

# Radiological spectrum of rhino-occulo-cerebral mucormycosis

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## Research Article

**Keywords:** Rhino-occulo-cerebral mucormycosis (ROCM), Fungal, Mucormycosis Infection, Radiological spectrum

**Posted Date:** April 18th, 2023

**DOI:** <https://doi.org/10.21203/rs.3.rs-2816661/v1>

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# Abstract

## Aim and objectives

### Aim

To study the spectrum of imaging findings in patients Rhino-occulo-cerebral mucormycosis (ROCM).

### Objectives

I To study the demographic profile of patients with ROCM

I To detect the associated extrasinus complications of ROCM

I To aid in clinical diagnosis of ROCM

### Materials & methods

This retrospective descriptive study was performed in histopathologically confirmed cases of ROCM. The case records of patients with radiological, culture and histological evidence of acute invasive rhinocerebral mucormycosis were retrospectively evaluated for relevant radiological and clinical data between May 2021 to June 2022.

### Results

The radiological evaluation included CT and MRI scans were done in 52 patients. The patient's average age was 48 years. The ethmoid sinus was involved in 46 cases (88%) and the maxillary sinus in 27 cases (52%). Biltaral (45, 86%) and pansinus (27, 52%) involvement were the most common. The orbit was involved in 39 cases (75%), the face in 25 cases (47%), and retroantral fat stranding in 24 cases (46%). Mucosal thickening (91%) was the most common pattern of involvement, followed by complete opacification (37%). Osseous involvement was seen in 17 of 44 patients who had CT scans, and the majority of patients had extrasinus extension with intact bone. MRI revealed variable T2SI, with T2 hyperintensity being the most common pattern. Heterogeneous enhancement in post contrast imaging was the most common.

### Conclusion

Rhinocerebral mucormycosis is characterised by a variety of imaging abnormalities on CT and MRI. In determining the degree of involvement and consequences, imaging is crucial.

## Introduction

Over more than 400,000 fungal species are known, approximately 400 are human pathogens, only 50 of which cause systemic or central nervous system infection. Most of these fungi are ubiquitous in our

environment. Many people are colonized by fungi, but the infection is prevented by an intact immune system.(1)

Rhinocerebral mucormycosis is a life-threatening infection caused by saprophytic fungi belonging to the genera *Mucor*, *Rhizopus* and *Absidia*. All of these belong to the order Mucorales and class Zygomycetes. (3)

Rhinocerebral mucormycosis is seen almost exclusively in immunocompromised patients. (3) In the early stages the disease typically presents with fever, headache, facial pain, nasal discharge, nasal obstruction and crusting. The disease progresses rapidly within a period of a few hours to days leading to cranial nerve palsies and features of CNS involvement. (3)

The disease is often misdiagnosed disease process involving the paranasal sinuses. It is a serious condition and associated with a high mortality rate.(1)

Early imaging is helpful in assessing the extent of involvement of this lethal disease which requires prompt and aggressive treatment. (3)

Huge surge in the number of Coronavirus disease (COVID19) associated mucormycosis has been observed recently in india.(2) Imaging forms the cornerstone of management in patients with rhinoorbitalcerebral mucormycosis (ROCM). (2)

In patients with clinical suspicion and imaging evidence of ROCM, empirical antifungal therapy can be started even before confirmation of the diagnosis by microbiology or histopathology.(4)

In patients where biopsy is planned, imaging can be used to help guide the site for biopsy to ensure maximum diagnostic yield. In patients with proven ROCM, imaging plays an important role in determining the extent of disease, which is critical in making a decision about further line of management.(2)

## Materials And Methods

We retrospectively evaluated the imaging and clinical data of 52 patients (38 male & 14 female), 19 to 73 years old, with invasive mucormycosis of the rhinooculocerebral areas. Patients were chosen for the study if they had a confirmed diagnosis of mucormycosis by biopsy or culture, and if computed tomography (CT) scans or magnetic resonance (MR) images were available for review over a period of 2 months during the 2nd wave of COVID 19 disease between May 2021 to June 2022.

The Computed Tomography (CT) and/or Magnetic Resonance Imaging (MRI) images were retrieved from the Picture Archiving and Communication System (PACS).

CT scan was performed on a TOSHIBA (Aquilion 64 TSX-101A) or CANAN (Aquilion Lightning, Canon Medical Systems' 16-row 32 slice) machine using a routine CT Paranasal sinus (PNS) &/or skull protocol with 130kVP and 150–220 mA tube current. Intravenous contrast medium (low osmolar, non-ionic, 350

mg/ml iodine content) was used routinely at a dose of 1 ml/kg administered by pressure injector. Conventional MR PNS &/or brain &/or orbit imaging including axial, coronal and sagittal T1 weighted, T2-weighted images and fat suppressed T1-weighted images after intravenous injection of gadopentetate dimeglumine (0.1 mmol/kg). were acquired. MRI imaging was performed using GE 1.5T MRI OPTIMA MR360 1.5T.

**Image analysis**-Three staff radiologists conducted a consensus retrospective review to look for sites and extent of involvement, signal characteristics, and complications.

**Image interpretation**-The sinuses involvement on CT or MRI were recorded in each case. Three patterns of sinus involvement on CT was recorded, mucosal thickening, complete opacification and air fluid level. Involvement of bone was evaluated on CT. Signal intensity on T1W and T2W images were recorded. Fat stranding and soft tissue extension that resembled the intrasinus soft tissue were interpreted as indicators of involvement in the orbit, retroantral, masticator, and pterygopalatine.

