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MRI Evaluation of Covid 19 Associated Rhinoorbital Cerebral Mucormycosis

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ABSTRACT

Background and Objective: Parallel opportunistic infections have been identified as an additional illness spectrum since the COVID-19 pandemic began. One of these opportunistic diseases that needs attention is mucormycosis, which has seen a sharp rise in cases and rapid dissemination when compared to the pre- COVID-19 era. Following COVID-19, there have been instances of immune suppression. in addition to the presence of comorbid illnesses, which raises the possibility that mucormycosis will be deadly. Early detection and prompt diagnosis can save lives. Magnetic resonance imaging (MRI) imaging is the cornerstone of care for individuals with ROCM. The use of MRI imaging in ROCM was reviewed in this review, with particular attention paid to the optimal MRI protocol in a ROCM case, the routes by which infection spreads, the conventional diagnostic features, MRI for disease staging, MRI for prognostication, MRI for follow-up, and imaging characteristics of common differentials in ROCM.

Materials and Methods: This hospital-based prospective study was conducted on 20 people who tested positive for COVID-19 RTPCR over the course of six months, from March 2021 to August 2021, at the Department of Radiodiagnosis, Alluri Sitarama Raju Academy of Medical Sciences, Eluru. Patients had PNS, orbits, and brain MRIs, which were then analyzed. The statistical analysis employed descriptive statistics.

Image reconstruction: Volume rendering approaches for all axial, coronal, and sagittal reformats have been applied. For vascular assessment, projection images with the maximum and average intensities are used. As noted, clinical and radiological follow-up was done on the cases.

Results: 20 patients were discovered to have rhino orbital cerebral mucor mycosis out of 50 COVID 19 RTPCR positive cases; follow-up biopsies confirmed this diagnosis. Out of 20 individuals with mucor, 11 patients had involvement in the nasal cavity and paranasal sinuses, 6 patients had orbital involvement, and 4 patients had central nervous system involvement.

Conclusion: Imaging is essential for guiding surgical treatments even before clinical symptoms appear and for assessing the severity of the disease, which facilitates a timely diagnosis. When mucor spreads into the orbits and neck regions early in the disease, fat stranding may be the only imaging indicator of extra-sinus dissemination. Therefore, it is critical to thoroughly assess fat-suppressed sequences on MRI when making a diagnosis.MRI is used as a screening method to assess mucormycosis even in the absence of clinical symptoms. Therefore, MRI is essential for determining the severity, stage, and prognosis of a disease, information that is useful for therapy planning.

Key Words: *MRI Evaluation; Mucormycosis*

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INTRODUCTION

The opportunistic, potentially lethal infection known as mucormycosis is caused by the ubiquitous fungus of the order Mucorales, which are commensals of healthy nasal mucosa but create fulminant infection in an immunosuppressed host. The rhino-orbito- cerebral type (ROCM) is the most common form of mucormycosis; other variants include pulmonary, cutaneous, gastrointestinal, and disseminated. An huge increase in ROCM instances occurred during the second COVID-19 pandemic that hit India between March and July 2021, leading the nation to declare an epidemic of this once-rare disease. The term COVID associated mucormycosis (CAM) was created in consideration of this connection.

An analysis of the literature revealed that 81% of instances of CAM were reported from India. A deficient innate immune system, impaired CD4 and CD8 cell counts, elevated ferritin levels, immunological dysregulation resulting in an elevated immature neutrophil count, preexisting uncontrolled diabetes, a diabetogenic state caused by COVID-19, and the improper use of steroids to treat COVID pneumonia are just a few of the likely causes. The extensive use of iron and zinc supplements, industrial oxygen, and contaminated oxygen humidifiers are other possible culprits.

Clinical characteristics, epidemiology, and etiopathogenesis of CAM

Following tissue invasion, thrombosis, and necrosis from the nose to the paranasal sinuses, orbit, and brain, the fungal spores are inhaled into the nasopharynx. Recent research indicates that the condition primarily affects men in their middle years, and most of them manifest 0– 14 days following a positive COVID-19 test. Clinical manifestations include face pain or swelling, paresthesia, loosening of teeth, unpleasant odor, black nasal discharge, epistaxis, nasal mucosal discoloration or eschar, nasal stuffiness, and involvement of the sinonasal and perisinus.

Pathways of spread

The primary mode of transmission for mucormycosis is direct tissue invasion. Through natural pathways such as the nasolacrimal ducts, lymphatics, and neurovascular bundles, or by breaking through bone deterioration, it can spread throughout anatomical areas. Anatomical routes implicated in the evolution of ROCM are summarized in Fig. 1. For a comprehensive assessment of the disease's severity, each of these anatomical areas on MRI needs to be carefully considered.

