the brain parenchyma. Mucor enter the brain through the cavernous sinus, superior orbital fissure, and orbit. The cribiform plate, ethmoid and frontal sinuses walls are the most prevalent sites of direct intracranial distribution. The pterygopalatine fossa and the internal carotid artery both extend into the middle cranial fossa. Infection from cavernous sinus spreads perineurally down the trigeminal nerve, leading to mainly posterior fossa involvement.

**Imaging Findings**

**Cavernous and major arterial involvement:**

- In ROCM, heterogeneously enhancing soft tissue that involves the cavernous sinus can be seen extending from the superior orbital fissure.

- On coronal and axial images, the lateral walls of the sinuses are typically straight or concave laterally.

- A symptom of involvement is the loss of the cavernous sinus concavity. Early signs include a large cavernous sinus with a convex lateral wall.

Images after contrast reveal sinus filling abnormalities.

- The superior ophthalmic vein may become occluded as a result of soft tissue compression at the orbital apex or as a result of disease extending along the vein.

**Intracranial extension**

- Mucormycosis frequently causes intracranial involvement by direct spread across the cribiform plate, walls of the ethmoid, and frontal sinuses. The pterygopalatine fossa and the internal carotid artery both extend into the middle cranial fossa.

- Predominant posterior fossa involvement may result from perineural spread along the trigeminal nerve from the cavernous sinus.

- In contrast-enhanced T1W images, early intracranial spread is easier to see when the meninges are enhanced. Abscesses and infarcts are two more intracranial manifestations.

- As a result of fungus invading the brain parenchyma, ill-defined regions of changed signal intensity, typically T2 hyperintensity, are seen in nonvascular distribution. Variable peripheral enhancement and minimal perilesional edema are visible.

**Skull base involvement**

- A rare consequence that typically manifests in the advanced stages of the disease is skull base osteomyelitis. Because the fungus angioinvasive nature makes it easier for the infection to spread widely into the deep soft tissues through the perivascular channels even before bone deterioration, bone involvement happens relatively late in the course of the disease.

- Early bone normal fat signal involvement. On T1W and STIR pictures, the bone marrow appears hypointense, and postcontrast images display heterogenous enhancement.

- With infiltration into the bones, there is vast heterogeneously enhancing soft tissue in the advanced stage.

**CONCLUSION**

- Invasive fungal sinusitis is frequently brought on by ROCM in diabetics and other immunosuppressed patients. Patients with COVID-19 have been shown to have ROCM co-infection since 2020, making patient care difficult. ROCM has a severe clinical course when it first appears, necessitating quick and forceful intervention.

- Imaging facilitates quick diagnosis and is essential in determining the extent of the disease, which directs surgical procedures. The black turbinate sign is a typical finding in the majority of ROCM patients, however it can also be observed in other IFS and duplicated by healthy cavernous tissues in the turbinates.
• The angio invasive nature of fungus makes it easier for it to spread outside of the sinus without directly destroying bone. As a result, mucor spreads into the orbits and neck areas at an early stage of the illness; fat stranding may be the only imaging sign of extra-sinus dissemination. Thus, it is crucial to carefully assess fat-suppressed sequences on MRI and soft tissue algorithms on CT when making a diagnosis.

• Although the fungus has the potential to move along peripheral nerves in the base of the skull into the cerebral compartment, more precise imaging of the base of the skull must be taken into consideration in suspected cases of MCR. Intracranial symptoms of the infection might range from the development of abscesses to ischemic problems linked to vasculitis, all of which are warning signs of a worse outcome.

• MRI imaging of PNS, orbits and brain plays a crucial role in evaluating pathway of spread, extent of disease, prognostication of disease even before clinical symptoms of disease arise. Thus MRI acts as diagnostic and screening aid in the early treatment of rhinoorbital cerebral mucormycosis that is rampant during COVID era which might be due to immunosuppression and other factors. Early diagnosis with MRI imaging which further helps in early treatment significantly reduces morbidity and mortality of patients.

REFERENCES

1. Kanduri Sreshta#, Tarjani Vivek Dave1, Dandu Ravi Varma, Akshay Gopinathan Nair2,3, Nandini Bothra1, Milind N Naik1, Srinivas Kishore Sistla4 A. Magnetic resonance imaging in rhino orbital cerebral mucormycosis DOI: 10.4103/ijo.IJO_1439_21