Cavernous sinus and internal carotid artery involvement was seen as thickening and non enhancement on post contrast scans and loss of flow void in ICA in MRI. Dural enhancement, the presence of extradural collections, infarcts, cerebritis, and intracerebral abscess were all evaluated in patients with intracranial extension.

**Statistical analysis**-Descriptive statistical methods were used for statistical analysis.

## Results

A total of 52 patients were selected for the radiological evaluation, of whom 44 underwent CT, 25 underwent MRI, and 17 underwent both. NCCT was performed in 34 cases, CECT in ten, and plain MRI in 11, while 14 underwent CMRI.

The Picture Archiving and Communication System (PACS) was used to retrieve the images from the computed tomography (CT) and/or magnetic resonance imaging (MRI).

**Demographic and clinical background:** Our study group included 38 males and 14 females ranging in age from 2 to 75 years (mean = 48 years). Patients over the age of 40 made up the majority (78.8%), with people in their 40s and 60s (65%) suffering the most.

Out of 52 patients selected, 47 (90.4%) were diabetic; 32 (61.5%) patients had a recent (within the last 2 months) history of COVID-19 disease; 24 (46.2%) patients had recent systemic (oral or IV) steroid use; and 17 (32.7%) patients had a history of nasal oxygen use. Out of 52 cases, 46 were histopathologically proven, and the remaining six were microbiologically proven (culture positive).

### Imaging findings

#### (a) Sinonasal involvement

The ethmoid sinus was the most common sinus involved in our study (46, 88%), followed by the maxillary sinus (27, 52%), and the frontal was the least commonly involved (8, 15%). B/L sinus involvement (45, 86%) was a more common finding as compared to unilateral involvement. With the exception of one case with isolated maxillary involvement, the majority of patients (27, 52%) had pansinusitis, followed by unilateral involvement of the ethmoid, maxillary, sphenoid, and frontal sinuses (11, 21%), and the remaining cases had multiple sinus involvement. Details of sinus involvement are shown in Table 1.

**Table 1:**

**Sinuses involved in mucormycosis**

<b>Sinus involved</b>	<b>Number (%)</b>
Maxillary	27 (52%)
Ethmoid	46 (88%)
Sphenoid	26 (50%)
Frontal	14 (52%)
Pansinusitis	11 (21%)

**(b) Extrasinus involvement**

Orbit was the most common site involved in our study, in which extraconal fat stranding or soft tissue opacification and/or altered signal intensity were most commonly seen (39, 75%) (Fig 1), followed by extraocular muscle thickening or altered signal intensity (22, 42%). Face involvement was seen in 25 (47%) patients, and retroantral fat stranding was seen in 24 (46%) patients (Fig 2). Optic nerve thickening or altered signal intensity was observed in 10 patients (19%) (Fig 1c). Other extra-sinus involved sites were pterygopalatine, infra-temporal fossa and optic nerve. Intracranial involvement included the cavernous sinus, meninges, brain parenchyma, and internal carotid artery. Tables 2, 3 and 4 provide additional information on extra-sinus extension, including the type of involvement.

**Table 2:**

**Orbital structure involved in mucormycosis**

**Table 2:****Orbital structure involved in mucormycosis**

<b>Orbital structures involved</b>	<b>Number (%)</b>	<b>Pattern</b>
Extraconal compartment	39 (75%)	Fat stranding or abnormal SI
Intraconal compartment	19 (36%)	Fat stranding or abnormal SI
Extraocular muscle involvement	22 (42%)	Thickening or abnormal SI or enhancement
Optic nerve	10 (19%)	Thickening or abnormal SI or enhancement
Globe tenting (guitar pick sign)	9 (17%)	
Exophthalmos	6 (6%)	

**Table 3:****Extrasinus involvement other than orbit and intracranial structure**

<b>Structures involved</b>	<b>Number (%)</b>
Face/preantral	25 (48%)
Retrorantral	24 (46%)
Infratemporal fossa	16 (31%)
Pterygopalatine fossa	20 (38%)
Skull bone	3 (0.6%)

**Table 4:****Intracranial involvement**

<b>Structures involved</b>	<b>Number (%)</b>	<b>Pattern</b>
Cavernous sinus	3 (0.6%)	Filling defect or abnormal SI
Meninges	2 (0.4%)	Meningeal enhancement
Brain parenchyma	2 (0.4%)	Infarction and cerebritis
Internal carotid artery	2 (0.4%)	Loss of flow void and vessel luminal attenuation

