The Seybold Report

ISSN 1533-9211

DOI: 10.5281/zenodo.10153275

IMAGING FEATURES OF COVID-19 ASSOCIATED RHINO-ORBITO-CEREBRAL MUCORMYCOSIS - A REVIEW OF CURRENT UPDATES OF BLACK FUNGUS

VIJAYA KAMBLE *

Professor, MBBS, MD, Department of Radiodiagnosis, School of Medical Sciences and Research, Sharda University, Greater Noida (U. P). *Corresponding Author Email: vijayashelkar@gmail.com

MOIRANGTHEM NITESHORE SINGH

Senior Registrar, MBBS, MD, Department of ENT, Shija Academy of Health Sciences, Langol, Imphal -West, Manipur.

Abstract

Mucormycosis is a severe, fatal, opportunistic fungal infection. History of diabetes, longer intensive care unit stay, overuse of steroids, oxygen therapy are the significant risk factors for contracting mucormycosis infection. Recently, India has closely observed a rapid surge of post covid-19 associated Rhino-orbito-cerebral mucormycosis (CAROCM) in the second wave of covid. This rapid rise of CAROCM cases is attributed to the complex interplay of metabolic factors and corticosteroid therapy. Radiologists need to have a high index of suspicion for early diagnosis, which incites immediate administration of antifungal therapy. As a result of which morbidity and mortality can be significantly limited. This review aims to provide the comprehensive cross sectional imaging features of CAROCM and its complications. It also aims to study if there is any difference between CAROCM and ROCM in pre covid era which generally occurred in immunocompromised individuals. All the cases discussed in this review are microbiologically and /or histopathologically turned out ROCM with associated Covid-19 infection.

Keywords: Rhino-Orbito-Cerebral Mucormycosis, Covid-19 Associated Rhino-Orbito Cerebral Mucormycosis (CAROCM), Diabetes, Magnetic Resonance Imaging, Computed Tomography.

INTRODUCTION

A potentially fatal condition of Rhino-orbito-cerebral Mucormycosis is generally associated with increased morbidity and mortality which is caused by saprophytic fungi of generamucor, Rhizopus and absidia. These fungi are of the order Mucorales and class zygomycetes.[1]

Cross sectional imaging offers rapid, prompt, probable diagnosis and provides model template for management. MRI has an upper hand over CT as it gives superior anatomic soft tissue details, tissue characterization even without administering intravenous gadolinium based contrast agent.

Contrast administration in MRI study is useful in differentiating a viable from a non-viable dead necrotic tissue. MRI accurately detects the uncommon complications of fungal sinusitis i.e cavernous sinus involvement and perineural spread. Radiologists need to be well versed with the imaging manifestations of CAROCM for the prompt and early diagnosis. The causative organism of this angio-invasive disease is saprophytic fungi of the order Mucorales of the phylum Zygomycota.[2]

The Seybold Report
ISSN 1533-9211
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This review aims to provide the comprehensive imaging features of CAROCM, to explain the current state of knowledge and to analyse if the imaging features of CAROCM are different from the ROCM in precovid era.

Imaging features of ROCM

Sinonasal involvement:

On MRI, all paranasal sinuses appears hypointense on all sequences as they are air filled. In ROCM, maxillary and ethmoid were the most commonly involved sinuses. [3-9] whearas few studies say ethmoid sinus is more commonly involved followed by maxillary sinus.

Bilateral sinus involvement is commonly seen than unilateral sinus involvement. [4,10] However few studies says that unilateral involvement is more commonly observed than bilateral sinus involvement. [7,11,12]

Sinonasal mucosal thickening is commonly observed [3,5]. Air fluid level, collection and debri are the contents of sinuses in fungal sinusitis. On CT, hyperdense nasal or paranasal content is seen. Unenhanced CT appearance of involved sinuses, turbinates varies from hypodense, heterogenous to hyperdense soft tissue filling the sinuses. Contrast enhanced computed tomography (CECT) showed heterogenous enhancement. [5,12]

In the sinonasal compartment, T2W, DWI and post contrast T1W were most useful sequences [13]. On T1W MRI, the mucosal thickening is hypointense to isointense and on T2W mucosal thickening is hyperintense [Fig 1a]. Some cases may show T2 hypointense thickening. [Fig1 a,b] [5,8]Three types of enhancement patters are observed on CE-MRI; 1) homogenous and regular mucosal enhancement 2) central non enhancement with peripheral mucosal enhancement [Fig 1 c] and 3) Complete lack of enhancement indicating necrosis. Restricted diffusion is seen in some cases [5,8]

