Spectrum of Imaging Findings in Rhino-Orbito-Cerebral Mucormycosis (ROCM) in Post COVID Patients - A Pictorial Review with Clinico-Radiological Correlation

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ABSTRACT

BACKGROUND

Rhino-orbito-cerebral mucormycosis (ROCM) is a devastating fungal infection with very high rates of mortality. Many patients post corona virus disease (COVID) infection are increasingly being diagnosed with mucormycosis (black fungus). Imaging being central to the early diagnosis of the infection, the study aims to characterize the major radiological patterns of involvement of mucormycosis. Computed tomography (CT) & magnetic resonance imaging (MRI) findings of 10 patients who were subsequently conformed to have mucormycosis were analyzed and 7 major patterns of involvement were detected. Imaging plays a vital role in the early diagnosis of ROCM. Knowledge about the common patterns of spread helps in picking the subtle signs of infection

KEYWORDS

Mucormycosis, Post COVID, Fungal Sinusitis, ROCM

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BACKGROUND

Rhino-orbito-cerebral mucormycosis is a rare, but devastating fungal infection, predominantly affecting immune compromised individuals.[1,2] Recent spike in the number of rhino-cerebral mucormycosis cases, in COVID patients has renewed interest in the topic in medical circles.[3] Hence, it becomes necessary for radiologists to familiarize themselves with the spectrum of findings encountered in rhino-cerebral mucormycosis and to look for early findings of mucormycosis in post COVID patients. The rapidity of progression, angio-invasive nature and need for multidisciplinary approach makes early detection of mucormycosis vital for patient management. In this scenario, imaging modalities like contrast CT & MRI play a key role in suspecting early disease and quantifying the spread of established disease. CT primarily helps in assessing the bone involvement, whereas MRI aids in quantifying the extent of soft tissue invasion and cerebro-vascular involvement.[4] The proposed work is meant to be a pictorial review summarizing key imaging findings of 10 cases of rhino-cerebral mucormycosis reported in Government Medical College, Kozhikode, Kerala. The primary objective of this study is to highlight the early and common radiological findings, patterns of spread and the use of appropriate imaging protocols (CT & MRI) that would facilitate early diagnosis and timely intervention in patient with mucormycosis. The study also emphasizes on the need of clinic-radiological correlation which is necessary to differentiate angio-invasive fungal sinusitis from other fungal aetiologies which can closely mimic the former. Post-operative follow-up cases have also been included in the study to distinguish post-operative changes from recurrence/residual foci of mucormycosis infection.

Review of Literature

Various studies conducted in the past have thrown light into the imaging manifestations of invasive fungal sinusitis; however studies that specifically look into the imaging features of mucormycosis are rather limited. Almost all of the studies invariably consider MRI to be of superior diagnostic value in comparison to CT, the most recent one being a paper published by El Gropo et al in 2021, titled, 'CT & MR imaging characteristics of acute invasive fungal sinusitis. In this study, MRI was found to have 87% sensitivity and 86% specificity in detecting invasive fungal sinusitis as compared to CT which had a sensitivity of 57% and specificity of 69 %. Diego Herrera's paper,[5] Imaging findings in rhino cerebral mucormycosis, published in 2009 detailed the various MRI features for detecting early intra orbital spread and he proposed that signal alteration extending to orbits from paranasal sinuses in a immunosupressed patient should prompt the diagnosis of mucormycosis. Many studies have specifically looked into the common imaging patterns in mucormycosis, in a study by Jacob Therakathu[1] in 2018 on a cohort of 43 patients, only 2% of the patients had sinus limited disease, 16% patients had extra sinusoidal spread and 25% of the patients had features of intracranial extension. Use of MRI for assessing the vascular complications was described as early as in 2005 by Minif et al.[6] Imaging modalities have also been used to evolve staging systems, to assess the severity of the disease process. Middlebrooks paper[7] on 'Comprehensive update on CT findings', for the first time proposed a 7 variable CT model to screen and triage patients of acute fungal sinusitis. In a recent study by Honnavar et al titled 'guidelines in the management of rhino orbital cerebral mucormycosis,[8] a four stage classification has been proposed to assess the severity of the disease based on the anatomical extend. According to this system, patients are classified according to the increasing order of disease severity as follows, patients with disease limited to nasal mucosa, disease extending to parananasal sinuses, disease extending to orbit and disease with intracranial extension. Although signal alteration was considered as a sign of spread in almost all of the previous studies, there appears to be very less agreement regarding the MRI sequences in which the altered signal need to looked for, In Diego Herrera's study[5] only 20% of the patients showing extra sinusoidal T2 hyper intensity, had histopathologically proven spread. However a recent study by Lone et al in 2015[9] have proposed 65% sensitivity for T2 hyper intense signal, in signifying extra sinusoidal spread. There appears to be very less studies highlighting the use of MRI sequences like T2FS and STIR in detecting extra sinusoidal spread.