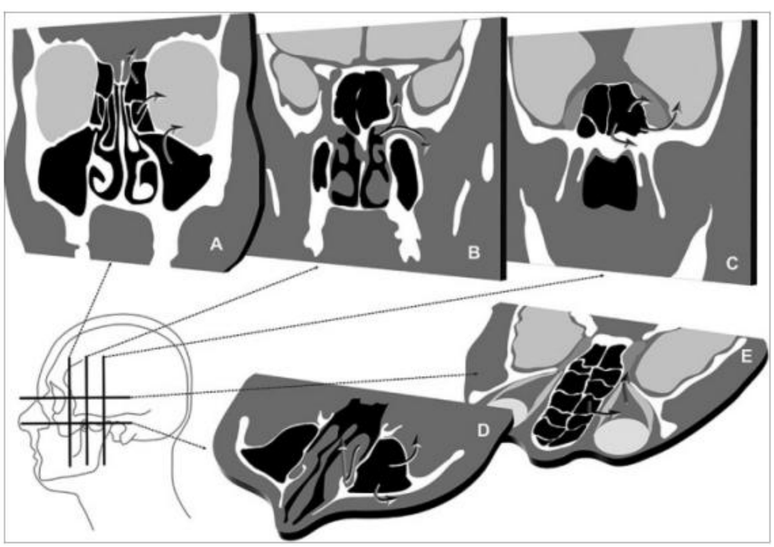

Figure 1 shows the rhinoorbital cerebral mucormycosis dissemination pathways. direct spread into the orbit or cerebral compartment from the ethmoid and maxillary sinuses (a). At the base of the skull, the pterygopalatine fossa serves as a crossroads where nasal disease may disseminate into the infratemporal fossa and cavernous sinus (b). Cavernous sinus, the brain, and the base of the skull may all be affected by sphenoid sinus illness (c). Maxillary sinus disease may affect the face, retroantral, and nasolacrimal soft tissues (d). The orbital apex and cavernous sinus may get infected by intraorbital illness (e)

Diagnosis

While histology and fungal culture are the gold standard for definitively diagnosing mucormycosis, imaging is essential for early diagnosis, early detection of complications, and patient follow-up. MRI is the preferred imaging modality because of its excellent soft tissue contrast resolution for detecting early extrasinus enlargement, especially in cases of intracranial disease in the context of CAM. With the exception of cortical bone involvement, MRI is more sensitive than CT in identifying all cerebral problems associated

MATERIALS & 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, Alluri Sitarama Raju Academy of Medical Sciences, Eluru.

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

The study was carried out in the Department of Radio diagnosis at ASRAM medical college and hospital over a period of 6 months (March 2021-August 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 1.5 TESLA MRI SCANNER, SIEMENS MAGNETOM AVENTO SYNGO (MR D-13) channel 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.

OBSERVATIONS & RESULTS

The research population comprised of 20 patients who were COVID 19 RTPCR positive at March 2021 & August 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 20 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.

DISCUSSION

Mucormycosis is a severe opportunistic fungal infection caused by a fungus belonging to the order Mucorales. India is currently experiencing a sharp rise in coronavirus cases. mucormycosis associated with disease (COVID-19).Individuals with compromised immune systems or altered metabolic processes, such as those who have just become infected with COVID-19, may see a swift advancement of this fungal infection. When it comes to mucormycosis therapy, the most important factors that impact outcome are early suspicion, prompt diagnosis, and treatment initiation. Imaging is the cornerstone of care for individuals with rhino-orbital-cerebral mucormycosis (ROCM). Fifty of the 200 MRI-screened individuals who tested positive for COVID-19 RTPCR had imaging characteristics that may point to ROCM.MRI imaging provides fine detail regarding the degree of involvement, disease spread, and prognosis regardless of clinical symptoms and indicators, which aids in treatment planning.

SINONASAL INVOLVEMENT

The paranasal sinuses are most frequently affected in ROCM, followed by the orbit and central nervous system. Of the twenty-one patients with PNS involvement, ten had ethmoidal sinus involvement, five had maxillary sinus involvement, and three had sphenoidal and frontal sinus involvement. : The air-filled, hypointense normal paranasal sinuses are present on all sequences. A sign of fungal sinusitis is soft tissue opacification of the sinuses. Approximately 50% of ROCM cases involve several sinuses. MRI signal properties vary depending on the sinus contents. T2 weighted hypointense signal is caused by the quantity of necrosis (which induces T2 hyperintensity) and the presence of paramagnetic elements (iron and manganese) within the fungal hyphae. There are several ways that the sinus contents can show up on postcontrast imaging.

1 complete core nonenhancement with or without a thin, uneven rim of peripheral enhancement.2. Intense homogeneous enhancement. 3 Variable enhancing and nonenhancing zones. Invasive fungal sinusitis is typified by the lack of enhancement in areas that should be enhanced on postcontrast T1W imaging. This results in tissue necrosis and microthrombosis in the afflicted areas and is caused by the fungus's angiogenic propensity. This appearance, also referred to as the "Black Turbinate sign," on imaging represents the necrotic eschar found on clinical or rhinoscopic examination. Observing this symptom may help in the early identification of ROCM.