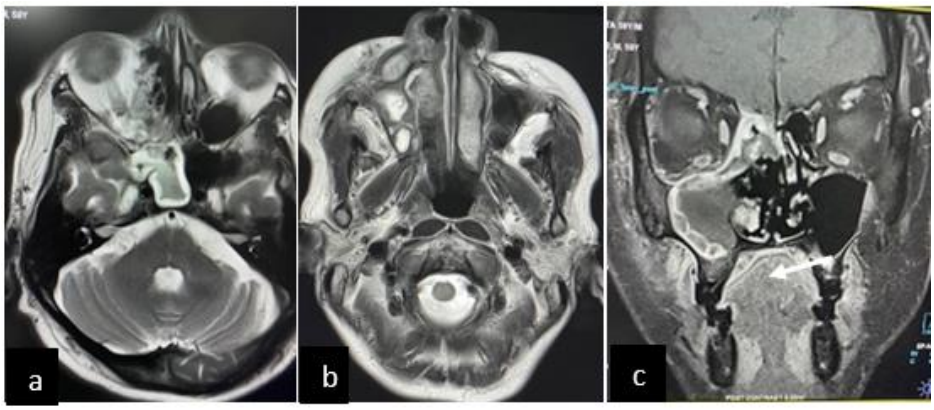

Figure 1

Fig 1.Sinonasal involvement in CAROCM (a) Axial T2-Weighted(T2W) image showing mucosal thickening in the right sphenoid sinus with T2 hypointense contents and right sided hypointense mucosal thickening in ethmoidal air cells. Axial (b) T2W image showing hypointense right nasal mucosal thickening in its posterior aspect and right maxillary sinus

The Seybold Report
ISSN 1533-9211
DOI: 10.5281/zenodo.10153275

mucosal thickening with hypointense periphery.Also anterior premaxillary fat infiltration in right side.Coronal (c)post contrast fat suppressed T1W image shows the abnormal inflammed mucosa in the right maxillary sinus i.e peripheral enhancement with central non enhancement.Non enhancing mucosa over the right superior and inferior turbinate-"Black turbinate sign"(white arrows).This suggests necrotic eschar.

Nasal cavity involvement:

Non specific mucosal thickening, hypertrophy, irregular mucosal thickening, destruction of turbinates are observed when nasal cavity is involved.[5]Non enhancement or mild enhancement of nasal mucosal thickening, destruction of turbinates or septum or floor of nasal cavity is observed. Middle turbinate is found to be most frequently involved. [10]

On CE-MRI, post contrast T1W images shows lack of enhancement in the regions which otherwise shows normal enhancement. This is because of microthrombi within vessels which eventually causes necrosis of underlying tissues in the affected areas. These changes within tissues are attributed to the natural angioinvasive quality of the fungus. This appearance is termed as 'Black turbinate sign' [Fig1,c] which represents the necrotic eschar seen on clinical examination and rhinoscopy.

Recognizing this sign may assist in early diagnosis of ROCM [15,16]. However normal individuals may also exibit focal non enhancement of sinonasal soft tissues which is a physiological fluctuation normally observed. Hence interpretation of this finding need to be done in view of clinical context.[17]

Extrasinus Spread: In Angioinvasive fungal Rhinosinusitis (AIFR), extrasinus extension is considered to be highly specific finding. Retroantral fat streakiness is commonly seen followed by preantral /pre maxillary fat stranding. [3,18].

The fat infiltration can also extend into adjacent buccal fat, facial muscles, pre frontal soft tissue, pterygopalatine fossa, masticator space, infratemporal fossa, parotid space, orbit, cavernous sinus, internal carotid artery, trigeminal nerve and its branches, intracranial extension, brain infarction[18,19] (Fig 2,a,b,c)