Clinical Profile of Patients with Mucormycosis

The most common clinical presentation of mucormycosis is rhino-orbital-cerebral infection, which is presumed to start with inhalation of spores into the paranasal sinuses of a susceptible host. Rhino orbital mucormycosis commonly presents with fever, rhino rhea and headache.[2] Subsequently as disease progresses, patients develop facial oedema and ocular pain which are indicators of regional spread of the disease. In a study done by Cammara Lemmaroy and Carlos Rodrigo in 2014, the overall mortality in patients treated for mucormycosis came close to 50 %, but there was significant reduction in the mortality in cases where early surgical debridement was done.[2,4] Death rates were significantly higher in patients with CNS spread and pulmonary involvement.[2]

Hyperglycaemia, usually with an associated metabolic acidosis, is the most common underlying condition. A review of 179 cases of rhino-orbital-cerebral mucormycosis found that 126 (70 percent) of the patients had diabetes mellitus and that most had ketoacidosis at the time of presentation. There are rare reports of rhino-orbital-cerebral mucormycosis in the absence of any apparent risk factors. The infection usually presents as acute sinusitis with fever, nasal congestion, purulent nasal discharge, headache, and sinus pain. All of the sinuses become involved, and spread to contiguous structures, such as the palate, orbit, and brain, usually progresses rapidly over the course of a few days. However, there have been some reports of rhino-orbital-cerebral mucormycosis with an indolent course that progresses over the course of weeks.

The hallmarks of spread beyond the sinuses are tissue necrosis of the palate resulting in palatal eschars, destruction of the turbinates, perinasal swelling, erythema and cyanosis of the facial skin overlying the involved sinuses and or orbit. A black eschar, which results from necrosis of tissues after vascular invasion by the fungus, may be visible in the nasal mucosa, palate, or skin overlying the orbit.

Signs of orbital involvement include periorbital oedema, proptosis, and blindness. Facial numbness is frequent and results from infarction of sensory branches of the fifth cranial nerve. Spread of the infection from the ethmoid sinus to the frontal lobe results in obtundation. Spread from the sphenoid sinuses to the adjacent cavernous sinus can result in cranial nerve palsies, thrombosis of the sinus, and involvement of the carotid artery. Haematogenous spread to other organs is rare unless the patient has an underlying hematologic malignancy with neutropenia.

A review of 208 cases of rhino-orbital-cerebral mucormycosis published in the literature between 1970 and 1993 found the following frequency of symptoms and signs: Fever – 44 percent, nasal ulceration or necrosis – 38 percent, periorbital or facial swelling – 34 percent, decreased vision – 30 percent, ophthalmoplegia – 29 percent, sinusitis – 26 percent and headache – 25 percent.