ORBITAL INVOLVEMENT

The orbit is the most frequently implicated extra sinus structure in ROCM, followed by the face. The masticator space, palate, skull base, pterygopalatine fossa, retroantral soft tissue, and other areas are also affected. The lamina papyracea, nasolacrimal duct, ethmoid foramina, and vascular channel perforations of the medial orbital walls are examples of pathways of least resistance that are commonly employed 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

Edoema of the retroorbital fat around the extraocular muscles and soft tissue involvement are signs of an early orbital infection. It is better to observe the retroorbital fat infiltration on fat-saturated T2W sequences. Due to the frequent invasion of the orbit through the medial wall, lateral displacement, and edoema of the medial rectus muscle, it is possible to see inflammatory tissue or the formation of an abscess along the medial aspect of the orbit. Potential involvement of the nerves of vision Sudden onset of blindness can be brought on by an optic nerve infarction, direct invasion of the optic nerve, or ophthalmic or central retinal artery occlusion. A high signal intensity of the nerve in diffusion-weighted imaging indicates optic nerve infarction. Direct invasion of the optic nerve can cause changes in signal strength and increased nerve diameter. When there is isolated involvement of the optic nerve, it indicates that the infection may have spread through branches of the ophthalmic artery and warrants the initiation of vigorous treatment. Globe tenting and severe proptosis are signs of broad orbital infection. The globe's involvement, although its rarity, might be considered an upgrade and augmentation of the ocular coverings. Increased soft tissue at the orbital apex that spreads into the optic canal and superior orbital fissure may be the cause of orbital apex syndrome. When orbital apex syndrome is associated with aberrant sinusitis imaging, suspicion of a fungal cause needs to be raised.

CNS INVOLVEMENT

Infection traveled from the sinuses to the brain by constant spread and, less frequently, bone invasion. Mucus from the nasal cavity and paranasal sinuses directly extends to the brain parenchyma, resulting in brain abscess and cerebritis. Mucor reach the brain via the orbit, superior orbital fissure, and cavernous sinus. The most common locations of direct cerebral distribution are the walls of the frontal sinus, ethmoid, and cribriform plate. Both the internal carotid artery and the pterygopalatine fossa reach into the middle cranial fossa. Infection from cavernous sinus travels perineurally down the trigeminal nerve, leading to predominantly posterior fossa involvement.

IMAGING FINDINGS

Cavernous and major arterial involvement:

Heterogeneously increasing soft tissue extending from the superior orbital fissure involves the cavernous sinus in ROCM. The lateral walls of the sinuses are usually straight or laterally concave on coronal and axial imaging. The disappearance of the cavernous sinus concavity is one sign of involvement. A big cavernous sinus with a convex lateral wall is one of the early symptoms. Abnormal sinus filling is revealed in images following contrast. Disease that spreads throughout the vein or soft tissue compression at the orbital apex can both cause the superior ophthalmic vein to become blocked.

Intracranial extension

Mucormycosis often spreads directly over the frontal sinuses, ethmoid walls, and cribriform plate, resulting in intracranial involvement. Both the internal carotid artery and the pterygopalatine fossa reach into the middle cranial fossa. Perineural spread from the cavernous sinus down the trigeminal nerve may cause predominant posterior fossa involvement. Early intracranial spread is more visible in contrast-enhanced T1W images when the meninges are improved. Two other intracranial symptoms include infarcts and abscesses. Nonvascular distribution shows ill-defined areas of altered signal intensity, usually T2 hyperintensity, due to fungal invasion of the brain parenchyma. There is obvious little perilesional edema and variable peripheral enhancement.

Skull base involvement

1. Skull base osteomyelitis is an uncommon outcome that usually appears in the latter stages of the illness. Bone involvement occurs relatively late in the course of the disease because the fungus's angioinvasive nature makes it simpler for the infection to disseminate widely into the deep soft tissues through the perivascular channels even before bone degeneration. Early involvement of the typical fat signal in bone. The bone marrow looks hypointense on T1W and STIR imaging, and postcontrast images show heterogeneous enhancement. There is a large amount of heterogeneously enhancing soft tissue in the advanced stage because to infiltration into the bones.

CONCLUSION

• ROCM frequently causes invasive fungal sinusitis in patients with diabetes and other immune compromised conditions. It has been established that individuals with COVID-19 have ROCM. co-infection since 2020, which complicates patient treatment. When ROCM first manifests, it has a severe clinical course that calls for prompt and vigorous care.

• Quick diagnosis is made easier by imaging, which is also crucial for figuring out the disease's extent, which guides surgical approaches. The majority of ROCM patients often exhibit the black turbinate sign, however it can also be seen in other IFS and replicated by healthy cavernous tissues in the turbinates. The fungus can expand outside of the sinus without directly harming bone because it is angioinvasive. Because of this, mucor invades the orbital and neck regions early in the illness; the only imaging indicator of extra-sinus dispersion may be fat stranding. Therefore, when reaching a diagnosis, it is critical to carefully evaluate soft tissue algorithms on CT and fat- suppressed sequences on MRI.

