Original Article

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Institutional Review of Spectrum of Covid and Post-Covid Central Nervous System Mucormycosis

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Abstract

Background: The objective of the study is to describe the various central nervous system imaging findings and manifestations of the mucormycosis. **Subjects and Methods:** A retrospective analytical observational study was done on 20 individuals who had biopsy /culture proven invasive rhinocerebral mucormycosis. The case records of these patients were reviewed and the MRI images were retrieved from the Picture archiving and communication system and were analyzed. Statistical analysis was performed using descriptive statistics. **Results:** MRI imaging of 20 patients with exclusive central nervous system was evaluated which showed predominantly cavernous sinus thrombosis in 5 patients, internal carotid artery thrombosis in 4 patients, cerebral infarction in 4 patients, cerebral abscess was noted in 2 patients, in cerebritis in 2 patient, meningitis in 2 patients and subarachnoid hemorrhage in 1 patient. **Conclusion:** MRI shows a spectrum of findings Sin central nervous system in rhinocerebral mucormycosis. It plays a major role in assessing the route of spread, extent of involvement and complications.

Keywords: Cns mucormycosis, cavernous sinus thrombosis, rhino cerebral mucormycosis.

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Introduction

Cerebral mucormycosis is a life-threatening infection seen almost exclusively in immunocompromised patients with diabetes mellitus and hematological malignancies. It is caused by members of the Mucoraceae family including Mucor, Absidia, Rhizopus. The clinical presentation of mucormycosis depends upon the immune characteristics of the host. The patients with diabetes mellitus develop rhino orbital cerebral mucormycosis and patients with hematological malignancies tend to develop the sinopulmonary disease. Mucormycosis involves the central nervous system by direct extension from infected paranasal sinuses or hematogenous dissemination from the lungs. The involvement of central nervous system represents one of the most severe manifestation of mucormycosis. The most common clinical presentations of ROCM are headache, fever, facial swelling, nasal obstruction and crusting. Symptoms like headache, altered sensorium, hemiplegia and focal seizures signal brain invasion and infarction. MRI helps in early diagnosis, extent of involvement, complications that require prompt and aggressive treatment. To study the imaging findings of the central nervous system involvement of the mucormycosis we performed a retrospective study of all patients with the diagnosis who presented to our hospital.

Subjects and Methods

Source of Data

Case records of biopsy/culture-proven rhinocerebral mucormycosis who have undergone MRI of the brain at NARAYANA MEDICAL COLLEGE AND HOSPITAL, Nellore, between august 2020 and august 2021 were included in the study.

The ethical clearance was obtained from our Institutional Review Board.

Investigations

All subjects underwent MRI Brain Scan by GE 3 tesla discovery 750W MRI machine.

An emergency kit to manage adverse reactions due to contrast was made available if necessary.

Technique of Examination

All subjects were screened before entering the MRI scanning room for ferromagnetic objects, cardiac pacemakers, aneurysmal clips, etc.

Subjects were examined in the supine position after proper positioning and immobilization of the head. The standard head coil was used for the scan.

Imaging Protocol

The following sequences will be taken:

T1 weighted, T2 weighted, Fluid attenuation inversion recovery (FLAIR), T1FS, T2FS, 3D FSPGR BRAVO(thin slices), Post-contrast T1weighted images, DWI, and SWI sequences will be obtained.

Results

A total of 20 patients with exclusive intracranial involvement of rhinocerebral mucormycosis having preoperative contrast MRI imaging and histopathology confirmation were identified. Demographics, clinical features and various imaging presentations of these patients were analyzed and interpreted. Follow up of these 20 patients was done and the prognosis of the patients was evaluated.

