ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 7, Issue – 5, September – 2022 , Page No. : 21 – 29

Imaging features in COVID-19 associated Rhino-Orbito-Cerebral Mucormycosis (ROCM) on CEMRI

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Citation this Article: Dr. Manisha Lokwani, Dr. Suraj Makhija, Dr. Sunit Lokwani, "Imaging features in COVID-19 associated Rhino-Orbito-Cerebral Mucormycosis (ROCM) on CEMRI", IJMSIR- September - 2022, Vol – 7, Issue - 5, P. No. 21 – 29.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Introduction: Rhino-orbito-cerebral mucormycosis is an acute, fulminant rapidly progressing and often lethal opportunistic infection. Early diagnosis and timely intervention are key to successful treatment. MRI plays a key role in assessing the locoregional spread of infection and its complications.

Objective: The objective of this study is to describe the spectrum of imaging findings of COVID-19 associated mucormycosis on Contrast enahnaced MRI and to study the extent of loco-regional spread of the infection in affected individuals.

Materials And Methods: 115 patients with laboratory proven mucormycosis were included in the study, and CEMRI studies of brain, sinuses and orbit of these patients were retrospectively evaluated. All the patients with sinusitis due to other cause were excluded.

Results: Mucosal thickening was seen consistently in all cases(115,100%). T2 hypointense soft tissue elements were observed in 98 cases (85%). Maxillary sinus was the most common sinus involved (96%)
followed by anterior group of ethmoid (91%). The classical black turbinate sign was observed in 37 patients (32%) on post contrast images. Retro maxillary fat pad stranding was noted in 83 cases (72%). Extension of disease to pterygopalatine fossa was observed in 76 cases (66 %). Involvement of infra temporal fossa structures was noted in 78 cases (68%). Orbit was seen to be involved in 65 cases (57%), where most common finding was orbital fat stranding. Extension of disease to cavernous sinus was noted in 28 cases (24%), with concomitant occlusion of cavernous ICA in 14 cases (37%). Intracranial involvement was noted in 37 cases (32%) with most common finding in brain being parenchymal infarct (11 cases, 9%).

Conclusion: CEMRI plays a major role in assessing the extent of involvement of mucormycosis and its complications, which guides the operating surgeon in prompt decision making.

Keywords: COVID-19. Mucor my cosis, Immuno compromised, micro vessel invasion, orbital and intracranial involvement.

Introduction

Rhino- orbito- cerebral mucor mycosis is an acute, fulminant rapidly progressing and often lethal opportunistic infection. It typically affects the immuno

compromised patients, especially diabetic patients. In the second wave of COVID pandemic in March 2021 in India, there was an alarming rise in the number of these not so common infections in post COVID phase due to multiple reasons. The causative agent is one of Absidia, mucor or Rhizopus fungus. Patients usually present with non-specific symptoms like headache, low grade fever, facial or peri-orbital swelling, orbital or paranasal sinus syndrome [1,2].

The most common predisposing immuno compromised condition was diabetes mellitus in India with injudicious use of steroids whereas in developed countries, the predisposing conditions were Haematological malign an cies and organ trans plants [1].

We retrospectively reviewed the MRI findings in a series of patients with rhino-orbito-cerebral mucormycosis to establish common features which may prove as useful predictors of diagnosis of this lethal infection.

Objective

The objective of this study is to describe the spectrum of imaging findings of COVID-19 associated rhino-orbito-cerebral mucormycosis on Contrast enhanced MRI and to study the extent of loco-regional spread of the infection in affected individuals.

Materials and methods

We retrospectively evaluated the imaging features of 115 patients in a span of 6 months. The inclusion criteria included established case of mucormycosis by micro scopy/ culture/autopsy and were evaluated by CEMRI.

All patients were evaluated on 1.5 T MR system by GE electronics, USA. A contrast study was also obtained in all cases by administering IV injection of gadopentetate Di meglumine (0.1 mmol/kg). Axial, coronal and sagittal T1 weighted (TR/TE 40/12 Ms), T2- weighted images (TR/TE 4000/100 Ms) and fat suppressed post contrast T1 weighted images were acquired.