More accurate imaging of the base of the skull must be considered in suspected cases of MCR, even if the fungus has the ability to travel along peripheral nerves in the base of the skull and into the cerebral compartment. The development of abscesses and ischemia issues associated with vasculitis are examples of intracranial symptoms of the infection that are warning indicators of a worse course of events. Even before noticeable symptoms appear, MRI imaging of the brain, orbits, and PNS is essential for determining the course and severity of a disease. Thus, rhinoorbital cerebral mucormycosis, which is common during the COVID era and may be caused by immunosuppression and other causes, can be diagnosed and screened for early treatment using magnetic resonance imaging (MRI).

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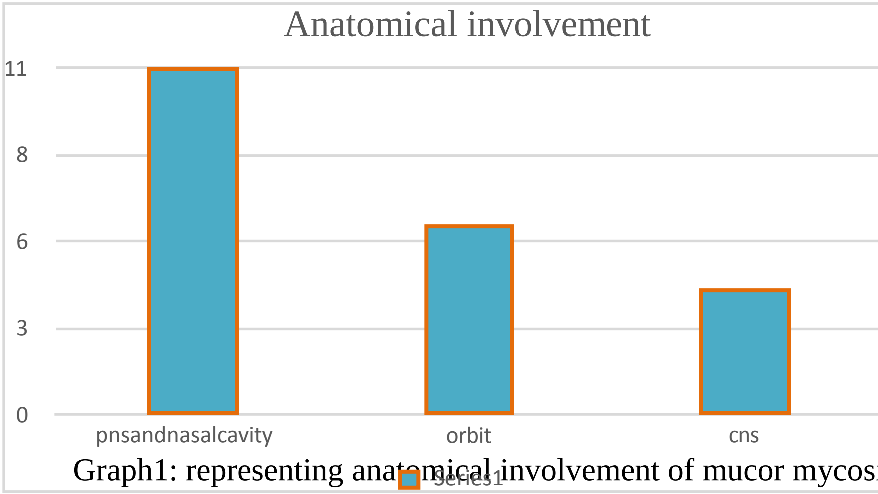
IMAGINGFINDINGS

Table1: showing anatomical involvement.(predominant)

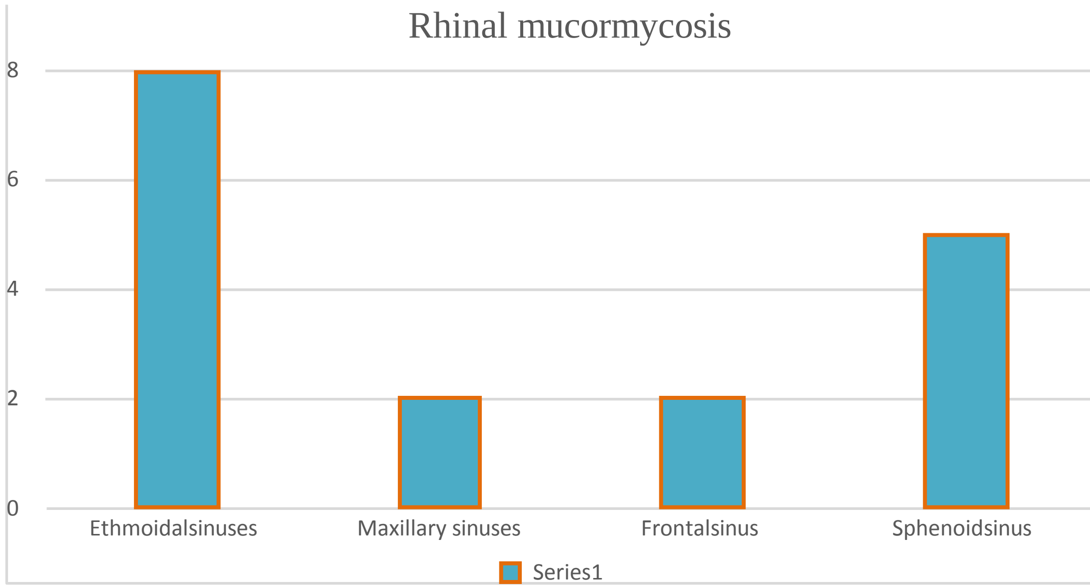
Structure of involvement	No. of patients	Percentage
PNS and nasalcavity	11	55
Orbit	6	30
CNS	4	20



