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MUCORMYCOSIS IN POSTCOVID ERA: DIAGNOSTIC AND THERAPEUTIC CHALLENGES

Dr. Rahul Gosavi	Assistant Professor, Department of ENT, Sanjeevan Medical Foundation ENT post graduate training Institute, Miraj
Dr. Chinmayi Suhas Kulkarni*	Junior Resident, Department of ENT, Sanjeevan Medical Foundation ENT post graduate training Institute, Miraj*Corresponding Author
Dr. Vishal Magdum	Associate Professor, Department of ENT, Sanjeevan Medical Foundation ENT post graduate training Institute, Miraj
Dr. Shishir Gosavi	Professor and HOD, Department of ENT, Sanjeevan Medical Foundation ENT post graduate training Institute, Miraj
Dr. Manali Gosavi	Senior Resident, Department of ENT, Sanjeevan Medical Foundation ENT post graduate training Institute, Miraj
Dr. Saurav Sabnis	Junior Resident, Department of ENT, Sanjeevan Medical Foundation ENT post graduate training Institute, Miraj

ABSTRACT **Background :** Mucormycosis, first identified in 1885, has surged in incidence, especially post-COVID-19, primarily affecting immunocompromised individuals such as those with uncontrolled diabetes and patients undergoing chemotherapy. The immunosuppressive effects of COVID-19 and steroid treatments that cause temporary hyperglycemia have heightened the risk. Additionally, factors like nasal mucosa drying and unsterilized oxygen delivery may contribute to its spread. The aim of this study is to study the various clinical presentations and management of mucormycosis in the post-COVID era and educate the clinicians in early diagnosis and treatment of this fateful disease. **METHODOLOGY** Clinically suspected and histologically reported 117 cases of mucormycosis depending upon their clinical presentation, nasal endoscopy, and radiological evidences were included in this study. Pus culture and sensitivity of sinus discharge as well as fungal staining by KOH mount were done. MRI were done in all cases to understand the extent of disease. Endoscopic surgical debridement was choice of surgical intervention followed by histopathological examination and administration of injection liposomal amphotericin B. All cases diagnosed as mucormycosis such as mixed fungal infection with mucormycosis as well as isolated mucormycosis were included in this study and all other types of fungal infections were excluded from this study. **RESULTS** Out of 117 patients with mucormycosis, 71 had paranasal sinus involvement, 27 had sinus with palatal complications, 28 had orbital involvement, 18 experienced intracranial involvement, and 8 had mixed presentations. Of the patients, 102 (87.17%) were immunocompromised, emphasizing the need for careful monitoring.81 patients fully recovered, 27 experienced some morbidity, 5 lost follow-up, and 4 passed away. Management included endoscopic surgical debridement along with administration of liposomal amphotericin B. Orbital decompression or exenteration and partial or total maxillectomy was required in certain cases depending on the clinical and radiological presentation. **Conclusion :** Post-COVID, clinicians should be alert to the possibility of mucormycosis in cases of fungal sinusitis until ruled out. Recognizing specific symptoms is crucial, and while endoscopy and MRI are key diagnostic tools, attention to ocular, palatal, and intracranial signs is essential. A low threshold for initiating Amphotericin B treatment is important, as mucormycosis can affect even otherwise immunocompetent patients who may experience sudden rise in blood sugar level after use of steroids or any other cause in COVID-19. A multidisciplinary approach is vital for effective management.

KEYWORDS : Mucormycosis, Post-COVID, Fungal infection, Antifungal therapy

INTRODUCTION

Mucormycosis was first identified as a cause of human disease in 1885, but in the past two decades, there has been a significant increase in invasive fungal infections worldwide, largely due to a growing population at risk. Mucormycosis, typically an acute necrotizing fungal infection characterized by a fulminant course and angioinvasion, has seen a notable rise in incidence, particularly post-COVID-19. This infection was primarily observed in immunocompromised individuals, including those with uncontrolled diabetes, HIV/AIDS, patients undergoing chemotherapy or radiotherapy, and organ transplant recipients. COVID-19 itself has been shown to compromise immunity, and its prevalence among diabetic patients has further exacerbated the situation. [1,2]

The use of steroids for COVID-19 treatment, both prophylactically and therapeutically, has led to temporary hyperglycemia, creating a transient immunocompromised state conducive to mucormycosis development. Additionally, theories suggest that drying of the nasal mucosa from high oxygenation and the use of unsterilized equipment for oxygen delivery may contribute to the spread of the disease, although these ideas remain unproven. [3,4]

The aim of this study is to investigate the various clinical presentations and management of mucormycosis in the post-COVID era. Specifically, we seek to conduct a detailed analysis of the different clinical manifestations of mucormycosis, including involvement of the nose, paranasal sinuses, orbits, palate, and intracranial extensions. We will discuss various diagnostic techniques and treatment modalities, encompassing surgical interventions, antifungal medications, and rehabilitation strategies. Additionally, the study will explore potential complications associated with mucormycosis and their impact on patient outcomes, emphasizing the need for effective management in this evolving clinical landscape.

