IRIA-ICRI Guidelines and Recommendations

(INDIAN RADIOLOGICAL AND IMAGING ASSOCIATION- INDIAN COLLEGE OF RADIOLOGY AND IMAGING)

Imaging in Acute Invasive Fungal Rhinosinusitis / Mucormycosis

Indian Radiological & Imaging Association

IRIA House, C-5, Qutab Institutional Area, Behind Qutab Hotel

New Delhi-110 016,INDIA

Tel. +91-11-26965598, +91-11-41688846. Fax: +91-11-26565391

E-mail: iria37@gmail.com, Website: www.iria.org.in

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Prepared by Indian College of Radiology and Imaging (Academic wing of Indian Radiological & Imaging Association) Head and Neck Subspciality group in association with Indian Society of head and neck radiology (ISHNR).

- Fungi are ubiquitous. Acute invasive fungal rhinosinusitis (AIFRS) is a result of weakened host immune system and a **rapidly progressive** disease.
- Rapid rise has been seen in incidence of AIFRS in association with COVID 19 especially in the setting of concomitant diabetes mellitus and steroid administration.
- The disease carries a high mortality with a large meta-analysis showing mortality rate of 50%[1]. Most disease in the current situation is caused by mucormycosis but aspergillus and other bacterial infections can also show similar changes.
- A high index of suspicion with knowledge of various clinical and imaging red flag signs helps in early diagnosis, early initiation of treatment and aids to reduce morbidity and mortality from the disease.
- Nasal endoscopy and biopsy with microbiological/histopathological analysis remains the gold standard for diagnosis.

Remember: The diagnosis and management, like in any disease, is a team work – we need to work in the team and effectively communicate for the best outcome for the patients – Physicians, ENT surgeons, Ophthalmologists, Oral/maxillofacial surgeons, Neurologists, Neurosurgeons and pathologists etc are involved in the management of AIFRS.

CLINICAL SYMPTOMS AND SIGNS

- Nasal congestion
- Nasal discharge (bloody or brown/black)
- Pain over cheek
- Facial pain, numbness or swelling
- Blackish discoloration over bridge of nose /palate
- Focal palatal / alveolar swelling / discharge
- Toothache, loosening of teeth
- Blurred vision or double vision with eye pain, sudden ptosis, proptosis
- Fever
- Worsening headache
- Mental status change/ seizures/ stroke
- Variations of the above symptoms are common.
- **Clinical signs** picked by the referring doctors may be – swelling, discharge, loosening of teeth, black discolouration of mucosa, mild proptosis, eye movement restriction, cranial nerve palsy.

Role of Imaging

- **Early diagnosis** – Radiologist should diligently evaluate to make the early diagnosis as it can be rapidly progressive; the findings to be communicated to clinician in a quick and clear manner.
- **Assessment of disease extent** – as described below.
- **Planning surgery** – discussion with surgeon is important to understand the clinical / scopy findings.
- **Follow up evaluation –** comparison is essential

Imaging modalities

- **Computed tomography (CT):**
    - Commonly used for evaluation, quick and cost effective.
    - Often sufficient for initial diagnosis when there is high index of suspicion but has limitations as described below.
- **Magnetic Resonance Imaging (MRI):**
    - Imaging modality of choice due to superior soft tissue contrast resolution, intracranial, neural and vascular assessment.

CT Technique

- Contrast enhanced CT scan of PNS and nasal cavity performed after iv bolus injection of non- ionic iodinated contrast administered at a dose 1-1.25 ml/kg body weight.
- Thin axial scans of 1- 2mm thickness obtained and evaluated in both soft tissue and bone windows. Multiplanar images to be reconstructed along coronal and sagittal planes from these axial set of images.
- Area of coverage-
    - superior – from top of frontal sinus [include cavernous sinuses]
    - Inferiorly- to include jaws
    - Anteriorly – including ala of nose
    - Brain to be included in case of suspected involvement

MR technique

- MR examination of PNS and nasal cavity done in supine position with dedicated head coils. Brain should be included when extension suspected or when orbital / skull base involvement present.
- An initial scout T1 weighted sagittal view obtained to act as a localizer and then used to obtain T1, T2 and STIR images in multiple planes followed by contrast

enhanced 3 plane T1 W fat saturated images. Diffusion weighted imaging may also be done.

- 3-4 mm thick slices are acquired including the top of frontal sinuses superiorly and level of the jaws inferiorly. Ensure the inclusion cavernous sinuses and orbits.
- Brain assessment include – FLAIR, T2, T1, DWI images and post contrast scans. Thinner sections to be used at skull base level –for orbital apex, cavernous sinus, cranial nerve / vascular assessment.
- MR angiography TOF technique to be done to assess the ICA and its branches.

Staging :

There are proposals in non-peer reviewed literature and few society guidelines to classify mucormycosis into stages - namely - 1. Sinonasal 2. Orbital and 3. Intracranial disease. Please note, these stages are not fully validated widely in literature – the limitations being: intracranial extension can occur without orbital involvement, masticator space extension and extracranial neural involvement is not addressed and other organ involvement in not included (Mucormycosis can involve lungs, stomach, intestine, skin etc – depending on the host). As per most peer reviewed journals, at this time, mucormycosis is described as per the organs / tissues involved. However, this classification may help in clear description of findings and clarity in communication.

CT findings: (Fig 1-4 & 9)

A: Nasal cavity and sinuses.