Figure 1.1

Figure 1.2

Figure 1.3

Figure 1. Images in the Upper Row are Clinical Photos of Mucormycosis Patients with Orbital (1.1) and Palatal (1.2) Involvement. Fig. 1.3 is an Endoscopic Image Showing Greyish Brown Eschar Covering Nasal Turbinates in a Patient with Mucormycosis

Relevant Anatomy[10]

Skull Base, Orbit & PNS

The paranasal sinuses include paired frontal, ethmoid, maxillary, and sphenoid sinuses. The frontal sinuses are located superior to the orbits. Both the superior and posterior walls of the frontal sinus separate the sinus from the cranial vault. The floor of the frontal sinus forms the orbital roof. The paired ethmoid sinuses are located medial to the orbits, inferior to the frontal sinuses, and anterior to the sphenoid sinuses. The roof of the ethmoid sinus (fovea ethmoidalis) separates the ethmoid sinus from the anterior cranial fossa. The medial margins consist of the middle turbinates and lateral lamella, while the lateral margins are formed by the medial orbital walls. The maxillary sinuses are located inferior to the orbits, with the orbital floor representing the roof of the maxillary sinus. Medially, the maxillary sinus communicates with the nasal cavity by opening into the middle meatus. The posterior wall of the maxillary sinus constitutes the anterior margin of the pterygopalatine fossa. The sphenoid sinuses are located within the body of the sphenoid bone posterior to the ethmoid sinuses. The cavernous sinuses with its contents are located on either side of the sphenoid sinus. The major soft tissue spaces in relation to skull base from the perspective of imaging of rhino cerebral mucormycosis include the paired masticator, infratemporal, premaxillary, buccal and parotid spaces.The orbit is a pyramidal socket of the skull that is formed by the frontal, sphenoid, ethmoid, lacrimal, zygomatic, and palatine bones and the maxilla. The orbital contents are divided into compartments comprising the globe, muscle cone, intraconal space, and extraconal soft tissues. The muscle cone (formed by the extra ocular muscles) separates the intraconal and extraconal compartments.

Protocols for Mucormycosis Imaging[3]

CECT Skull Base, Orbit & PNS3

CT imaging of the paranasal sinuses is the initial modality used in the imaging of mucormycosis. Helical CT allows for rapid acquisition and multiplanar reformations. Unenhanced axial images are typically obtained at 0.625-mm intervals, with reformatted images in the coronal and sagittal planes obtained at 1 – 2 mm intervals. Both high-resolution bone and soft-tissue algorithms should be obtained in all three imaging planes. Post contrast acquisition further helps in estimating the extent of involvement. Image guidance systems allow the surgeon to visualize CT images in all three imaging planes during endoscopic debridement. In CT, attention is given to the extent of bony involvement. However, significant soft tissue extension can also be identified by means fat stranding and soft tissue thickening adjacent to the involved sinuses-

A. MRI PNS, Orbit, Skull Base & Brain

MRI has become the primary modality of choice to stage the soft tissue and cerebrovascular involvement. Major sequences used include:

a. Axial T1 & T2
   - Aids in anatomical delineation of structures and enables the identification of epicentre of the infection and major sinuses involved.

b. Axial and coronal STIR/T2 Fat Suppressed
   - Most important sequence that helps in early identification of soft tissue spread, the involved areas appear hyper intense on STIR/T2 FS.

c. Axial and coronal post-contrast fat suppressed sequences
   - Involved areas shows heterogeneous post contrast enhancement. Lack of normal contrast opacification provides indirect evidence of vascular invasion.

d. DWI (Diffusion Weighted Imaging)
   - Helps in early detection vasculitic infarcts which precede frank cerebral invasion.

