

Imaging in Covid-19 associated mucormycosis: a case series

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Date of Submission: 22/05/2022

Date of Review: 25/06/2022

Date of Acceptance: 12/07/2022

ABSTRACT

Introduction: Mucormycosis is a very rare saprophytic, opportunistic fungal infection with high morbidity and mortality. With the Covid-19 pandemic, there is a sudden increase in the incidence of this disease due to causes not clearly known.

Methods: Retrospective clinic-radiological analysis of a series of seven microbiologically confirmed cases of Covid-19 associated mucormycosis (CAM) treated at our tertiary care center in 2021 was done.

Results: All patients were middle-aged with a mean age of 47 years. All patients had poor glycemic control. Three patients were on oxygen support and were given steroids during Covid-19 treatment. Symptoms were facial pain, swelling, headache, eyelid swelling, and nasal block. All patients underwent contrast MRI to study the extent of tissue involvement. MRI helped in complete surgical debridement with minimal deformity.

Conclusion: Judicious use of immunosuppressants and strict glycemic control vital during covid-19 treatment. Contrast MRI is the investigation of choice to identify the extent of involvement in surgical planning.

KEYWORDS: Imaging, Covid-19, Mucormycosis, Amphotericine

INTRODUCTION

Severe acute respiratory syndrome (SARS) caused by Coronavirus 19, has affected a large number of people all over the world every day, and causing millions of deaths resulting in a global health crisis. It affects primarily the respiratory system with severity varying from simple common cold to severe pneumonia. It spreads among people mainly by inhalation of droplets or by touching the infected surfaces.^[1]

Mucormycosis is a rare, opportunistic invasive fungal infection used to be seen in immune-compromised individuals commonly uncontrolled diabetics. However, after the start of the SARS Covid-19 pandemic, there was a sudden and significant increase in the number of invasive mucormycosis cases. Possible causes could be the use of steroids or immunosuppressants in SARS Covid-19 patients to avoid the progression of the disease requiring mechanical ventilation or a huge number of diabetic patients in India who are diagnosed late affecting the immunity of the individuals.^[2] Diabetic patients with SARS Covid-19 infection have hyperglycemia, hypoxia, acidic medium, and high iron levels and associated impaired phagocytic function of white blood cells causing defective intracellular killing by oxidative and non-oxidative mechanisms. This provides an ideal environment for this angio-invasive fungus.^[3] Imaging is very crucial in the diagnosis and assessing the extent of the disease. It is also very useful in assessing the clearance of the disease in the postoperative period. Contrast-enhanced magnetic resonance imaging (MRI) is the investigation of choice.^[4]

In this article, we are presenting a series of seven cases of post-covid-19 associated mucormycosis, who underwent treatment at our center.

METHODS

We are presenting clinic-radiological profile of seven confirmed cases of mucormycosis managed in our institute from May 2021 to August 2021.

RESULT:

Case No.1: A 50-year-old male patient presented with Facial swelling, Facial pain, and Nasal block on the left side for a few days. He was a diabetes mellitus patient on irregular treatment. He also gave a history of receiving oxygen supplementation during the Covid-19 infection history of Diabetes mellitus on irregular treatment. Nasal endoscopy

showed Mucopus, polypoidal tissue, and slough in the left middle meatus. Slough sent for KOH mount was positive for mucormycosis. Contrast MRI of the paranasal sinuses showed extensive mucosal thickening of bilateral maxillary, ethmoid, sphenoid and frontal sinus with areas of T2W hypo intensity in the right maxillary sinus and pseudo pneumatization on T2W in the bilateral ethmoid sinus, suggestive of fungal sinusitis. There were areas of mucosal necrosis involving the left maxillary and ethmoid sinus. There was marrow edema involving the posterolateral wall of the left maxillary sinus with periantral soft tissue thickening and enhancement, associated extensive soft tissue thickening, and enhancement involving the left pterygopalatine fossa and left soft palate. There was no evidence of extra sinus soft tissue necrosis and no evidence of intracranial extension of the disease Figure 1. The patient underwent endoscopic debridement under general anesthesia. Tissue was positive for invasive mucormycosis. The patient received Amphotericin B and posaconazole. No recurrence in the follow-up period of 3 months.