- Predilection for unilateral involvement
- Most common sites are middle turbinate, maxillary, ethmoid and sphenoid sinuses. Bilateral disease may also be seen.
- Early findings–ulcerated/ emphysematous nasal septum mucosa and turbinates, Inflammatory mucosal thickening at nasal cavity and sinuses with or without fluid level – these of the changes occur in all types of sinusitis.
- *Disease can extend through perivascular channels and hence can be seen outside the sinuses without intervening bone destruction*

- Soft tissue infiltration of peri-antral fat planes – premaxillary and retromaxillary fat plane.
- Erosion or infiltration around nasolacrimal duct/ sac.
- Fat stranding and soft tissue pterygomaxillary fissure, pterygopalatine fossa and extending into the infratemporal fat / masticator space muscles.
- Bony erosions: Nasal septal destruction / turbinate erosions/ floor of maxillary sinus erosion, infiltration, erosions and reduced density of maxillary alveolar bone around tooth sockets and hard palate infiltration and erosions – either alone or in various combinations.
- Bone dehiscence, orbital invasion and intracranial extension are late findings but disease can spread fast and involvement can occur in a matter of hours.

B: Orbital extension

- Preseptal and eyelid thickening.
- Edema and thickening of extra ocular muscles,
- Stranding at extraconal and intraconal orbital fat with or without enhnacement.
- Phlegmon / inflammatory mass with or without abscess.
- Optic nerve involvement
- Orbital apex disease.

C: Intracranial extension

- can lead to cavernous sinus thrombosis and involvement of carotid artery.
- This may result in narrowing, thrombosis, dissection or pseudoaneurysm formation.
- Arterial involvement can result in mycotic aneurysms, leading to subarachnoid hemorrhage and occlusion leading to acute infarcts.
- Leptomeningeal enhancement can be seen with intracranial extension of the disease.
- Other manifestations are intracranial granulomas and abscess formation.

D: Limitations of CT:

a. Limited assessment of intracranial disease - cerebral cortical, meningeal , perineural, vascular invasive detection and extension.

b. Bone infiltration changes occur later than MRI as early marrow changes can be missed and therefore true extent can be underestimated.
c. Enhancement pattern is less obvious compared to MRI

MRI findings: (Fig 5-11)

A: Nasal cavity and sinuses.

- Predilection for unilateral involvement
- Most common sites are middle turbinate, maxillary, ethmoid and sphenoid sinuses. Bilateral disease may also be seen.
- Early finding s–ulcerated nasal septum mucosa and turbinates,
- Inflammatory mucosal thickening at nasal cavity and sinuses with or without fluid level – these changes occur in all types of sinusitis.
- Soft tissue infiltration of peri-antral fat planes – premaxillary and retromaxillary fat planes – seen best on fat suppressed sequences – T2FS, STIR or T1FS contrast.
- The lesions are intermediate to hypointense on T2 weighted images. However, hyperintense signal may also be seen.
- Lack of contrast enhancement is highly suggestive of tissue necrosis and is a sign of angioinvasive fungal sinusitis (“black turbinate sign”). However, homogeneous and heterogeneous patterns of enhancement may also be seen.

B: Orbital extension

- Preseptal and eyelid thickening – seen on high signal on T2FS /STIR.
- Edema and thickening of extra ocular muscles – high signal and post Gd enhancement.
- Stranding at extraconal and intraconal orbital fat.
- Optic nerve involvement – enhancement along optic nerve; DWI restriction may occur due to nerve infarction – blindness in these patients[8].
- Orbital apex disease.
- The thickening of the extra ocular muscles, fat infiltration and edema can raise the intra orbital pressure, resulting in compression and distortion the globe – resulting in ‘guitar pick sign’.

C: Intracranial extension

- Cavernous sinus thrombosis – poor enhancement of cavernous sinus with convex bulging / enlargement on post Gd images.
- Internal carotid artery (or its branches or any other arteries) involvement due to angioinvasion by the fungus – look out for stenosis, thrombosis, dissection or pseudoaneurysm formation – these can lead to acute infarcts (DWI restriction)
- Mycotic aneurysm can lead to subarachnoid hemorrhage; stenosis and occlusion can lead to acute infarcts (post contrast MRI/ TOF MRA)
- Leptomeningeal enhancement and thickening (low signal T2/ enhancing on Post Gd images)
- Early cerebritis – best picked up by MRI as high signal on FLAIR images and enhancement on Post Gd images
- Intra-cerebral granulomas (as hypointense on both T1 and T2 weighted images with minimal enhancement)
- White matter edema (high signal on FLAIR/T2W images)
- Abscess formation (rim enhancement with central necrosis; diffusion restriction)
- Perineural spread / cranial nerve infiltration – Trigeminal nerve (or its branches) is most commonly affected as expected – look for thickening and enhancement along the nerve course upto brain stem, Meckel's cave T2 fluid signal loss /enhancement on post Gd,

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Checklist for interpretation of findings on CT/MR