Demographics

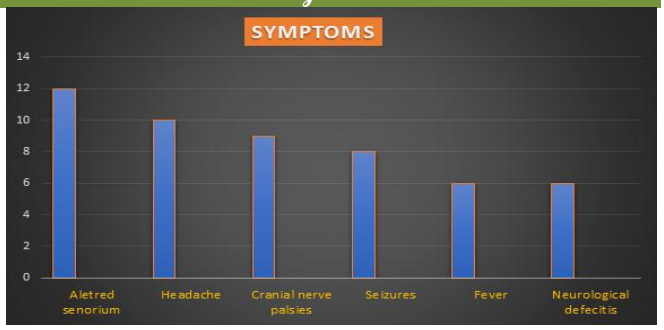
Our study group comprised 20 members with ages ranging from 24 to 75 years (mean =49 years). Out of which 13(65%) were male and 7(35%) were female The majority of patients (75.6%) were aged over 40 years, with those aged 43–64 years (55%) being most affected. Seventeen patients (85%) had a history of uncontrolled diabetes, three patients (15%) had other risk factors like predisposing hematological condition (acute myeloid leukemia), post-organ transplant patient on immunosuppressive drugs and other one patient had a history of IV drug abuse.

Clinical features

The clinical symptoms of the 20 patients who had involvement of the central nervous system by mucormycosis were assessed and they were headache, fever, altered consciousness, cranial nerve palsies, neurological deficit, seizures.

Table 1: showing clinical features and their percentage among the patients

Clinical feature	No. of patients	Percentage
Altered sensorium	12	60%
Headache	10	50%
Cranial nerve palsies	9	45%
Seizures	8	40%
Neurological deficit	6	30%
Fever	6	30%



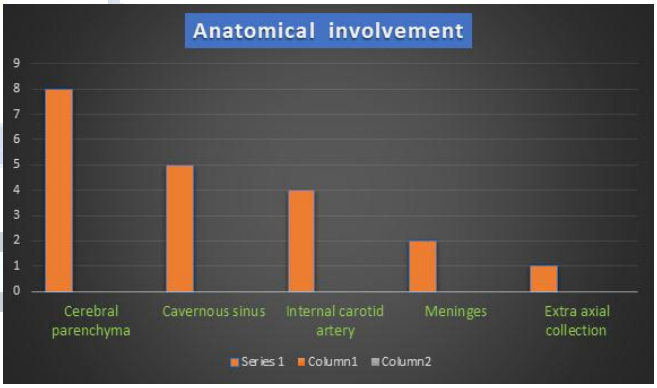
Graph 1: Graphical representation of clinical features among the patients

The most common symptom of presentation in our study was altered sensorium (60%) followed by headache (50%), cranial nerve palsies(45%), seizures(40%), neurological deficits & fever in (30%) cases.

Imaging Findings

Table 2: showing anatomical involvement.

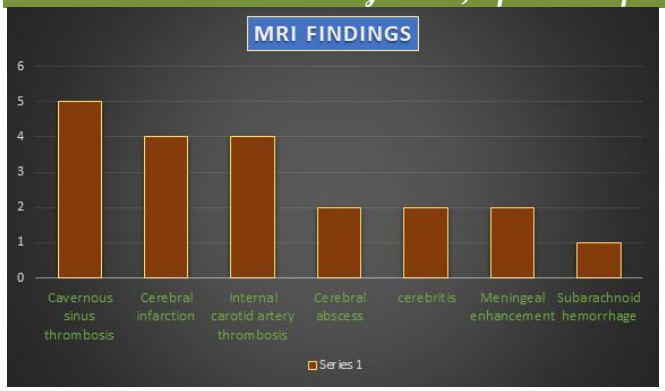
Structure of involvement	No. of patients	Percentage
Cerebral parenchyma	8	40%
Cavernous sinus	5	25%
Internal carotid artery	4	20%
Meninges	2	10%
Extra axial collections	1	5%



Graph 2: Graphical representation of anatomical involvement.