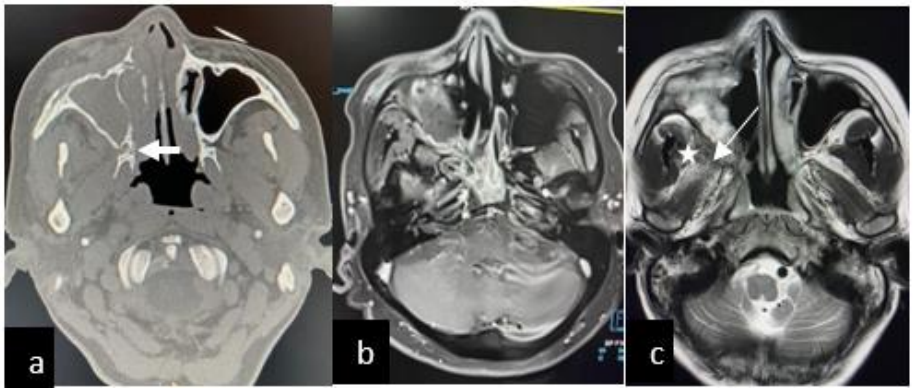

Figure 2

The Seybold Report
ISSN 1533-9211
DOI: 10.5281/zenodo.10153275

Figure 2:Extra sinus extension in CAROCM. Axial (a) CT image bone window shows right preantral and retro antral fat stranding with obliteration of retroantral fat. Fat infiltration is noted along the right pterygopalatine fossa with subtle expansion of fossa (thick white arrow).Compare with opposite side wherein the retroantral fat is maintained. Also note the thinning of anterior bony wall of right maxillary sinus. Axial post contrast T1W fat suppressed image (b)shows enhanced mucosal thickening extending into preantral and retroantral fat. Also enhancement of muscles of infratemporal fossa is appreciated. Axial T2W image (c) shows inflammation extending into retroantral fat,infratemporal fossa (white star),lateral pterygoid muscle(thin white arrow) with expansion of pterygopalatine fossa.

Medial pterygoid is the commonly involved muscle. Extension of inflammation can also be seen in temporal fossa, infratemporal fossa, palatal mucosa, maxillary and mandibular arch. All these findings are generally seen in combination [3] (fig 3)

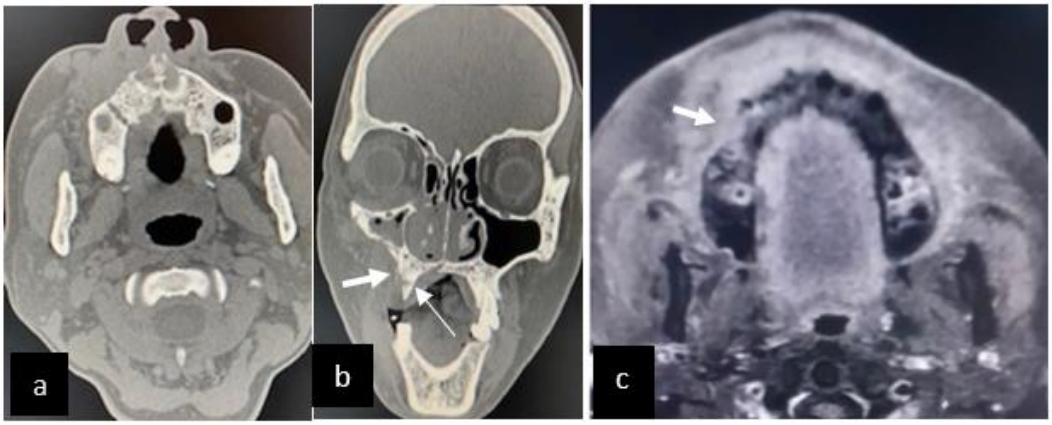

Figure 3

Figure 3:A patient with CAROM , Axial CT bone window (a) showing inflammatory soft tissue swelling along the anterior wall of maxillary arch on right side with erosion of anterior wall of maxillary alveolar arch.Compare with left side where the anterior cortical margin of alveolar arch is seen continuous and intact.Coronal CT bone window (b) shows dehiscence (opening up) of the lateral walls of right maxillary sinus and bony erosion along the floor of the sinus and permeative lytic areas in alveolar process of maxilla and hard palate (thick arrow) with soft tissue thickening along the undersurface and lateral aspect of hard palate on right side.(white thin arrow).

Axial T1W fat suppressed post contrast image (C) shows inflammatory soft tissue thickening with post contrast enhancement, along the anterior wall of maxillary alveolar arch on right side.There is focal discontinuity of the cortical margin anteriorly (white arrow).

