International Journal of Radiology and Diagnostic Imaging

E-ISSN: 2664-4444
P-ISSN: 2664-4436
www.radiologypaper.com
IJRDI 2025; 8(1): 26-31
Received: 19-12-2024
Accepted: 20-01-2025

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Imaging and clinico-pathological correlation of mucormycosis in post covid patients

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DOI: https://doi.org/10.33545/26644436.2025.v8.i1a.432

Abstract

Aim's & Objective

1. To study the imaging characteristic and clinico-pathological relationship of mucormycosis in post covid patients.
2. To study the relationship between development of mucormycosis in post covid patients who received various treatment therapies (Including use of Corticosteroids/ Oxygen supplementation / Ivermectin / Remdesivir).
3. To assess the sensitivity & specificity of the abbreviated MRI protocol used in this study in diagnosis of mucormycosis.

Materials and Methods: A total of 75 Post COVID patients with clinical suspicion of mucormycosis referred to Department of Radiodiagnosis for an MRI scan in a Tertiary care Government Medical college, Maharashtra, India between May 2021 to July 2021 were included in this study. A 3T GE machine was used in this study with abbreviated Protocol for imaging PNS with screening of Brain & orbits. Axial T_2 Propeller, Cor T_2 STIR 3 mm, 3D Axial T_1 Bravo, Axial T_1 Fat Sat Pre-Contrast, Axial T_1 Fat Sat Post Contrast and 3D Sag T_2 CUBE sequences were used in this study. Gadoterate meglumine (DOTAREM) was used as the intravenous contrast. Along with the imaging features, data of all the volunteers including their symptoms, day/week of presentation with symptoms (For mucormycosis), co-morbidities, blood reports and therapy (For COVID treatment including drugs & supplemental Oxygen) were also recorded. All the images were analysed by three Senior Radiologists and the data obtained was analysed using appropriate statistical tests.

Results: In this study, mucormycosis was seen most commonly in 48 to 59 years age group with no predilection for either of sex (Male to female ratio: 1.2:1). Most patients presented with symptoms of facial pain and swelling (50/75, 66.6%) followed by headache (45/75, 60%) in 3rd week post discharge (24/75, 32%). Patients with history of Diabetes Mellitus (P value-0.001286) and those who had high ferritin levels (P value-0.000096) during their treatment course had positive correlation in development of mucormycosis. Maxillary (61/75, 81%) and ethmoid sinuses (52/75, 69%) were the most common sinuses involved with presence of Black Turbinate sign having significant correlation with development of mucormycosis (P value-0.03). No significant correlation with Oxygen supplementation (P value-0.45), use of corticosteroids (P value-0/187), low leukocytes counts (P value-0.485), Chronic Kidney Disease (P value-0.1117), Hypertension (P value-0.6047), Ivermectin (P value-0.1695) and Remdesivir (P value-0.4838) were obtained in this study. The sensitivity & Specificity of the MRI with Abbreviated Protocol was 82% and 55% respectively, with 17.3% and 10.6% false positivity & negativity. KOH mount / Histopathology was used as the Gold standard.

Conclusions: The abbreviated MRI protocol has significantly higher sensitivity and specificity in diagnosis of mucormycosis with reduction in scan time an additional feature. Most patients presented in 3rd week of post discharge in this study, suggesting special care and MRI evaluation if clinically indicated. Further studies are advised in validation of our abbreviated protocol and further developing a protocol for screening of mucormycosis in post covid patients particularly with presence of Diabetes Mellitus and High ferritin levels during their treatment. No significant correlation between oxygen therapy, Corticosteroids /Ivermectin and Remdesivir therapy in development of mucormycosis.

Keywords: MRI imaging, mucor-mycosis, post covid-19 patients, diabetes mellitus, ferritin, corticosteroids

Introduction

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been associated with a wide range of opportunistic bacterial and fungal infections. Mucormycosis is an acute opportunistic infection caused by fungi of the order Mucorales

like Rhizopus, Mucor, Cunninghamella, Apophysomyces, Saksenaea and Absidia [1]. In India during pre Covid times the prevalence of mucormycosis was approximately 14 cases per 1,00,000 population; about 80 times the prevalence globally.[2] Recently the cases of mucormycosis in post covid patients have increased particularly in India [17].