Case No.2: 39-year-old female patient presented with headache, eyelid, and facial swelling on the right side for a few days. Nasal endoscopy showed slough and polypoidal tissue in the right middle meatus. KOH mount of the slough was positive for mucormycosis. Contrast MRI of the PNS showed Mucosal thickening of right maxillary ethmoid, frontal and bilateral sphenoid sinus. Mucosal necroses in right maxillary sinus and right nasal cavity. Erosions of posterolateral wall of the maxillary sinus with associated significant periantral, pterygopalatine, para pharyngeal and masticator space edema and enhancement. Erosions of the right frontal bone and lamina papyracea with significant soft tissue thickening and walled-off collection in the right orbit with mild proptosis of the right eye. Similar soft tissue thickening and walled-off collection was seen in the right perifrontal region. Right periophtic soft tissue thickening and enhancement were seen, suggestive of optic neuritis. There was a focal small ring-enhancing lesion in the medial right temporal lobe with surrounding perilesional edema, suggestive of brain abscess Figure 2. The neurologist advised intravenous Amphotericin B therapy. Endoscopic debridement tissue was positive for mucormycosis. Endoscopic debridement was repeated after a week as symptoms didn't improve and a repeat MRI showed residual avascular tissue. The patient received Amphotericin B and Posaconazole. No recurrence of disease in the follow-up period of 3 months after the second surgery.

Case No.3: 38-year-old male patient presented with headache and eye pain on the left side. Nasal endoscopy showed crusting and mucopus in the nose, sent for KOH mount was positive for mucormycosis. Contrast MRI showed mucosal thickening of the left maxillary and ethmoid sinus. There were erosions of the posterolateral of the maxillary sinus with periantral soft tissue thickening and enhancement. No evidence of intraorbital and intracranial involvement Figure 3. Endoscopic debridement was done.

The tissue was negative for mucormycosis. No recurrence in the follow-up period of 3 months.

Case No.4: 54-year-old male patient presented with left-sided facial pain and swelling. Nasal endoscopy showed crusts and mucopus in the left nasal cavity. KOH mount was positive for mucormycosis. A contrast MRI of the PNS showed mucosal thickening of the left maxillary and ethmoid sinus with areas of mucosal necrosis involving the left maxillary sinus. There is soft tissue thickening and enhancement involving the left perimaxillary and periorbital space. No evidence of intraorbital and intracranial involvement Figure 4. Endoscopically debrided tissue was positive for mucormycosis. The procedure was repeated again after a week for residual necrotic tissue. Patient doing well in the 3 months follow-up period.

Case No.5: 55-year-old female patient presented with headache, facial pain, and swelling on the right side. KOH mount of the nasal mucopus was positive for mucormycosis. A contrast MRI of the PNS showed mucosal thickening of the right maxillary, ethmoid and frontal sinus. There were areas of mucosal necrosis in the right ethmoid sinus. There was soft tissue edema and enhancement involving the right perimaxillary, perinasal, pterygomaxillary, masticator, and parotid space with few enlarged right intraparotid nodes and a small focal area of necrosis in the superficial lobe of the right parotid gland. There was orbital spread in the form of thickening and enhancement of extra conal fat and the inferior rectus muscle. There was thickening and enhancement of the right cavernous sinus Figure 5. Debridement under general anesthesia followed by Intravenous Amphotericin B therapy was done. There was no recurrence in the 3 months follow-up period.

Case No.6: 47 yr old male patient presented with left-sided ptosis, nasal block, headache, and facial pain. Nasal mucosa was pale and insensitive with crusting and its KOH mount was positive for mucormycosis. Contrast MRI PNS showed mucosal thickening involving the left maxillary and ethmoid with mucosal necrosis on the maxillary sinus and left middle turbinate. Features of osteitis of anterior and posterolateral wall of the maxillary sinus and associated soft tissue thickening and enhancement involving left periantral space, pterygopalatine, infratemporal, and masticator spaces. There were focal areas of non enhancement involving posterior part of pterygoid muscles. There was intracranial extension of soft tissue thickening and enhancement involving left orbital apex causing thrombosis of left cavernous sinus and inferior petrosal sinus Figure 6. Retro orbital Amphotericin-B injection and Endoscopic debridement done. Post operative Amphotericin B continued. No recurrence in follow up period of 3 months.