We looked for MR signal intensity of the sinus contents, presence or absence of mucosal thickening, different sites involved, orbital, ptery go palatine fossa, infratemporal fossa, caver nous sinus, vascular or intra cranial involvement. The MR signal intensity was compared to that of gray matter on T1 and T2.

Results

The results have been summarized in TABLE 1 and TABLE 2.

Out of 115 patients, 86 were males, 29 females. The age varied from 37 yr to 86 yr with the average age being 51 yrs.

Mucosal thickening was seen consistently in all cases (115,100%). T2 hypointense soft tissue elements were observed in 98 cases (85%) [FIG. 1]. A few cases demonstrated diffusion restriction of necrosed mucosa on DWI.

The classical black turbinate sign was observed in 37 patients (32%) on post contrast images [FIG. 2].

Maxillary sinus was the most common sinus involved (96%) followed by anterior and posterior group of ethmoids (91%).

Extension of disease to pterygopalatine fossa was observed in 76 cases (66 %). Involvement of infra temporal fossa structures was noted in 78 cases (68%) [FIG.-3]

Orbit was seen to be involved in 65 cases (57%), where most common finding was orbital fat stranding [FIG.4]. Proptosis was observed in 25 cases (21%). Other orbital manifestations on MRI were- orbital abscess (3, 2%), optic neuritis/nerve infarction (22, 19%), Superior ophthalmic vein thrombosis (6, 5%). A few cases demonstrated posterior global tenting i.e., GUITAR PICK SIGN.

Extension of disease to cavernous sinus was noted in 28 cases (24%), with concomitant occlusion of cavernous ICA in 14 cases (37%) [FIG.-5].

Intracranial involvement was noted in 37 cases (32%) with most common finding in brain being parenchymal infarct (11 cases, 9%) [FIG.-10]. Other parenchymal findings were cerebritis (9, 7%), cerebral abscess (9, 7%) [FIG. 6], meningeal enhancement (6, 5%).

Table 1: anatomic site distribution

Site	Number/115	%
Nasal cavity	98	85
Maxillary sinus	110	96
Ethmoid sinuses	105	91
Sphenoid sinus	97	84
Frontal sinus	87	76
Retro maxillary fat pad	83	72
Pterygopalatine fossa	76	66
Infratemporal fossa	78	68
Orbital involvement	65	57
Optic nerve	22	19
Superior ophthalmic vein	6	5
Intracranial involvement	37	32
Brain parenchyma	29	25
Cavernous sinus	28	24
ICA	14	12
Meninges	6	5

Table 2: imaging features on cemri

Imaging feature	Number out of 115	Percentage
Sino nasal		
Mucosal thickening	115	100
Black turbinate sign	37	32
T2 hypointense contents	98	85
Sinus involvement	115	100
Pansinusitis	77	67
Orbit		
Orbital fat stranding	65	57
Proptosis	25	21
Orbital abscess	3	2
Optic neuritis/ nerve infarction	22	19
Superior ophthalmic vein thrombosis	6	5
Intracranial		
Cerebritis	9	7
Cerebral abscess	9	7
Cerebral infarct	11	9
Meningeal enhancement	6	5
ICA occlusion	14	12
Caver nous sinus involvement	28	24
Bone erosions	63	55