Graph1: representing anatomical involvement of mucor mycosis

Tab2 representing anatomical involvement of cerebral mucor mycosis

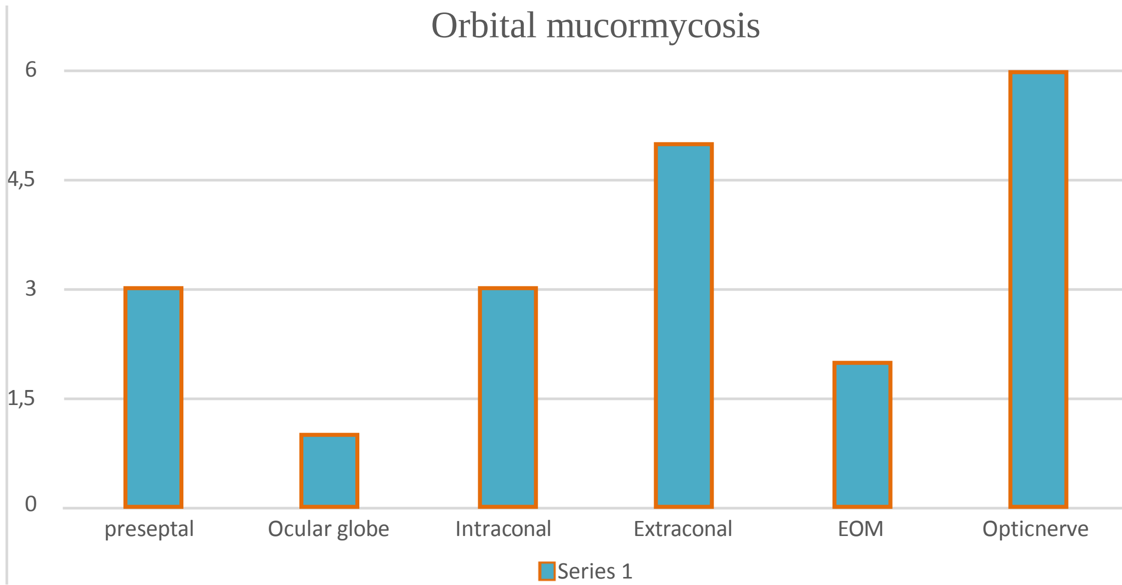
Paranasal sinus involved	Noof patients (n=11)	Percentage
Ethmoidal sinuses	8	72,7
Maxillary sinuses	2	19
Frontal sinuses	2	19
Sphenoid sinus	5	45



Graph2 representing anatomical involvement of rhinal mucormycosis

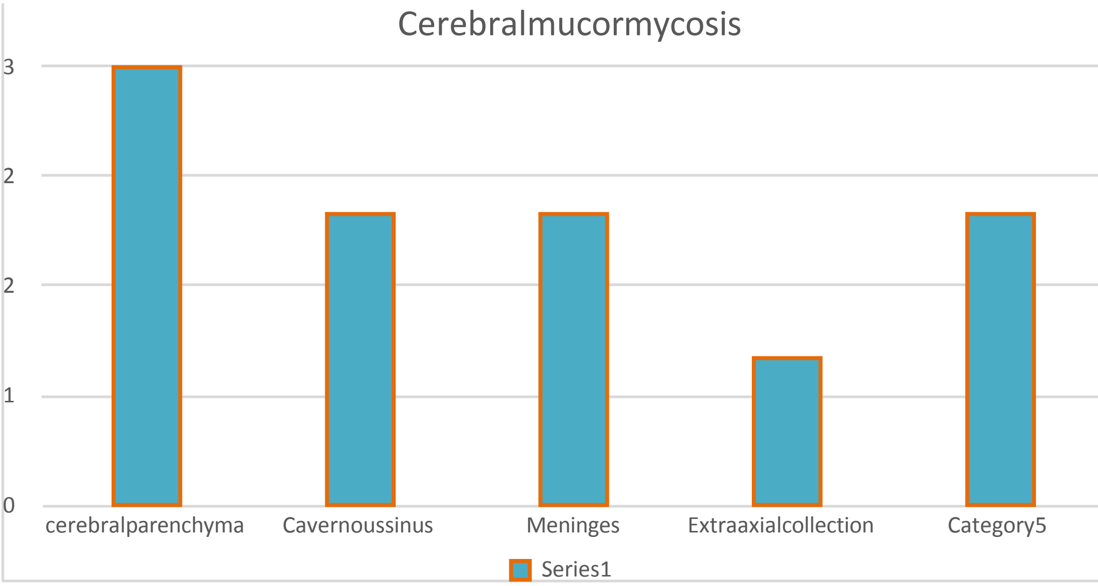
Tab 3 representing anatomical involvement of orbital mucormycosis

Orbital structure involved	No of patients(n=6)	Percentage
Preseptal	3	50
Ocular globe	1	16,6
Intraconal	3	50
Extraconal	5	83,3
EOM	2	33,3
Optic nerve	6	100



Tab4 representing anatomical involvement of cerebral mucor mycosis

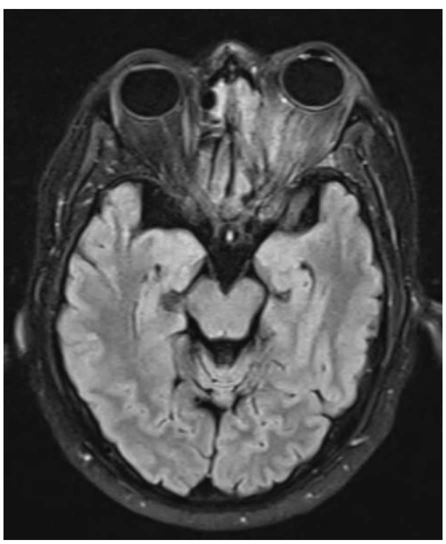
Structure involved	No of patients(n=4)	Percentage
Cerebral parenchyma	3	75
Cavernoussinus	2	50
Meninges	2	50
Extra axial collection	1	25
Internalcarotid artery	2	50