**(c) Imaging appearance and signal characteristics**

Mucosal thickening (40%) was the most common pattern of sinus involvement, followed by complete sinus opacification (34%), and air fluid level (15%) (Fig. 2). Hyperdense content within the sinuses was noted in 7 patients. A combination of patterns was most commonly seen in individual patients. Nasal cavity involvement (46, 88%) was seen as nonspecific mucosal thickening, fluid or soft tissue content in

the nasal cavity, and heterogeneous or nonenhancing nasal mucosa. Intraconal or extraconal orbital involvement was observed in the form of fat stranding, soft tissue opacification, or altered signal intensity (Fig 1 & 3). Extraocular muscle and optic nerve involvement were found to have thickened or altered signal intensity. Exophthalmos and globe tenting were observed as a result of increased orbital tension caused by optic nerve stretching of the posterior globe. Extrasinus involvement was observed in 39 patients out of 44 who underwent CT, whereas sinus wall involvement was seen in only 16 patients, suggesting extrasinus spread of disease through intact bone. Bone involvement in the form of bone rarefaction, erosion, and permeative destruction was seen in 16 patients, involving the sinus wall (16) and skull base (3) (Fig 4). Face, retroantral, infratemporal fossa, and pterygopalatine fossa involvement was observed in the form of fat stranding, altered signal intensity, or abnormal enhancement. Cavernous sinus filling defect, or abnormal enhancement were observed in cavernous sinus involvement in 2 patients (Fig 5). Abnormally enhancing meninges were observed in 2 patients. Loss of flow void and filling defect were seen in the internal carotid artery. Brain parenchymal involvement was seen as brain abscess, infarction, and cerebritis (Fig 6 & 7).

Homogeneous enhancement of mucosa was observed in 4 patients, heterogeneous enhancement was seen in 5 patients, and one patient showed no enhancement in total of 14 patients who underwent CECT. Six patients showed homogeneous enhancement, and eight patients had heterogeneous enhancement with nonenhancing areas on post-contrast T1FS in 14 patients who underwent contrast enhanced MRI. Black turbinate sign was present in five patients (Fig 8). Details of patterns of disease, signal intensity and enhancement patterns are enlisted in Table 5 and 6.

**Table 5:**

<b>CT features (34 NCCT &amp; 10 CECT)</b>	
Mucosal thickening	40 (91%)
Air fluid level in sinuses	15 (34%)
Sinus opacification	34 (77%)
Hyperdense content in sinuses	7 (16%)
Osseous involvement	17 (38%)
<b>Enhancement Pattern (10)</b>	
Non enhancing	1 (10%)
Mild homogeneous enhancement	4 (40%)
Heterogeneous enhancement	5 (5%)

**Table 6:**

<b>MRI features (11 plain &amp; 14 contrast enhanced)</b>	
<b>T1 weighted</b>	
Hypointense	25 (100%)
Hyperintense content	5 (20%)
<b>T2 weighted</b>	
Hyperintense	15 (60%)
Isointense	6 (24%)
Hypointense	4 (16%)
Hypointense content in sinus	9 (36%)
<b>Enhancement Pattern (14)</b>	
Homogeneous enhancement	6 (43%)
Heterogeneous enhancement	8 (57%)
Black turbinate sign (non enhancement)	5

## Discussion



Mucormycosis is an invasive fungal infection that was first described in 1885 by Paulltauf A (4). Although it can affect various body organs, the rhinocerebral form is the most common (5). These fungal spores can be found in abundance in the environment, including the skin, soil, air, dust, and spoiled food. In most cases, infection is acquired through inhalation of Phycomycetes fungi spores, most commonly from the genera *Mucor*, *Rhizopus*, and *Absidia* (5). These organisms can become pathogenic in immunocompromised patients, as well as those with poorly controlled diabetes mellitus and diabetic ketoacidosis. Organ transplantation, hematologic malignancies, chronic corticosteroid treatment, and haemochromatosis are all examples of immunocompromised states (5). 47 patients in our study were diabetic, 32 patient had recent COVID-19 disease and majority of them received systemic steroids making them susceptible for Mucormycosis.

The infection begins in the nasal cavity and spreads to the paranasal sinuses. Early fungal implantation is typical in the maxillary sinus, where there is no bone degradation. The middle turbinate is the most commonly involved site in mucor, followed by the middle meatus and septum(6).

Fungi can spread through perivascular channels beyond paranasal sinuses with intact bony walls (Fig. 1) (7).

It virtually penetrates all of the tissues nearby. Then, it advances to the brain either through angioinvasion or ethmoid sinuses, orbital apex, and bone erosion (6). Imaging aids in the assessment of osseous destruction, which is followed by intracranial, cavernous sinus, and intraorbital extension, however (7) early radiological changes, such as mucosal thickening, are indistinguishable from nonspecific sinusitis on either MRI or CT (7).

Although sinus CT is the preferred imaging modality for evaluating signs of invasion, bone destruction is frequently observed late in the infection course after soft tissue necrosis. Magnetic resonance imaging is more sensitive in identifying the intradural and intracranial extent of ROCM, cavernous sinus thrombosis, and thrombosis of the internal carotid artery's cavernous portions (8).

The Middlebrooks et al. proposed 7 variable CT based model was found to be useful as a screening tool to identify patients at risk for acute invasive fungal sinusitis. Pterygopalatine fossa, bone dehiscence, orbital invasion, septal ulceration, lacrimal sac, and periantral fat were among the factors. In their study, involvement of periantral fat was the best individual predictor of invasive fungal sinusitis (9).

Patel et al. found bony erosion in 75% of Covid-ROCM patients, whereas DelGaudio et al., Gupta K. et al., and Jacob Therekattu et al. found bony erosion in only 33–40% of pre-COVID ROCM cases (10, 11, 12, 3). Osseous involvement in our study was seen in 38% of cases in the form in the form of bone

erosions (most common), rarefaction and permeative destruction. Erosions were frequently found in the walls of the maxillary antrum and orbital walls, allowing them to spread into the retromaxillary soft tissue and orbit, respectively. CT images helped to visualise the erosion or rarefaction of bony walls.