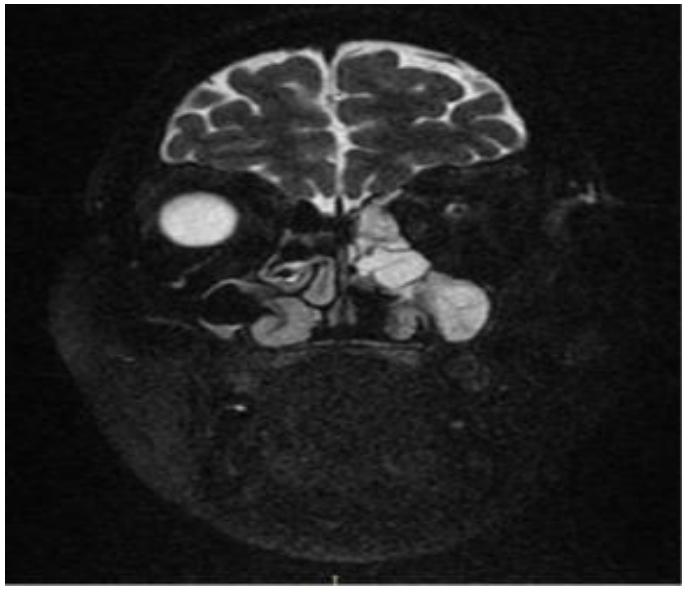

Fig. 1: Sino - nasal involvement in post COVID mucormycosis. Coronal T2 fat sat. MR image shows mucosal thickening with internal hypointense contents along bilateral maxillary and ethmoid sinuses, more prominent on left side.

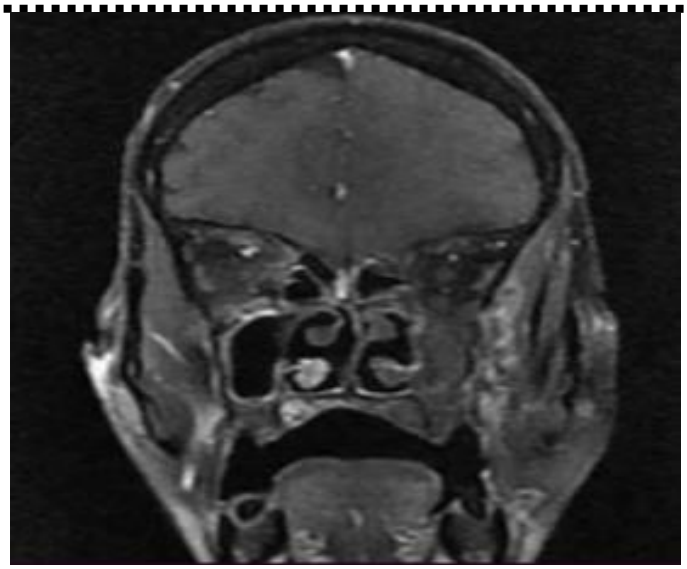

Fig. 2: Coronal T1 post contrast image shows non-enhancing right middle and left middle and inferior turbinate in a case of post-COVID mucormycosis; findings suggestive of BLACK TURBINATE SIGN. Note the normally enhancing right inferior turbinate

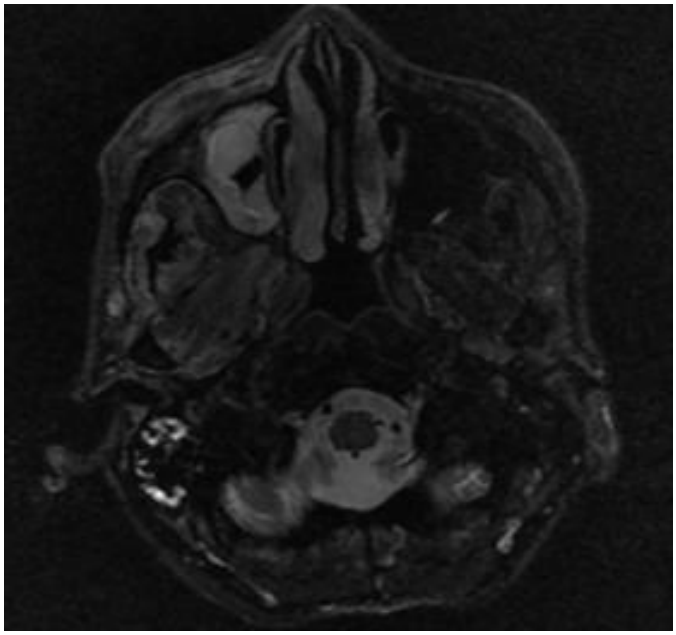

Fig. 3: Axial T2 Fat sat. MR image demonstrates mucosal thickening along the right maxillary sinus. There is evidence of stranding along right preantral and retro antral fat pads. Fat stranding is also noted in Right masticator space and right infratemporal fossa.