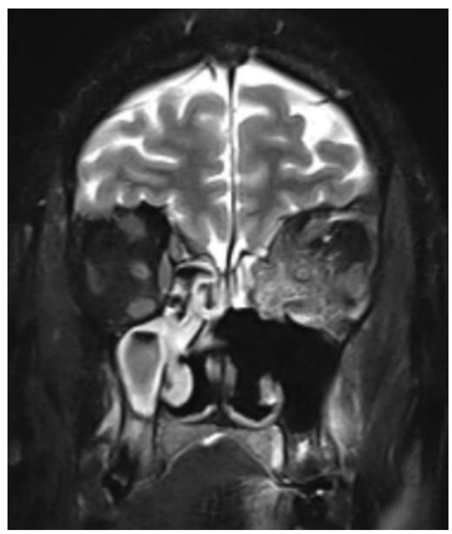


Graph4 representing anatomical involvement of cerebral mucormycosis

IMAGE GALLERY

ORBITALMUCORMYCOSIS





a **b**

Fig 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

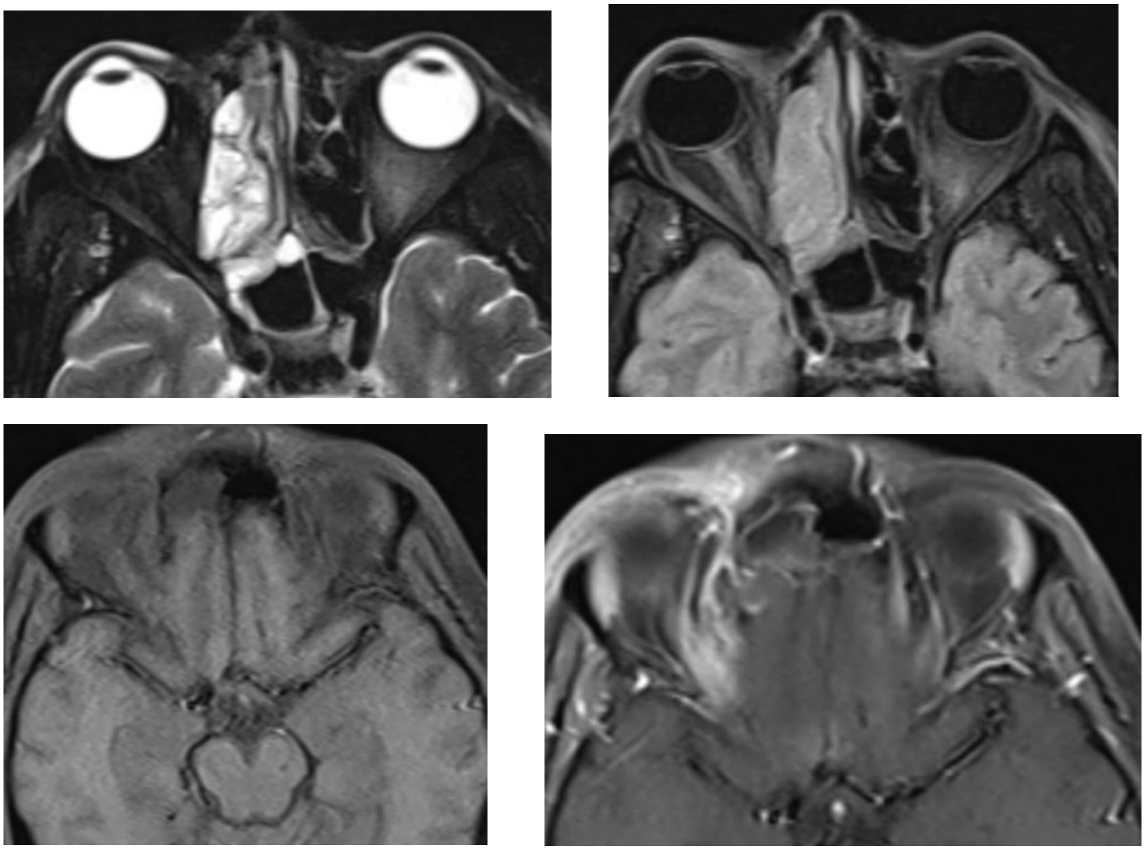


Fig 2 Orbital disease in ROCM Axial T2FS(a),FLAIR(b),T1FS pre contrast(c),T1FS post contrast (d) showing right pre septal involvement of orbit in orbital mucor