(Mucorales enters the nasal cavity and paranasal sinuses via inhaled dust particles. It sporulates in tissues and then disseminate hematogenously from site of infection to other organs. They have predication for vascular invasion causing thrombosis and infarction with resultant tissue necrosis in affected tissue. Direct spread through the cribriform plate into the anterior cranial fossa, may also occur via perineural spread. Further elevated serum iron compromises phagocyte killing of Mucorales) [13].

The mucorales spores germinate in patients with COVID-19 as there is an ideal environment of low oxygen (hypoxia) [4], increased blood glucose levels (Diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia) [4], acidic medium (Metabolic acidosis, diabetic ketoacidosis)[2], increased iron levels (Increased ferritins) [2] and decreased phagocytic activity of white blood cells [2] due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated or background comorbidities)[4] coupled with prolonged hospitalization with or without mechanical ventilators [4].

Material and Methods

It was an observational cross sectional prospective study in post covid patients with clinical suspicion of mucormycosis. All 75 patients were referred to Department of Radiodiagnosis for an MRI scan in a Tertiary care Government Medical college, Maharashtra, India between May 2021 to July 2021 were included in this study.

The MRI scans in these patients was performed using 3T GE Machine with limited protocol using

- AXIAL T_2 PROPELLER
- COR T_2 STIR 3mm
- AXIAL T_1 FAT SAT PRE CONTRAST
- Post contrast 3D AXIAL T_1 BRAVO
- 3D SAG T_2 CUBE sequences
- Gadoterate meglumine (DOTAREM) was used as the intravenous contrast

For all the sequences Field of vision included entire PNS, entire Brain and bilateral Orbits.

Data including patients age, clinical complaints, Post discharge day/week of presentation with symptoms, associated co-morbidities (Diabetes Mellitus, Hypertension, CKD or any other previous illness including malignancies if any), Corticosteroid / Ivermectin/ Redmisivir /O2 therapy if given during the treatment of COVID 19, Imaging findings (sinus / intracranial /orbital involvements) Laboratory reports (Ferritin level, Total leucocyte count) were recorded. KOH mount report/ Hp report from nasal swabs/scrapping was used as the Gold Standard.

Three radiologists with an experience of more than 15 years analysed all the MRI scans.

Appropriate statistical tests were applied for analysis of the data recorded.

Results

A total 75 post covid patients (41 males and 34 females) between the ages of 15 to 75 years with clinical suspicion of mucormycosis were studied using abbreviated MRI protocol and KOH Mount / Histopathology were used as the gold standard for diagnosis of mucormycosis.