Case No.7: 47 yr male patient had headache and pain in the periorbital region on the right side. There was mucopus with crusts in the nose. KOH mount was positive for mucormycosis. Contrast MRI of the PNS showed mucosal thickening involving right maxillary, ethmoid, frontal and

sphenoid sinus with areas of mucosal necrosis involving right maxillary and ethmoid sinus. Erosions of posterolateral wall of right maxillary sinus and right lamina papyracea. There was periantral, pterygopalatine, infratemporal and right masticator space soft tissue thickening and enhancement with areas of necrosis of soft tissue along the posterolateral perimaxillary space. Intraorbital involvement in the form of thickening and enhancement of extraconal fat, intraocular muscles and intraconal fat with thickening involving right optic canal and supraorbital fissure encasing optic nerve was seen. There is intracranial extension in the form of right cavernous sinus infiltration and meningeal thickening and enhancement along the medial lobe of right temporal lobe Figure 7. Endoscopic debridement done and post-operative intravenous Amphotericin B therapy was given. No recurrence in the follow up.

All patients were middle-aged with mean age of 47 years. The youngest patient was 38 yr and oldest patient was 55 years with male to female ratio of 5:2. All patients had history of diabetes mellitus. Five patients had recovered from Covid-19 infection and two patients didn't give any history of suffering from Covid-19 infection. Out of the five patients who had recovered from Covid-19, three patients were on oxygen support and were given steroids. Most of the patients had presented with facial pain, swelling, headache, eyelid swelling and nasal block. Nasal endoscopy showed decreased sensation of the nasal mucosa, crusting, slough commonly in the middle meatus. All patients nasal crust/slough KOH mount showed branched aseptate/pauciseptate hyphae. All patients underwent contrast MRI to study the extent of tissue involvement. MRI findings were very well corresponding with operative findings. Apart from strict glycemic control, surgical debridement was undertaken under general anesthesia to remove all avascular, necrotic tissue in all cases. Histopathology of the excised tissue confirmed the mucormycosis in six patients. These six patients were given intravenous Amphotericin B followed by oral posaconazole therapy. There was no recurrence in follow up period.

DISCUSSION

Mucormycosis is a saprophytic fungus commonly found in the environment. It can affect a variety of tissues and organs in the body. The most common tissues affected are the nose, sinuses, facial tissues, orbits, and intracranial structures. Normally lymphocytes and polymorphonuclear phagocytes are involved in immunity against tissue invasion by opportunistic Mucorales by generating free oxidative metabolites. In SARS Covid 19 infection there is lymphopenia. Also, high blood sugar levels in severe cases of SARS Covid 19, due to glucocorticoid usage as per protocols, result in disruption of these defense mechanisms against this fungus. [4, 5]

Imaging plays a key role in the early detection of mucormycosis. MRI with its high soft tissue resolution makes the detection of mucosal necrosis and extra mucosal spread

of the disease evident much before the clinical suspicion. MRI is necessary before the biopsy to know the area of necrosis and biopsy site, in order to get a high yield in microscopy/ culture. Antifungal therapy can be started with corroborative imaging evidence in a clinically suspected mucormycosis. [6]