Patterns of Involvement in Selected Cases from our Institute

1. Sinus Limited Disease

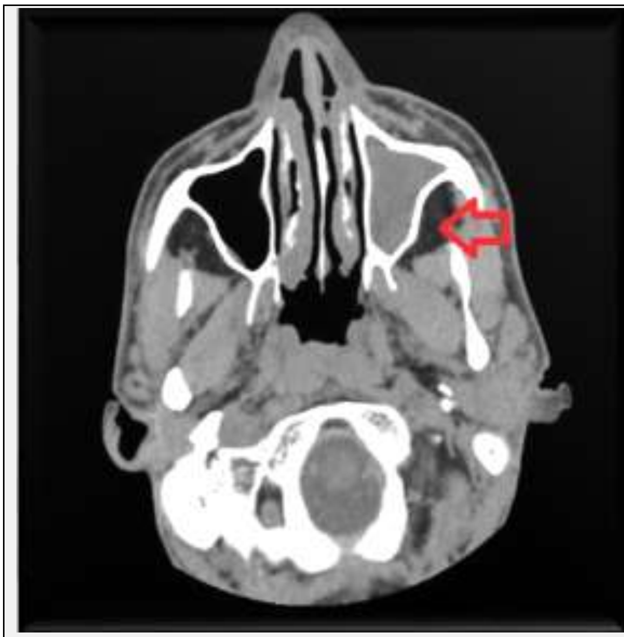


Figure 2.1 is an Axial CT Section Showing Soft Tissue Opacification of Left Maxillary Sinus. Red Arrow Shows Clear Retroantral Fat on the Left Side which is Comparable with Right. The Diagnosis Given was Chronic Sinusitis, Which was Later Proven to be Mucormycosis After Endoscopic Debridement and Histopathologic Analysis.

Teaching Point

It is impossible to diagnose mucor aetiology in CT when the disease is limited to sinuses. However T2 hypo-intensity in MRI can be a helpful feature that can aid in diagnosis of sinus limited mucormycosis.

2. Early Stage of Extra Sinusoidal Extension

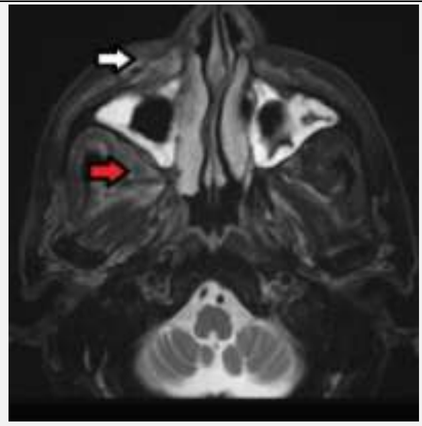


Figure 3.1

Figure 3.2

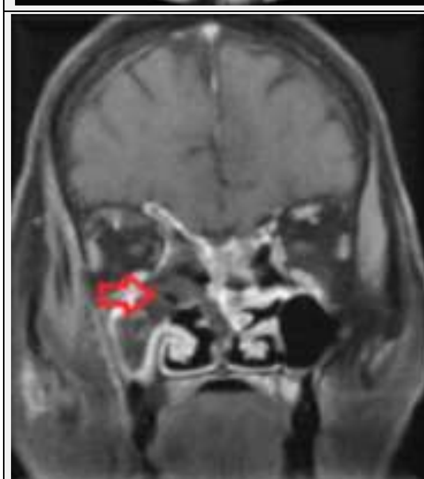


Figure 3.3

Figure 3. Axial CT Section (FIG 3.1) Showing Early CT Features of Extra-Sinusoidal Spread in the Form of Left Premaxillary Stranding (White Arrow), Retroantral Stranding (Red Arrow) and Swelling of Adjacent Turbinate (Blue Arrow). Axial T2 FS Image (FIG 3.2) Showing Subtle Hyperintense Signal in Left Premaxillary Space and Left Masticator Space. FIG 3.3 Shows the Classic 'Black Turbinate Sign' on the Right Side, Which is Due to the Non Enhancement of Mucosa of Turbinates Affected by Mucor.[11]

Teaching Point

Absence of extra-sinusoidal soft tissue does not preclude extra-sinusoidal extension. Subtle fat stranding/fat plane obliteration in CT and perisinusoidal STIR hyper intensity in MRI can be the earliest signs of invasive fungal sinusitis.

