

## Neuroimaging of Mucormycosis in COVID-19 Patients: Case Series

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Received: 15-03-2022 / Revised: 20-04-2022 / Accepted: 15-05-2022

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Conflict of interest: Nil

### Abstract

Recent COVID19 pandemic was evident with increase in cases of mucormycosis which primarily affects the paranasal sinuses, orbits and central nervous system. Depending on organ of involvement, Mucormycosis is further sub-classified of which rhino-orbital-cerebral mucormycosis (ROCM) is most common. In this case series of 5 patients we will see the pattern of neuroaxis involvement along with their radiological features. All patients were suffering with COVID19 confirmed by positive RT PCR results and mucormycosis with KOH mounts. First case was of right frontal abscess with pachymeningeal thickening of right cavernous sinus, right ICA thrombosis and right 5<sup>th</sup> cranial neuritis. Second case was of right temporal abscess, right ICA & cavernous sinus thrombosis. Third case was of right temporal abscess with pachymeningeal thickening of right cavernous sinus. Fourth case is of right temporal abscess with right middle cranial fossa pachymeningitis and final fifth case was with left ICA thrombosis with skull base osteomyelitis with clivus involvement of mucormycosis. Diagnosis of neuroaxis involvement was done by Computed tomography and Magnetic resonance Imaging. Imaging is very important in diagnosing and studying the pattern of neuroaxis involvement of mucormycosis along with further treatment planning.

**Keywords:** Rhino-orbital-cerebral mucormycosis (ROCM), Abscess, Internal Carotid Artery thrombosis, Cavernous Sinus Thrombosis, Cranial Neuritis, Pachymeningitis, Computed tomography (CT), Magnetic resonance Imaging (MRI)

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### Introduction

After aspergillosis, mucormycosis is the second most frequent invasive mold disease caused by filamentous fungi belonging to the order Mucorales [1].

Depending on organ of involvement, Mucormycosis is further sub-classified, of which rhino-orbital-cerebral mucormycosis (ROCM) is most common

(2). Recent COVID-19 pandemic is associated with increased frequency of mucormycosis which involves paranasal sinuses, orbits and brain mostly due to irrational use of antibiotics, steroids and association with diabetes[3]. Mucormycosis causes tissue invasion, necrosis and thrombosis helped by SARS-CoV-2 virus mediated disruption of cell mediated immune response[4]. The survival and functional outcome of the patient is often determined by the central nervous system (CNS) involvement by mucormycosis which is one of its most severe manifestations[5]. Various patterns of neuroaxis involvement along with its radiological correlation are of vital importance in helping achieve early diagnosis, predicting the ROCM natural history and achieving favourable outcome. In this case series, we will see the CNS involvement of mucormycosis in COVID-19 patients encountered in our tertiary care institute.

### Case Description

#### Case 1

A 44-year-old male diabetic patient presented with facial pain of 5 days duration and fever, dyspnoea since last 3 days. He was known case of diabetes mellitus on treatment and had received treatment for COVID-19 pneumonitis few days back. On examination there was no e/o blackish discoloration or crustation in

nose or necrotic patch in buccal mucosa and palate. A non-contrast CT Paranasal sinus (PNS) was done which showed mucormycosis involving bilateral frontal-ethmoid sinusitis without evidence of bony destruction. Endoscopic sinus surgical debridement was done with right uncinectomy and tissue was sent for histopathological examination which showed mucormycosis. Patient was treated with Injection Amphotercin and Augmentin. After few days he developed right eye swelling, pain with mild proptosis and headache. MR brain was done which showed rhino-orbital cerebral mucormycosis with oval T2 hyperintense right basifrontal abscess which showed small air fluid level and perilesional edema. Loss of right ICA flow void was seen s/o thrombosis of right ICA. Right cavernous sinus involvement was seen which appeared bulky with pachymeningeal thickening. Right trigeminal nerve appeared thickened with hyperintensity extending from Meckel's cave to intrapontine course along nerve s/o Perineural extension of infection. No acute infarct was seen. Patient underwent right orbital exenteration and was treated with intra-venous anti-fungal drugs. Follow up MRI brain after 2 weeks showed response to treatment with reduction in size of abscess & perilesional vasogenic edema. Patient was discharged on oral Pseudoconazole and advised follow up.