METHODOLOGY

This study encompassed 117 cases of mucormycosis that were clinically suspected and histopathologically confirmed from 1st January 2021 to 31st December 2021. The methodology included the following steps:

CLINICAL PRESENTATION

Early signs and symptoms included headaches, facial pain, and neurological issues like facial numbness and ophthalmoplegia. Patients reported nasal symptoms such as blockage and loss of smell. As the infection advanced, it affected the orbit, causing vision problems and inflammation. Oral cavity involvement led to palatal necrosis and loosening of teeth, potentially resulted in oroantral fistulas. If the infection spread to the central nervous system, it could cause altered mental status and cranial nerve deficits, leading to life-threatening conditions.

Fig No.01: Classical black nasal crust as seen on a OPD nasal endoscopy

Fig No.02: Palatal necrosis with impending fistula

Fig No.04: Preoperative and Post operative status

Fig No.05: ORBITAL AND PALATAL INVOLVEMENT

1. DIAGNOSTIC PROCEDURES:

Nasal endoscopy: Diagnostic nasal endoscopy was the first step to diagnose mucormycosis when the patient presented to the outpatient department from which we could identify the presentation of lesion and did the following microbiological tests.

Pus Culture and Sensitivity: Sinus discharge was collected for culture and sensitivity testing to identify the fungal organism and determine its susceptibility.

FUNGAL STAINING: The classical presentation of aseptate hyphae on KOH mount was characteristic of mucormycosis.

Biopsy and Histopathological correlation: Biopsy of the affected sinus tissue was taken to confirm the diagnosis and identify the type of fungal infection.

3. IMAGING:

MRI: All patients underwent magnetic resonance imaging (MRI) to assess the extent of the disease and involvement of surrounding structures.

MRI was preferred for mucormycosis due to its better visualization of soft tissue and intraorbital/intracranial extension. While CT was effective for assessing bone involvement, it often complicated evaluation by revealing necrosis.

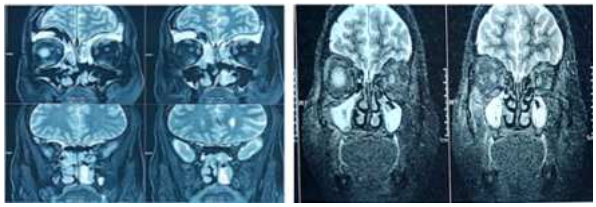

Fig No.06: MRI of Brain, PNS and Orbit

4. SURGICAL INTERVENTION:

Endoscopic debridement was performed for mucormycosis management, starting with the resection of the middle turbinate for better access. A wide middle meatal antrostomy facilitated drainage, while ethmoidectomy and sphenoidotomy removed fungal infections from the respective sinuses. Medial maxillectomy was done to excise necrotic tissue, and a modified Denker's procedure was employed as needed. In cases requiring orbital decompression, the lamina papyracea was typically pierced, and a medial orbitotomy was performed to decompress the orbit.

In cases with temporal or frontal lobe involvement, a neurosurgeon was consulted. For palatal necrosis, infrastructure maxillectomy or palatectomy was performed based on severity. An obturator was inserted post-debridement to aid closure and restore function. Histopathological examination of excised tissue was conducted afterward.

PREOPERATIVE STATUS

Fig No.07: Intraoperative pictures

POST-OPERATIVE CARE

Post-operative care included nasal endoscopy every three days for site assessment and douching, with scabs cleaned and rebiopsies performed if recurrence was suspected. Blood tests monitored glucose, serum creatinine, and electrolytes. Collaboration with physician colleagues ensured effective management of complications and improved patient outcomes.

FOLLOW-UP CARE

Post-operative follow-up involved weekly visits for two weeks, biweekly for one month, and monthly for six months, with nasal endoscopies to assess healing and detect mucormycosis recurrence. Patients who had palatal debridement were referred to a maxillofacial surgeon for further dental care, ensuring comprehensive oversight and prompt management of concerns.

5. MEDICAL MANAGEMENT:

Liposomal Amphotericin B is the primary treatment for mucormycosis, given at 5-10 mg/kg/day for at least three weeks, mixed with 5% dextrose. For stable disease, posaconazole was prescribed as 2 x 300 mg on day 1, then 1 x 300 mg daily for at least three weeks.

This study included all diagnostically and histopathologically proven cases of mucormycosis. Specifically, it encompassed cases of isolated mucormycosis, diagnosed without the presence of other fungal infections, as well as cases involving mixed infections where mucormycosis coexisted with other fungi. Conversely, patients with infections other than mucormycosis were excluded from the study. Additionally, cases lacking definitive histological confirmation, despite presenting with similar symptoms, were also excluded to ensure the accuracy of the findings.

