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Radio-Diagnosis

COVID-19: MUCORMYCOSIS OR 'BLACK FUNGUS

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ABSTRACT

Introduction: Mucormycosis is an acute and often fatal infection caused by a fungus of the Mucorales order of the Zygomycetes class. In the majority of cases, it is associated with an underlying disorder, such as diabetes mellitus with ketoacidosis, or with immunocompromising factors, but it appears in long term use of steroid in recovered covid patients and may appear in healthy people, although rarely. Early diagnosis and treatment are critical to prevent an otherwise fatal outcome.

Aim: This study aimed to early detection by using of imaging techniques and evaluate the use of amphotericin B and endoscopic management of rhinocerebral mucormycosis and follow up.

Materials And Methods: We review 40 cases of mucor mycosis admitted in our government generalhospital, Nizamabad from 1st MAY to 15th June of 2021. 38 patients had diabetes mellitus, 2 patients had non diabetic and two patients had CKD

20 patients with infection limited to the nose and sinuses were selected. Patients underwent endoscopic debridement of all necrotic tissue; cottonoidpledgets soaked in amphotericin B solution were then placed in the nasal cavity. Subsequently, long-term antifungal therapy was administered.17 patients had orbital involvement, out of which 3 cases loss of vision, 4 cases had hard palate involvement and one case cavernous sinus thrombosis

Results: All patients had previous history of covid-19 positive with diabetes mellitus. 4 patients hard palatal necrotic ulcers and/or black eschars. 17 patients had orbital involvement with 3 patients had unilateral blindness, and one case had cerebral involvement with cavernous sinus thrombosis and four patients died because of a delayed diagnosis.

Conclusions: Early diagnosis is critical in the prevention of intracranial extension of the infection, which is the cause of death in 80% of cases. Therefore, a high index of clinical suspicion is essential in immunocompromised or diabetic patients with acute sinus infection.

Identification of a fungal organism on histopathology is the most specific element for diagnosis. Topical use of amphotericin B combined with endoscopic surgical debridement, followed by intravenous amphotericin B treatment, may constitute acceptable management for selected patients, with less morbidity than conventional treatments.

KEYWORDS : Covid-19, Mucor mycosis, Diabetes mellitus, Sinus endoscopy, Computed tomography, magnetic resonance imaging

INTRODUCTION

Mucormycosis is a term used to refer to any fungal infections of the order Mucorales, which belongs to the class Zygomycetes[3] In India, patients who have recovered from COVID-19 are increasingly being detected with Mucormycosis or black fungus. This is a rare fungal infection caused by a group of fungi called mucoromycetes, commonly found in the environment. Though this condition is rare and attacks individuals with compromised immune systems, not treating it in time can be potentially life-threatening.

COVID-19 patients with uncontrolled diabetes and weaker immune systems are particularly at a higher risk of developing this condition.

Mucor mycosis occurs when a person inhales the fungal spores in the air. These spores can be found both outdoors and indoors, especially in hospital settings. Mucormycosis is not a contagious disease and does not spread from an infected person or animal. The coronavirus disease 2019 (COVID-19) infection caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may be associated with a wide range of disease patterns, ranging from mild to life-threatening pneumonia. A wide range of bacterial and fungal co-infections may exist and may be associated with pre-existing morbidity (diabetes mellitus, lung disease). India has a high prevalence rate of type 2 diabetes mellitus, which is a well-known risk factor[2]. We report the case of a patient with COVID-19 infection, who during the course of the treatment, developed rhino-orbital Mucor mycosis.

It can involve upper aerodigestive tract, lungs, central nervous system, gastrointestinal tract and skin (usually in burn patients). Most fatal presentation is rhino-cerebral involvement, which is usually initiated with paranasal sinus involvement and may progress to the orbit and the brain. Loss of vision is one of the dreaded complications apart from fatality. Intraoperative nasal endoscopic examination is the most informative test for possible fungal involvement of nasal cavity and paranasal sinuses.

The mainstays of therapy are treatment of immunocompromised status, systemic high dose Amphotericin B, and surgical debridement of necrosed or nonviable tissue.3 Following cases highlight the importance or early diagnosis governed by endonasal endoscopic examination and surgical decision of endoscopic management of mucormycosis, resulting in favourable outcome and lesser complications, especially pertaining to vision. Clinical data Patient information We retrospectively reviewed data of our six patients managed in a short span of four months, ranging from 28 -71 years (median age of 62 year). All cases were immunocompromised in form of having uncontrolled diabetes mellitus, chronic kidney disease, leading to sepsis. one patient was a renal transplant recipient on immunosuppressive treatment.