SINO NASAL AND NECK SPACES	ORBIT	INTRACRANIAL
Nasal cavity ○ Emphysematous /ulcerated mucosal thickening- especially unilateral ○ Nasal septum ulceration/abscess ○ Necrotic turbinate/ black turbinate sign / lack of enhancement.	• Bony orbit • Preseptal oedema • Extraconal fat involvement, subperiosteal abscess • Orbital muscle cone involvement, proptosis • Intraconal fat involvement • Sub periosteal collection • Orbital apex involvement, superior and inferior orbital fissure • Globe involvement • Optic nerve involvement. • Superior ophthalmic vein thrombosis	○ Skull base involvement –clivus ,frontal , ethmoid, sphenoid and basi occiput ○ Skull base foramen & Perineural extention , pterygoid plates ○ Meningitis ○ Cortical edema – focal cerebritis.(frontal, anteromedial temporal lobe) ○ Intracranial granulomas/ abscess ○ Extra-axial/ parenchymal collection ○ Infarct/hemorrhage ○ Cranial nerve / Meckel's cave involvement. **Vascular complications** ○ Cavernous sinus thrombosis ○ Internal carotid artery narrowing/ thrombosis/ pseudoaneurysm
Paranasal sinuses and their drainage pathways ○ Mucosal thickening- ethmoid/ maxillary/ sphenoid/ frontal ○ Bony erosion		
Soft tissue infiltration ○ Peri-antral fat pads (anterior premaxillary and posterior retroantral) ○ Pterygopalatine fossa ○ Infratemporal fat, zygoma ○ Masticator space, buccal space, parapharyngeal space ○ Naso pharynx and prevertebral muscles		
Nasolacrimal Duct and Nasolacrimal Sac		
Hard palate, floor or maxillary sinus / alveolar process of maxilla, Mandible and oral cavity		
Other Bone dehiscence/ destruction including skull base.		

Co-existent pulmonary fungal involvement (mucormycosis / aspergillosis)

- Pulmonary mucormycosis may also occur in the setting of COVID19 and accompanying immune suppressed state. It may be seen co-existing with rhino-orbito-cerebral mucormycosis.
- The findings on chest CT are usually non-specific and include peri-bronchial ground glass opacity, nodules, consolidations, multiple lesions with a predilection for peripheral location. Peri-lesional ground glass halo and cavitation may also be seen. Reverse halo sign has been considered to be a relatively specific sign.

Key points to remember

- Sinus opacification may be minimal to mild. Look around the sinuses.
- Bone destruction is not necessary to classify it as AIFRS
- Unilateral nasal ulcerated mucosal thickening and peri-antral fat stranding are early findings.
- Bilateral disease may also be seen.
- Widen the CT window settings for evaluating fat infiltration.
- Narrow the CT window settings to look for cavernous sinus involvement.

Recommendations:

- Every suspected case of rhino-orbito-cerebral fungal disease should ideally have an MRI of sinuses / orbits and brain with Gadolinium contrast as per the protocol suggested above.
- CT is a good test, cost effective, fast and can provide most of the information needed when disease is confined to extracranial sites (see limitations above)
- To be interpreted and reported by qualified Radiologist.
- Communication and discussion with clinical team is essential as this is a dreaded disease with complications, disfiguring surgery and rapid progression.

Suggested reading :

1. Turner JH, Soudry E, Nayak JV, et al. Survival outcomes in acuteinvasive fungal sinusitis: a systematic review and quantitative synthesis of published evidence. Laryngoscope 2013;123:1112–18
2. Ni Mhurchu E, Ospina J, Janjua A, Shewchuk J, Vertinsky A. Fungal rhinosinusitis: a radiological review with intraoperative correlation.Can Assoc RadiolJ 2017;68(2):178-86.
3. Silveira M, Anselmo-Lima W, Faria F, Queiroz D, Nogueira R, Leite M et al. Impact of early detection of acute invasive fungal rhinosinusitis in immunocompromised patients. BMC Infect Dis 2019;19(1):310-5.
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5. Epstein V, Kern R. Invasive fungal sinusitis and complications of rhinosinusitis.Otolaryngol Clin North Am 2008;41(3):497-524.
6. Aribandi M, McCoy V, Bazan C. Imaging features of invasive and noninvasive fungal sinusitis: a review. RadioGraphics 2007;27(5):1283-96.
7. Mossa- Basha M, Ilica T, Karakok O, Izbudak I, Aygun N. The many faces of fungal disease of the paranasal sinuses: CT and MRI findings. DiagIntervradiol 2013;19: 195-200.
8. Ghabrial R, Ananda A, van Hal SJ et al. Invasive Fungal Sinusitis Presenting as Acute Posterior Ischemic Optic Neuropathy. Neuroophthalmology. 2018; 42(4): 209–214.
9. Hammer M, Madan, R, Hatabu H. Pulmonary Mucormycosis: Radiologic Features at Presentation and Over Time: AJR 2018; 210:742–747

Figures and legends

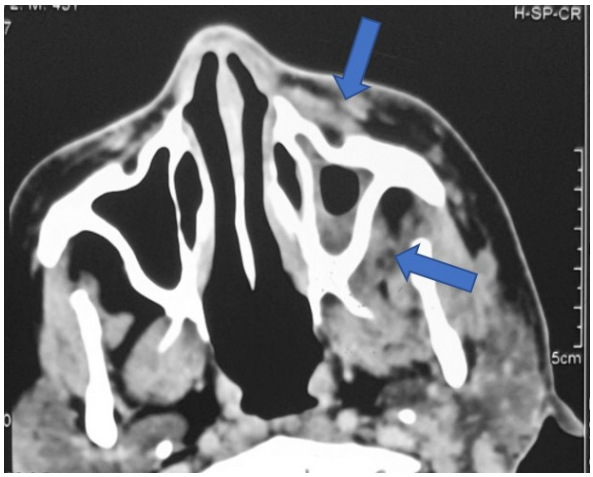

Fig 1. Axial CT shows left maxillary sinus mucosal thickening with peri-antral fat stranding without intervening bone destruction in a case of AIFRS. *Note the retroantral fat plane infiltration is also in proximity to pterygomaxillary fissure and pterygopalatine fossa*