Table 3: showing MRI findings in Cerebral mucormycosis

MRI Findings	No of patients	Percentage
Cavernous sinus thrombosis	5	25%
cerebral infarction	4	20%
Internal carotid artery thrombosis	4	20%
cerebral abscess	2	10%
Cerebritis	2	10%
Meningeal enhancement	2	10%
Subarachnoid hemorrhage	1	5%



Graph 3: Graphical representation of MRI findings in Cerebral mucormycosis

The earliest and most common structure of the central nervous system to get involved in our study was cavernous sinus (25%) and presented with imaging features of cavernous sinus thrombosis and involvement of the III, IV, V and VI cranial nerve was also seen and were presented with symptoms of loss of corneal reflexes, ophthalmoplegia and loss of sensation over the face in ophthalmic and maxillary distribution of the trigeminal nerve. Amananda chikley et al noted that cavernous sinus is the first and most common site of intracranial involvement of the mucormycosis. Various manifestation of involvement of Cerebral parenchyma involvement was seen (40%) in patients with cerebral infarctions in (50%) of cases, cerebritis in (25%) and cerebral abscess in (25%). Involvement of the internal carotid artery was seen in (20%) of cases and Meningeal involvement was seen in about (10%) of cases and extra-axial collections in (5%) of cases.

On MRI imaging involvement of cavernous sinus was demonstrated as T2 heterogenous hypointense soft tissue thickening in the region of cavernous sinus and on Post gadolinium images as abnormal enhancement of cavernous sinus. Areas of T2 and FLAIR hyperintensity showing diffusion restriction was noted in bilateral cerebral parenchyma demonstrated the cerebral infarction due to mucormycosis. Areas of T1 iso to hypointense and T2 hyperintense with minimal perilesional edema and variable peripheral contrast enhancement indicated the fungal invasion into cerebral parenchyma with features of cerebritis. Mucor invasion and formation of brain abscess were seen in two cases one case showing T2 hyperintensity showing diffusion restriction with surrounding perilesional edema and peripheral ring enhancement on post-contrast images and in other case imaging, there was minimal perilesional edema and lack of complete peripheral enhancement due to lack of wall formation around the abscess due to poor immunogenic response by the compromised patient. In one patient intracranial spread to meninges presented as Pachymeningeal enhancement along the bilateral frontal lobe on T1 post-contrast images. Diffuse vasculitis due to mucormycosis weakens the blood vessels and forms aneurysms and rupture of these aneurysm causes Extraaxial hematomas. In our study, we have seen 1 case of subarachnoid hemorrhage due to rupture of the aneurysm of the basilar artery.

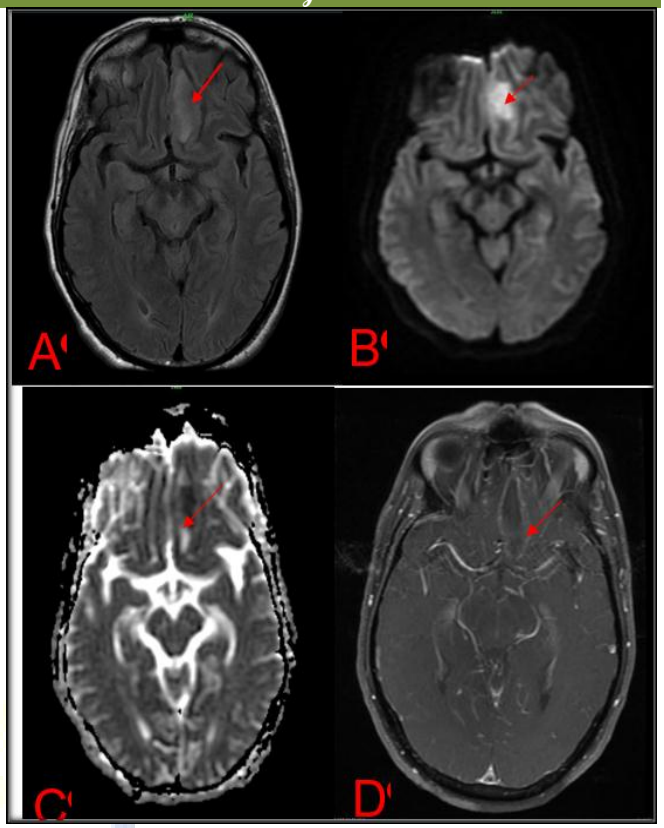


Figure 1: Axial sections of brain FLAIR (A) images show area of hyperintensity in left basi frontal lobe which is showing hyperintensity on DWI(B) and hypointensity on ADC(C) images. Gadolinium enhanced axial T1 W MR images(D) shows peripheral rim enhancement.