Our patients presented with symptoms ranging from high grade fever not controlled on broad spectrum parenteral antibiotics, facial swelling and pain, peri orbital oedema, diminished or loss of vision, ophthalmoplegia, proptosis, palatal ulcer , and purulent discharge from nose.

The renal transplant recipient patient also had lower cranial nerve palsies apart from above mentioned symptoms and signs.

Workup All patients underwent urgent rigid nasal endoscopy which revealed black brown crusts which did not bleed on removal and tenacious pus filling nasal cavity, appearing to be arising from middle meatus. There was erosion of middle turbinate and posterior end of inferior turbinate with posterior septal perforation.

Examination of oral cavity revealed perforation of hard palate with black eschar formation in one patient. There was erosion of lamina papyracea in one patient, with invasion of periorbital fat in 6 patients as presented in Figure 1A-1D.

Biopsy was taken in all cases which was positive for mucormycosis. All patients also underwent ophthalmologic examination, in view of diminished or loss of vision. The distant visual acuity ranged from 6/36 to complete loss of vision in affected eye.

CT / MRI scan of PNS was done in all cases to determine the extent of infection as depicted in Figure 2A-2C. Apart of these routine complete blood counts, various other biochemical and serological tests were performed.

All patients had neutropenia, grossly deranged glycaemic control, and deranged serum urea and creatinine values suggestive of chronic kidney disease.

What Is Mucormycosis

Mucormycosis previously termed zygomycosis, is a rare fungal infection, instigated by the mucormycete mould, that occurs extensively in soil, leaves, decayed wood and putrefied manure. It mainly affects people who have health problems or take medicines that lower the body's ability to fight germs and sickness.

Sinuses or lungs of such individuals get affected after they inhale fungal spores from the air. In some states have noted a rise in cases of Mucor mycosis among people hospitalized or recovering from Covid 19, with some requiring urgent surgery. Usually, mucoromycetes does not pose a major threat to those with a healthy immune system.

METERIALS AND METHODS:

We evaluated the imaging and clinical data of four males and one female, 3 to 72 years old, with mucormycosis of the craniofacial areas. Patients were selected for study if the diagnosis of mucormycosis was established by means of biopsy, culture, nasal endoscopy and computed tomography (CT) scans or magnetic resonance (MR) images were available for review. All the patients were immun osuppressed in the form of diabetes mellitus, and two had CKD conditions. All patients had MR imaging with a 1.5-T system. Both T1- and T2-weighted images were obtained as well as T1-weighted images after intravenous injection of gadopentetate dimeglumine (0.1 mmol/kg).

All patients had CT scans available for review.

Images were evaluated for density, signal intensity, and contrast enhancement characteristics. The CT density was evaluated in non-enhanced images and compared with muscle/brain. The MR signal intensity was compared with grey matter on the T1- and T2-weighted images.

All studies were reviewed by two radiologists and the anatomic structures involved by the infection were defined by consensus. Clinical information about the presentation, management, and evolution of disease was obtained from medical history in all cases.

Pathophysiology

It originates in the paranasal sinuses and can frequently invade to orbital and cerebral regions. If detected and treated early, involvement can be limited to the nasal cavity and paranasal sinuses.

It is caused by fungi of order Mucorales which can include Mucor, Rhizopus, and Absidia spp. The fungi themselves are ubiquitous, subsisting on decaying vegetation and diverse organic material [12]. Given the opportunity, fungal spores can invade the nasal mucosa (which are often not phagocytised due to poor immune response). They then germinate, forming Angio invasive hyphae that cause infarction of the involved tissue, giving in a "dry" gangrene appearance.

Imaging Findings Of Mucormycosis

Radiographic Features

Can show varying degree of sinus opacification with most having a tumefactive nature [6]. They generally demonstrate a rim of soft-tissue thickness along the paranasal sinuses. Complete sinus opacification, gas-fluid levels and obliteration of the nasopharyngeal tissue planes can also occur.

Computed Tomography Findings

Paranasal mycosis manifests as two distinct entities, a benign type of non-invasive infection and the more serious type of invasive infection, which occurs in immunocompromised individuals and is characterized by its rapid onset, ability to invade tissues and cause destruction. It is important to distinguish the invasive disease from the noninvasive because treatment and prognosis are different in each. Early diagnosis is vital in these infections because delay in initiation of treatment can be life threatening due to the propensity of the fungi to invade adjacent blood vessels and embolize to distant organs including brain.