In angio-invasive fungal sinusitis, avascular tissue acts as a nidus for fungal growth, hence it is important for the treating surgeons to decide on the areas of debridement to arrest the disease spread. Post-contrast MRI differentiates vascular and avascular tissues in the region involved, thereby helping clinicians to plan the area of resection beforehand. [7] Since MRI clearly shows the extent of the disease spread, surgeons can plan accordingly so that there will be a maximum clearance of dead tissue and minimal disfigurement/Prognostication of the patient and triaging accordingly is critical in angioinvasive fungal sinusitis since there will be intraorbital and intracranial involvement much before the clinical signs and symptoms. MRI is a cornerstone in staging the disease process and predicting the prognosis. Disease spread beyond the paranasal sinus with areas of necrosis, intraorbital and intracranial involvement is associated with poor prognosis. [8] MRI also plays a key role in the follow-up of patients to assess the therapeutic response and guides in optimizing the treatment of the patients accordingly. Early diagnosis of invasive fungal sinusitis on MRI requires knowledge and experience. There are physiological variations that can mimic "the black turbinate sign". [9] It is only possible to diagnose invasive fungal sinusitis on MRI and is impossible to predict the microbiological subtype of the causative organism. [10]

In a study published in 2010 by Yang et al. has shown that the SARS coronavirus affects Islets cells of the pancreas. This could result in patients developing diabetes mellitus or worsening glycemic control. [11] This could be the reason for high blood sugars in most of the SARS covid-19 cases, which in turn predisposes to mucormycosis.

All the cases in our case series were diabetics with poor glycemic control, some pre-existing and others newly diagnosed. The majority had recovered from RTPCR confirmed Covid-19 illness; others had a history suggestive of mild Covid-19 infection symptoms. All cases were diagnosed early in the course of illness, evaluated quickly, and treated with strict glycemic control, aggressive endoscopic debridement of all necrotic tissue followed by systemic Amphotericin B and posaconazole therapy. Contrast-enhanced MRI was very helpful in differentiating inflamed tissue from necrotic tissue, which helped in planning the debridement of the necrotic tissue with minimum possible deformity.

The mortality rate in mucormycosis varies between 37% to 50% depending on the presence of chronic diseases, time on surgical intervention, and antifungal therapy. [12] In our series, all patients were doing well in 3 months of the postoperative follow-up period. We believe it was due to multiple reasons. Increased public awareness created by

the media about mucormycosis (Black fungus), aggressive screening of all Covid-19 recovered patients for signs and symptoms of mucormycosis. Sending all patients samples for KOH mount and getting Contrast MRI done in all suspected cases.

CONCLUSION

As the Covid-19 pandemic continues to come in waves across the globe, mucormycosis remains a possibility among

these cases receiving immunosuppressives in both diabetic and non diabetic patients. Judicious use of immunosuppressants and strict glycemic control is very crucial for the prevention of mucormycosis. Contrast MRI is the investigation of choice to identify the extent of involvement and for surgical planning.