3. Bone Erosions

Figure 4.1

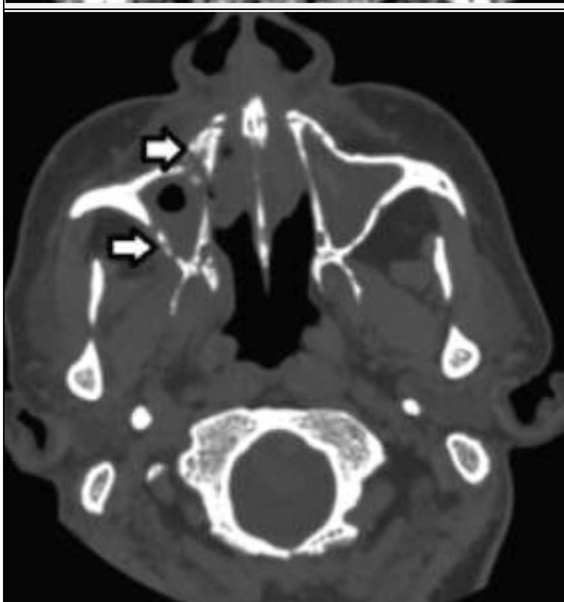


Figure 4.2

CT Coronal Reconstruction (FIG 4.1) Showing a Differential Density Area in Right-Half of Sphenoid Sinus Eroding the Lateral Wall and Extending to Optic Canal (White Arrow). Axial CT Section in Bone Window (FIG 4.2) Showing Extensive Erosions of All Walls of Right Maxillary Sinus

Teaching Point

Bone involvement can be considered as a definitive sign of invasive fungal sinusitis.[3] Bone involvement can take in the form of permeative destruction, ill-defined rarefactions of sinus walls or even frank bony erosions with soft tissue.

4. Orbital Extension

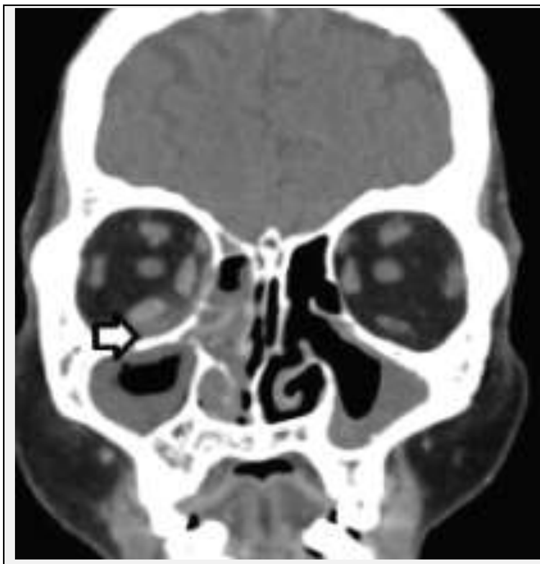


Figure 5.1

Figure 5.2

CT Coronal Reconstruction (FIG 5.1) Showing Right Intra-Orbital, Extraconal Fat Stranding with Bulky Inferior Rectus Muscle (White Arrow). Axial T2 FS Image (FIG 5.2) Showing Hyper Intensity within the Intraconal Compartment of Right Orbit (White Arrow) Suggesting Orbital Extension of Infection

Teaching Point

Orbital spread often occurs rapidly and can further progress to cavernous sinus thrombosis by retrograde spread through superior ophthalmic vein. A patient presenting with periorbital oedema, eye pain, opthalmoplegia or proptosis should alert the radiologist of possible orbital extension and should actively look for subtle signs of orbital involvement. Timely intervention by orbital exentration can prevent further intracranial spread.