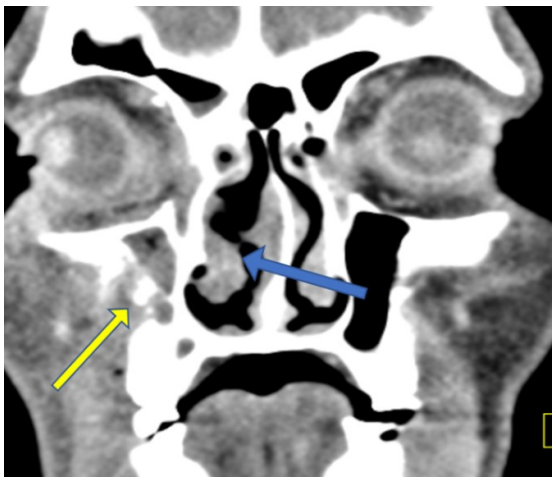

Fig 2.Coronal CT shows ulcerated mucosal thickening in right nasal cavity (blue arrow) and maxillary sinus mucosal thickening with bone destruction (yellow arrow)in a case of AIFRS.

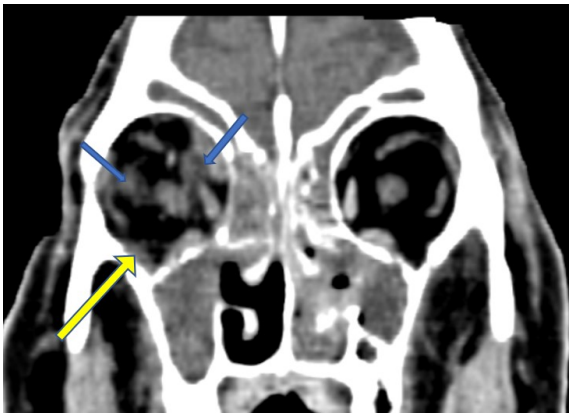

Fig 3.Coronal CT shows nodular thickening and stranding in right orbital fat involving both extraconal(yellow arrow) and intraconal (blue arrow) compartments.

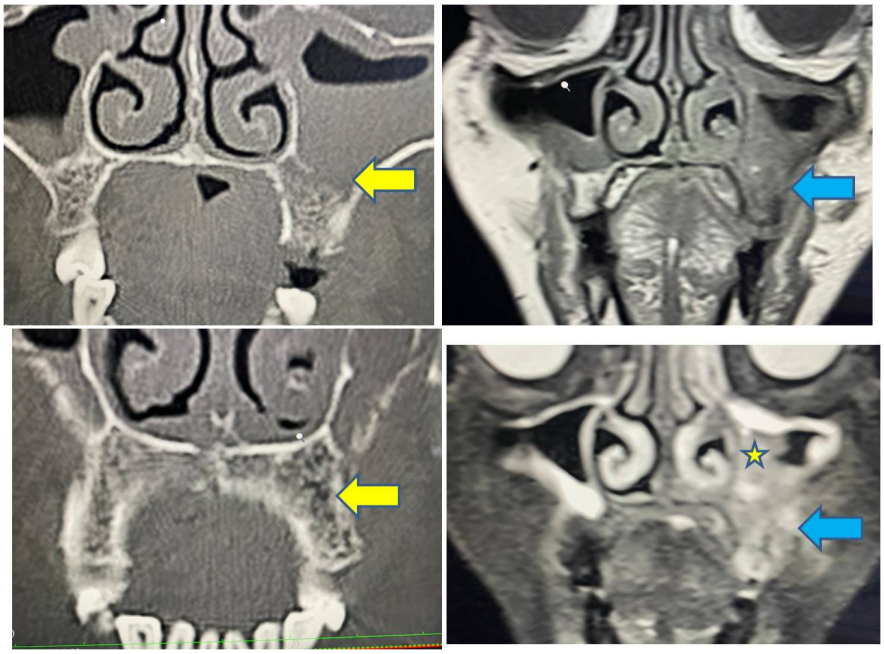

Fig 4 a/b/c/d. Bone infiltration by Mucormycosis. Coronal CT (above/below) shows erosion of floor of left maxillary sinus; there is also rarefaction of rest of alveolar bone but actual infiltration is rather difficult to appreciate; Coronal T1/T2FS (above and below) MRI shows complete replacement of marrow fat at left maxillary alveolar bone compared to right side. T2W images show infiltrative tissue; bone marrow infiltrative changes are easily appreciated on MRI. Note the T2 low signal changes within the left maxillary mucosal disease (yellow star) shows erosion of left and intraconal (blue arrow) compartments.