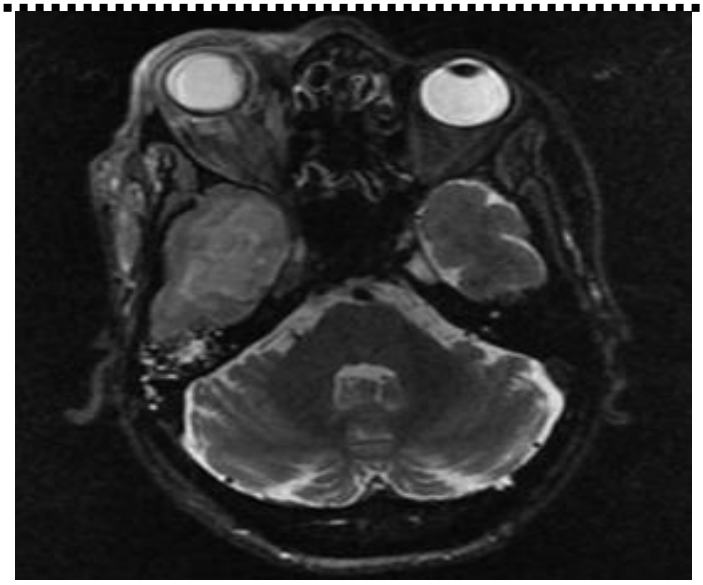

Fig. 4: Orbital extension of mucormycosis. Axial T2 Fat sat. MR image demonstrates right sided retro-orbital fat stranding with resultant proptosis. Also, note the presence of mucosal thickening along bilateral anterior and posterior group of ethmoids.

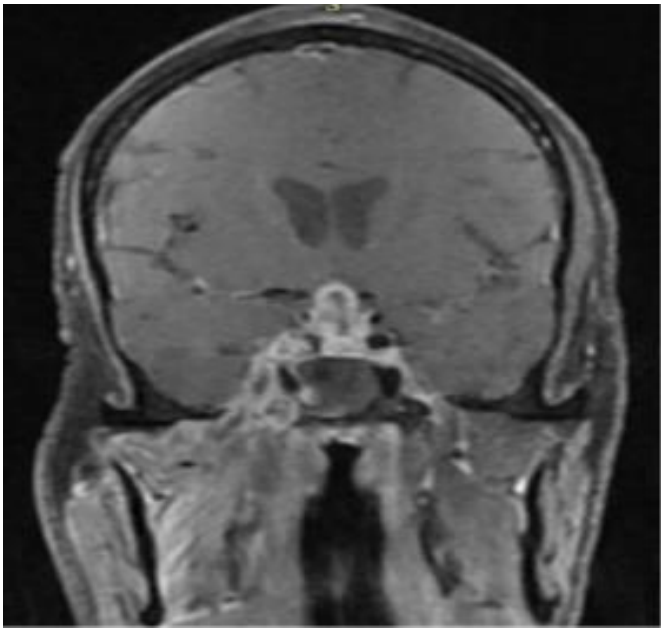

Fig.5(A)

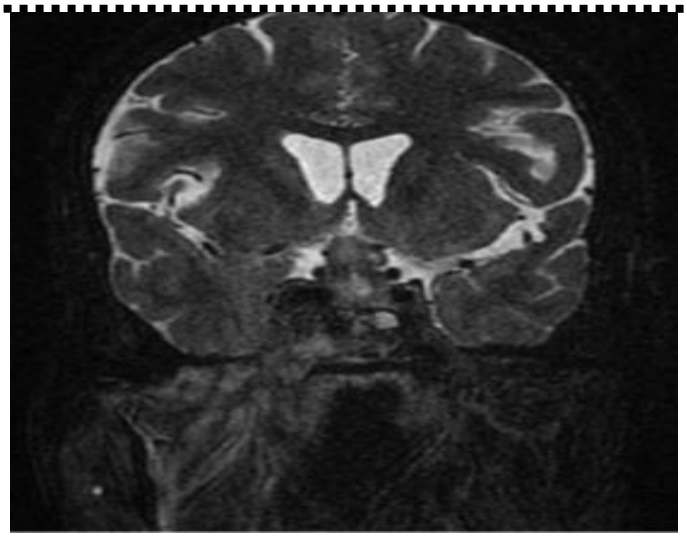

Fig. 5(B)

Fig. 5: Cavernous sinus involvement. Fig 6(A) shows bulky right cavernous sinus with loss of lateral concavity and internal T2 hypointense contents. Fig 6(B) T1 post contrast coronal image showing bulky right cavernous sinus with reduced caliber of cavernous ICA (occlusive/ compressive).