Computed tomography (CT) with axial and coronal sections is a highly accurate and non-invasive modality of accurately imaging sinonasal mycosis.

of the 40 patients who had CT scans available for review, 30 (75%) had isodense to muscle/brain lesions. Only 10 patient (25%) had hyperdense lesions relative to muscle/brain in the non-invasive portion suggesting secondary obstructive changes.

Pre and post contrast CT scan of the paranasal sinuses revealed a soft tissue density mass lesion arising from the right maxillary antrum with contiguous extension into the nasal cavity, causing destruction of its medial wall. The soft tissue mass lesion showed a small speck of hyperdensity . Bone windows revealed erosion of the medial wall of the right maxillary antrum, middle turbinate and the uncinate process of the ipsilateral side (Fig 1 & 2).

Mucosal thickening of the left maxillary and right ethmoidal sinuses was also present. There was no erosion of the anterior or lateral wall of the right maxillary antrum. Based on the CT findings, a diagnosis of fungal sinusitis was made. Patient underwent an extended antrostomy of the right maxillary antrum and the antral wash revealed necrotic mucosa and pus. Histopathological examination of the mucosa showed broad aseptate hyphae with right angled branching consistent with fungal hyphae resembling mucor.

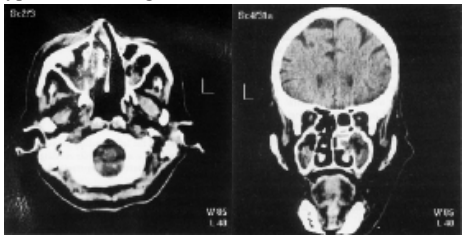


Fig.1:CT of paranasal sinuses (axial section) showing soft tissue mass lesion in right maxillary sinus with destruction of its medial wall

Fig. 2:CT of paranasal sinuses (coronal section) showing soft tissue mass lesion in right maxillary sinus extending to the ipsilateral nasal cavity with erosion of uncinate process and middle turbinate.

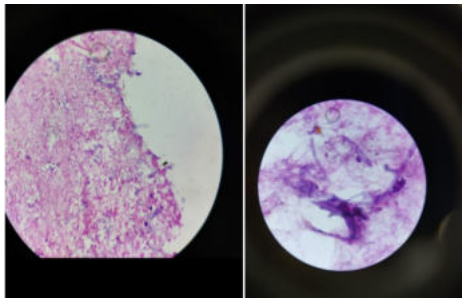


Fig.3-Histologic sections of periorbital tissue with multiple, broad nonseptate hyphae surrounded by inflammatory infiltrate.

MAGNETIC RESONANCE IMAGING

Most of the patients 16 out of 20(80%) had isointense lesions relative to brain in T1-weighted images. The signal intensity in T2-weighted images was more variable, with only four (20%) patients showing hyperintensity. The rest of the lesions were either hypointense or isointense in long retention time images.

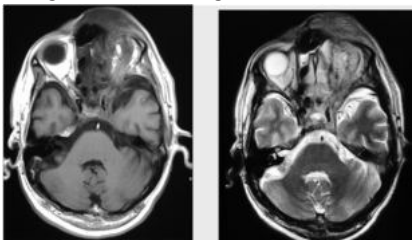


Figure 3: MRI T1 W –axial section: shows hypointense mucosal thickening of left ethmoid cells. Soft tissue swelling is seen anterior to left eyeball.

Figure 4: MRI T2 W –axial section: shows hyperintense left ethmoid cells. Soft tissue swelling is seen anterior to left eyeball. Left orbital hyperintense signal intensity lesion is seen extending along orbital apex into left cavernous sinus lateral to left internal carotid artery.

Enhancement Pattern

One patient out of five (20%) didn't have enhancement of his inflammatory process after the administration of gadolinium. Two patients (40%) had variable enhancement, with mixed non-enhancing and marked enhancing portions of their inflammatory lesions. One patient (20%) had mild enhancement and the remaining patient (20%) had no enhancement at all.