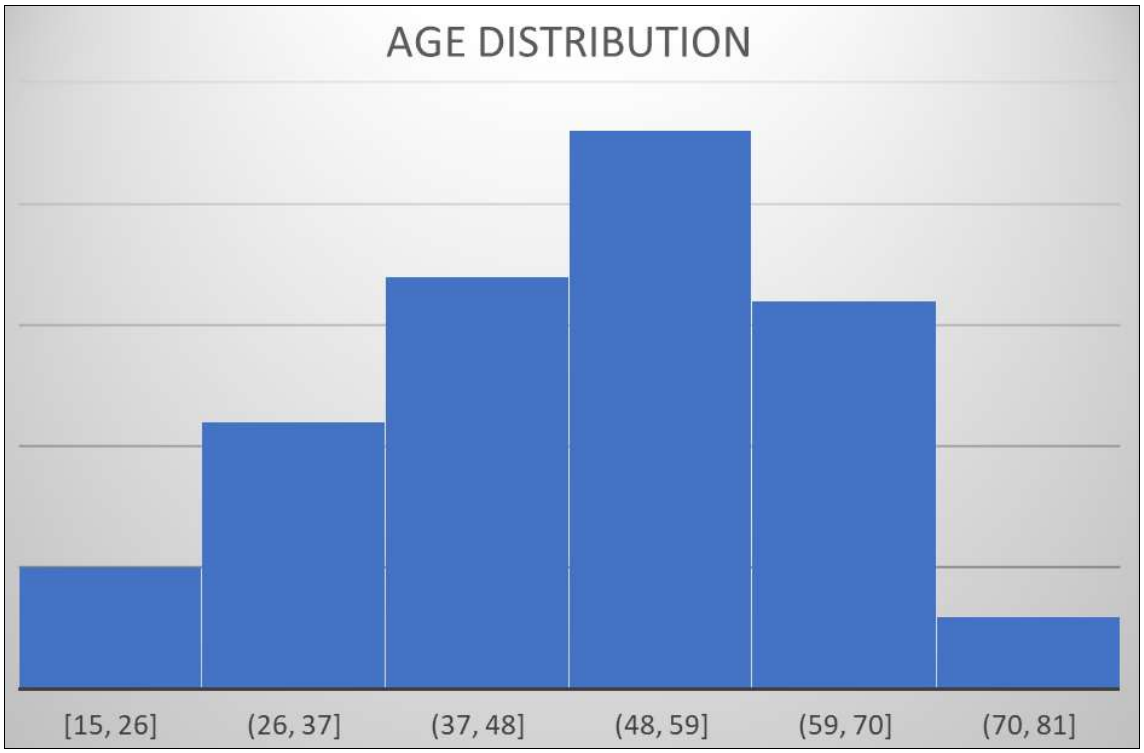

Fig. 1: As per our study, most common age group for development of mucormycosis is between 48 to 59 years. [18]

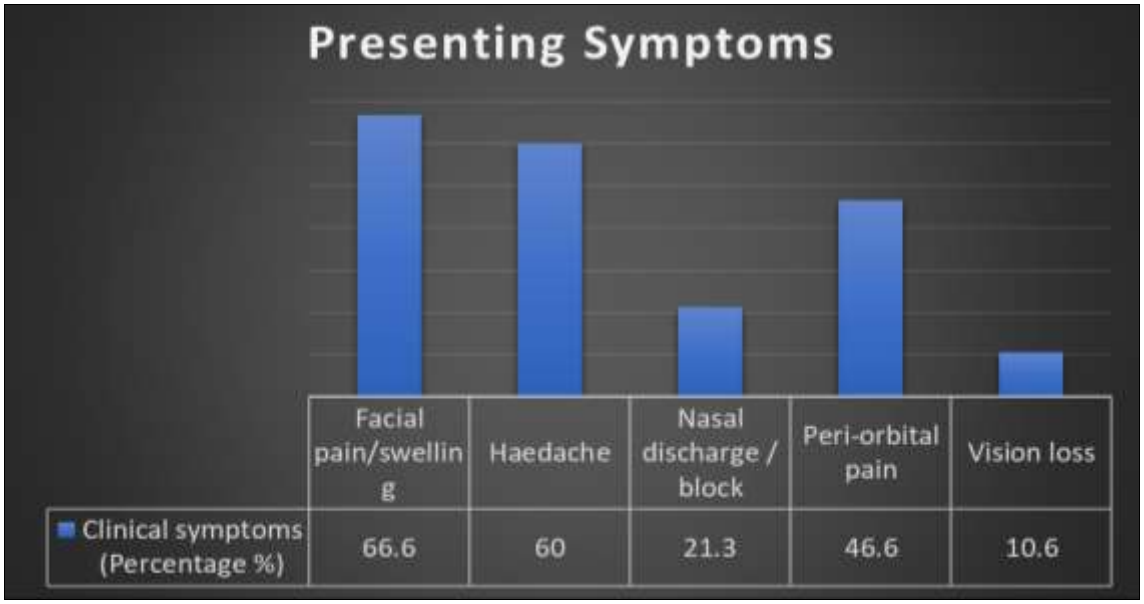

Fig 2: Presenting symptoms: In our study the most common presenting symptoms was facial pain followed by headache.