Air within bony sinus structures is also noted [20]. When the pre maxillary area, orbital fat and pterygopalatine fossa shows fat stranding, these features are suggestive of extrasinus extension. These imaging features supports the early diagnosis of invasive fungal infection in an appropriate clinical scenario.

The Seybold Report
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Pterygopalatine fossa (PPF) infiltration: Relative expansion of PPF, fat stranding and sometimes bony erosion along the posteromedial wall of the maxillary sinus suggests PPF infiltration. (fig 2) [18]

Orbital involvement:

Orbital fat and extra ocular muscles inflammation is an early sign of orbital involvement (Fig 4) [21]. Lateral displacement of medial rectus muscle suggests early subtle changes of orbital invasion as orbital invasion usually recurs through medial orbital wall. (Fig 4, b) [17,22]

Medial rectus thickening, patchy enhancement of the orbital fat involving the orbital fissures and orbital apex with associated bony destruction of the paranasal sinuses relative to orbit are indicative of severe disease. [22,23]

Posterior globe tenting as ‘guitar pick sign'is a radiological marker of tense orbit and profound vision loss (24) also known as conical globe. [3]

In patients with dacrocystitis, Non contrast CT and MRI shows the imaging features of enlarged lacrimal sac with associated fat stranding and contrast CT and MRI studies reveal peripheral wall enhancement of lacrimal sac and hyperenhancement along the course of lacrimal duct. [18]

The pathways of least resistance, from where CAM can spread are congenital dehiscence or breach of lamina papyracea, perivascular channels, foramina ethmoidalis along the medial wall of orbit, foramina along the inferior wall of orbit (infraorbital foramina).

The natural pathways from where CAM can spread are along the inferolateral wall of orbit (inferior orbital fissure) and along the inferomedial wall of orbit (nasolacrimal duct) [17,25,26,27,28]

In Orbital cellulitis, imaging reveals preseptal edema, extraconal fat stranding and very occasionally intraconal fat stranding, underlying edema, enlarged extraconal muscles ([6,8,18] extraconal abscess, subperiosteal abscess [3] perineuritis, optic neuritis, endophthalmitis, choroid membrane detachment. [5]

Engorgement or thrombosis of the superior ophthalmic vein peculiarly shows loss of flow void on fat saturated T2 images with exophthalmos in Orbital cellulitis. [8]

Hypointense optic nerve on STIR and T2W imaging implies optic nerve engagement by mucormycosis and perineural spread of infection. Stretching of optic nerve and increased enhancement alongside the posterior wall of globe, within the ocular coats, restricted diffusion on DWI in optic nerve and ocular globe coats is observed as well [18] Optic nerve infarction or direct infiltration of the optic nerve can cause sudden blindness. [29,30]. Other causes of sudden blindness are ischemic causes like central retinal artery occlusion or ophthalmic artery occlusion. Perineural extension along the optic nerve and consequent midbrain involvement is also observed [29]

Increased calibre of optic nerve with altered signal intensity within suggests direct invasion of optic nerve. (fig 4 c)

The Seybold Report
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When the optic nerve is exclusively involved, it indicates that the infection spread is through the arterial branches of ophthalmic artery. This is an evidence of infiltration of optic nerve and needs aggressive treatment. [17]

Marked proptosis and posterior tenting of the globe is also caused by diffuse orbital infection.

Involvement of Orbital apex:

Presence of soft tissue in the region of orbital apex and extension of this soft tissue into the optic canal and into the orbital fissure. On post contrast study, this soft tissue shows enhancement. These features suggest orbital apex syndrome.

Fungal Infection should be suspected if the imaging features provide evidence of orbital apex syndrome and sinusitis. [17] Spread of infection from orbital apex can happen posteriorly into the cavernous sinus via superior orbital fissure. Similarly, infection can spread into the infratemporal fossa across pterygopalatine fossa via the inferior orbital fissure. [17]