In fungal sinusitis, hyperdense intraluminal contents represent fungal hyphae and debris (1). According to Patel et al., approximately one-third of patients with ROCM had hyperdense material (10), but we discovered this finding in 16% of instances.

Due to the angio-invasiveness by fungi, extrasinus involvement can occur without bony erosions by spreading through small vascular channels (3, 13). This finding was seen in 20 (45%) patients in our study.

Another early sign of ROCM is superficial cellulitis, as involvement of the superficially located subcutaneous fat is uncommon in non-fungal sinusitis. Patel et al. found superficial cellulitis in 35% of cases, with premaxillary fat stranding/soft tissue replacement being the most common (10). 48% of patient had superficial cellulitis in our study.

In sinuses, Agarwal et al. observed variable signal intensity on T2WI and predominantly (90%) hypointensity on T1WI (14). In our study, we also found variable signal intensity on T2WI (60% hyperintense, 25% isointense and 4% hypointense) and all showed hypointensity on T1WI. The accumulation of hemosiderin and paramagnetic materials such as calcium, iron, magnesium, and manganese has been linked to hypointensity on T1WI and T2WI in fungal disease (3, 14, 15).

ROCM is also characterised by periantral fat invasion, which can manifest as stranding of premaxillary/retroantral fat, increased signals on fat-saturated T2-weighted imaging, or enhancement on contrast sequences. Fat stranding can also be seen on CT images. In our study, 59.6% of patients had periantral fat involvement. Agrawal et al. showed periantral involvement in 75.83% of cases (15).

In the early stages, there is intense homogeneous enhancement of the mucosa, similar to bacterial sinusitis. The presence of heterogeneous enhancement or non-enhancing areas within the lesion suggests that it is caused by an invasive fungal aetiology. The disease is known to devitalize the sinonasal mucosa through vascular invasion and infarction, resulting in non-enhancing tissues on contrast administration (15).

Only 5 of the 14 patients with available post-contrast MRI had the black turbinate sign described by Safder et al. as a feature of early nasal mucormycosis (16).

## **Limitation Of Study**

Single centered and retrospective nature were the the limitation of our study and all patient did not undergo contrast enhanced study.

## **Abbreviations**

ROCM: Rhino-occulo-cerebral mucormycosis

MRI : Magnetic resonance imaging

T1WI: T1 weighted image

T2WI: T2 weighted image

T1 FS: T1 fat saturated

CT: Computed tomography

NCCT: Non contrast computed tomography

CECT: Contrast enhanced computed tomography

ICA: Internal carotid artery

## Declarations

**Ethical approval and consent to participate:** – Ethical clearance was obtained from Office of ethical committee, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, for the conduct of this study. Informed written consent was taken from all participants.

**Consent for publication-** Not applicable

**Availability of data and materials-** Yes

**Competing Interests** – None

**Funding** – No funding received for the study

**Authors' contribution** – D- Preparation of manuscript and analysis of data, UP- Review of manuscript, SKS- Editing of manuscript and references MK & VW- Preparation of manuscript and images.

**Acknowledgements** – We are highly grateful to Medical record department of our institute who help and cooperated in data collection.

**Statement:** All methods were carried out in accordance with relevant guidelines and regulations.

**Conflict of interest**

There was no conflict of interest in our study.