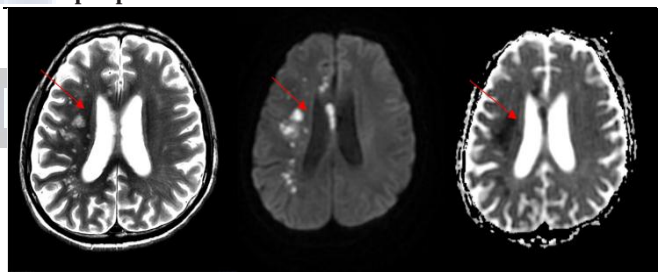


Figure 2: Axial T2W images (A) showing hyperintense areas in right fronto parietal lobe, genu and body of corpus callosum Axial DWI and ADC (B and C) showing corresponding areas of diffusion restriction.

We have followed up the 20 patients and all the patients received antifungal therapy using amphotericin B deoxycholate therapy was given and adjuvant empirical antimicrobial therapy was also given using higher antibiotics like meropenem and vancomycin for secondary bacterial infections. In the follow-up period we have lost the follow up of 5 patients and the rest of 15 cases were completely followed. Along with antifungals and antimicrobials Patients with cavernous sinus involvement were given anticoagulants and the prognosis in patients with cavernous sinus involvement was better when compared to other patients and mortality was seen in 3 (60%) of cases. 2 patients with brain abscess had 100% mortality rate and the among the 4 patients with infracts and ICA thrombosis 3 patients died with a mortality rate of (75%). The overall mortality rate in 15 followed up patients was high and around 73%.

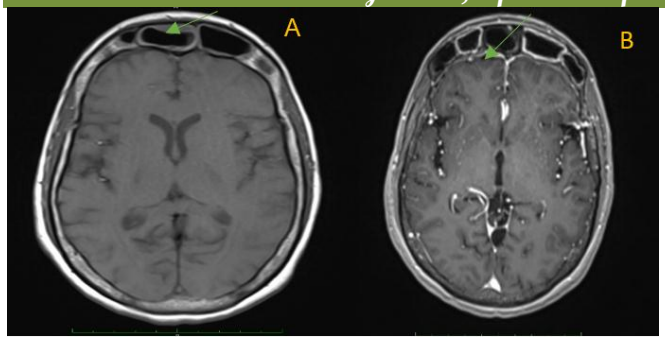


Figure 3: Axial T1 W images (A) shows mucosal thickening in frontal sinus. Gadolinium enhanced axial T1 W image(B) showing unenhanced frontal sinus mucosal thickening and focal meningeal enhancement over bilateral frontal lobes.

Figure 4: MR angiogram (A) showing right carotid artery occlusion. Image (B) Gadolinium enhanced axial T1W image showing swollen non enhancing right cavernous sinus (open arrow) with narrowed ICA flow void (green arrow) and focal meningeal enhancement over the right temporal lobe (white arrow).

Discussion

Mucormycosis, previously called zygomycosis, was first described by Paultauf in 1885.[1] It refers to several different diseases caused by infection with fungi of genera Mucor, Absidia, Rhizopus belonging to the order Mucorale.[1]

It is a life-threatening infection requiring early prompt diagnosis and treatment. These aggressive and highly destructive lesions predominantly affect the immunocompromised hosts, especially patients with diabetes mellitus, predisposing hematological conditions, solid organ transplant patients who are on immune suppressive drugs and Iv drug abusers.[1,2,3,4] Fungi predominantly affect the orbits, sinuses, central nervous system and pulmonary system.[2] Diabetic patients showed the rhino-orbital-cerebral spectrum of the disease but a higher likelihood of Cns invasion rather than sinus and orbits is seen in the solid organ transplant patients.[4,5,6]

These fungi are ubiquitous in nature and occur in soil, air, skin, body orifices, manure, spoiled food, dust and grow rapidly and release large numbers of spores that can become airborne so all humans have ample exposure to these fungi in day to day activities but a person with intact immune system rarely contracts the infection.[7] Infection occurs in patients with underlying predisposing factor.