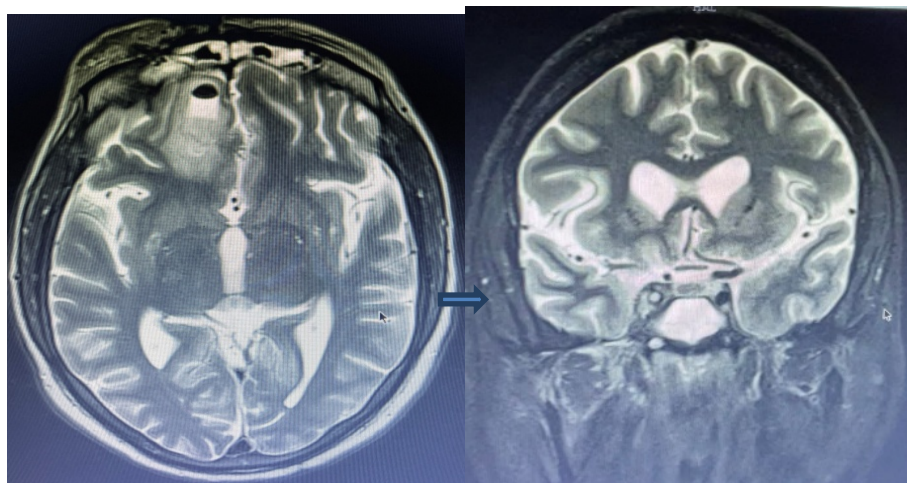


Figure a

Figure b

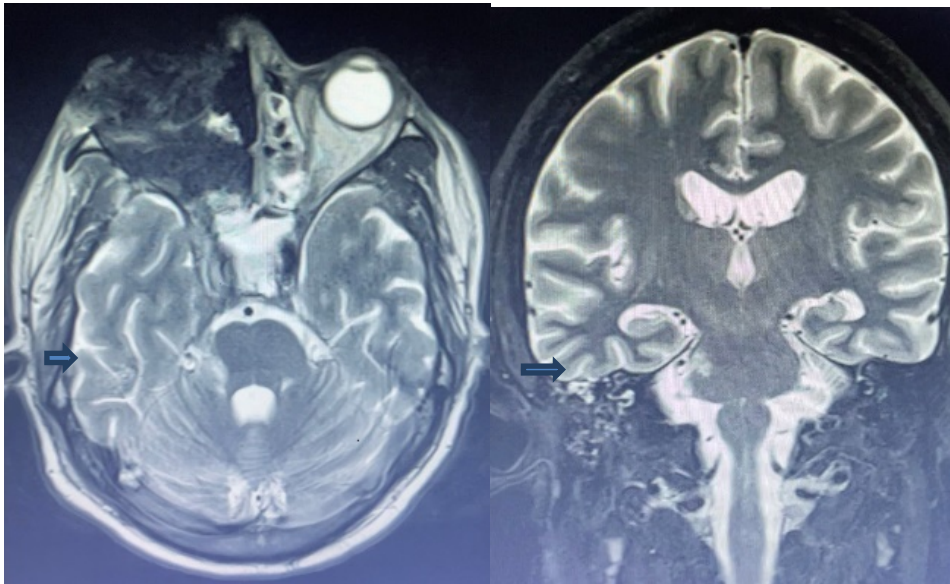


Figure c

Figure d

**Case 1 figures:** T2W axial image (fig a ) shows hyperintense abscess in right basifrontl lobe with surrounding edema with airfluid level. Right cavernous sinus and right ICA thrombosis on T2W coronal image ( arrow Fig b). Axial and coronal T2W images hyperintensity with perineural extension along right trigeminal nerve in cisternal segment and in pons ( arrow Fig c and d). Note post operative status exenteration of right globe.