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## Figures

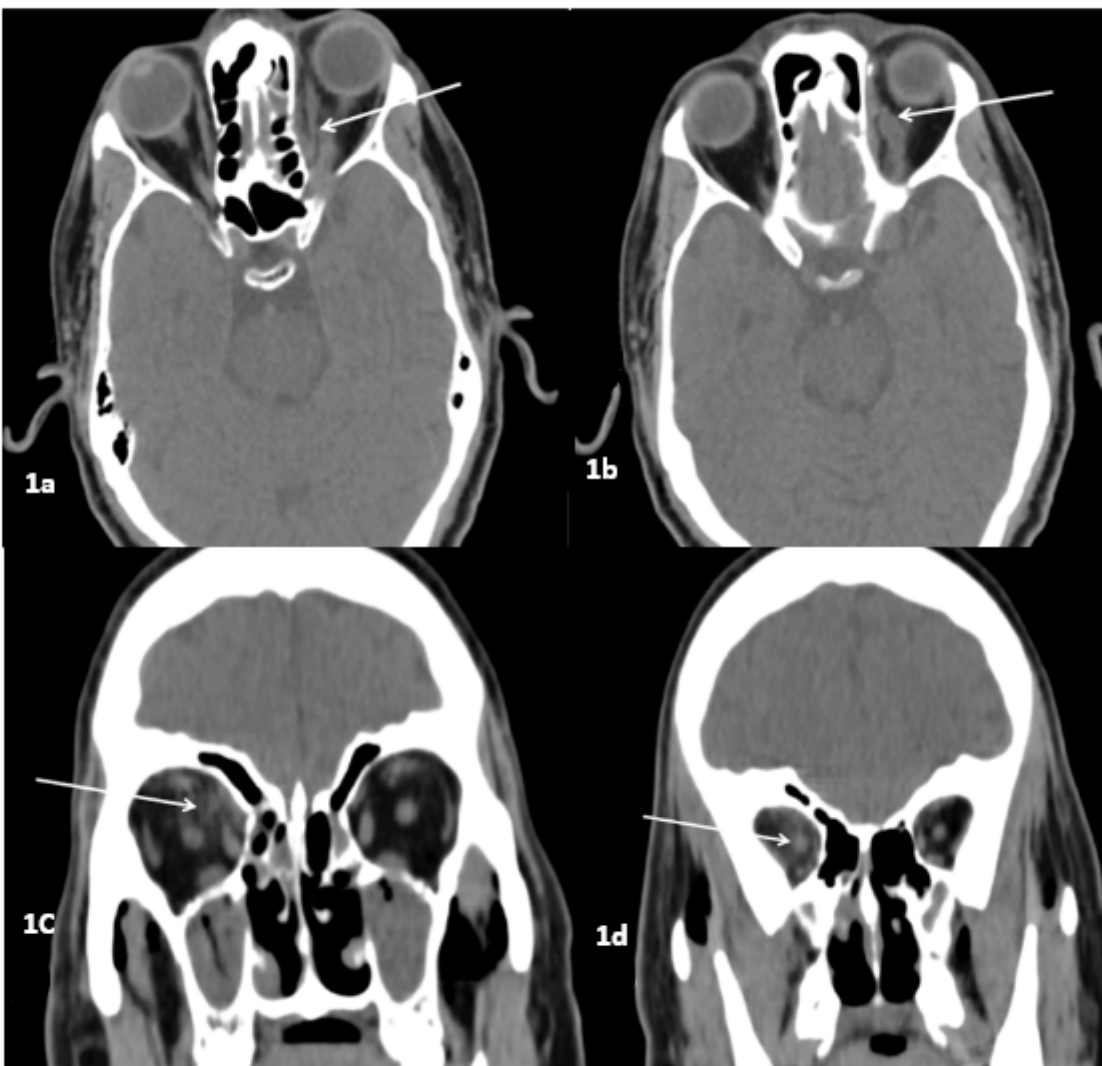
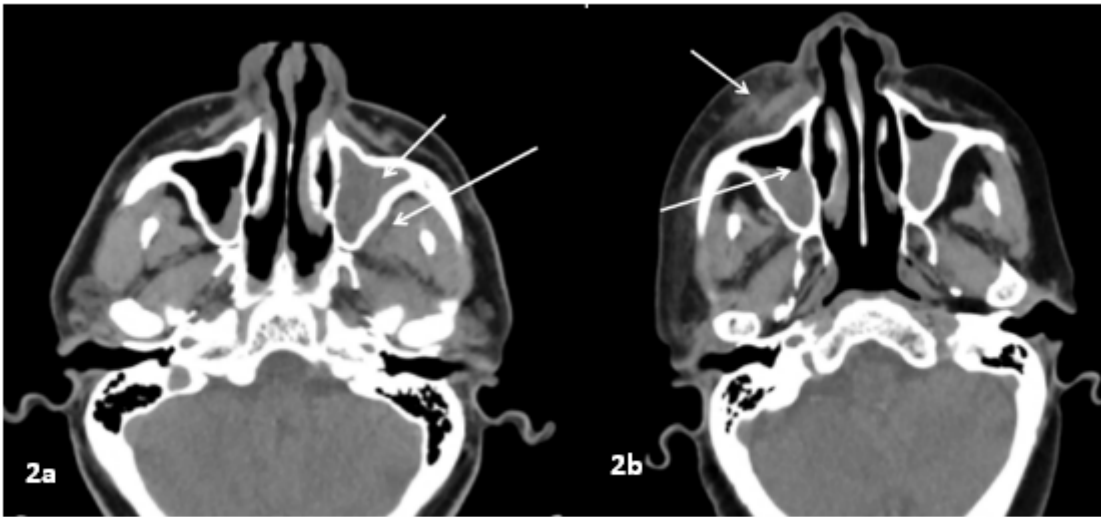