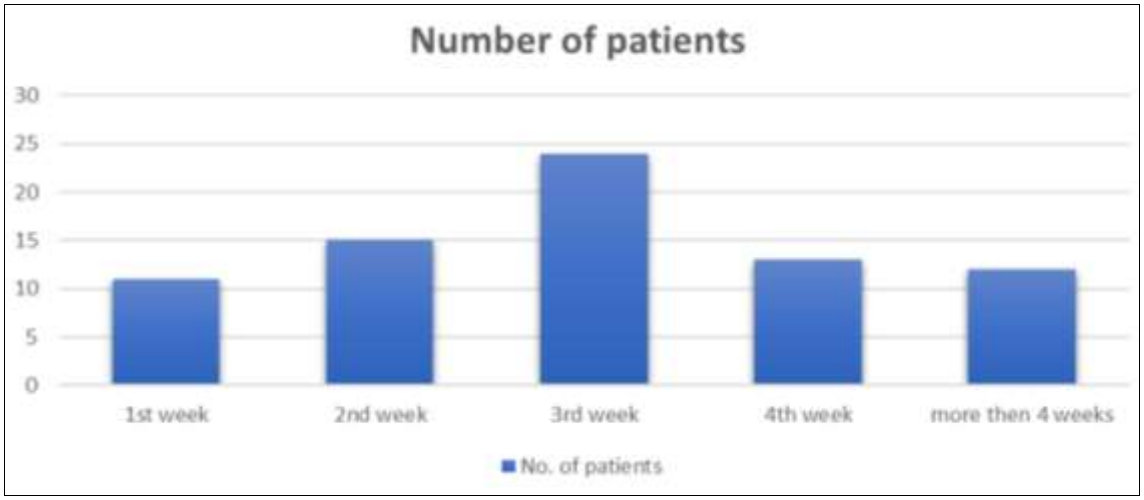

Fig 3: Distribution of patients according to the week of presentation post discharge. The most common week of presentation for mucormycosis was 3rd week after post covid.

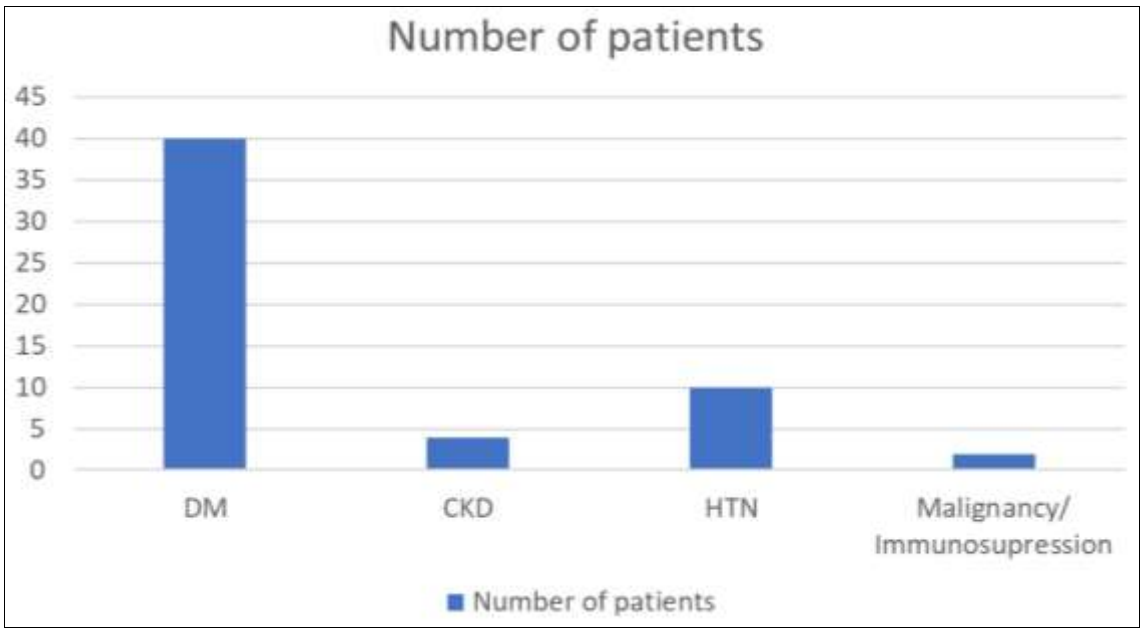

Fig 4: Co morbidities. In our study the commonest comorbidly found was diabetes which has shown positive correlation with incidence of mucormycosis with P value: 0.001286.

Correlation of co morbidities with mucor mycosis

In our study- 30/75(53, 3%) patients had DM (P value-0.001286), 4/75(5.3%) patients had CKD (P value-0.1117), 2/75 (2.6%) patients had Malignancy/ Immunosuppression (P value-0.3409). However only presence of DM showed significant correlation in development of mucor mycosis (P value- 0.001286).

	Mucormycosis	
	Present	**Absent**
KOH Mount / Histopathology	46	29
MRI Findings	51	24

The sensitivity & Specificity of the MRI with Abbreviated Protocol in the diagnosis of mucormycosis was 82% and 55% respectively. The False positivity was 17.3% and false negativity was 10.6%.