RESULT

The clinical presentation of patients with mucormycosis varied significantly across the cohort of 117 individuals. A total of 71 patients exhibited involvement of the paranasal sinuses alone. Additionally, 27 patients had paranasal sinus involvement accompanied by palatal complications, while 28 patients presented with orbital involvement. Furthermore, 18 patients experienced intracranial involvement, and 8 patients had mixed presentations.

The distribution of patients with mucormycosis based on preexisting immunocompromised status reveals that 102 patients (87.17%) had some form of immunocompromised condition, while 15 patients (12.82%) were not immunocompromised. This data emphasizes the significant association between immunocompromised states and the development of mucormycosis, highlighting the need for vigilant monitoring and management in at-risk populations.

RECOVERY OF PATIENT

EVENT	NO. OF PATIENTS
COMPLETE RECOVERY	81
RECOVERY WITH SOME MORBIDITY	27
LOSS OF FOLLOW UP WITH INCOMPLETE TREARMENT	5
SAD DEMISE	4

Out of the total 117 patients, 81 achieved complete recovery from mucormycosis, while 27 experienced recovery with some morbidity. Five patients lost follow-up due to incomplete treatment, and sadly, four patients passed away.

In managing mucormycosis, 27 patients underwent partial or total maxillectomy. Five received retrobulbar Amphotericin B injections post-operatively, and three with extensive eye involvement had orbital exenteration. Additionally, 10 patients were transferred to the Critical Care Unit for close monitoring. The use of systemic glucocorticoids for COVID-19 complications posed a risk of opportunistic fungal infections, complicating patient management.

DISCUSSION

In the present study of 117 patients with mucormycosis, 71(60.68%) exhibited isolated paranasal sinus involvement, while 27(23.07%) had sinus involvement with palatal complications, and 28(23.93%) presented with orbital involvement. Additionally, 18(15.38%) patients experienced intracranial involvement, and 8(6.83%) had mixed presentations. Jadhav et al.[5] reported peri-orbital invasion in 15.62% of cases and intracranial involvement in 3.12%. Similarly, Pathak et al.[6] noted extensive radiological involvement, with 90% of patients affected in the maxillary sinus, 85% in the ethmoid sinus, and 80% in the frontal sinus, and an intracranial extension rate of 10%.

Among the 117 patients in this study, 102 (87.17%) were found to have an immunocompromised condition, while 15 (12.82%) did not, underscoring the strong association between immunocompromised states and mucormycosis. In a study by Hoenigl et al.,[7] comorbidities included hypertension (12%), kidney disease (7%), and obesity (2%). Additionally, Eldsouky et al.[8] reported that 86.7% of patients had diabetes mellitus and 66.7% had hypertension, further highlighting the significant role of underlying health issues in the risk and severity of the disease.

In the present study involving 117 patients with mucormycosis, 81 achieved complete recovery, 27 recovered with some morbidity, five lost follow-up, and four sadly passed away. Management strategies included maxillectomy for 27 patients, retrobulbar Amphotericin B injections for five, and orbital exenteration for three patients with extensive eye involvement. Additionally, 10 patients were monitored in the Critical Care Unit. The use of systemic glucocorticoids for COVID-19 complications was noted to increase the risk of life-threatening opportunistic infections. In a study by Hoenigl et al.,[7] 33 patients (56%) survived, while 22 (37%) died, and 4 (7%) had an unknown status; notably, 19 patients (32%) experienced vision loss. Similarly, Singh et al.[9] reported that among 101 patients, 56 (55.4%) were alive and improving, 5 (5.0%) remained unchanged, 31 (30.7%) had died, and 9 (8.9%) had unknown status due to loss to follow-up.

CONCLUSION

In the post-COVID era, clinicians must maintain heightened awareness that any case of fungal sinusitis could potentially be mucormycosis, and this possibility should be considered until definitively excluded. It is crucial for clinicians to recognize specific symptoms and clinical findings that may indicate mucormycosis in patients with fungal sinusitis. Diagnostic nasal endoscopy and MRI are considered the gold standard for diagnosis; however, practitioners should remain vigilant for signs of ocular symptoms, palatal involvement, and intracranial extension. A low threshold for initiating treatment with injection Amphotericin B is essential for managing mucormycosis effectively. Furthermore, distinguishing between aggressive, invasive, and non-invasive forms of the disease is critical. The traditional notion that mucormycosis exclusively occurs in immunocompromised individuals is somewhat outdated; it can also affect patients who appear immunocompetent, particularly following temporary changes in glycemic status or a history of COVID-19. Lastly, a multidisciplinary team approach is necessary to ensure comprehensive care for affected patients.

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