### Case-2

Female aged 45 years came with right eye swelling, pain, reduced vision with bleeding from nose intermittently. She was diagnosed with COVID-19 one month back. On examination of right eye it showed proptosis, chemosis and periorbital edema with restriction of extra-ocular muscle movements. Her random blood sugar level was 470mg/dl and was started on insulin injection. CT Paranasal sinuses was done which showed extensive mucormycosis involving right maxillary sinus, ethmoid sinus with bony destruction, right intra-orbital extension demonstrating inflammatory changes in intra-extraconal compartments. Intracranial extension was seen with bulky right cavernous sinus with hypodensity in

right temporal lobe s/o vasogenic edema. On contrast study, filling defects were seen in right cavernous sinus s/o thrombosis with small ring enhancing lesion in right temporal lobe s/o abscess. MRI brain study revealed bulky right cavernous sinus which showed T2 hypointense signal with loss of flow void signal of right ICA with T2 hyperintense signal in lumen s/o ICA thrombosis. Small oval shaped well defined T2 hyperintense lesion was seen in right temporal lobe with diffusion restriction, tiny foci of T1 hyperintensity & blooming on SWI s/o abscess with microhemorrhages likely of fungal origin. Involvement of paranasal sinuses was seen with mucosal thickening, collection and right orbit congestion, inflammatory changes. No acute infarcts noted. Patient underwent endoscopic sinus debridement with right uncinectomy and mucormycosis was confirmed on histopathology examination. Patient was treated with intravenous Amphotercin along with retrobulbar Amphotercin injections in right eye. She was also started on injection heparin, Mannitol and prophylactic anti-epileptic medication. She was later discharged with oral antifungal drugs and advised follow up.



Figure a

Figure b

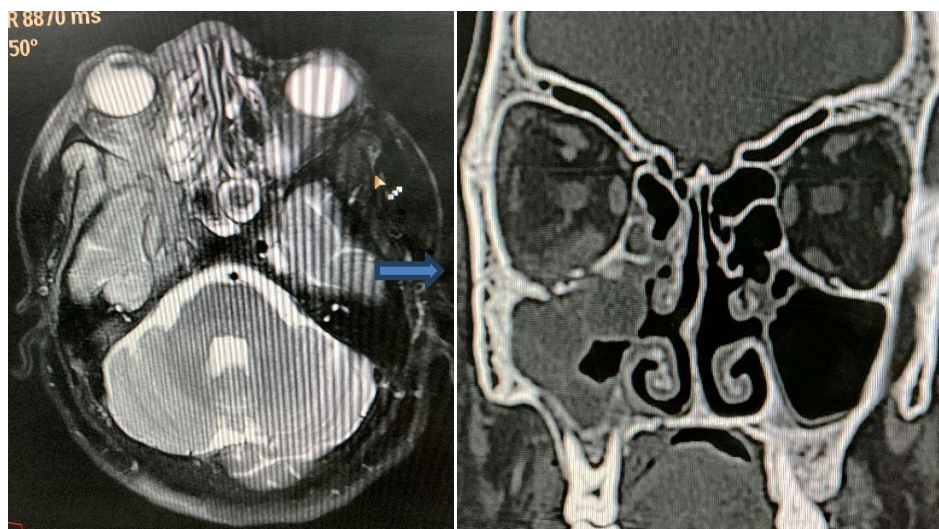


Figure c

Figure d

**Case 2 figures:** Ring enhancing abscess with surrounding edema in right temporal lobe in Axial post contrast CT image (Fig a), axial T2W images (Fig b, c) showing right ICA thrombosis with loss of flow void signal. Note is made of right globe proptosis, soft tissue hyperintensity in right orbital intra and extra-conal compartments, (Fig c). Right maxillary sinusitis is seen with rarefaction of roof of sinus. (Arrow Fig d) with right orbital extra-conal soft tissue thickening with involvement of right inferior rectus muscle is seen on CT.

### Case-3

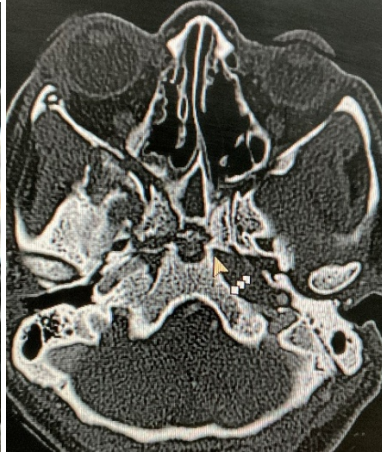
A 54 year old female with known diabetes and hypertension on treatment came with right facial pain, swelling with similar complaints in past 2 months. She was

diagnosed with COVID-19 pneumonitis 2 months back and was treated for same. On examination nasal crustations were seen bilaterally. CT Paranasal sinuses and Brain plain & contrast study was done which showed enhancing soft tissue involving paranasal sinuses, right orbit and skull base osteomyelitis with involvement of sphenoid bone. Bone destruction was seen in sinus walls and skull base region. CT Brain reveals enhancing soft tissue thickening involving lateral wall of right cavernous sinus. Ring enhancing right temporal lobe abscess was seen with perilesional vasogenic edema. Findings were s/o rhino-orbital & cerebral mucormycosis (ROCM) confirmed by histopathology. Patient underwent function endoscopic sinus surgery (FESS) and was treated with injection Amphotericin B.