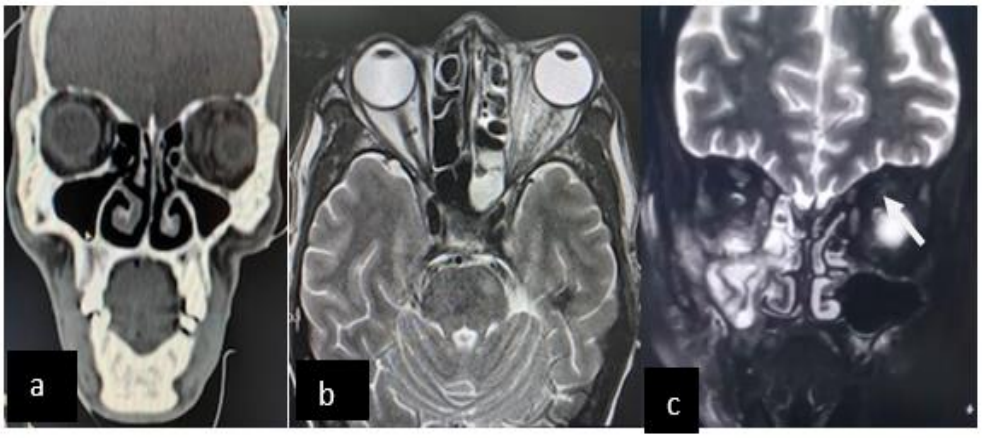

Figure 4

Fig 4: Orbital invasion in covid related mucormycosis patient.Coronal CT image soft tissue window(a) shows shows lateral displacement of medial rectus in Left orbit, suggests early subtle changes of orbital invasion as orbital invasion usually recurs through medial orbital wall . Also thickening of the coats of eyeball noted T2W MR image (b) reveals proptosis of left eye, intraconal fat stranding, signal intensity changes in medial rectus and optic nerve,thickened optic nerve and crowding at left orbital apex (white arrow). Fat suppressed T2W image(c) shows inferior oblique pushed superiorly with hyperintense signal intensity (inflammatory) changes within, on right side.

Cavernous Sinus involvement: On axial and coronal imaging, the lateral wall of the cavernous sinuses are straight or shows concavity in a normal study.

Loss of this straightness and concavity of the cavernous sinus is an evidence of involvement of cavernous sinus. Cavernous sinus shows loss of concavity replaced by lateral convexity and bulging, in its early stage of involvement. On post contrast study, filling defects within the sinus, asymmetric enhancement of lateral wall of cavernous sinus are observed.

The Seybold Report
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Other findings such as outward bulging of lateral wall of cavernous sinus, outward convexity of lateral wall of cavernous sinus or thickened wall of cavernous sinus can also be seen. (Fig 5) [18]Thrombosed superior ophthalmic vein is seen as a dilated cord like structure, crossing from medial to lateral side and is appreciated superior to the optic nerve.Soft tissue compression at the orbital apex or spread of pathology along the vein can cause superior ophthalmic vein occlusion. On post contrast imaging, thrombosed superior ophthalmic vein exhibits filling defect and the loss of normal flow void. [29]

Cavernous segment of the internal carotid artery may be involved by soft tissue within or thrombus within, causing narrowing or occlusion of that segment. Direct invasion of the arterial wall by fungus shows wall enhancement on post contrast imaging. (Fig 5)[30].Narrowing, Occlusion or invasion of the internal carotid artery in its cavernous part causes cerebral infarcts in watershed zones.[18]

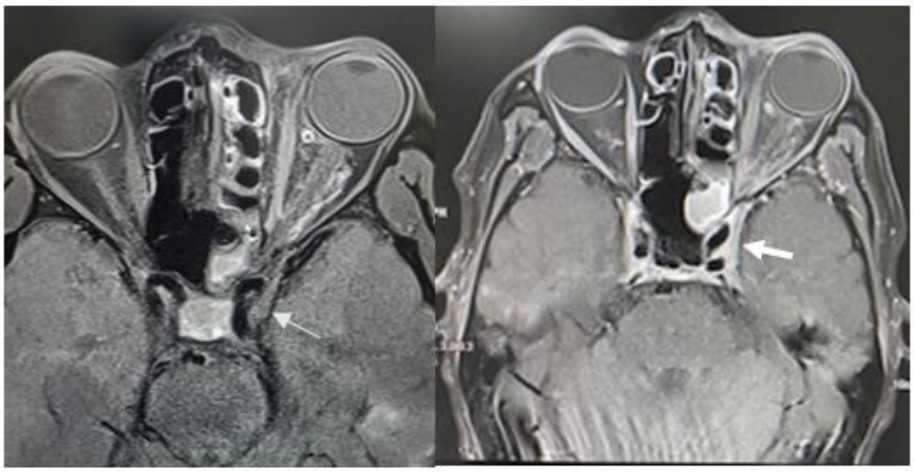

Figure 5

Fig 5: Patient with covid associated mucormycosis (CAM) post contrast fat suppressed T1W axial (a) and (b) image reveal intermediate signal intensity(Thin arrow) in left cavernous sinus causing convexity along its lateral wall,subtle narrowing of cavernous segment of internal carotid artery.Also crowding at orbital apex,intraocular fat stranding, enlarged and enhancing medial rectus , left sided ethmoidal and sphenoid sinusitis are noted. Image (b) reveal arterial wall thickening and hyperenhancement along its lateral wall (white arrow) suggesting Fungal arteritis.