5. Extensive Sinonasal Disease with Intracranial Extension

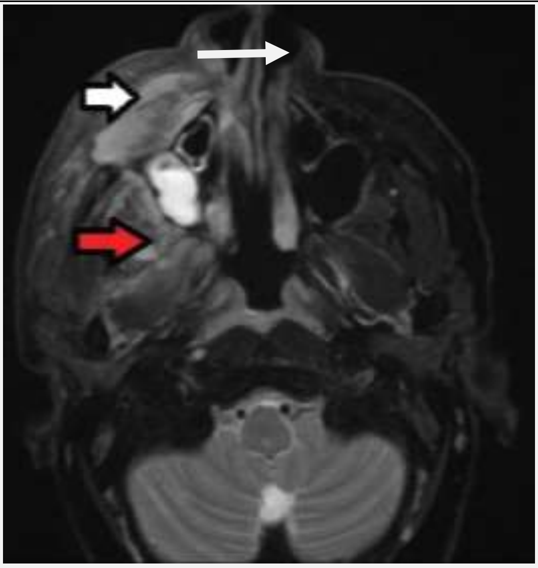


Figure 6.1

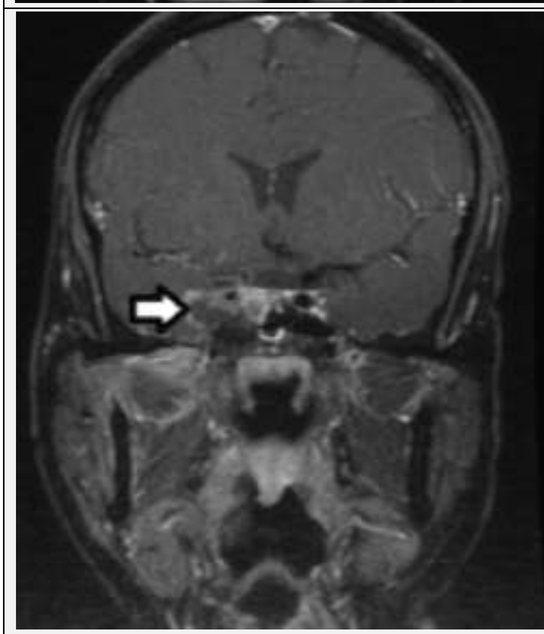


Figure 6.2

Axial T2 FS Image (FIG 6.1) Showing Extensive Spread of Infection into the Pre-maxillary Space (White Arrow) and Right Masticator Space (Red Arrow). Coronal T1 FS+C Image of Same Patient (FIG 6.2) Showing a Peripherally Enhancing Altered Signal Intensity Area in Right Paracavernous Location.

Teaching Point

Most common imaging findings of intracranial extension include cerebrovascular involvement in the form of sinus thrombosis and vasculitic infarcts secondary to internal carotid artery occlusion. Other uncommon manifestations include subdural and epidural abscess and mucor encephalitis with parenchymal changes generally involving basifrontal lobes.

6. Vascular Invasion

Figure 7.1

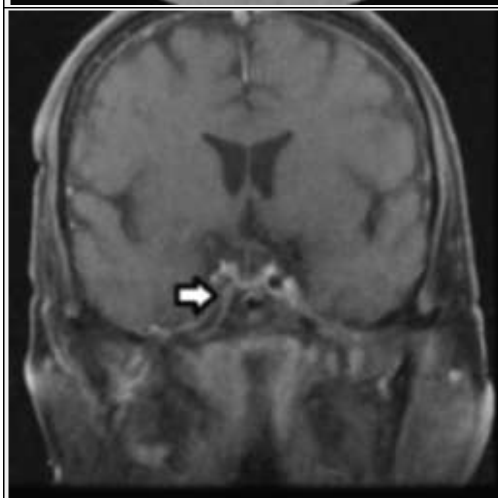


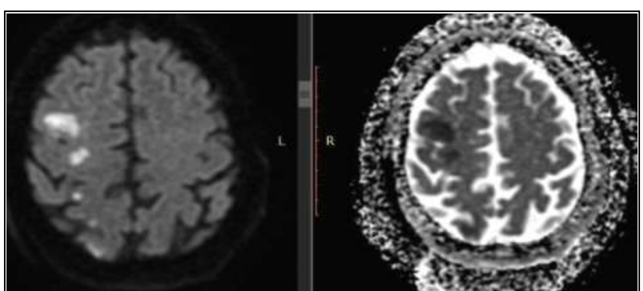
Figure 7.2

Axial CT Section (FIG 7.1) Showing Relatively Prominent Right Superior Ophthalmic Vein Which is an Indirect Evidence of Ipsilateral Cavernous Sinus Thrombosis. Axial T1 FS+C (FIG 7.2) Showing Non Contrast Opacification of Right Cavernous Sinus