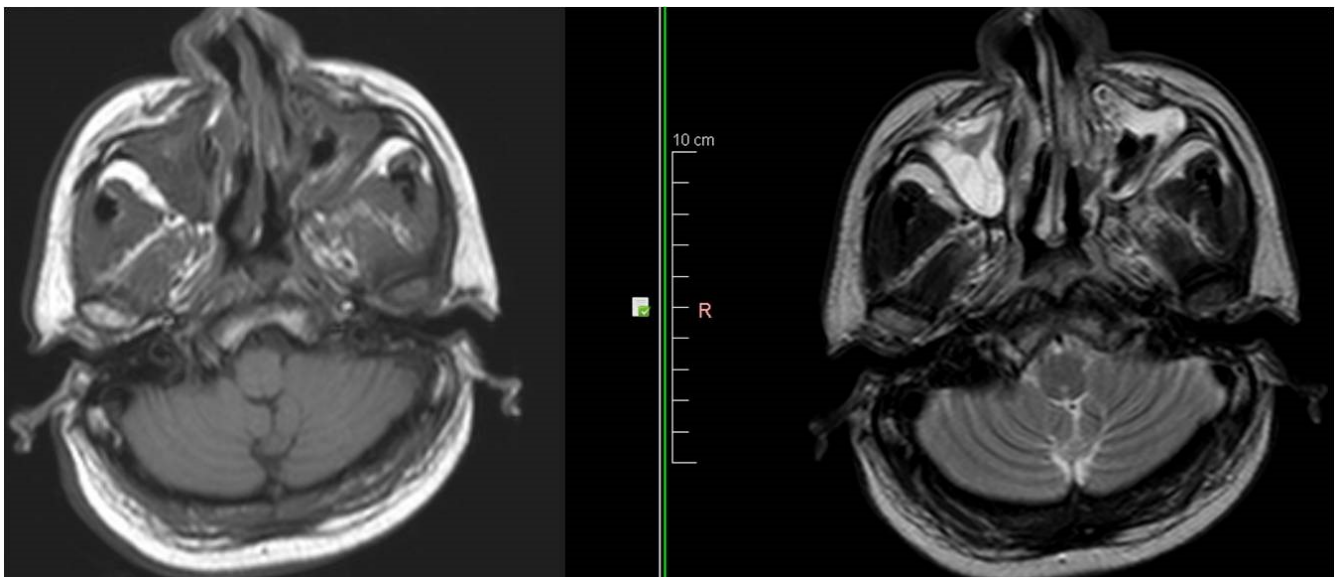


Figure 1: Mucosal thickening in right maxillary sinus showing T1 hyper intensity and T2hypointensity , suggesting fungal sinusitis.

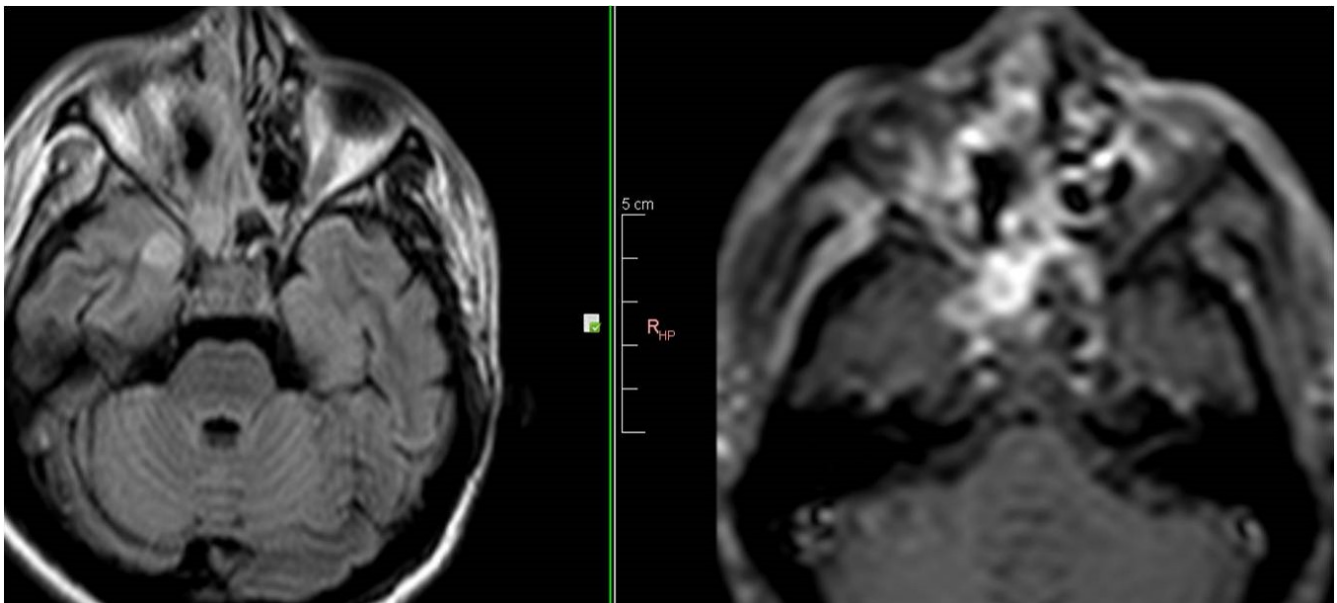


Figure 2: Features of mucosal thickening of right sphenoid and ethmoid sinus with a ring enhancing lesion in the adjacent right medial temporal lobe.