The imaging findings obtained in the patients with mucormycosis was

Sino nasal involvement: The maxillary sinus was the most common paranasal sinus involved in our study (61/75, 81%), followed by Ethmoidal (52/75, 69%) Sphenoid (43/75, 47%) and frontal (37/75, 52%). In the majority of patients (57/75, 77.3%) multiple sinuses were involved. The combination of maxillary and ethmoid was most frequently seen in (49/75, 65.33%) of patients.

Rhino-orbital mucormycosis was seen in 22/75 (29.3%) and most common in patients having ethmoidal sinus involvement in all patients. Rhino orbitocerebral involvement was seen 18/75, (23.9%), in the form of meningitis & cerebral abscess formation (14/75, 18.6%), cavernous sinus involvement (4/75, 5.3%).

MR findings had significant correlation in diagnosis of mucormycosis (P value <0.05).

Presence of Black turbinate sign was seen in 18/75 (24%) patients and its presence had significant correlation in diagnosis of mucormycosis (P value -0.03).

In our study 63/75 (84%) (P value- 0.485) patients showed low TLC counts and 29/75 (38.6%) (P value-0.000096) patients showed increased serum ferritin counts. High ferritin levels showed significant correlation with development of mucormycosis, while low TLC count had no significant correlation in development of mucormycosis.

In our study 55/75(73.3%) patients had obtained Corticosterorid (P value-0.187), 6/75(8%) patients had Ivermectin (P value-0.1695), 49/75(65.3%) patients had Oxygen supplementation (P value-0.45), and 53/75(70.6%) patients had Remdesivir (P value-0.4838), while under treatment for COVID 19. However, none of them showed any significant correlation in development of mucor mycosis.

Discussion

Mucormycosis was first described by Paulltauf in 1885 [5]. Though mucoreles can involve different parts of body organs the most common type is the rhinocerebral form [6, 7]. In post covid patients, it occurs most commonly as a result of chronic corticosteroid treatment, reduced leukocytes counts, increased ferritin levels, as well as controlled diabetes mellitus and diabetic ketoacidosis [4, 7].

In our study, mucormycosis was seen most commonly in 48 to 59 years age group [18], with no predilection for either of sex (Male to female ratio:1.2:1).

The sensitivity & Specificity of the MRI with Abbreviated Protocol in the diagnosis of mucormycosis was 82% and 55% respectively. The 17.3% False positivity can be attributed to the inter observer difference in the interpretation of the images. The False negativity 10.6% can be attributed to non-contrast scan performed some of these patients due to impaired renal function and very early stage of presentation.

Instillation of fungus in body occurs preliminary by inhalation, when spores reach the nasal cavity and nasopharynx. The fungus may then spread to the paranasal sinuses and subsequently to the orbit, meninges, and brain by direct extension. Orbital involvement results from spread through the nasolacrimal duct and medial orbital wall [5], the fungus can invades the walls of the blood vessels resulting in vascular occlusion, thrombosis and infarction. Spread to the brain may occur via the orbital apex, orbital vessels, or via the cribriform plate [5].

Imaging helps in diagnosis of Rhino-orbito-cerebral disease; to evaluate the extent of disease, plays a crucial role in early diagnosis and timely intervention. All this helps in timely management with antifungal agents and surgical debridement in mucormycosis patients and also helps to reduce morbidity and mortality [5, 6]. In our study 51/75(61%) have shown positive findings for mucormycosis on MRI with P value of 0.00046 which is highly significant.

On MRI, the lesions were isointense or mildly hypointense on T1W, On T2W images mucosal lesions were seen as isointense to mildly hypointense, heterogeneous soft tissue lesions, hyperintense mucosal thickening and intrasinus T_2 hyperintense fluid. The T2W signal intensity is determined by the extent of necrosis (causing hyperintensity) and the presence of paramagnetic elements such as iron and manganese within the fungal hyphae (causing hypointensity) [10, 12]. On contrast examination the lesions has shown variable patterns of enhancements ranging from polypoidal/ irregular/ uniform/ uneven.

Angio invasive property of Fungi has results in infarction of turbinate, leading to the “dry gangrene” appearance which appear as contiguous foci of non-enhancing tissue on MRI, so-called “black turbinate sign,” which presents in early stages in nasal mucormycosis and can aid in earlier detection [8, 9, 15]. In our study, Presence of Black turbinate sign was seen in 18/75 (24%) patients and its presence had significant correlation in diagnosis of mucormycosis (P value -0.03). As described in fig 5 &6.