Teaching Point

Angioinvasion is the hallmark feature of mucormycosis. A practical dilemma faced by the radiologist is the inability to administer contrast as many mucormycosis patients have transiently deranged renal function after intravenous Amphotericin course and pre-existing diabetes. Hence, indirect signs of angioinvasion like prominence of superior ophthalmic vein in NCCT and absence of ICA flow void in non-contrast MRI should be carefully looked for.

7. Cerebrovascular Complications



Diffusion Weighted MRI (FIG 8) of a 53-Year-Old Patient who Had Extensive Craniofacial Involvement, Showing Multiple Foci of Diffusion Restriction in Right Middle Cerebral Artery Territory, Consistent with Multiple Vasculitic Infarcts.

Teaching Point

Both arterial and venous infarcts can occur in mucormycosis secondary to arterial occlusion and sinus thrombosis. MRI is superior CT in the assessment of cerebrovascular complications as it can distinguish vasculitic infarcts from mucor encephalitis and abscess. It is important to note that the vasculitic infarcts can be remotely located from the brain parenchyma that lies in contiguity with primary focus of infection.

8. Postoperative Imaging

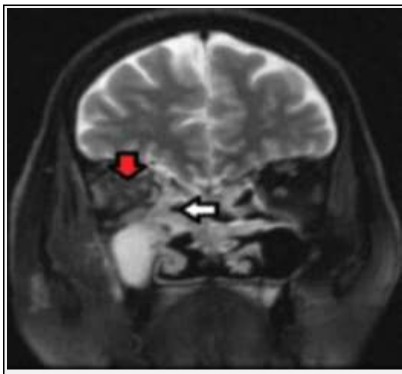


Figure 9.1

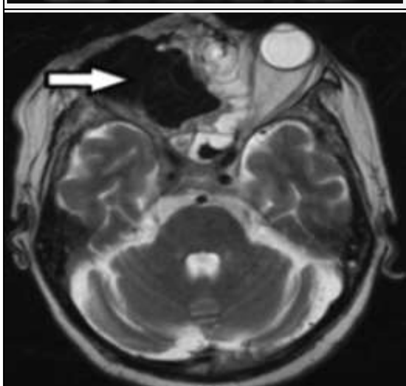


Figure 9.2

Coronal T2 FS Image (FIG 9.1) Showing Altered Signal Intensity Areas Epicentred to the Right Maxillary Sinus. Signal Alteration is Noted within the Right Orbit (Red Arrow) and Right Ethmoid Sinus (White Arrow). The Patient Underwent Right Orbital Exentration with Right Maxillary Antrectomy and Ethmoidectomy, the Post-Operative Changes are Seen in FIG 9.2.

Teaching Point

It is important to distinguish between mucor related mucosal thickening from simple inflammatory thickening that can occur as a part of post-operative changes following endoscopic debridement. It is important to describe the areas of involvement in comparison to pre-operative imaging.

CONCLUSIONS

Rhino-orbito-cerebral mucormycosis has become an established complication in post COVID patients, especially those in immunocompromised states and those who have received long term oxygen therapy. Early clinical suspicion complemented with CT & MR imaging is imperative for early detection and prompt intervention. Recurrence of illness in post-debridement patients, calls for mandatory post op imaging in all successfully treated patients. Thus, radiologists working in post COVID era have a key role to play in eliminating the scourge of black fungus.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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