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Original Article

Rhino-Cerebral-Orbital Manifestations of Mucormycosis an Opportune in COVID Pneumonia Patients

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Abstract

Introduction: Invasive fungal infections are serious complications in immunocompromised patients with hematological diseases, after chemotherapy or transplantation, leading to a high morbidity and mortality but in a current scenario of COVID19 pandemic and its treatment along with comorbidity of uncontrolled diabetes the risk of such fungal infections has risen.

Materials and Methods: A total of 100 patients with a positive microbiological culture or DNA analysis of Mucorales species taken from sinuses during the time period of 2 months (May 2021 and June 2021) which were referred to the department of radio diagnosis, Gandhi Medical College and Hamidia Hospital Bhopal, Madhya Pradesh. All the patients which were included in our study had previous or concurrent history for COVID-19 infection which was proven by reverse transcription polymerase chain reaction test and were or had been on steroid therapy.

Results: 100 patients which were proven cases of mucormycosis and had history of COVID-19 infection and subsequently steroids treatment. Most common age group involved was of 49–57 years 41/100 with male predominance 72/100. Among all the patients, Type 2 diabetes mellitus as a clinical history was present in about 67/100 cases.

Conclusion: MRI provides a better delineation of the blood vessel involvement and intracranial extension of the infection. The Infiltration of the orbital fat and areas of cellulitis on the eyelids can be observed more clearly. Our study recommends MRI as an ideal choice for determining the anatomic involvement of the infection which in turn helps in surgical planning in all the three compartments.

Key words: COVID complications, Mucormycosis, Rhino-orbital-cerebral, RCOM

INTRODUCTION

Invasive fungal infections are serious complications in immunocompromised patients with hematological diseases, after chemotherapy or transplantation, leading to a high morbidity and mortality but in a present scenario of COVID-19 pandemic and its treatment along with comorbidity of uncontrolled diabetes, the risk of such fungal infections has risen.[1] Infections caused by members of the order Mucorales are termed "mucormycosis." Among the different invasive mycoses, mucormycosis has emerged as a life-threatening infection.[2] The challenges of this infection are magnified only further by the paucity of diagnostic tools and therapeutic options. Mucormycosis is characterized by a rapidly evolving course of angioinvasion and tissue necrosis in immunocompromised hosts.[3-5] This study was focused principally on sinus, sino-orbital, and rhinocerebral infection as a disease process and the role magnetic resonance imaging (MRI) as an imaging tool in the present situation.[6] As the traditional term of "rhinocerebral" mucormycosis omits the critical involvement of the eye, we will refer to the more clinically comprehensive term as rhino-orbital-cerebral mucormycosis (ROCM).

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METHODOLOGY

This retrospective study was approved by the institutional review board, also waiving the need for informed consent. We could identify a total of 100 patients with a positive

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Table 1: Case distribution as per age

Age (years)	*n* (100)
17–25	1
25–33	6
33–41	14
41–49	16
49–57	41
57–65	15
65–73	7

Table 2: Summary of anatomical regions/tissues predominantly involved as a findings in cases of rhino-orbital-cerebral as shown by magnetic resonance imaging

Para nasal sinus	
Pan sinusitis	
Unilateral	29
Bilateral	41
Sinuses	
Maxillary	84
Ethmoidal	88
Frontal	61
Sphenoidal	72
Black turbinate sign	28
Orbits	
Normal	22
Orbital cellulitis and proptosis	77
Preseptal cellulitis	45
Optic neuritis	26
Extraocular muscle involvement	
No involvement	33
Medial rectus	57
Inferior rectus	39
Superior rectus	14
Lateral rectus	8
Superior oblique	11
Inferior oblique	3
Brain	
Normal	57
Superior ophthalmic vein thrombosis	6
Cavernous venous thrombophlebitis	9
Internal cerebral artery thrombosis	13
Infarcts	21
Frontal lobe	10
Temporal lobe	7
Cerebellum	3
Occipital lobe	2
Parietal lobe	1
Abscess	13
Frontal	8
Temporal	5
Meningitis	3
Cerebritis	6
Frontal	4
Temporal	2

microbiological culture or DNA analysis of Mucorales species taken from sinuses during the time period of 2 months (May 2021 and June 2021) which were referred to the department of radio diagnosis, Gandhi Medical College and Hamidia Hospital Bhopal, Madhya Pradesh all the patients which were included in our study had previous or concurrent history for COVID-19 infection which was proven by reverse transcription polymerase chain reaction test and were or had been on steroid therapy.

For each patient, the MRI examination was performed on HITACHI 1.5T machine and the protocol consisted of unenhanced axial T1-weighted sequences without fat-suppression as well as axial and coronal T2, contrast-enhanced T1-weighted sequences with fat-suppression, and short tau inversion recovery sequences.