Patient condition improved and was discharged with follow up advice.



**Figure a**



**Figure b**



**Figure c**

**Case 3 figures:** Reconstructed sagittal and axial images (fig a & b) shows erosion of squamous part of right temporal bone, right zygomatic bone, superior portion of clivus (arrow head) near sphenoid sinus. Axial contrast CT image (fig c) shows ring enhancing abscess in right temporal lobe with adjacent right cavernous sinus pachymeningeal thickening.

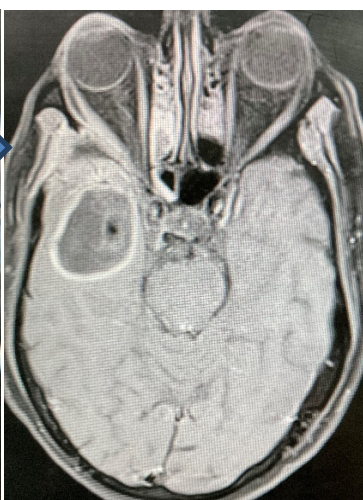
#### **Case-4**

54 year old diabetic male presented with headache, right sided facial pain and was treated with steroids for COVID-19 fifteen days back. MRI brain was done which revealed mucosal thickening, collection in paranasal sinuses with extension of disease in pterygoid fossa, masticator space with right sphenoid wing osteomyelitis, adjacent extension in right middle cranial

fossa showing pachymeningeal enhancement. Well defined oval shaped T2 hyperintense lesion with diffusion restriction is seen in right temporal lobe showing perilesional edema & compression on temporal horn of right lateral ventricle. He was started on antifungal drug injection Amphotericin. Patient underwent functional endoscopic sinus surgery debridement for sino-nasal disease with uncinectomy and histopathology confirmed invasive mucormycosis. Patient progressed to osteonecrosis of right maxilla which was treated with partial maxillectomy. Diagnostic nasal endoscopy at time of discharge showed healthy mucosa. Oral Posaconazole was started and follow up was advised.



**Figure a**



**Figure b**



**Figure c.**

**Case 4 figures:** Axial T2W (Fig a) shows a well defined round to oval hyperintense lesion in right anterior temporal lobe, peripheral rim enhancement (Fig b) on axial T1 fat sat post Gd contrast enhanced image. The lesion shows central T1 hypointense focus with blooming on axial GRE (Fig c) likely s/o air. Pachymeningeal enhancement is seen along right anterior temporal lobe (arrow Fig b) with involvement of right sphenoid wing and adjacent soft tissue.

**Case-5**

Young male aged 33 years non-diabetic patient with post COVID-19 status 2 months back treated with steroids presented with headache, left eye swelling.

On examination crustations were seen in both nostrils. Patient underwent MR brain study which revealed heterogeneous signal intensity soft tissue involving sphenoid sinus, clivus with destruction of clivus bony cortex s/o skull base osteomyelitis. Left ICA shows thrombus with absent flow void signal. No acute infarcts were seen. T2 hyperintense intra-osseous lesion seen in left sphenoid wing likely s/o intra-osseous abscess. Mucosal thickening/soft tissue was seen in paranasal sinuses. Patient underwent functional endoscopic sinus surgery (FESS) with debridement for paranasal sinus disease involvement. He was treated with injection Amphotericin B. He was discharged on day 24 and follow up was advised.