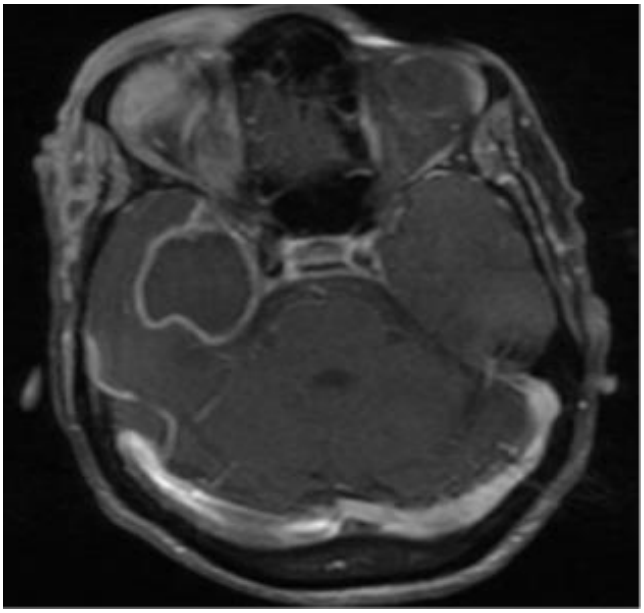

Fig. 6(A)

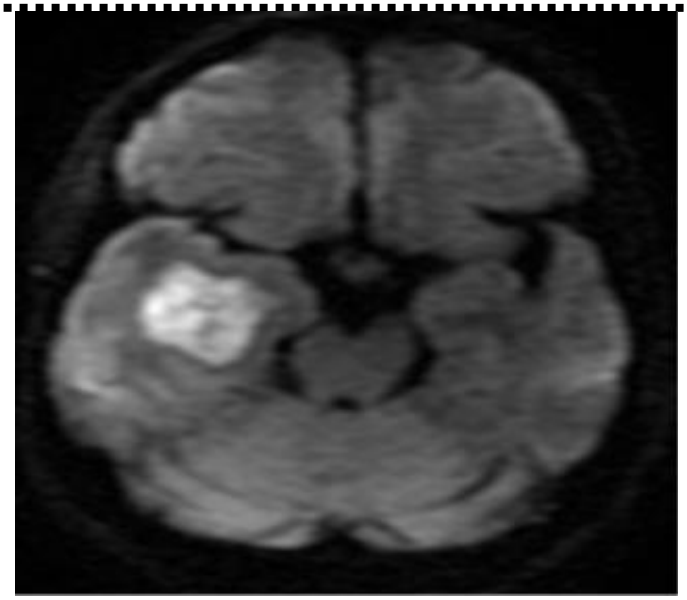

Fig. 6 (B)

Fig. 6: Temporal lobe abscess in a case of mucormycosis. A ring enhancing lesion was observed in right temporal lobe (A), which demonstrated internal diffusion restriction on DWI (B).

Discussion

Rhino-orbito-cerebral mucormycosis is an acute, fulminant rapidly progressing and often lethal opportunistic infection caused by an angio-invasive opportunistic fungus of order Mucor ale. Following the inhalation of fungal spores present in the environment, the fungi colonize and infect the nasal/sinus mucosa first, before spreading to surrounding anatomical areas including the orbit, cavernous sinus, and brain [3]. Risk factors were concurrent or recent (<6weeks) treated for COVID, uncontrolled diabetes mellitus and treatment with steroids and tocilizumab like immunomodulators [4].