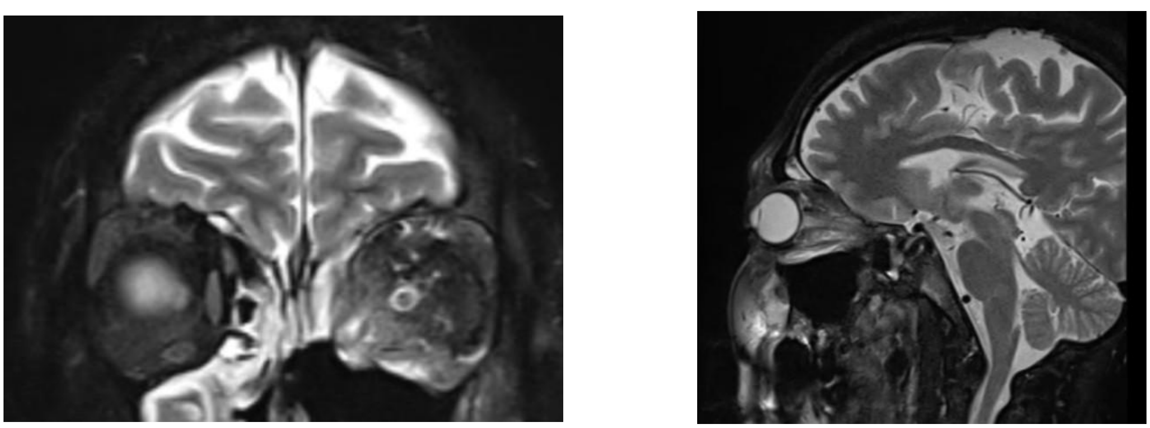


Fig 3 Orbital disease in ROCM Coronal T2w(a),Sagittal T2w (b) showing mild bulky optic nerve with heterogenous signal intensity suggestive of optic neuritis

PARANASALINVOLVEMENT

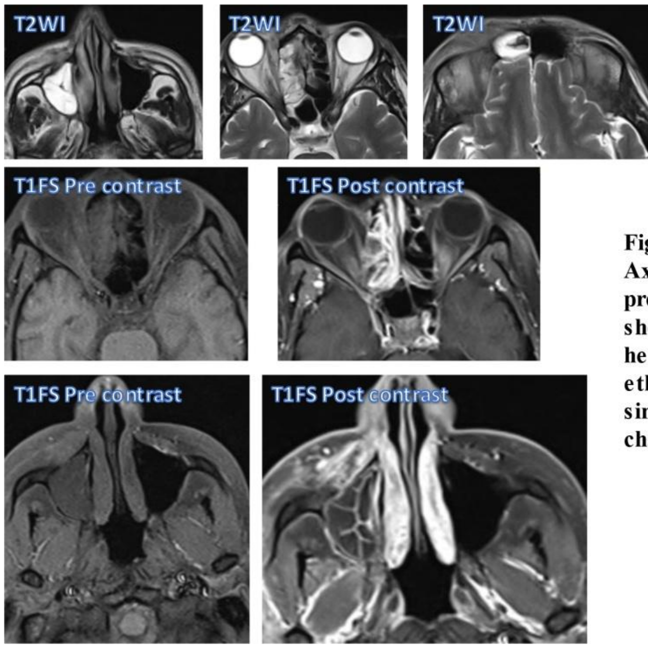


Fig 4 Sinonasal disease in ROCM Axial T2w(a-c),T1FS precontrast(d,f),post contrast(e,g) showing mucosal thickening and heterogenous enhancement of right ethmoidal,maxillary and frontal sinuseswith adjacent soft tissue changes

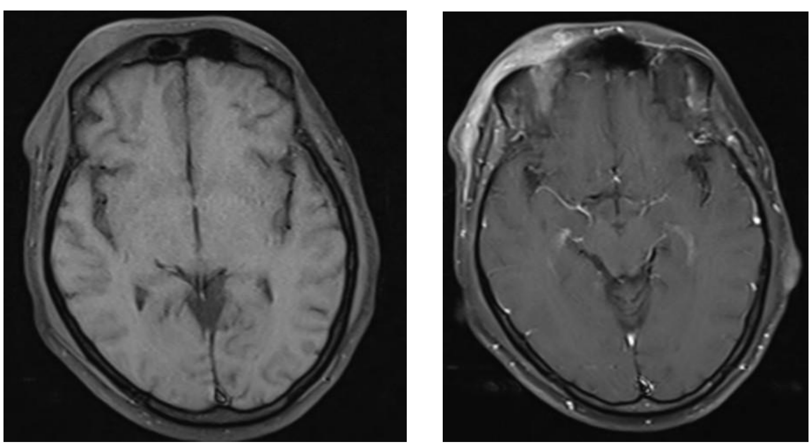


Fig 5 Axial T1FS pre contrast (a),post contrast(b) images of brain showing mild bulky,heterogenous enhancing right temporalis muscle