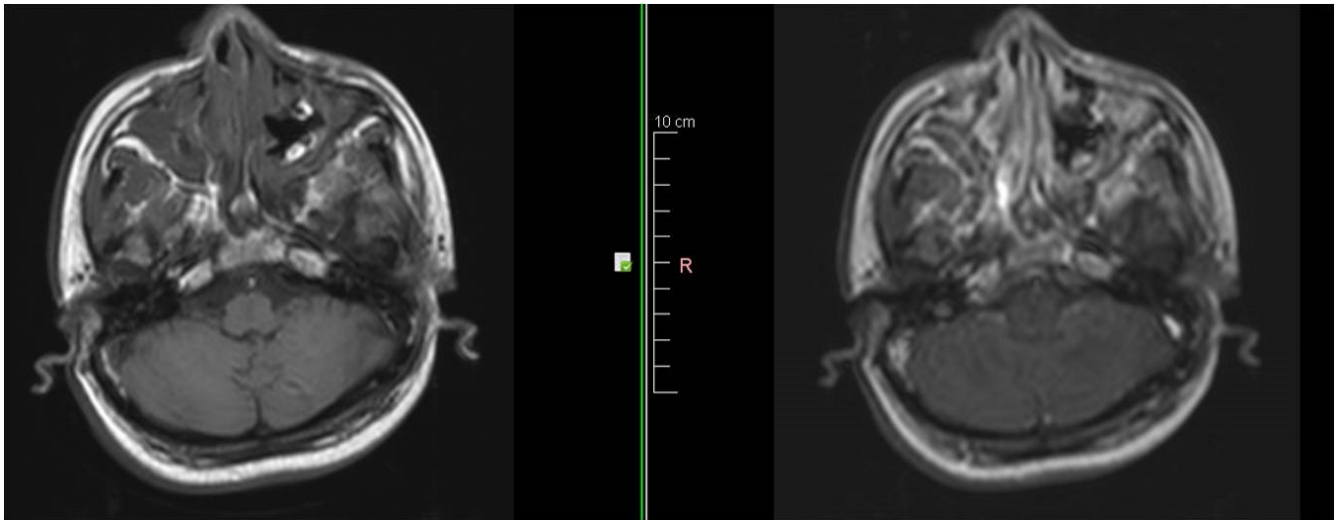


Figure 3: Areas of mucosal non enhancement in the left maxillary sinus , indicating necrosis.