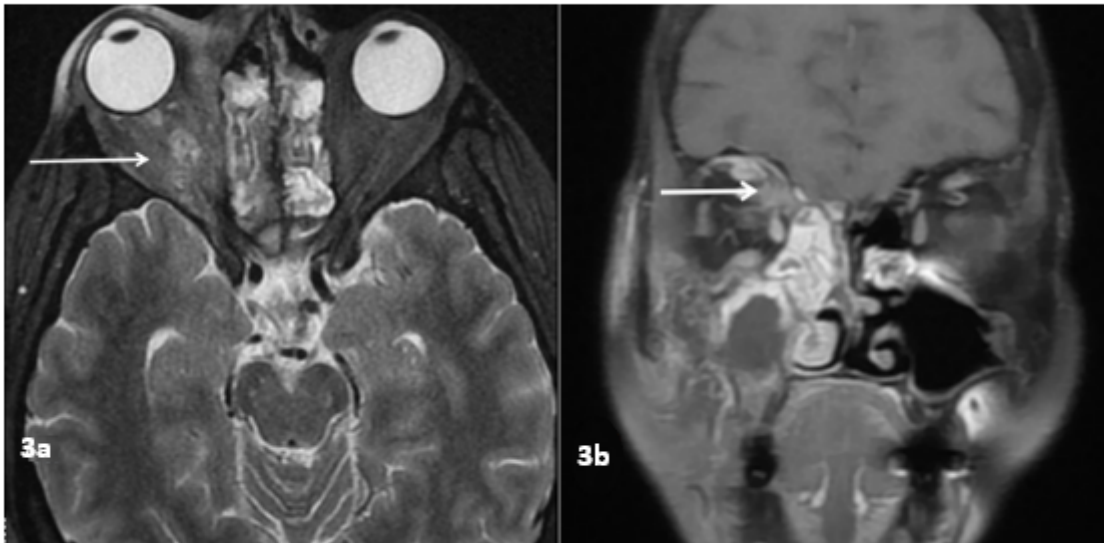
Figure 1

Orbital involvement in different patients. Figure (a) & (b): Axial CT image of 57 years old diabetic patient of rhino-ocular mucormycosis showing left intra and extraconal fat stranding with soft tissue opacification of left orbital apex (arrow in 1a) and thickening of left superior ophthalmic vein (arrow in image 1b). Figure (c) & (d): Coronal CT scan of another 68 years old patient of rhino-ocular mucormycosis showing right intra and extraconal fat stranding (arrow in image 1c) with thickening of right optic nerve (arrow in 1d).



**Figure 2**

Periantral involvement in different patients. (a). Axial CT image of 52 years old patient of mucormycosis showing complete sinus opacification of left maxillary sinus (short arrow) with retroantral fat stranding (long arrow). (b). Axial CT scan of 57 years old patient of mucormycosis showing air fluid level in right maxillary sinus (long arrow) with preantral fat standing (short arrow). Both (a) and (b) images showing periantral involvement with intact bony wall, suggestive of perineural spread of the infection.



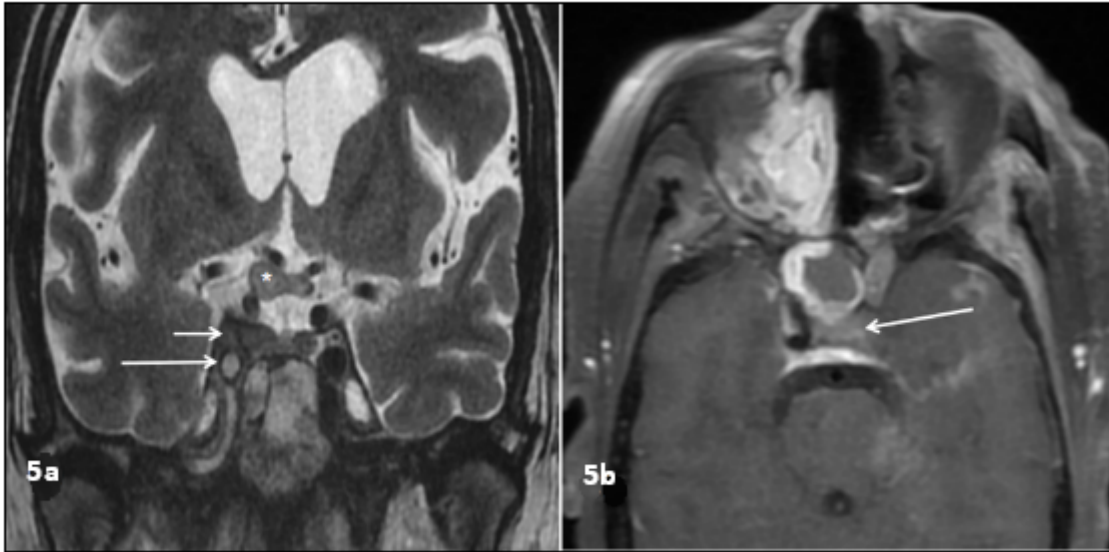
**Figure 3**

Orbital involvement. (a). Coronal T2WI of 43 years old patient of ROCM showing altered signal intensity in right intra and extraconal compartment (arrow). (b). Coronal T1 FS post contrast image showing abnormal enhancement of right intra and extraconal fat (arrow).