Inoculation occurs primarily by inhalation when spores reach the nasal cavity and/or nasopharynx leading to invasive sinopulmonary infection.[2] In cases of Iv drug abuser's inoculation of fungi is due to hematogenous spread of sporangiospores present in contaminated drugs and drug injection.[2]

The disease spreads from sinuses to the central nervous system by contiguous spread and uncommonly through bony invasion.[5] Direct extension of mucor from the nasal cavity and paranasal sinuses to brain parenchyma leads to the formation of brain abscess and cerebritis. Mucor access the brain via orbit, superior orbital fissure and cavernous sinus route. Intracranial spread commonly occurs by the direct spread across the cribriform plate, walls of the ethmoid, and frontal sinuses.[5] Extensions into the middle cranial fossa from the pterygopalatine fossa and along the internal carotid artery are also seen. Infection from cavernous sinus spreads perineurally along the trigeminal nerve, leading to predominant posterior fossa involvement.[5] When routed through the cavernous sinus, intracranial infection leads to mandibular and maxillary nerve palsies and ICA thrombosis and pseudoaneurysms in rare cases. From the sphenoid sinus, mucor can travel across and reaches basal meninges and basilar artery leading to thrombosis or rupture with subarachnoid hemorrhage. The most common presentation of intracranial spread is cavernous sinus thrombosis, internal carotid artery occlusion and brain infarction.[2] Other imaging findings in CNS involvement are cerebral abscess, cerebritis, meningitis and extra-axial collections. In isolated cerebral involvement, basal ganglia are usually involved[2] and manifest as basal ganglia mass showing diffusion restriction, hemorrhage, perilesional edema and varying degrees of contrast enhancement.[8]

Bony erosion by the fungi is a rare complication because the angioinvasive nature of the fungus facilitates the extensive spread of infection into the deep soft tissues through the perivascular channels even before bone destruction.[9,10,11]

MRI is the choice of modality in diagnosis, staging, follow up of the disease and it is superior in evaluating soft tissue, assessing intracranial and vascular invasion.[5,12] However Early mucormycosis on MRI appears as non-specific sinus wall thickening so early clinical pick up is required to diagnose the disease.[13]

The imaging characteristics on MRI are sinonasal mucosal thickening appearing predominantly as T1 isointense and T2 heterogenous mucosal lining with central non enhancing areas on post-contrast imaging, the early disease shows non enhancing turbinate's often referred to as ' black turbinate sign' on post-contrast imaging and extra sinus involvement of orbits is most common followed by face, pterygopalatine fossa,[13-16] masticator space, infratemporal fossa, orbital apex, maxillary antrum, extraocular muscles. Extension into the cavernous sinus appears as T1, T2 hypointense heterogeneously enhancing soft tissue with loss of concavity of the cavernous sinus.[15] Cerebral parenchyma involvement is seen as areas of infarction in non-vascular distribution and cerebral abscess as a well-defined mass with liquified T2 hypointense core showing diffusion restriction but may not show characteristic rim enhancement

due to poor immunogenic response by the compromised host. Meningitis as a focal area of Pachymeningeal enhancement.

Our study of 20 patients of proven mucormycosis showing central nervous system involvement shows many of the above-mentioned findings. And predominant patients were diabetic and showed intracranial extension of disease to involve cavernous sinus thrombosis, cerebral infarction, cerebral abscess, cerebritis, internal artery thrombosis, meningitis and extra-axial collection.[17,18]

Conclusion

MRI shows a spectrum of findings in the central nervous system in rhinocerebral mucormycosis. It plays a major role in assessing the early and severe stages of the disease, route of spread, extent of involvement and complications.

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