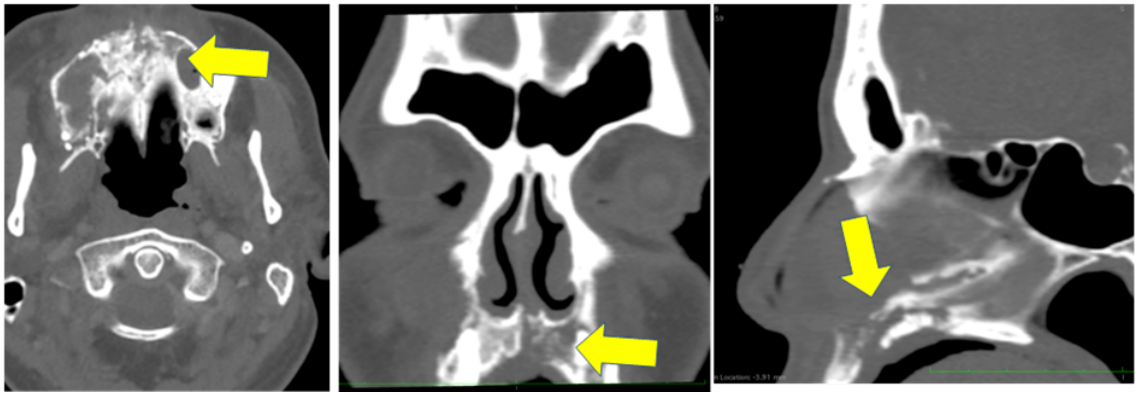

Fig 5 a/b/c. Bone infiltration by Mucormycosis. Axial CTshows erosion of floor of left maxillary sinus with involvement of hard palate; the erosion and destruction of hard palate can be seen on coronal and sagittal reconstructed MDCT images.

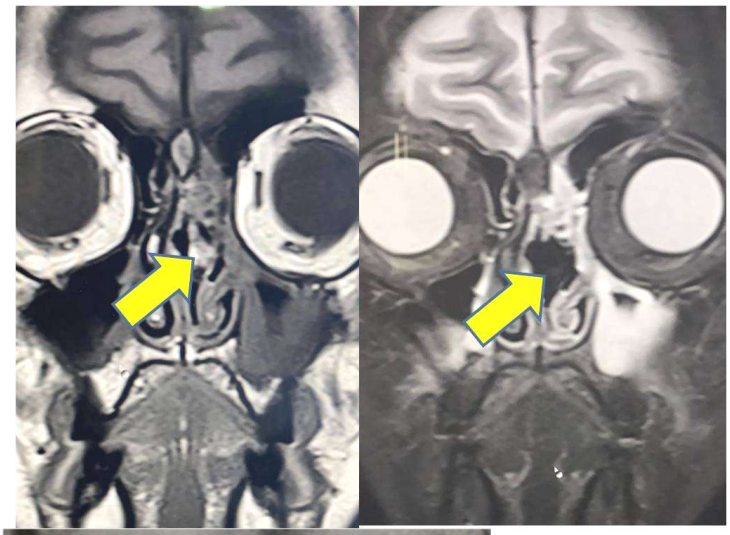

Fig 6. Turbinate mucormycosis. Coronal T1 and T2FS MRI: focal high signal at left middle turbinate on T1W (arrow); the same area appears low signal on the T2FS MRI (arrow. Inflammatory changes at ethmoid and maxillary sinuses.

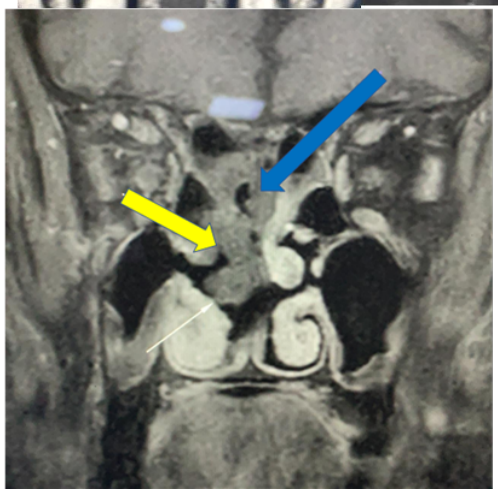

Fig 7: Mucormycosis: Sinonasal disease. Post contrast T1FS in a different patient: the right middle turbinate and nasal septum show no significant enhancement – 'black turbinate sign'; note the normal enhancement of mucosa over both inferior and left middle turbinate. Further inflammatory changes with poor enhancement noted at right ethmoid sinus and both maxillary sinuses.

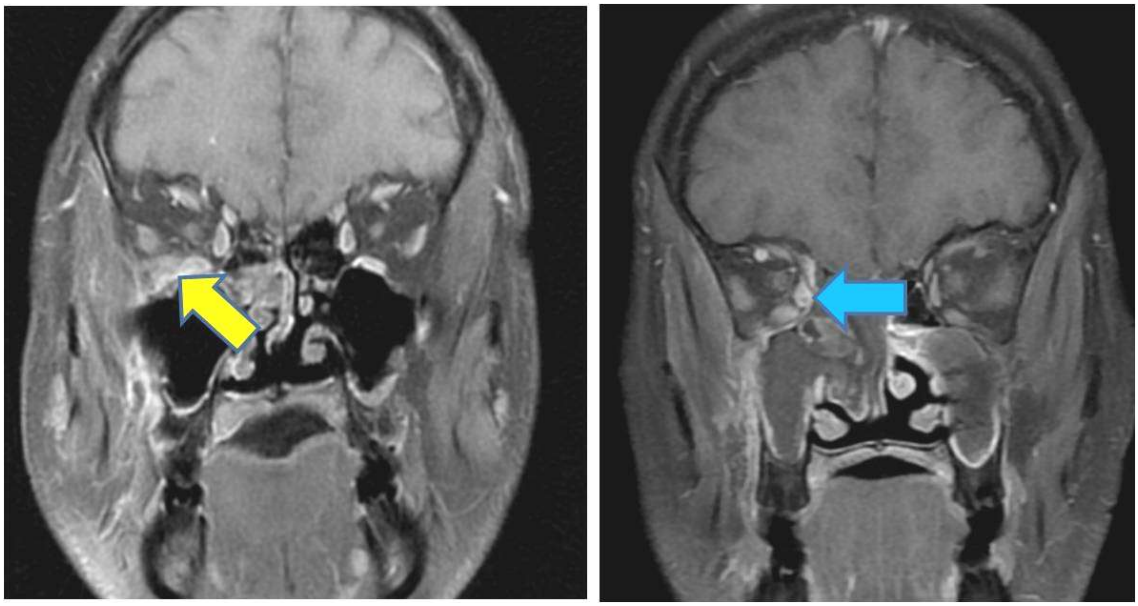

Fig 8: Mucormycosis – sinonasal and orbital disease: T1FS post contrast coronal image. show early orbital infiltration, seen as enhancing tissue at right orbit, inferior extra conal space with thickening of inferior rectus (yellow arrow); different patient with medial orbital disease with thickening of medial rectus muscle (blue arrow). Note the inflammation at sinuses with retained fluid at maxillary sinus and poorly enhancing tissue at right ethmoid sinus region