RESULTS

In our study of 100 patients which were proven cases of mucormycosis and had history of COVID-19 infection and subsequently steroids treatment. Most common age group involved was of 49–57 years 41/100 with male predominance 72/100 [Table 1].

Among all the patients, Type 2 diabetes mellitus as a clinical history was present in about 67/100 cases. In all our patients with paranasal Mucorales infiltration, bilateral pan sinusitis was seen in 41 cases, ethmoidal sinus was most commonly involved sinus 88/100, and least involving frontal sinus in 61 of total cases. We found hypointense mucosal areas at the inferior turbinate predominantly known as black turbinate sign. It was seen in 28 cases.

Among the orbital involvement, orbital cellulitis and proptosis were seen in 77 cases, preseptal cellulitis and optic neuritis in 45 and 26 cases, respectively. The most commonly rectus muscle involved was medial rectus in 57 cases followed by inferior rectus muscle and least commonly involved was inferior oblique. Extraocular muscle involvement was spared in about 33 of the total cases. Incidentally, intraconal-extraorbital abscess formation was encountered in two cases, vitreous hemorrhage and retinal hemorrhage in one case each.

Among all 100 patients, cerebral findings were seen only in 43 of the cases, out of which focal infarct was the most common finding encountered, that is, in 21 cases (ten involving frontal lobe, seven involving temporal, two involving occipital lobe, one involving parietal lobe, and two cerebellar hemisphere). Abscess was seen in 13 of the cases (eight in frontal lobe and five in temporal), meningitis and focal cerebritis were seen in three and six cases, respectively. Internal cerebral artery thrombosis was encountered as the most common vasculopathy in our study, it was seen in 13 of the cases, cavernous venous thrombophlebitis was seen in nine and superior ophthalmic vein thrombosis in six cases [Table 2].

DISCUSSION

ROCM is a severe and life threatening complication in patients who are typically immunocompromised and suffering especially from hematologic disorder, but diabetes seems to be an important risk factor (especially in those with diabetic ketoacidosis or increased serum ferritin); likewise in our study, Type 2 diabetes mellitus remains the most common comorbidity seen in 67 of the total patients. Early diagnosis and treatment are important factors for a good outcome in invasive fungal infections. Fifth decade was most common age group in our study with male predominance.

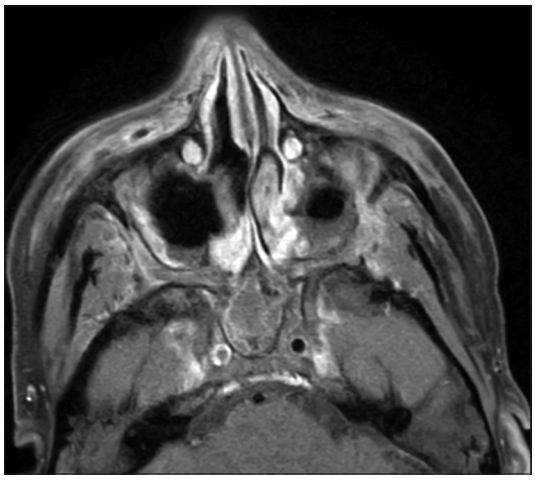

Figure 1: T1 axial image of post-COVID patient showing flow void in the right internal cerebral artery suggesting internal cerebral artery thrombosis

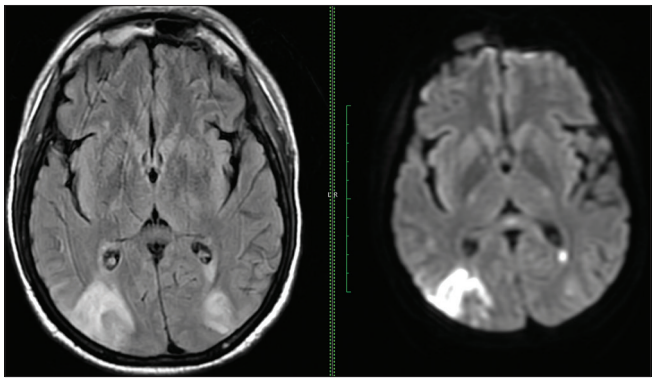

Figure 2: Magnetic resonance imaging shows diffusion-weighted imaging restrictions in the right parieto-occipital lobe suggesting acute infarct

Sinus infection is the most commonly reported presentation.[7,8] In all of our patients with paranasal Mucorales infiltration, we could find inflammatory soft-tissue changes extending from the sinuses into the facial subcutaneous tissue as well as infratemporal and temporal fossa. Among all sinuses ethmoidal sinus was most commonly involved followed by maxillary and least by frontal sinus, bilateral pan sinusitis was seen in 41% of the total cases. The black turbinate sign refers to lack of contrast-enhancement of invaded mucosal areas at the turbinate due to occlusion of small vessels; it was seen in 28 of 100 cases. This sign was described by Safder *et al.*[6]