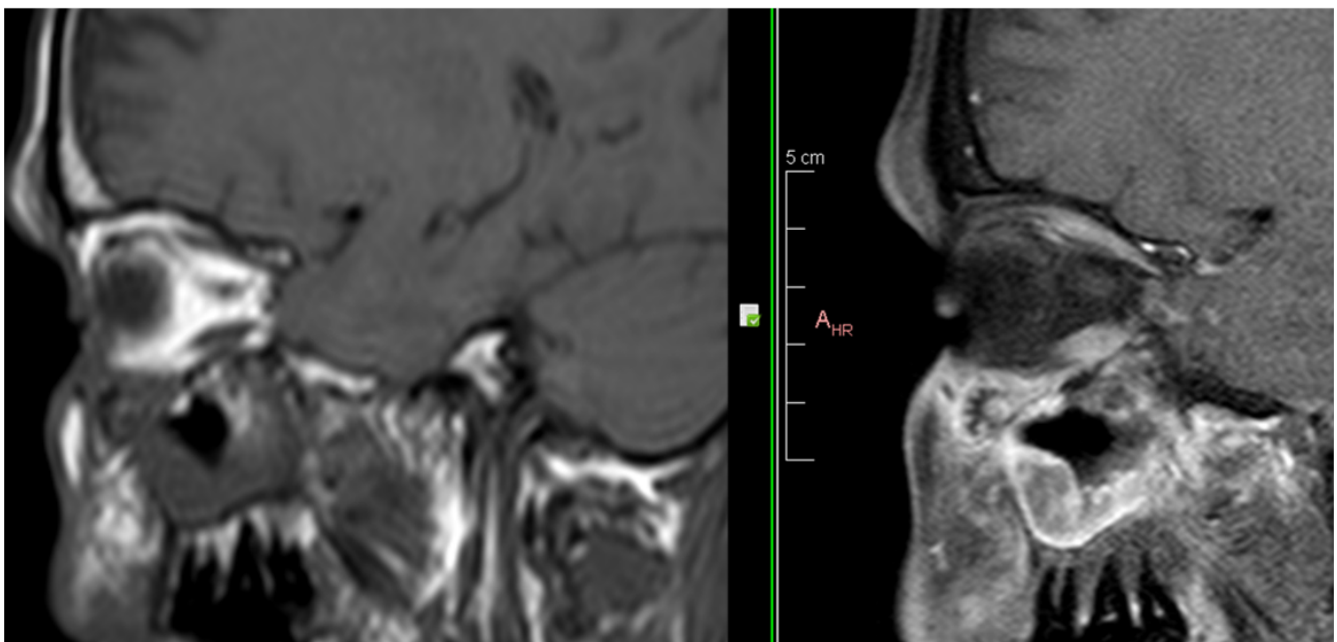


Figure 4: Erosions of posterolateral maxillary wall with adjacent soft tissue thickening and enhancement in the pterygomaxillary space.

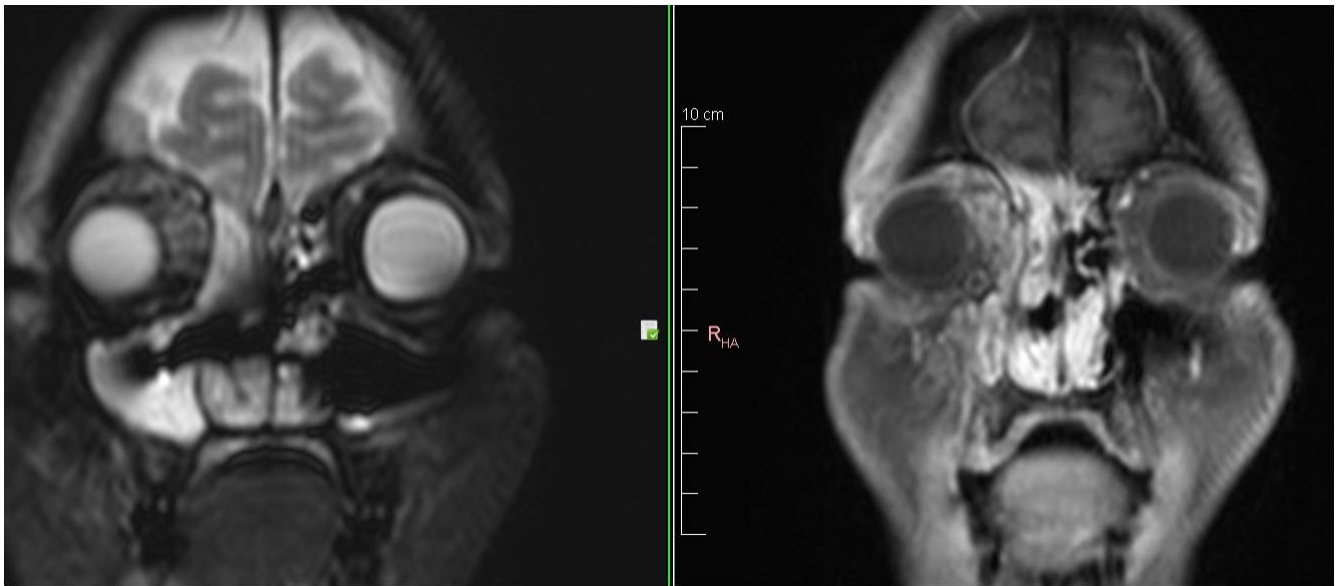


Figure 5: Mucosal thickening in right maxillary and ethmoid sinus with fat stranding in adjacent right orbit involving intra and extraconal fat.