Signal characteristics on MRI of the sinuses and brain include:

T1: isointense lesions relative to brain in most cases (~80%)[5]
T2: variable with around 20% of patients showing high T2 signal [5]
Fungal elements themselves tend to have low signal on T2

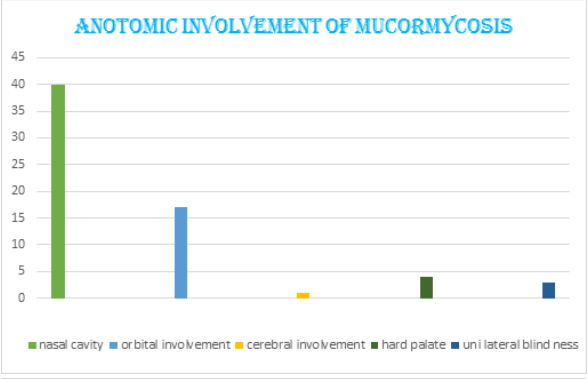
T1 C+ (Gadolinium): the devitalised mucosa appears on contrast-enhanced MR imaging as contiguous foci of non-enhancing tissue, leading to the black turbinate sign[10]

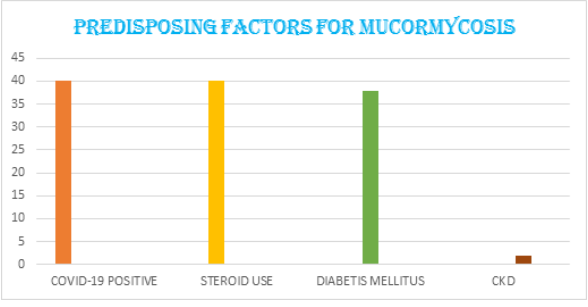
Anatomic Involvement

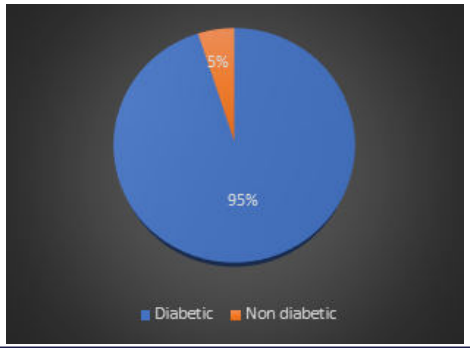
Total 40 patients (100%) have involvement affecting the nasal cavity, maxillary sinus, and ethmoid cells, 17 patients out of 40(42%) had orbital involvement,4 patients(10%) had hard palate involvement and one case had (2.5%)cavernous sinus thrombosisnoted.

Diagnostic nasal endoscopy revealed black-brown crust and tenacious pus filling up nasal cavity, erosion of turbinates and nasal septal perforation. Four patient showed erosion of hard palate and with abscess formation and loosening of tooth.

CE/MRI of PNS showed evidence of bony erosion, orbital involvement and cerebral involvement.







DISCUSSION

Upper airway Mucormycosis was first described in 1885 by Paltauf, who coined the term “mycosis mucorina”, which eventually became “Mucormycosis". In 1943, the more typical findings of advanced rhino cerebral mucormycosis, proptosis, and ophthalmoplegia were reported in a series of three fatal cases in patients with diabetic ketoacidosis." In 1955, Harris et al described the cure of mucormycosis.

Mucormycosis is a term used to refer to any fungal infections of the order Mucorales, which belongs to the class Zygomycetes.

Most pathogenic species are members of the family Mucoraceae. Rhizopusoryzae is the predominant pathogen and accounts for 60% of all forms of mucormycosis and 90% of rhinocerebral cases of mucormycosis. Apohysomyces elegans is the most recently recognised agent which causes mucormycosis in an immuno competent individual, Diabetics in ketoacidosis are disproportionately affected.

In our study 40 patients(100%) have previous history of covid positive with hospital admission and taking of steroid and oxygen therapy. 38 out of 40(95%) have type-II diabetis and only two patients non diabetic(5%) which are taking large dose of steroid and oxygen therapy in ICU with long period. 6 patients have denovadaibetis out of 38(15%). Two patients have CKD with diabetes.

A study has shown that dialysis and iron overload patients, an iron and aluminium chelator, are more susceptible to mucormycosis[5].

Other risk factors which increase susceptibility of an individual to mucormycosis include neutropenia, systemic steroid therapy, protein-calorie malnutrition, solid organ and bone marrow transplant, immunodeficiency, leukaemia, and intravenous drug abuse which involve the risk of injecting spores of Mucorales with drugs of abuse.

The presenting symptom is fever, which occurred in less than half of individuals, followed by nasal ulceration or necrosis, periorbital or facial swelling, or decreased vision; each occurred in approximately one third of cases.

Rigid endoscopic nasal examination should be performed on every immune-compromised patient who continues to have fever with or without localising signs despite appropriate broad spectrum parenteral antibiotics.