Orbital invasion commonly occurs through the medial wall, Edema and thickening of medial rectus muscle is early finding. Further the invasion of optic nerve present as optic neuritis and can lead to loss of vision[10]. In our study, Rhino-orbital mucormycosis was seen in 22/75 (29.3%). As described in fig 7 & 8.

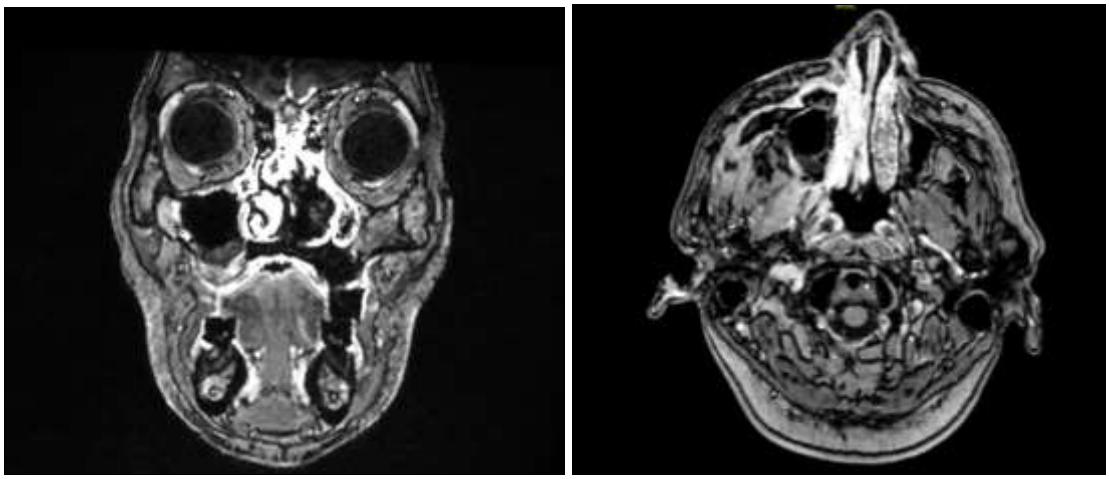

Fig 5 & 6: MRI imaging showing the presence of the "Black Turbinate Sign" as an early diagnostic feature of nasal mucormycosis

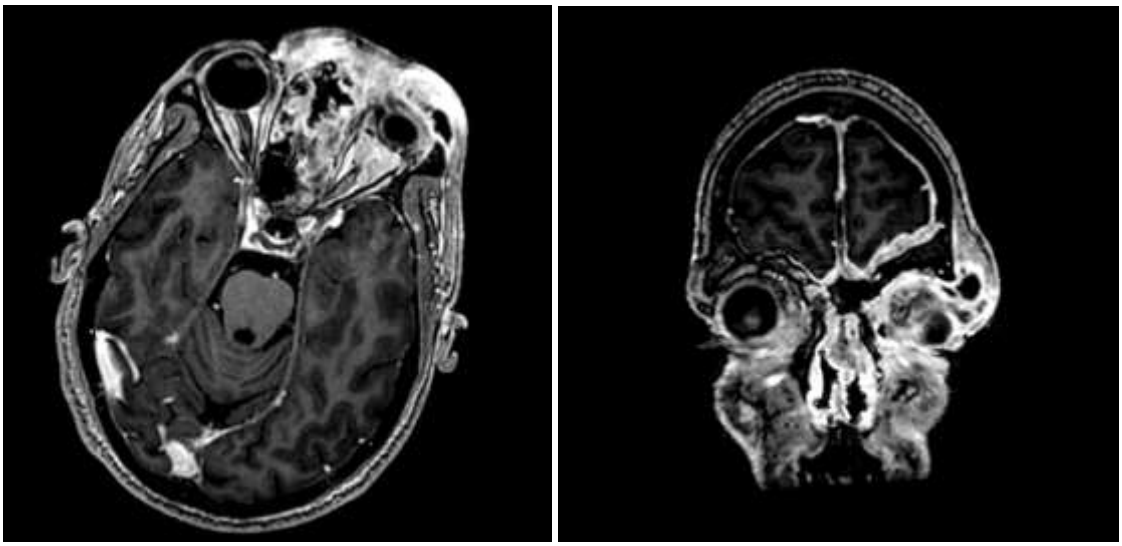

Fig 7 & 8: MRI depiction of orbital invasion in rhino-orbital mucormycosis, highlighting medial rectus muscle thickening and optic neuritis