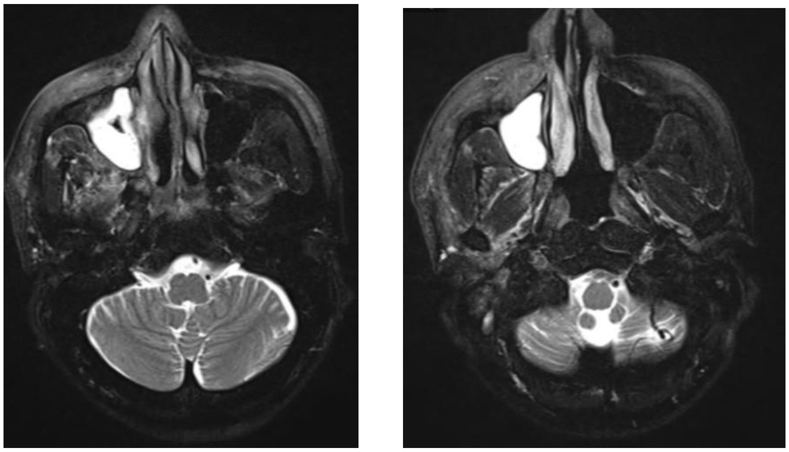


Fig 6AxialT2 w(a & b) images of brain showing hypersignal intensity in right maxillary sinus,heterogenoussignalintensitychangeswithfatstrandinginrightmasticatormuscles

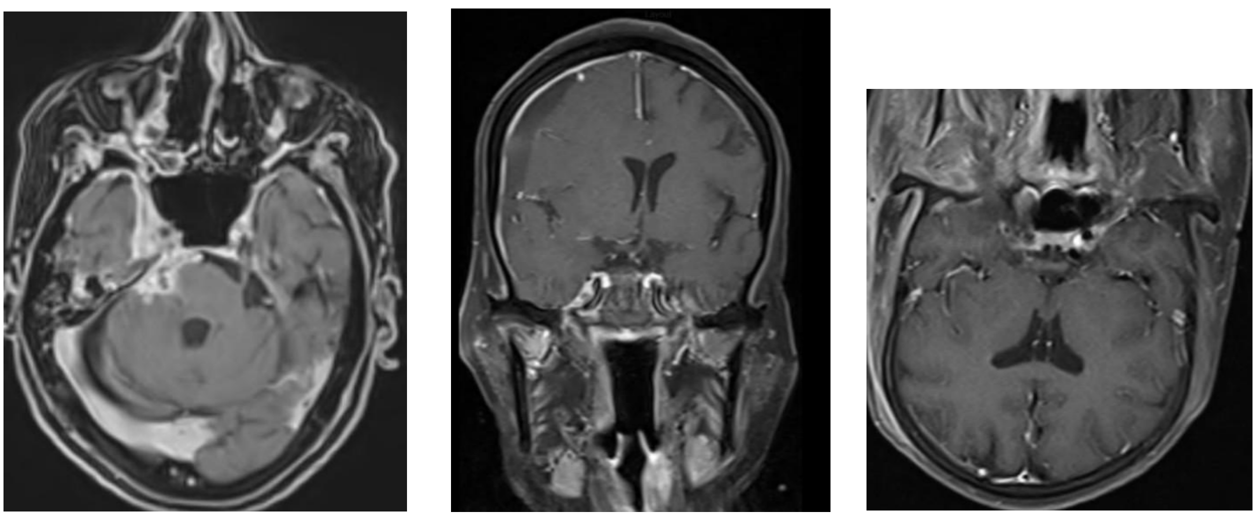


Fig 6 Extrasinus invasion in ROCM patient Axial T1FS post contrast(a) showing heterogenous enhancement of right meckels cave which is suggestive of trigeminal nerve involvement

Coronal(b) T1FS post contrast showing the involvement of bilateral cavernous sinus

Axial(c) T1 FS post contrast brain showing narrowing of right ICA flow void

CEREBRALMUCORMYCOSIS

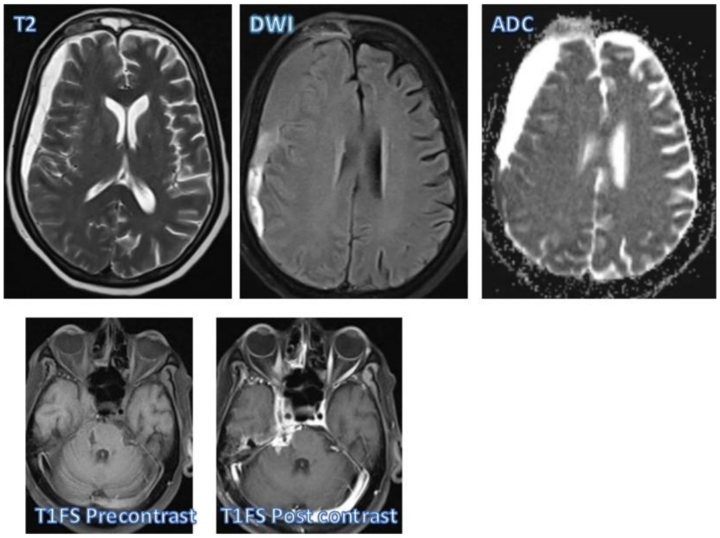


Fig 7 CNS involvement of ROCM T2 axial(a),DWI(b),ADC(c) showing well defined extra axial concavo convex collection with no diffusion restriction noted along right frontoparietalconvexity.T1FSprecontrast(d)andpostcontrast(e)showinginvolvementof right trigeminal nerve,cavernous sinus and orbital apex.