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NEUROSURGICAL PERSPECTIVES ON CEREBRAL MUCORMYCOSIS IN THE POST-COVID-19 ERA: A RETROSPECTIVE ANALYSIS

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ABSTRACT

Introduction: There has been a recent surge in cerebral mucormycosis cases among COVID-19 patients due to several factors, including compromised barrier defense mechanisms and the administration of immunosuppressive drugs such as steroids for COVID-19 treatment. The primary aim of this study was to delineate the pattern of cerebral mucormycosis involvement and identify associated factors in COVID-19 patients.

Materials and Methods: This observational study was conducted at a tertiary care Indian hospital. Data from 78 patients treated for post-COVID-19 mucormycosis with cerebral involvement were collected and analyzed. The study spanned nine months.

Results: The average age of patients was 52.81 years and Male to Female ratio was 1.3:1. Majority of patients presented with eye-related symptoms at the time of diagnosis. Diabetes Mellitus was the most prevalent comorbidity among these patients, followed by a combination of Diabetes Mellitus and Hypertension. The MRI findings revealed that a majority of patients exhibited involvement of the left cerebral hemisphere, followed by involvement of both hemispheres. Additionally, MRI scans indicated infarcts in most cases, followed by abscess formation and non-specific changes. Among the deceased patients, the highest number showed non-specific brain changes according to MRI reports, followed by cerebral infarction.

Conclusions: COVID-19 patients appear to be more vulnerable to this fungal infection due to compromised barrier defense mechanisms and the use of immunosuppressive medications such as steroids and tocilizumab. Most patients afflicted with mucormycosis also had diabetes. Vigilance for this fungal infection among high-risk patients can enhance patient care and outcomes.

Keywords: COVID-19, Mucormycosis, Neurosurgery, Fungal infection.

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INTRODUCTION

Fungal infections affecting the central nervous system, particularly cerebral mucormycosis, are uncommon. Typically, it is not an independent disease but rather a secondary opportunistic infection caused by fungi belonging to the Mucoraceae family. With the recent surge in COVID-19 cases, there has been a rise in reported cases of cerebral mucormycosis. This increase can be attributed to compromised barrier defenses, dysfunction of immune cells such as phagocytes and lymphocytes, and the use of immunosuppressive drugs like steroids and tocilizumab in COVID-19 treatment [1-3].

Cerebral mucormycosis exhibits an aggressive pattern of spread, rapidly involving surrounding structures. It can extend into the brain through direct extension, hematogenous spread, or perineural spread. Local invasion via the nasal and orbital routes accounts for most cases of intracranial mucormycosis. Tissue necrosis resulting from angioinvasion and subsequent thrombosis and endarteritis leads to the formation of necrotic, black eschars, which are characteristic of the disease [2-5]. Clinical manifestations may include nasal congestion, crusting, loss of smell, headache, blurred vision, facial pain, and, in cases of intracranial extension, atypical signs such as proptosis, ophthalmoplegia, or periorbital cellulitis [4].

In cases of perineural spread, enhancement of the affected nerve on MRI can indicate neuritis, which may progress to abscess formation [6]. MRI is the preferred diagnostic tool, providing detailed three-dimensional images to assess disease spread and guide management. Common imaging findings in intracranial mucormycosis include cavernous sinus thrombosis, brain infarction, brain abscess, and internal carotid artery occlusion, with the cavernous sinus often being the initial site of involvement [4].

Surgical debridement is the mainstay of treatment for mucormycosis and has been associated with improved outcomes in several case series. However, extensive surgical procedures such as orbital exenteration and craniofacial resection carry significant morbidity and mortality, with recent studies suggesting no survival benefit from such radical approaches. Therefore, the extent of surgical debridement should be carefully considered, taking into account the patient's underlying comorbidities and life expectancy. Decisions regarding surgical approach and goals should involve discussions among neurosurgeons, infectious disease specialists, radiologists, patients, and their families [7-11].

Accepted indications for neurosurgery in mucormycosis include relieving intracranial pressure, draining obstructive hydrocephalus, and excising lesions compressing the spinal cord. Radical excision of fungal brain abscesses or granulomas is generally discouraged [12].

This study primarily focused on various cerebral manifestations of mucormycosis in COVID-19 patients and provided a neurosurgical overview of its outcomes. All patients underwent clinical evaluation by a multidisciplinary team and treatment followed standard protocols, yielding promising results.

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MATERIALS AND METHODS

All patients admitted to the Departments of Medicine, Otorhinolaryngology, and Neurosurgical Units of General Surgery at an Indian tertiary care hospital for the treatment of post-COVID-19 mucormycosis, with MRI scans indicating cerebral extension of the disease, were included in this study. Patient details, including symptoms at presentation, co-morbidities, and MRI brain reports, were collected to analyze the pattern of disease occurrence.

Clinical evaluations were conducted by a multidisciplinary team comprising specialists from Otorhinolaryngology, Medicine, and Neurosurgery. All patients received treatment following established protocols for post-COVID-19 mucormycosis, utilizing the best available facilities in the hospital. Throughout the study, adherence to treatment protocols was maintained, and patient care remained uncompromised. The collected data underwent statistical analysis by Epi Info 6, and results were obtained for further interpretation.