Extension of inflammation beyond paranasal sinuses is not an exclusive hallmark of fungal invasions as it can also be seen in bacterial infections, Son *et al.* found a higher tendency for intraorbital extraocular muscle involvement and thickening of sinus mucosa in ROC patients compared to that of bacterial infection. Orbital involvement was seen as a complication in our study, orbital cellulitis and proptosis were seen in most of the cases, that is, in 77 of 100 cases. Extension from ethmoidal sinus through lamina papyracea may directly involve the contiguous medial rectus muscle and through the floor of the orbit from maxillary sinus may entrap the inferior rectus and inferior oblique muscles. Most commonly involved extraocular muscle in our study was medial rectus (ethmoidal sinus being the most commonly involved sinus) in 57 cases followed by inferior rectus muscle, similar findings were observed by few studies.[9,10] Optic neuritis as a finding was present in 26 patients. Apart from these findings, four cases encountered were showing intraconal-extraorbital abscess formation in two cases and one case each had vitreous and retinal hemorrhage.

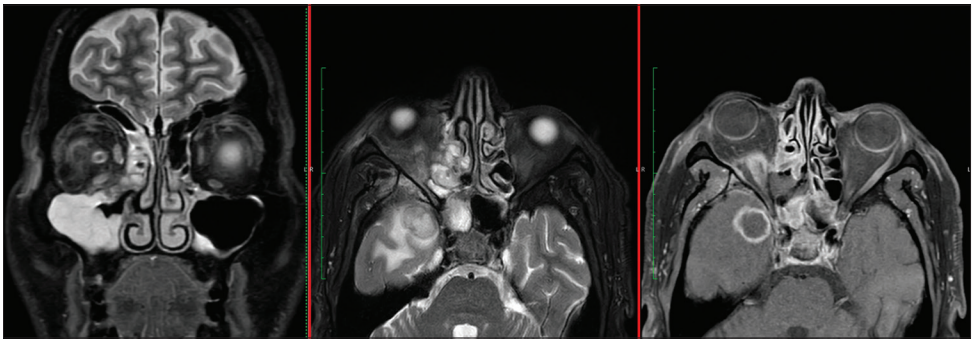

Figure 3: Case with a history of COVID infection, magnetic resonance imaging suggested a focal abscess noted in the right anteromedial temporal lobe with surrounding edema and adjacent pachymeningitis along with bilateral pan sinusitis

Development of cerebral mucormycosis as a complication of sino-orbital mucormycosis is a life threatening sequel. Invasion of brain tissue may develop through the ethmoidal and orbital veins that drain into the cavernous sinuses and superior ophthalmic veins, by invasion along optic nerve, and by direct extension into the cranial cavity from frontal, ethmoidal, and sphenoid sinuses. Cerebral involvement (43/100) was also seen frequently in our cohort. Internal cerebral artery thrombosis was encountered as the most common vasculopathy in our study [Figure 1], it was seen in 13 of the cases, cavernous venous thrombophlebitis was seen in nine and superior ophthalmic vein thrombosis in six cases.[11,12] Focal infarcts [Figure 2] were the most common findings among the cerebral complication encountered which was seen in 21 cases (ten involving frontal lobe, seven involving temporal, two involving occipital lobe, one involving parietal lobe, and two cerebellar hemisphere), Abscess [Figure 3] was seen in 13 of the cases (eight in frontal lobe and five in temporal lobe). Meningitis and focal cerebritis were seen in three and six cases, respectively.[13-15]

MRI provides a better delineation of the blood vessel involvement and intracranial extension of the infection. Infiltration of the orbital fat and areas of cellulitis on the eye lids can be observed more clearly. Diego *et al.* reported the usefulness of multimodality imaging in achieving prompt and early diagnosis and recommended MRI as an ideal choice for determining the anatomic involvement of the infection which in turn helps in surgical planning.

CONCLUSION

The signs of inflammatory involvement just outside the paranasal sinuses in immunoincompetent patient's and in the situation of the present pandemic of COVID-19 infection and its treatment with new facial, orbital swelling, or even vision impairments and new onset neurological symptoms should raise the suspicion of a fungal sinusitis possibly caused by the Mucorales species. The suspected diagnosis should be given to the referring physician and the microbiological laboratory to make early diagnosis, extension of the disease which may be very useful for the further follow-up, as a guide for surgical debridement[16,17] and prognosis.[18,19] MRI provides a better delineation of the blood vessel involvement and intracranial extension of the infection. Infiltration of the orbital fat and areas of cellulitis on the eye lids can be observed more clearly. Diego *et al.*[20] reported the usefulness of multimodality imaging in achieving prompt and early diagnosis and recommended MRI as an ideal choice for determining the anatomic involvement of the infection which in turn helps in surgical planning.

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