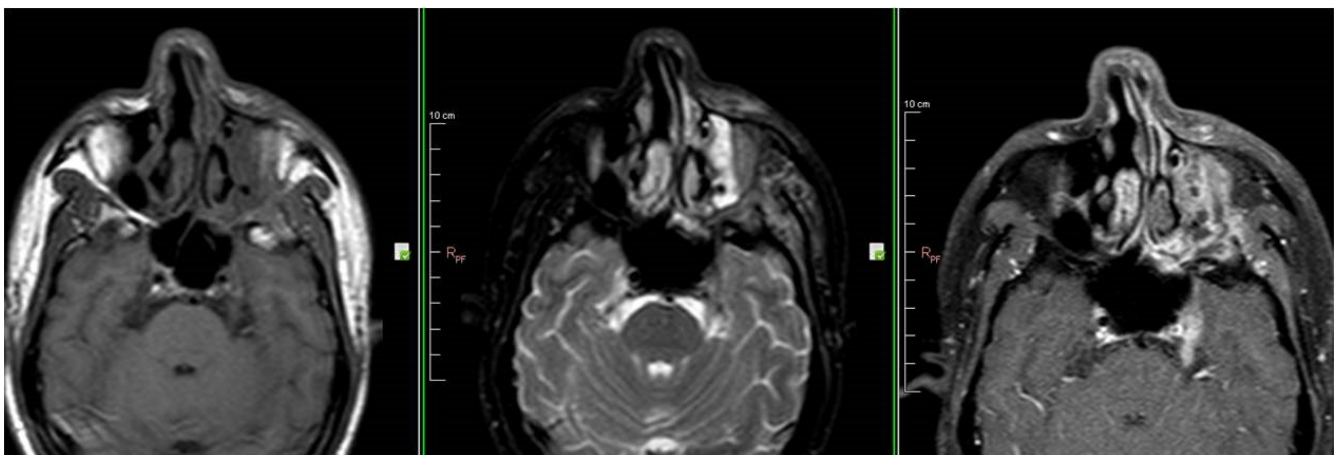


Figure 6: Thickening and non enhancement of left middle turbinate – Black turbinate sign. Bulky left cavernous sinus - cavernous sinus thrombosis.

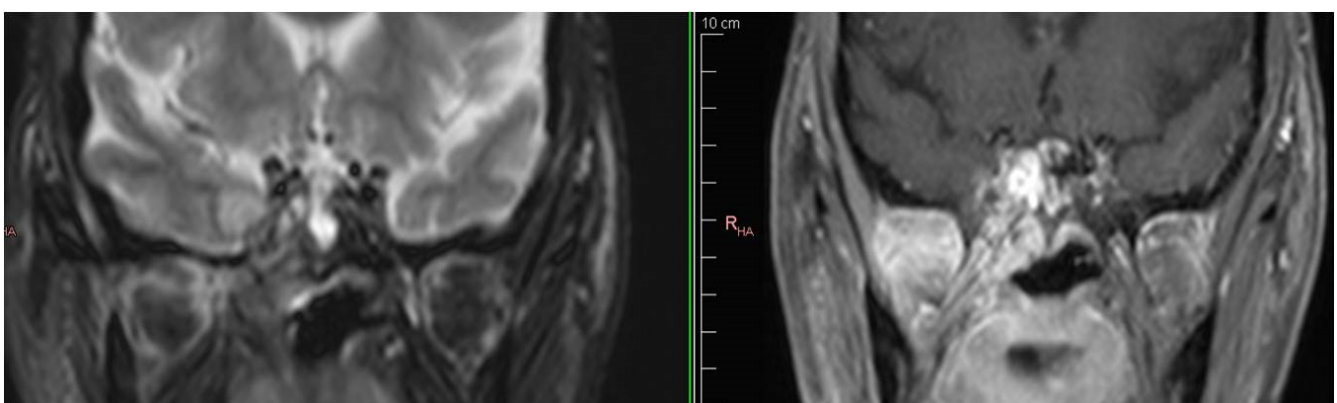


Figure 7: Thickening and delayed enhancement of right cavernous sinus — cavernous sinus thrombosis.

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How to cite this article: Prashanth S, Handi P, Prathap N, Shoorshetty Manohar R, Bhaskarn K. **Imaging in Covid-19 associated mucormycosis: a case series.** *Perspectives in Medical Research*. 2023;11(1):55-62
DOI: [10.47799/pimr.1101.09](https://doi.org/10.47799/pimr.1101.09)