RESULTS

A comprehensive analysis was conducted on a total of 78 instances of post-COVID-19 Mucormycosis, inclusive of cerebral engagement. The age range of the cases spanned from 23 years (the youngest) to 80 years (the eldest), with an average age of 52.81 years. Notably, the majority of patients fell within the 51-60 age bracket, while the fewest were distributed across the 21-30 and 71-80 age groups. Male to Female ratio was 1.3:1 (Table 1).

In the clinical presentation observed among the 78 cases examined, the majority of patients presented with eye-related symptoms at the time of diagnosis, such as eye pain, swelling, and/or decreased visual acuity. Diabetes Mellitus was the most prevalent comorbidity among these patients, followed by a combination of Diabetes Mellitus and Hypertension (refer to Table 2).

The MRI findings of cerebral mucormycosis in the study participants, as depicted in Table 3, revealed that a majority of patients exhibited involvement of the left cerebral hemisphere, followed by involvement of both hemispheres. Additionally, MRI scans indicated infarcts in most cases, followed by abscess formation and non-specific changes. Among the deceased patients, the highest number showed non-specific brain changes according to MRI reports, followed by cerebral infarction.

Table 1: Demographic variables of study participants

Age Group	n	%	Survived	Death
21-30 years	3	3.85	2	1
31-40 years	17	21.79	9	8
41-50 years	18	23.08	7	11
51-60 years	23	29.49	13	10
61-70 years	14	17.95	11	3
71-80 years	3	3.85	2	1
Total	78	100.00	44	34
Gender				

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Male	44	56.41	24	20
Female	34	43.59	20	14
Total	78	100.00	44	34

Table 2: Clinical presentation of patients in study participants

Presenting Complaints	**n**	**%**
Ocular	37	47.44
Hemiparesis	18	23.08
Headache	17	21.79
Others	6	7.69
Total	78	100.00
Co-Morbidity		
Diabetes Mellitus	50	64.10
Hypertension	1	1.28
Both	23	29.49

Table 3: MRI findings of cerebral mucormycosis in study participants

Site of involvement	**n**	**%**
Right Hemisphere Involvement	26	33.33
Left Hemisphere Involvement	30	38.46
Both Hemisphere Involvement	23	29.49
MRI Finiding		
Infarct	28	35.90
Abscess	16	20.51
Non-Specific	10	12.82
Mixed	9	11.54
Thrombus	7	8.97
Ischaemia	5	6.41
Thrombophlebitis	3	3.85

DISCUSSION

This research posited that intracranial mucormycosis in COVID-19 patients is not an independent disease but a secondary opportunistic infection, particularly in individuals treated with immunosuppressive medications like steroids and tocilizumab. Patients with COVID-19 who received such treatments were found to have a higher likelihood of developing secondary opportunistic infections like mucormycosis. Notably, almost all post-COVID-19 cerebral mucormycosis cases reviewed in the literature had type 2 diabetes mellitus as one of the most common comorbidities. The intracranial extension of this opportunistic fungal infection can occur through local invasion or hematogenous dissemination, resulting in a systemic disease [13-17].

Opportunistic fungal infections, particularly in nasal sinusitis, are rare but have been increasingly reported during the COVID-19 pandemic. Mucormycosis caused by mucormycetes molds has

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various forms, including rhino-orbito-cerebral, pulmonary, gastrointestinal, cutaneous, and disseminated [18-19]. The infection typically begins with inhalation of spores into the oral and nasal cavity. In individuals with intact immune systems, infection is rare as the fungal spores are phagocytized by macrophages. However, in patients with uncontrolled diabetes mellitus or severe immunocompromise, infection can develop due to weakened immune responses. From the nasal sinuses, the infection may spread to the orbit, resulting in orbital cellulitis and potentially extending to the brain parenchyma through various routes [20-22].

Diagnosis of mucormycosis involves clinical, radiological, and laboratory approaches. Clinical signs such as facial swelling, headache, nasal or sinus congestion, and blackish discoloration within the nose or palate can aid diagnosis. Radiological imaging through CT or MRI and laboratory tests including culture or pathology can further confirm the diagnosis [19-21].

The occurrence of 78 cases of cerebral mucormycosis in a single hospital represents a significant incidence of this rare opportunistic disease. The subsequent studies should aim to elucidate the disease's pattern of cerebral involvement, associated risk factors, and outcomes from a neurosurgical perspective.

CONCLUSION

Mucormycosis presents as an uncommon opportunistic infection, with COVID-19 patients displaying heightened susceptibility due to compromised barrier defenses and the administration of immunosuppressive drugs like steroids and tocilizumab. Predominantly, diabetic patients are affected. Nasal and orbital involvement is frequently observed in patients with cerebral mucormycosis. Healthcare providers should remain vigilant for signs of this fungal infection in COVID-19 patients with comorbidities, especially those exhibiting the described clinical features, facilitating prompt diagnosis and improved patient outcomes.

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