Figure a



Figure b

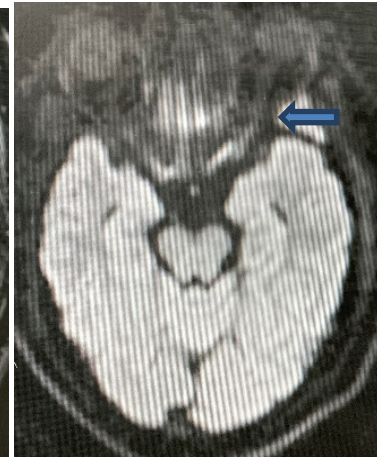


Figure c

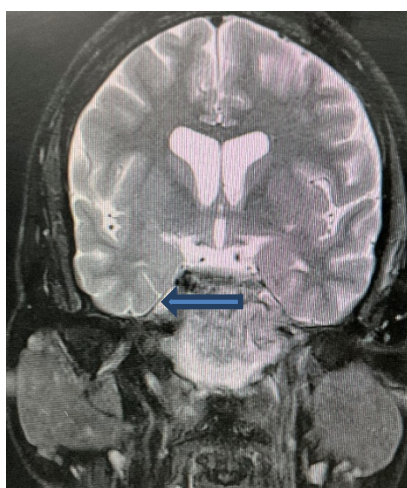


Figure d



Figure e

**Case 5 figures:** Axial T2 and FLAIR (Fig a and b) showing thrombosis of left ICA & bulky left cavernous sinus and left

sphenoid wing involvement showing diffusion restriction (Fig c arrow head). Heterogenous ill-defined lesion involving

sphenoid sinus and clivus (arrow Fig e) causing erosion of clivus, superiorly

involving left cavernous sinus on T2W coronal (arrow Fig d)

**Table1:- Distribution of Cases (Neuroimaging Finding) Accrediting to Presence of Abscess, Cavernous Sinus, ICA Thrombosis , Additional Finding And Histopathological Report (HPR)**

NAME	AGE	SEX	DM	MENINGITIS	ABSCESS	CAVERNOUS SINUS	ICA THROMBOSIS	ADD. FINDING	HPR
Case 1	44	M	Y		Right Frontal	Right-Pachymeningitis	Right	Right 5th Cr Nerve invasion, Air-fluid level in abscess	Positive
Case 2	45	F	Y		Right Temporal	Right-Thrombosis	Right		Positive
Case 3	54	F	Y		Right Temporal	Right-Pachymeningitis		Skull Base Osteomyelitis	Positive
Case 4	54	M	Y	Pachymeninitis-Right Middle Cranial Fossa	Right Temporal			Right Sphenoid wing-Osteomyelitis	Positive
Case 5	33	M	N			Left-Pachymeningitis	Left	Clival Osteomyelitis, Left Sphenoid wing abscess	Positive

## Discussion

Mucormycosis is an opportunistic fungal infection caused by saprophytic fungi belonging to the order Mucorales which is invasive and potentially fatal [1]. According to organ of involvement, Mucormycosis is sub-classified, of which rhino-orbital-cerebral mucormycosis (ROCM) is most common followed by cutaneous, pulmonary, disseminated, renal and gastrointestinal system involvement. Mucormycosis is the second most common pathogenic fungal infection in patients with haematological malignancy, haematopoietic stem cell transplantation, organ transplantation and are increasingly detected in diabetes mellitus patients[2]. The most frequent species responsible for mucormycosis confirmed by microbiology in majority of case series are Rhizopus species. Rhizopus, Mucor and Lichthemia collectively are responsible for 70-80% of reported cases of mucormycosis[6]. During COVID-19 Pandemic in India, increase is seen in incidence of mucormycosis. Hypoxia, prolonged

immunosuppression, uncontrolled blood sugar levels which may be caused by diabetes mellitus or indiscriminate steroid use are the proposed predisposing factors [7]. Inhalation of spores is the usual infection route leading to rhinosinusitis caused by invading the mucosa of nasal cavity and paranasal sinuses[8]. Neurological symptoms of mucormycosis include headache, ptosis, diplopia, proptosis, reduced vision, facial pain, facial numbness, facial paresis, convulsions and altered sensorium resulting from invasive fungal involvement of neurological structures[8]. Neuro-imaging with CT or MRI is of utmost importance and helpful in evaluating the structural involved and extent of disease which further guides in the need for aggressive antifungal treatment and or the surgical debridement.