Intracranial involvement in mucormycosis commonly occurs by direct spread across the cribriform plate, walls of the ethmoid, and frontal sinuses, extension from the pterygopalatine fossa and along internal carotid artery. Intracranial manifestations include meningitis, cerebritis, abscesses and infarcts, all these findings better appreciated on contrast images [10, 11] In cases involving the sphenoid sinus, bulky non enhancing extra sinus soft tissue was seen in the surrounding cavernous sinus, which can further invade into cavernous part of internal carotid artery with resultant thrombosis. Involvement of cavernous sinus can again present with orbital apex syndrome. In our study, Rhino orbitocerebral involvement was seen 18/75, (23.9%), in the form of meningitis & cerebral abscess formation (14/75, 18.6%), cavernous sinus involvement (4/75, 5.3%). As described in Fig 9 & 10.

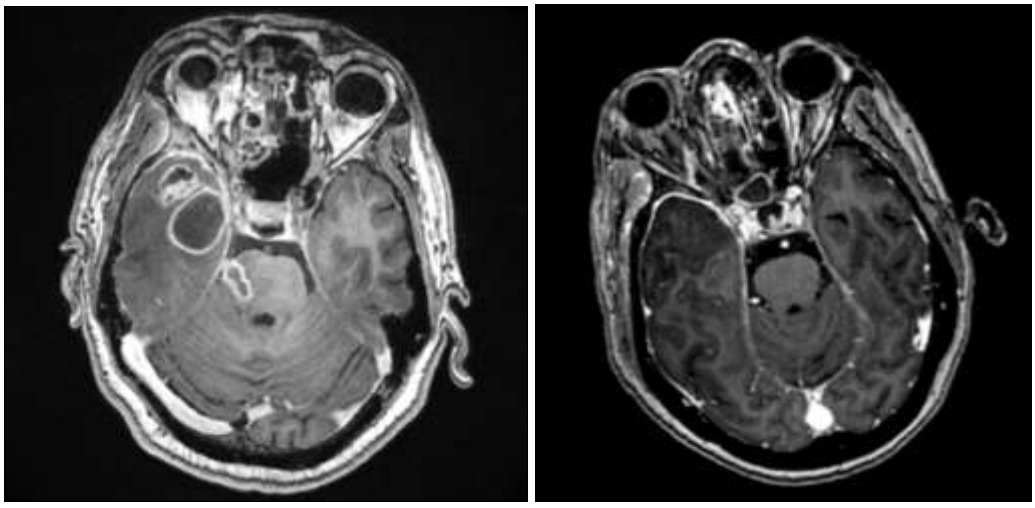

Fig 9 & 10: MRI scans illustrating intracranial involvement in mucormycosis, demonstrating cavernous sinus thrombosis and meningitis

Most patients presented with symptoms of facial pain and swelling (50/75, 66.6%) followed by headache (45/75, 60%) in 3rd week post discharge (24/75, 32%).

Iron is required by virtually all microbial pathogens including fungus for growth and virulence. However, Iron chelators are used as adjunctive antifungal therapy [13]. In our study, patients who had high ferritin levels (P value-0.000096) during their treatment course had positive correlation in development of mucormycosis.

Steroids treatment in COVID 19 positive patients reduces inflammations and is recommended for the treatment of viral pneumonia, but predisposing patients to secondary bacterial and invasive fungal infections (IFIs) whereby impacting morbidity and mortality [16]. COVID-19 infection makes the tissue environment hypoxic. The fungi can adapt itself for being survivable in hypoxic environment [14]. However, in our study there is no positive correlation with steroid use, hypoxic environment for development of mucor mycosis.

Histopathological follow up of all patients has taken for fungal elements on KOH mount. A biopsy was taken from left middle turbinated and demonstrated fungal granulomatous inflammation with broad aseptate fungal hyphae on PAS staining suggesting Mucor species [7].

Conclusions

The abbreviated MRI protocol has significantly higher sensitivity and specificity in diagnosis of mucormycosis with reduction in scan time an additional feature. Most patients presented in 3rd week of post discharge in this study, suggesting special care and MRI evaluation if clinically indicated. Further studies are advised in validation of our abbreviated protocol and further developing a protocol for screening of mucormycosis in post covid patients particularly with presence of Diabetes Mellitus and High ferritin levels during their treatment. No significant correlation between oxygen therapy, Corticosteroids /Ivermectin and Remdesivir therapy in development of mucormycosis.