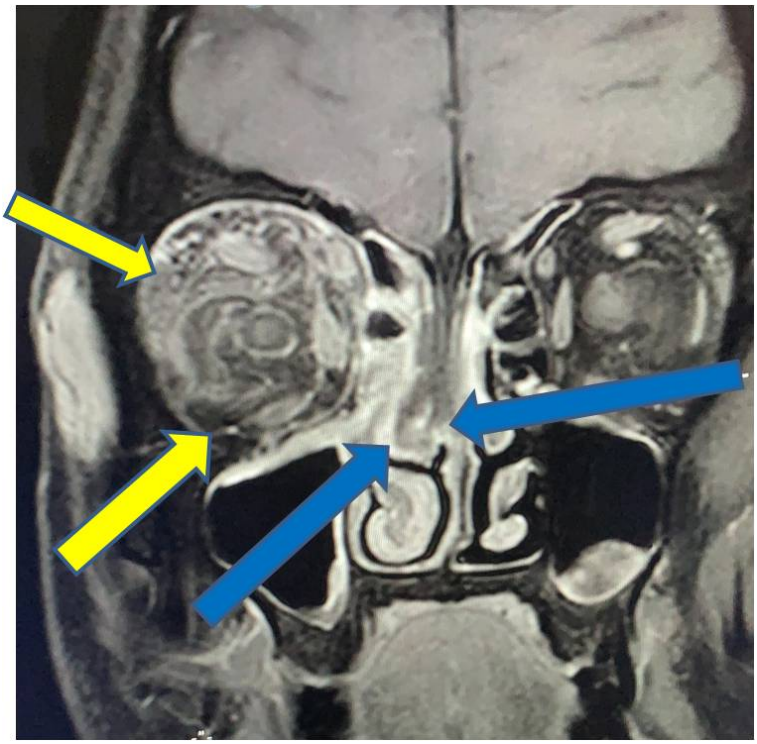

Fig 9: Mucormycosis – sinonasal and orbital disease: T1FS post contrast coronal image. Black turbinate sign at right middle turbinate (blue arrows); extensive fat stranding and infiltrative changes at right orbit at extra and intraconal regions (yellow arrows)

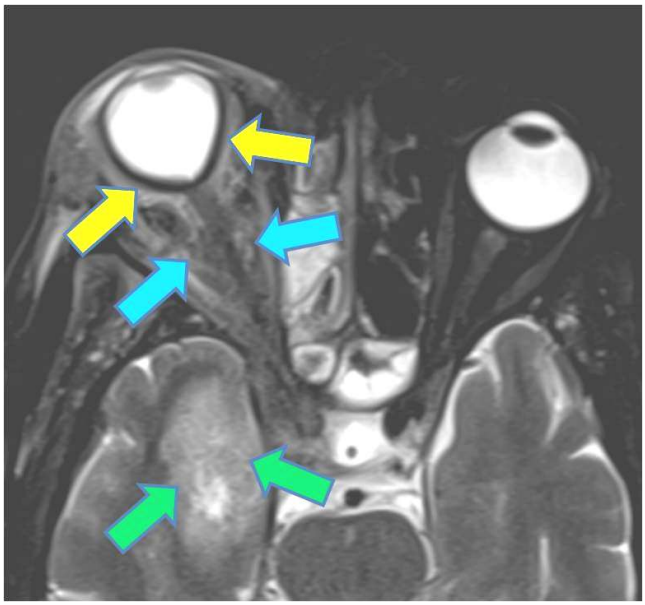

Fig 10: Mucormycosis – orbital, sinonasal and intracranial disease: T2FS axial image. Extensive fat stranding at intra and extra conal fat planes (blue arrow) with muscle edema resulting in distortion of globe which is shaped like a 'guitar pick' (yellow arrow) with proptosis. Note the cerebritis with possible early abscess formation at right temporal lobe (green arrow). Inflammatory changes at right ethmoid and sphenoid sinuses.

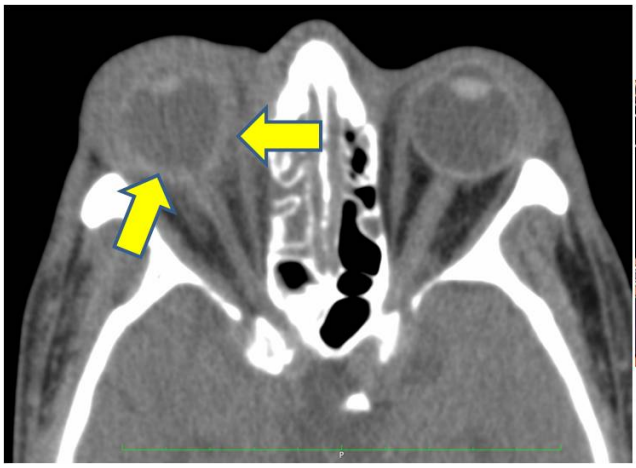

Fig 11 a/b: Axial CT in a different patient: note the shape of the globe is distorted like a "shape of guitar pick". This is a signs of extensive orbital disease with increase in intra orbital pressure – note the proptosis, increase in orbital fat density, preseptal edema and sinusitis.