Intracranial extension:

Anterior cranial fossa invasion by ROCM can occur directly via cribriform plate (fig 6, b), sphenoid sinus walls, walls of ethmoid and frontal sinuses.

Anterior cranial fossa invasion can also happen through natural cranial orifices such as orbital fissures, vidian canal and foramina ovale. [17]ROCM extension into middle cranial fossa can occur via internal carotid artery and via pterygopalatine fossa. [29]

The Seybold Report
ISSN 1533-9211
DOI: 10.5281/zenodo.10153275

ROCM extension into posterior cranial fossa can occur via perineural spread along trigeminal nerve from the cavernous sinus.

The commonest imaging feature suggestive of intracranial extension of ROCM is meningeal enhancement. (Fig 6, a)[17]. Cerebritis, brain infarcts and brain abscess are also seen.

On MRI study, ill-defined areas of altered signal intensity in non-vascular distribution, which are T2 hyperintense with surrounding mild perilesional edema and peripheral enhancement on post contrast study suggests brain parenchymal invasion.(fig7)

This perilesional enhancement is ill defined in its posterolateral wall (arrow fig 7, f).

The peculiar very well-defined, distinct, rim enhancement observed in bacterial abscesses is not appreciated in ROCM .This is because of the immunocompromised status of the host.[17]

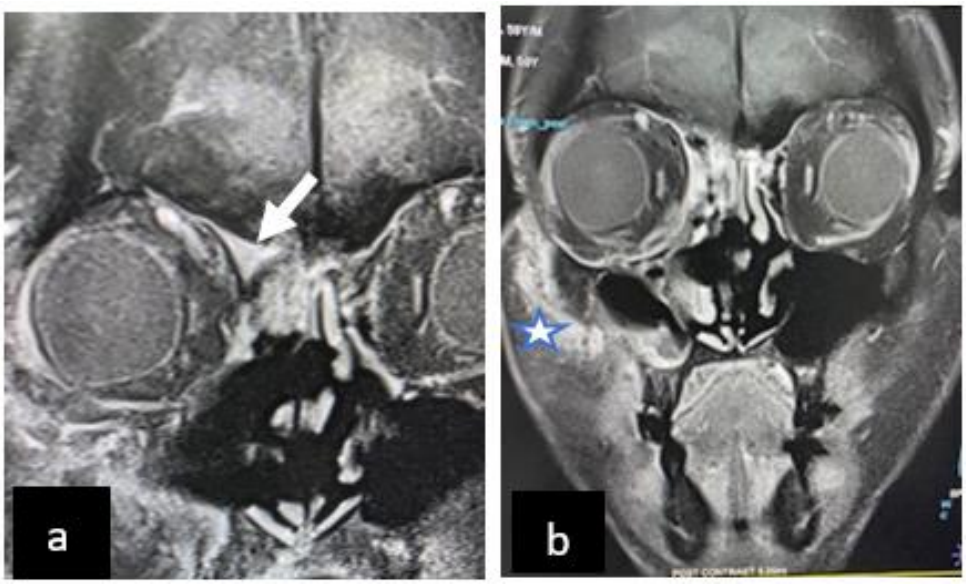

Figure 6

Fig 6: MRI of a brain in a 58 year-old patient with Rhino-orbito-cerebral mucormycosis (ROCM) post contrast fat suppressed T1W image(a) reveal dural thickening and enhancement (arrow) along the anterior cranial fossa right side with obliteration of subarachnoid space. Compare with left side where subarachnoid space is appreciated.Post contrast coronal fat suppressed T1W image (b) reveal enhancement of inferomedial wall of right orbit involving lamina papyracea and cribriform plate. Subarachnoid space is obliterated. Also anterior antral fat stranding (star)-representing Inflammation.