Pathogenesis

The fungus causes a necrotizing vasculitis and causes mucosal gangrene and death and sloughing of tissues due to micro vessel occlusion and perivascular and perineural spread leading to further rapid invasion of fungus to deeper and vital structures like orbit and brain. If only the

paranasal sinuses are involved, the survival rates are good (between 50-80%) but with brain invasion, the mortality rate spikes at more than 80%. Therefore, it is important to not only to make its early diagnosis but also treat it quickly and aggressively.

Pathways of spread of infection

The spread may occur across natural bony defects, along natural pathways such as the nasolacrimal ducts, lymphatics, and neurovascular bundles.

Spread into sinuses

Initially the fungus colonizes the nasal cavity mucosa, invades the mucosa and then spreads rapidly into the sinuses through anatomical contiguity and by bone erosive and angioinvasive properties.

Spread from sinuses

From the maxillary sinuses, it may spread either posteriorly into the retro antral fat and then the pterygopalatine fossa (PPF) and masticator space or superiorly into the inferior extraconal space of orbits. From the frontal and ethmoid sinuses, spread occurs to the orbit through the sinus wall erosion or from nose to orbits via nasolacrimal duct and commonly then the orbits.

Spread from orbits

(1) Spread into pterygo-palatine or infratemporal fossa through inferior orbital fissure.

(2) Infection may spread to cavernous sinus through orbital apex or superior orbital fissure.

Spread to intracranial compartment

Involvement of anterior cranial fossa can occur by direct spread through cribriform plate, ethmoid and frontal sinuses. Involvement of middle cranial fossa may occur through pterygopalatine fossa and along ICA [5].

MR Imaging features

Sino nasal findings

Opacification of sinuses and nasal cavity by soft tissue is seen. Contents may show variable signal intensity as they may be T2 hyperintense or T2 hypointense. T2 hypo intensity is due to presence of iron and manganese within fungal hyphae [6]. DWI may show restricted diffusion in necrosed mucosa [7].

Marrow edema and erosions in walls of sinuses (changes of osteomyelitis) may be seen. Variable enhancement of sinus mucosa is seen in CEMRI ranging from intense homogenous enhancement /mixed enhancing and non-enhancing areas and complete central non enhancement with peripheral enhancement. Characteristic feature is nonenhancement of sinus mucosa called black turbinate sign seen on fat sat post contrast T1W images.

This sign helps in early diagnosis of invasive fungal sinusitis [8].

Extra sinus extension itself gives an indication of fungal etiology.

Retro antral fat

Fat stranding and enhancement are commonly seen. Retro-antral fat stranding is best seen on fat sat T2W sequences.

A) Pterygopalatine fossa, masticator space and infratemporal fossa

Fat stranding, enhancing soft tissue and edema and enhancement of muscles of mastication are commonly seen.

Orbit

- Retroorbital fat stranding and enhancement is a sensitive and important sign to look for orbital involvement. It is best seen on fat saturated T2W sequences.

- There may be edema and infiltration of extraocular muscles and sometimes orbital abscess formation. The Medial rectus muscle is the earliest affected muscle.
- Direct invasion of the optic nerve may appear swollen with abnormal signal on T2W images. Optic nerve may show infarction seen as presence of restricted diffusion on DWI. Sudden blindness can occur due to direct invasion of optic nerve or optic nerve infarction due to central retinal artery or ophthalmic artery
- Due to excess retroorbital fat inflammation, proptosis and posterior tenting of globe may be seen resulting in guitar pick sign.
- Pan ophthalmitis is rare but may occur and is seen as diffuse thickening and enhancement of the coats of eyeball.
- Orbital apex which includes superior orbital fissure and optic canal may be involved seen as enhancing soft tissue in these areas. When imaging findings of sinusitis are associated with orbital apex syndrome, suspicion of fungal etiology must be raised. Orbital apex syndrome encompasses three elements: visual loss due to optic neuropathy, ophthalmoplegia due to third, fourth and sixth cranial neuropathy, and ocular-orbital pain &/or anesthesia due to involvement of the ophthalmic division of the trigeminal nerve [10].
- Superior ophthalmic vein may be thrombosed and seen as a dilated cord-like structure.