**Figure 4**

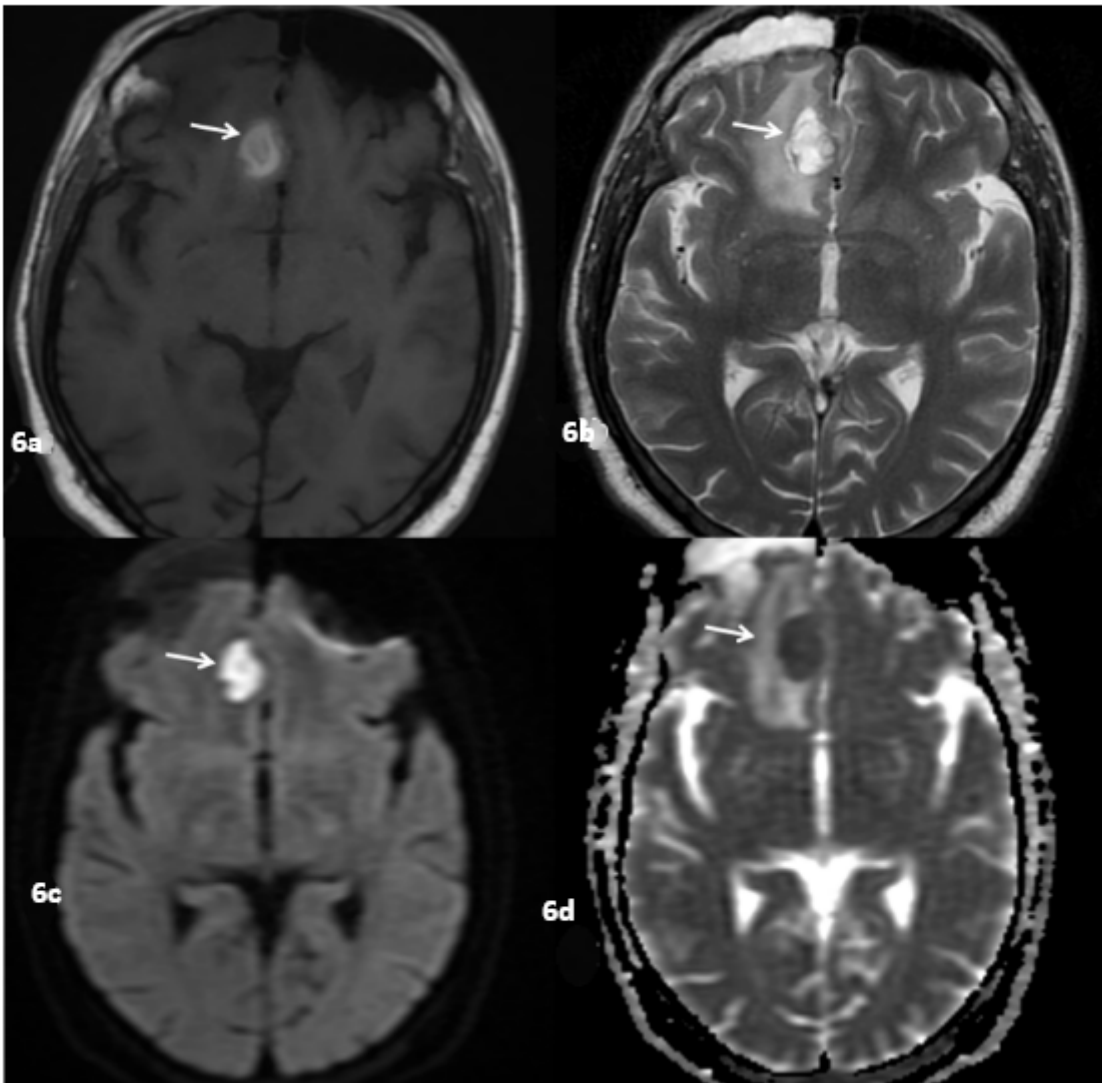
Osseous involvement. Axial CT bone window image of 65 years old diabetic patient who presented with facial pain and redness, showing erosion of anterior and posterior wall of left maxillary sinus (arrows).



**Figure 5**

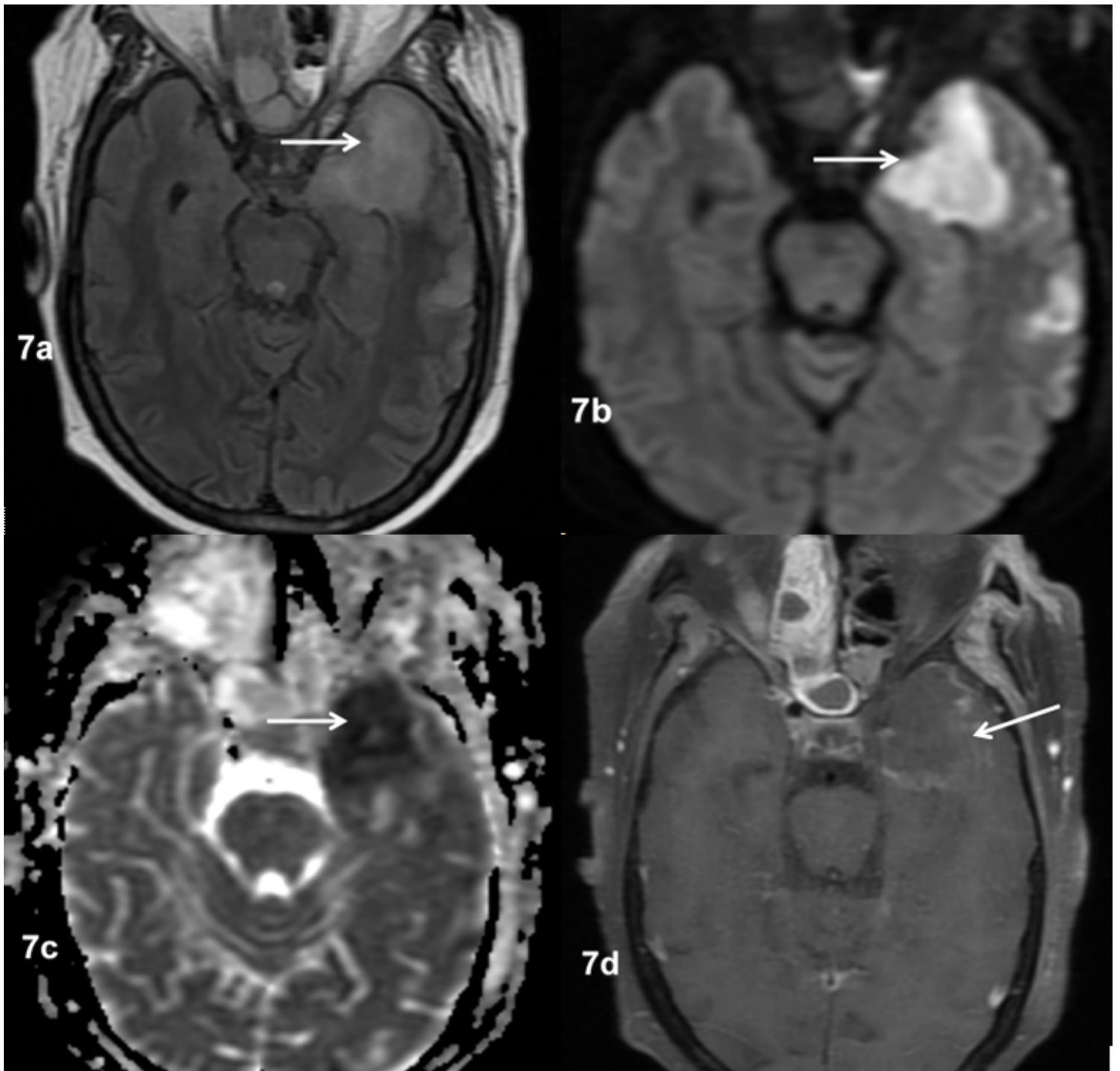
(a) Coronal T2WI of 42 years old patient who had recent COVID-19 disease and systemic steroid use presented with headache and right eye vision loss, showing loss of flow of void in right ICA (large arrow) with abnormal signal intensity in right cavernous sinus surrounding right ICA (small arrow) and thickening of right optic nerve upto optic chiasma (\*). (b) Axial post contrast T1 FS of 50 years old patient who had recent COVID-19 disease and systemic steroid use presented with headache and left eye vision loss, showing loss of flow void in left ICA (arrow).