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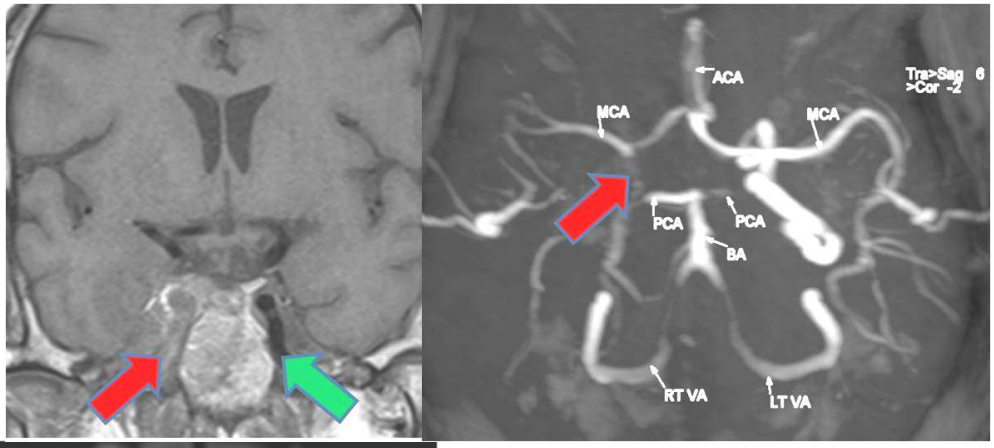

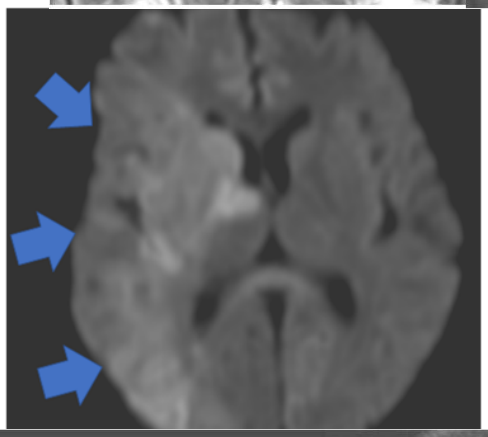

Fig 12 a/b/c: Right ICA occlusion: T1W coronal image show no flow void at right ICA at precavernous/cavernous segment (Red arrow); compare with normal left side. MR angiography show no flow signal at right ICA (Red arrow). Note the extensive right MCA territory infarct at right brain on DWI images (blue arrows).

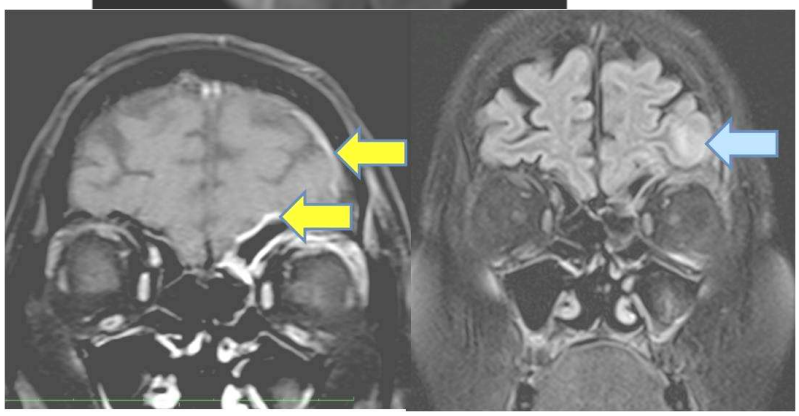

Fig 13 a/b: Meningeal and cerebral involvement: T1W +Gd coronal image show left frontal skull base and lateral frontal leptomeningeal enhancement (yellow arrow); FLAIR image show focal edema (cerebritis) at left frontal cortical and subcortical plane (blue arrow).

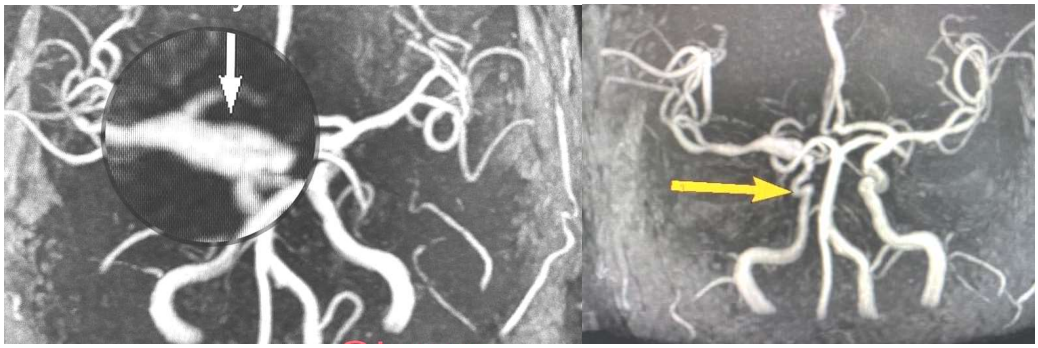

Fig 14 a / b: ICA stenosis and Pseudoaneurysm due to mucormycosis invasion. MR angiography of circle of willis in a patient with angioinvasive mucormycosis showing a dilated segment of right ICA and M1 segemnt of MCA – pseudoaneurysm (white arrow); note the stenosis of cavernous segment of right ICA (yellow arrow) proximal to pseudoaneurysm due to cavernous sinus invasion by the fungus.