Conflict of Interest: Not available

Financial Support: Not available

References

1. Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh T, Kontoyiannis D. Epidemiology and clinical manifestations of mucormycosis. Clinical Infectious Diseases. 2012;54(1):S23-S34.
2. Revannavar SPSS, Samaga LVKV. COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world?. BMJ Case Reports. 2021;14(4):e241663.
3. Wiersinga W, Rhodes A, Cheng A, Peacock S, Prescott H. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19). JAMA - Journal of the American Medical Association. 2020;324(8):782.
4. Herrera D, Dublin A, Ormsby E, Aminpour S, Howell L. Imaging findings of rhinocerebral mucormycosis. Skull Base. 2008, 18(S 01).
5. Therakathu J, Prabhu S, Irodi A, Sudhakar S, Yadav V, Rupa V. Imaging features of rhinocerebral mucormycosis: A study of 43 patients. The Egyptian Journal of Radiology and Nuclear Medicine. 2018;49(2):447-452.
6. Mondel PK, Udare AS, Raut AA. CT & MRI imaging features of rhinocerebral mucormycosis. European Congress of Radiology; c2012. DOI: 10.1594/ecr2012/C-2072.
7. Han Q, Escott E. The black turbinate sign, a potential diagnostic pitfall: evaluation of the normal enhancement patterns of the nasal turbinates. American Journal of Neuroradiology. 2019;40(5):855-861.
8. Chae H, Lim J, Lee S, Kim K. The significance of black turbinate sign on MRI. Ear, Nose & Throat Journal. 2019;99(6):395-396.
9. Sreshta K, Dave TV, Varma DR, Nair AG, Bothra N, Naik MN, *et al*. Magnetic resonance imaging in rhino-orbital-cerebral mucormycosis. Indian Journal of Ophthalmology. 2021;69(7):1915-1927. DOI: 10.4103/ijo.IJO_1439_21.
10. Sandron J, Hantson P, Duprez T. Intracranial brain parenchymal spread of mucormycosis through olfactory tract: a diffusion-weighted imaging-based concept. Acta Radiologica Open. 2020;9(12):205846012098099.
11. Aribandi M, McCoy V, Bazan C. Imaging features of invasive and noninvasive fungal sinusitis: A review. Radiographics. 2007;27(5):1283-1296.
12. Moorthy A, Gaikwad R, Krishna S, Hegde R, Tripathi K, Kale P, *et al*. SARS-CoV-2, uncontrolled diabetes and corticosteroids-An unholy trinity in invasive fungal infections of the maxillofacial region? A retrospective, multi-centric analysis. Journal of Maxillofacial and Oral Surgery. 2021.
13. Ibrahim A, Spellberg B, Edwards J. Iron acquisition: a novel perspective on mucormycosis pathogenesis and treatment. Los Angeles Biomedical Institute, David Geffen School of Medicine at UCLA, USA.
14. Chung H, Lee YH. Hypoxia: A double-edged sword during fungal pathogenesis?. Seoul National University, South Korea.
15. Taylor AM, Vasan K, Wong EH, Singh N, Smith M, Riffat F, *et al*. Black turbinate sign: MRI finding in acute invasive fungal sinusitis. Nepean Blue Mountains Local Health District, Sydney, Australia; Westmead Hospital, Sydney, Australia.
16. Ahmadikia K, Hashemi SJ, Khodavaisy S, Getso MI, Alijani N, Badali H, *et al*. The double-edged sword of systemic corticosteroid therapy in viral pneumonia: A case report and comparative review of influenza-associated mucormycosis versus COVID-19 associated mucormycosis.
17. Rising incidence of mucormycosis in patients with COVID-19: another challenge for India amidst the second wave? Lancet Respiratory Medicine. 2021 Jun 3. DOI: 10.1016/S2213-2600(21)00265-4.
18. Mucormycosis in tertiary care centre in South India: 4-year experience. Journal of Postgraduate Medicine. DOI: 10.5005/jp-journals-10071-23387.

How to Cite This Article
Pavankumar SV, Purbhe S, Rote V. Imaging and clinico-pathological correlation of mucormycosis in post covid patients. International Journal of Radiology and Diagnostic Imaging. 2025; 8(1): 26-31.