The Seybold Report
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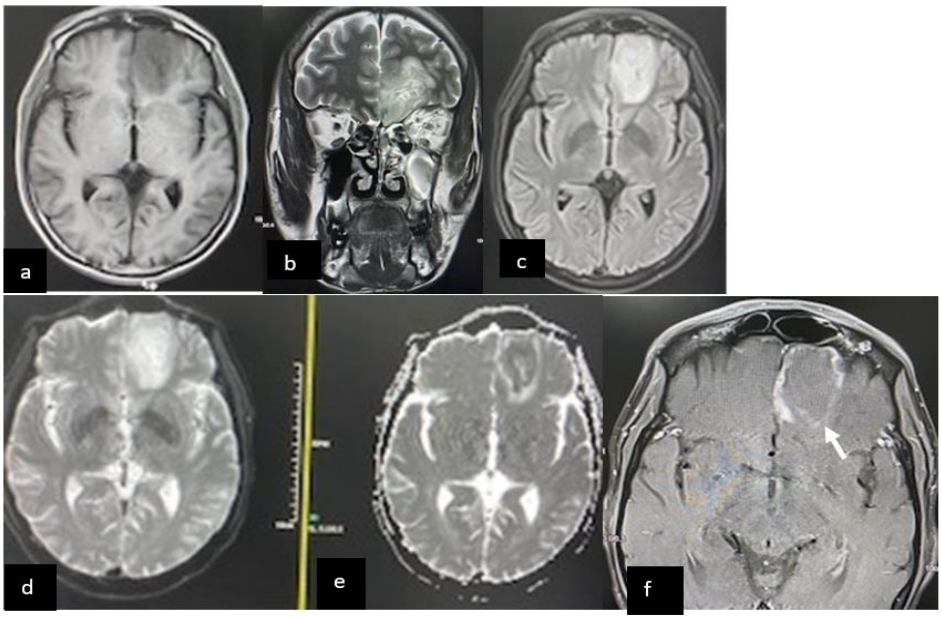

Figure 7

Fig 7: Cerebral parenchymal invasion reveal disease spread from the ethmoid sinuses across the cribriform plate into the left frontal lobe.(a) T1W axial (b) T2W coronal (c) FLAIR axial (d) DWI (e) ADC (f) Fat-Saturated Contrast enhanced T1W axial - reveals left frontal lobe abscess.This parenchymal lesion is hypointense on T1W image, hyperintense on T2WI,FLAIR, shows restricted diffusion on DWI and peripheral rim enhancement on post contrast T1W image.This perilesional enhancement is ill-defined in its posterolateral wall (arrow) due to poor immunogenic response by an already compromised host.

Skull base Osteomyelitis:

Late stages of ROCM may rarely show irregular lysis, rarefaction, sclerosis and thickening of the maxillary sinus. This was a rare complication observed in pre covidera. [1] Bone erosion was less frequent (17.40%) and remaining of the cases (26.60%) on imaging showed extrasinus extension across overall normal appearing intact bones. [1] Chronic mucormycosis may be considered in a patient presenting with history of Covid-19 infection spanning over 12 weeks, showing bilateral skull base osteomyelitis imaging features on CT and MRI. [31]

Bone erosion:

Nasal septum, nasal bones, maxillary sinus walls, lamina papyracea, cribriform plate, sphenoid sinus walls, pterygoid plates are the common anatomic sites of bone involvement. Few patients showed bone involvement of more than one anatomic site. [18]

CT imaging revealed bone involvement in the form of focal or diffuse bone erosion. CT also showed decreased bone density with rarefaction and thickening of the sinus wall. Thinning of the sinus wall, mottled air foci within bone, permeative appearance of bone are also noted. [Fig 2 a and Fig 3 a,b] MRI reveals sinus wall bone marrow edema [18]

The Seybold Report
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CONCLUSION

CAROCM follows quite aggressive course whereas ROCM of non covid era follows an indolent course and manifests late in terms of its soft tissue and bone involvement. It is recommended to do aggressive follow up of patients and scan the patient for brain and PNS after one month of his/her acquiring covid, with moderate and severe covid.

A defined and organized reporting format need to be followed by radiologists while reporting. Strict attention to minute details and precise reporting is adapted. These steps will allow for detailed evaluation, early detection of the disease and as well speed up the reporting process.

Further future studies comparing covid ROCM with Non covid ROCM need to be carried out to enlighten more on these.

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