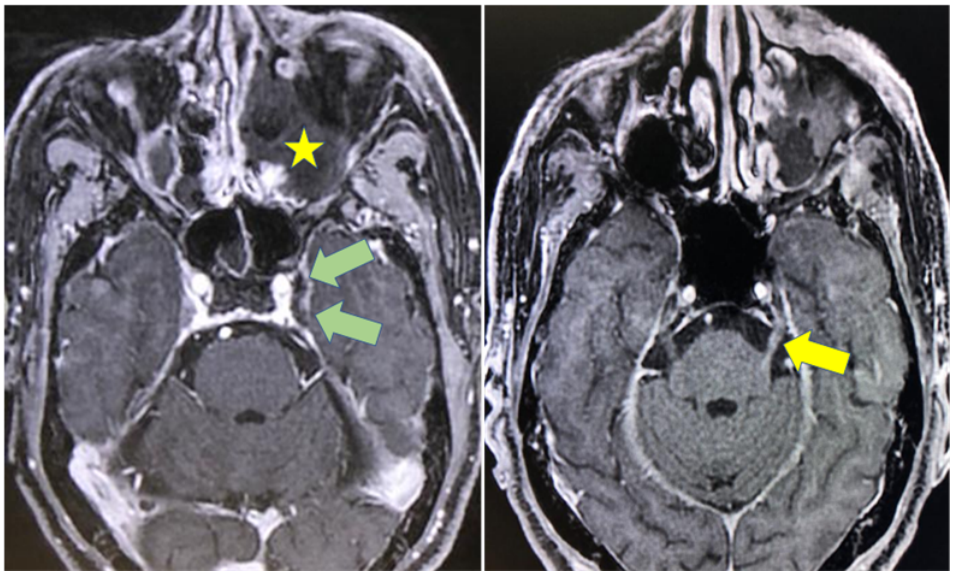

Fig 15 a/b: Cavenous sinus thrombosis and Trigeminal nerve invasion. Post contrast axial T1FS images. Cavernous sinus thrombosis with bulging lateral margin; infiltration and thrombosis are seen as poorly enhancing area at left cavernous sinus (green arrows) - compare with right side; note the extensive disease at left maxillary / ethmoid region showing no significant enhancement (yellow star); the next image show enhancement along the left trigeminal nerve and Meckel's cave region – consistent with perineural infiltration / cranial nerve involvement in the same patient.

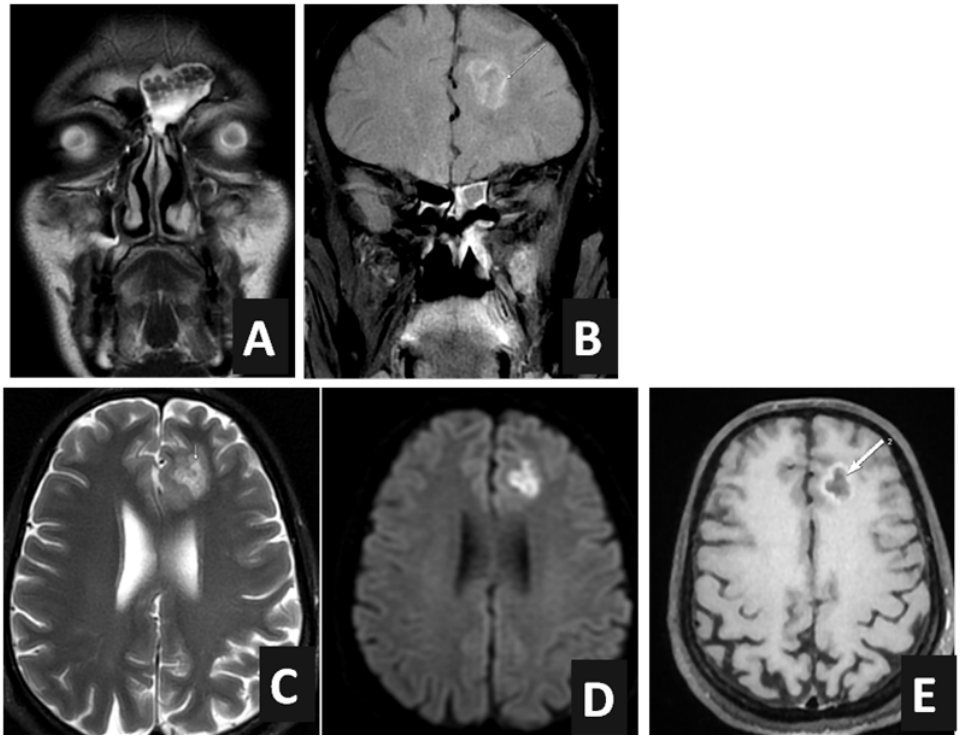

Fig 16 A to E: Intracerebral fungal abscess: Note left frontal sinus inflammation due to fungal disease in coronal T2W image (A); FLAIR coronal images show high signal area at left frontal lobe (B). Axial T2W image (C) show high signal heterogenous lesion at left medial frontal region at the same level as B. DWI images show diffusion restriction (D). Post contrast scans show mild rim enhancement (E- arrow).

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