Nasal endoscopy findings of discoloration, ulceration, and eschar formation mainly involving middle and inferior turbinates, are suggestive of invasive fungal rhinosinusitis.

Almost 80% of patients develops a necrotic lesion on either the nasal or oral mucosa[1,6].

Early detection of mucormycosis is essential and incorporates clinical suspicion with culture and microscopic examination of the specimens. Potassium hydroxide–calcofluor white method can be used immediately on culture aspirate material. Potassium hydroxide dissolves tissues, and an optic brightener (calcofluor white) binds to the cell wall of the hyphae. Fungal cell walls, including septations, fluorescence are viewed using a fluorescence microscope[7].

A presumptive diagnosis of mucormycosis can be made histologically based on the broad ribbon-like hyphae, 10 to 20 µ across, haphazardly branched, and the absence or paucity of hyphal septations.

Once organism becomes invasive, it shows a marked predilection for vascular invasion.

CT scan is initial investigation of choice. Fine-cut (2 mm) slices in the axial and coronal planes should be obtained in high-risk patients. Intravenous contrast is used if intracranial or intraorbital extension is suspected, but it is not necessary for most initial evaluations. Severe unilateral thickening of the nasal cavity mucosa has been shown to be the most consistent finding on CT, suggestive of underlying invasive fungal sinusitis. It has also been suggested that infiltration of the preantral fat planes may represent the earliest imaging evidence of mucormycosis. CT scans are helpful in defining individual variations in sinus architecture and possible periorbital and intracranial spread.

MRI is superior to CT in delineating the intracranial extent of the

disease and it may have a role in evaluating patients who demonstrate signs of intracranial invasion: altered mental status , orbital apex syndrome, seizure, or stroke[2].It is evident that prompt diagnosis and early initiation of management in form of surgical debridement with systemic antifungal therapy and correction of underlying predisposing risk factors, if possible; gives most promising results leading to decrease in morbidity and mortality[6,8].

According to few recent studies if treatment with antifungal is initiated within 5 days of diagnosis of mucormycosis, survival was markedly improved compared to late initiation of treatment. (83% vs. 49% survival)[9,10]

Medical antifungal therapy for most patients who have mucormycosis consists of systemic amphotericin B at intravenous doses of 0.25 to 1.0 mg/kg/d to a total dose of 2 to 4 g over sixweeks. The use of amphotericin B is limited in some patients secondary to renal toxicity, and they may be candidates for liposomal amphotericin B at a concentration of 3 to 5 mg/kg/d.2

Moreover, there is evidence available that treatment of mucormycosis with liposomal amphotericin B was associated with a 67% survival rate, compared to 39% survival when patients were treated with amphotericin B[9,11]

Antifungals alone are not sufficient in the treatment of invasive fungal sinusitis as blood vessels thrombosis and tissue necrosis results in poor bio-availability of antifungals at site of infection. In our study, aggressive endoscopic sinonasal debridement using microdebrider was performed on all patients who have biopsy-proven disease or any patient suspected of having fungal invasion. Microdebrider assisted endoscopic surgery facilitated in removal of necrotic tissue and also shortened the duration of surgery. This slowed the progression of the disease, reduced fungal load, and also provided a specimen for culture and histopathologic diagnosis. Debridement of the involved sinuses or structures was extended until clear bleeding margins were noticed[18]

Complications of mucormycosis range from relatively benign to potentially fatal and are divided into three categories: local, orbital, and intracranial.

Local- mucocele, pott's puffy tumor, and osteomylitis.
Orbital- preseptal cellulitis, orbital cellulitis, subperiosteal cellulitis, orbital abscess ,and cavernous sinus thrombosis[2].

Intracranial - meningitis, epidural abscess, subdural abscess, intracerebral abscess, and venous sinus thrombosis.

CONCLUSION

Mucormycosis is a very rare disease. It rarely affects a healthy individual. Hence, it is important to consult your doctor if you suspect a mucormycosis infection. If you or anyone you know is recovering or has recently recovered from COVID-19, closely follow the signs and symptoms of mucormycosis. The key to effective treatment of mucormycosis is prompt detection, accurate diagnosis and immediate and aggressive treatment. Mucormycosis is an aggressive fungal infection which can lead to fatal complications in immunoco mpromised patients if not managed promptly and energetically. Our experience shows that early detection of sinonasal mucormycosis in immunocompromised patients enables prompt aggressive treatment. Powered endoscopic debridement is efficient and feasible, leading to excellent local control and which ultimately led to reduced morbidity and mortality.

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