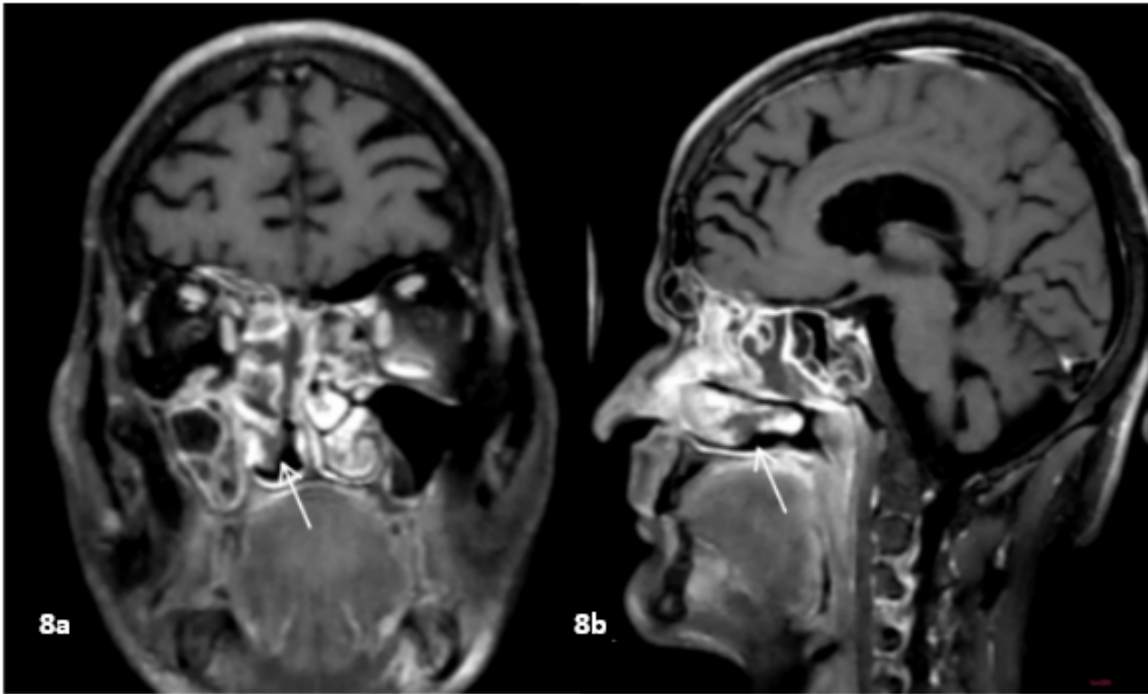
**Figure 6**

Brain abscess in a 68 years old diabetic patient with history recent systemic steroid use who presented with nasal symptoms and headache. (a) Axial T1WI image showing hyperintense lesion in right gyrus rectus, (b). Axial T2WI shows the lesion is hyperintense on T2WI as well with adjacent edematous changes, (c). Axial DWI showing the lesion shows diffusion restriction, and (d). ADC map shows the lesion is hypointense suggestive of true restriction.



**Figure 7**

Subacute infarct in patient of ROCM. (a) Axial FALIR image showing hyperintensity in left frontal lobe, (b) axial DWI at b=1000 showing diffusion restriction in left frontal lobe (b), (c) ADC map showing hypointensity in corresponding region, and (d) Axial post contrast T1 FS showing mild peripheral enhancement suggestive of subacute infarct.



**Figure 8**

Black Turbinate sign. (a). Coronal T1 FS image showing non enhancing right inferior turbinate (arrow). (b). Sagittal T1FS of the same patient showing non enhancing part of right inferior turbinate (arrow).