Intracranial involvement

- Cavernous sinus: Heterogeneously enhancing soft tissue may be seen extending from superior orbital fissure into cavernous sinus. Loss of concavity of the lateral wall of cavernous sinus on coronal or axial images may be seen. There may be nonenhancement of cavernous sinus.
- Cavernous segment of ICA: Encasement and narrowing of cavernous segment of ICA can occur due to soft tissue. Direct invasion of vessel wall leads to thrombotic occlusion leading to cerebral infarction and stroke. Loss of the normal flow void on T2W images is seen with or without peripheral enhancing soft tissue.
- Infarct in brain parenchyma seen as areas of abnormal signal with restricted diffusion.
- Fungal cerebritis is seen as an area of abnormal high T2 signal in gyri with swelling in non-vascular distribution with gyri form enhancement. This may later turn into a well-defined area of fungal abscess with non-enhancing T2 hyper intense center showing central restricted diffusion. The peripheral rim enhancement may be absent in a immuno compromised host [11].
- Pachymeningeal enhan cement suggests dural invasion by fungus.
- Lep to meningeal enhan cement suggests fungal meningitis.
- Fungal ventriculitis is rare but may occur and is seen as obstructive hydro cephalus and ependymal enhan cement.
- Skull base marrow edema and enhancement is a late feature and suggests bony invasion of skull base (skull base osteomyelitis) seen as loss of normal high fat signal of marrow fat on T1W images. The marrow appears hypointense on T1W images and hyperintense on STIR images with postcontrast images showing heterogenous enhancement [12].

MR STAGING by Honarvar SG [13];

Stage I: Disease limited to nasal mucosa

Stage II: Extending into paranasal sinuses

Stage III: Orbital involvement.

Stage IV: CNS involvement.

Importance of CEMRI

CEMRI is the cornerstone for early and prompt diagnosis, allowing evaluation of the entire extent of disease. Due to its inherent superior spatial and contrast resolution, MRI permits early detection of extra sinus extension, even before bone destruction is evident on CT scan. MRI helps in proper evaluation of the presence of necrosis (nonenhancement), extra sinus involvement-peri antral fat, orbital pterygopalatine fossa or ITF, cavernous sinus, vascular, cranial nerves, brain and skull base extension.

Thus it has a major role in guiding treatment strategy. Patients with disease limited to sinuses are taken for debridement of sinuses and nasal cavity with or without resection of nasal septum turbinates and medial orbital wall. In predominant orbital involvement, early orbital exenteration is done with Sino nasal debridement. In cerebral involvement, along with antifungal, debridement of necrotic issue is done.

Due to lack of ionizing radiation, MRI is also helpful in follow up of patients with ROCM.

Pitfalls of MRI

- In early disease confined to sinuses and nasal cavity, MRI may be normal or show non-specific findings. However, a repeat scan after 48 to 72 hrs can be done to look for progression of disease. Such rapid progression points to fungal etiology.
- Nonenhancement of sinus turbinate may be seen as a normal physiological variation. However, progressive enhancement in delayed phase, absence of extra sinus findings and lack of T2 hypointense soft tissue elements points to a benign cause such as a physiological variation rather than fungal etiology.
- MRI cannot differentiate between various species of fungi.
- It is time consuming, expensive and has limited availability.

Pitfalls of the study

This study is done in a tertiary care center so referral usually carries a bias of late-stage disease or progressed disease so the early MRI signs may not be seen.

Conclusion

Mucormycosis is a life-threatening invasive infection, which predominantly affects immunocompromised individuals. The disease originates in the Sino nasal mucosae and extends rapidly to neighboring structures, including orbit and brain.

Early diagnosis and timely intervention are key to successful treatment. Although definitive diagnosis is based on the demonstration of fungal hyphae typical for mucor my cetes in biopsies from affected tissues, imaging (MRI, in particular due to its high contrast and spatial resolution) plays an indispensable part in evaluation of the Sino nasal infection and its spread to the locoregional structures.

CEMRI plays a major role in assessing the extent of involvement of mucormycosis and its complications, which guides the operating surgeon in prompt decision making.

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