In intracranial Mucormycosis, the cavernous sinus thrombosis/extension, infarction and internal carotid artery

occlusion were the most common imaging findings[9]. Other imaging findings include cranial nerve involvement, septic emboli, cerebritis, abscess, lepto-pachymeningitis, hemorrhage and skull base involvement[10]. Spread of infection to cavernous sinus occurs through ethmoidal, orbital veins, direct extension from sphenoid sinus or through perineural spread from the neural foramina[8]. Ethmoid sinus involvement is associated with high risk of cavernous sinus thrombosis due to valveless emissary vein penetrating lamina papyracea and leading to orbital apex, cavernous sinus invasion [11]. Findings in cavernous sinus thrombosis include paracavernous soft tissue extension, lateral wall bulging, abnormal signal intensity of sinus lumen with T1 isointense or hypointense signal and T2 hyperintensity on plain study with filling defects and abnormal sinus lateral wall enhancement on post contrast study[12]. Findings of internal carotid artery involvement range from luminal narrowing to complete thrombosis which occurs from angioinvasion of sphenoid sinus or cavernous sinus disease and small ophthalmic artery Mucor thrombus with retrograde spread. MR imaging is much more sensitive for detection of angioinvasion with findings include abnormal wall thickening with T2 hyperintensity, wall enhancement on post contrast study causing luminal compromise and finally causing complete thrombosis with loss of flow void signal on T1/T2 sequences[13]. Angioinvasion by mucormycosis is hallmark of local tissue destruction and hematogenous spread[14]. Growth of fungal hyphae is seen along the internal elastic lamina and extending in the arterial lumen causing its obliteration and finally intravascular thrombosis with intimal hyperplasia[15]. Cerebral embolic infarcts due to internal carotid artery involvement may occur in watershed territory [13].

Frontal & temporal lobes are most common affected in cerebral abscess formation due to mucormycosis. Imaging

findings of abscess include marginated lesion showing T1 hypointense, T2 hyperintense core and T2 hypointense enhancing wall with restricted diffusion in core, wall of abscess with intra-cavitary projections. Fungal composition may be indicated by susceptibility artefacts seen in the abscess periphery [16]. Gas formation within abscess may indicate communication with paranasal sinus or nasal cavity communication or infection due to gas forming organisms/anaerobes [17]. One abscess in our series showed air-fluid level. Ventriculitis and subdural/extradural abscesses may rarely be seen in advanced disease.

Cranial nerve involvement is most commonly seen in optic and trigeminal nerves. Ischemic neuropathy may be caused due to angioinvasion, thrombotic occlusion of ophthalmic, central retinal artery or perineural direct fungal infiltration. On Diffusion sequence it shows restricted diffusion along the nerve with suppression on ADC maps[16]. Intracranial extension of orbital infection may occur with perineural spread along optic nerve or involvement of brainstem due to perineural spread along trigeminal nerve. MR Imaging findings of thickening, irregularity and abnormal enhancement of cranial nerve or its branch may suggest involvement. Additional findings of nerve involvement include loss of fat pad adjacent to neural foramina, abnormal signal intensity in cavernous sinus, Meckel's cave or pterygopalatine fossa with abnormal enhancement on post contrast study[18].

Pachymeningeal thickening is seen in middle cranial fossa, paracavernous dura and along cerebral convexities which may be focal or diffuse. On post contrast MR images, thick nodular meningeal enhancement is seen. Hydrocephalus and arachnoiditis may be seen due to gelatinous exudates with inflammatory cells, fibrin and hemorrhage [19]. Parenchymal hemorrhage may be seen in the anterior circulation is a rare



manifestation of ROCM possibly due to ruptured mycotic aneurysm [12, 19].

Skull base bony invasion is also common in mucormycosis with MR imaging being quite sensitive for detection of minor pathologic bone marrow abnormalities in the skull base especially plain T1 non-fat saturated sequence which shows replacement or loss of fatty T1 hyperintense bone marrow signal with T1 hypointense signal. Involved marrow shows STIR hyperintense signal intensity and heterogeneous marrow enhancement on post contrast MRI study [20].

Amphotericin B is the drug of choice for treatment of mucormycosis. Mainstay of ROCM mucormycosis treatment is surgical debridement [21]. Relief of intracranial pressure, drainage of obstructive hydrocephalus and excision of spinal cord lesions causing mass effect are indications for neurosurgery [22]. Fungal brain abscess or granuloma lesions radical excision should be avoided [23].

### Conclusion

In COVID-19 pandemic, Mucormycosis is increasingly common. Neuro-imaging is helpful in early diagnosis, defining the extent of disease and institution of prompt aggressive management plan. The survival and functional outcome of the patient is often determined by the central nervous system (CNS) involvement by mucormycosis which is one of its most severe manifestations.

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