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Case Report

Mucormycosis of oral cavity: a descriptive case report from a tertiary care hospital

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ABSTRACT

We presented an interesting case report of mucormycosis (*Rhizopus Oryzae*) in a recovered COVID-19 patient, its diagnosis and identification. The patient in past visited our institute with symptoms of COVID-19, she was a known case of tuberculosis and was taking ATT and diabetic (DM-2) patient. She was diagnosed COVID positive and successfully treated at our institution and discharged after recovering from the complications. After approximately two months of getting discharged from the hospital she again visited the post COVID clinic with symptoms of fever and numbness around face and on routine examination a blackish tissue like growth seen involving the hard palate and post nasal area. Mucormycosis (phycomycosis, zygomycosis) is an acute opportunistic infection generally develops secondary to debilitating diseases. But increased incidence was noticed in COVID-19 affected individuals. In head, neck and oral cavity the mold usually gains entry through respiratory route involving maxillary sinuses and oral cavity. The fungus causes great damage to the anatomical structures leading its necrosis. Hence an early diagnosis and surgical interventions is must for a good prognosis, decreasing morbidity and mortality. Extensive Research needs to be carried out in COVID patient specially treatment to prevent and reduce the cases of opportunistic infection in order to reduce its incidence and morbidity/mortality.

Keywords: COVID-19, Mucormycosis, Fungal infection, Opportunistic infection, H and E stain

INTRODUCTION

In the past one and half year outbreak of coronavirus disease (COVID-19) has spread rapidly and caused havoc on a global scenario.[1,2] Every preparation by any country and its health sector was proved insignificant and affected the general population in large. The classical picture of COVID-19 may vary in severity from very mild to moderately symptomatic to life threating pneumonia caused by bacterial or fungal superinfections associated with COVID-19.[3,4]

There have been reports of the development of severe opportunistic infections such as gram-negative bacteria, *Staphylococcus aureus*, oropharyngeal candidiasis, *Pneumocystis jiroveci* pneumonia (PCP), pulmonary aspergillosis, bloodstream candida infections in patients undergoing COVID-19. Opportunistic infections are especially common in patients who, apart from the current COVID-19 disease, also have other comorbidities such as diabetes or COPD.

In spite of all efforts, there is no definitive treatment protocol for the disease. However, prevention and symptomatic management are the best options.

The clinical presentations of mucormycosis are classified on the basis of anatomical localisation such as rhino-orbital-cerebral (ROCM), pulmonary, gastrointestinal, cutaneous, renal, and disseminated mucormycosis.[3,4] Patients with diabetes mellitus, haematological malignancy and chemotherapy, haematopoietic stem cells

and solid-organ transplant recipients on immunosuppressive therapy, with iron overload, on peritoneal dialysis, extensive skin injury, human immunodeficiency virus (HIV) infection and voriconazole therapy are at increased risk of acquiring mucormycosis.[3-5]

Secondary infections are a well-described complication in influenza, SARS, MERS and other respiratory viral illnesses. But super-infections and co-infections in COVID-19 pneumonia are still under exploration.[6] Secondary infections are reportedly common in hospitalized, severely ill COVID-19 patients, encompassing between 10 and 30% of cases, fungal being 10 times more common.[6] As the nature of the disease is still not completely unveiled, it can't be confirmed if it's a complication of the disease or its management.

Uncontrolled diabetes mellitus is the most common underlying disease associated with mucormycosis in India.[5-7]

The incidence rate of mucormycosis globally varies from 0.005 to 1.7 per million population.[8] Whereas, in Indian population its prevalence is 0.14 per 1000, which is about 80 times higher than developed countries.[9] The fatality rate of mucormycosis is 46% globally.[10] However, factors like intracranial or orbital involvement, irreversible immune suppression increases fatality to as high as 50% to 80%.[11] A high suspicion for this disease must be considered in patients who are immunocompromised. Tissue necrosis, a hallmark of mucormycosis is often a late sign.[10] Early diagnosis and treatment are essential. Delay of a week often doubles the mortality from 35% to 66%.[10]

CASE REPORT

A 42 year old female was admitted to our institution, a tertiary care centre with (past history of known COVID-19 positive about 12 months back) and a known case of pulmonary tuberculosis (on ATT) and DM-2. She presented with a high-grade fever, body ache, cough, numbness over face and loss of appetite with difficulty in swallowing for last 5-6 days. Patient was evaluated at post COVID ward by the concerned specialists and on local examination a black mass like lesion seen protruding from posterior nostrils. Upper alveolar and half of the hard palate was necrosed with normal tongue and oropharynx. Nostrils were filled with crust bilaterally. On diagnostic nasal endoscopy a fungating discharge seen which was removed with inferior turbinate. The removed mass was sent for 20% KOH and HPE examination. surgeons first clinical impression was hard palate osteomyelitis. Nasal endoscopic biopsy was taken from right nostril under local anaesthesia. FESS was done, lesion removed and nasopharyngeal swab was sent for RT-PCR which came negative. The patient was shifted to COVID ward and detailed clinical and physical evaluation was done. The patient was known diabetic (from past 5 years) and currently on ATT for the treatment of pulmonary TB. After admission routine biochemical test revealed deranged investigations: TLC 22400/ml, neutrophil count 92.4% (35-66%), lymphocyte count 5% (24–44%), fasting blood sugar (FBS) 186 mg/dl (70-110 mg/dl), post-prandial blood sugar (PPBS) 244 mg/dl (110-140 mg/dl), serum interleukin-84.64 pg/ml (<6.4 pg/ml), CRP >60 mg/l (0-6 mg/l), D-dimer 460 ng/ml (0-500 ng/ml) and PT was 56 seconds. The patient was conscious and maintaining SpO_2 at 96% by normal breathing.

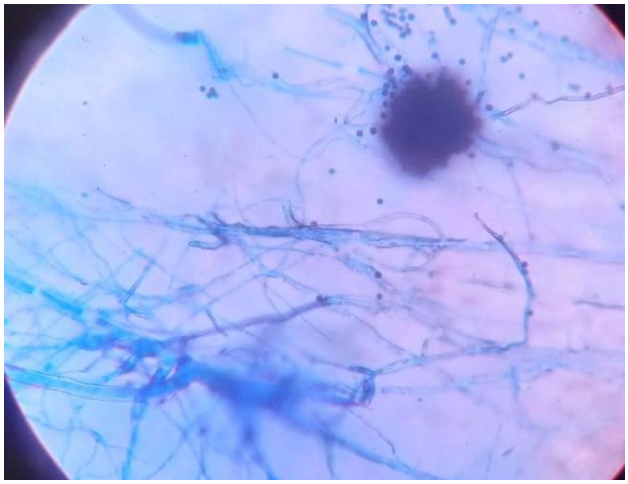

Figure 1: Mucor on lactophenol cotton blue staining, showing broad aseptate hyphae, with sporangium and aggregation of sporangiospores (original magnification-160).

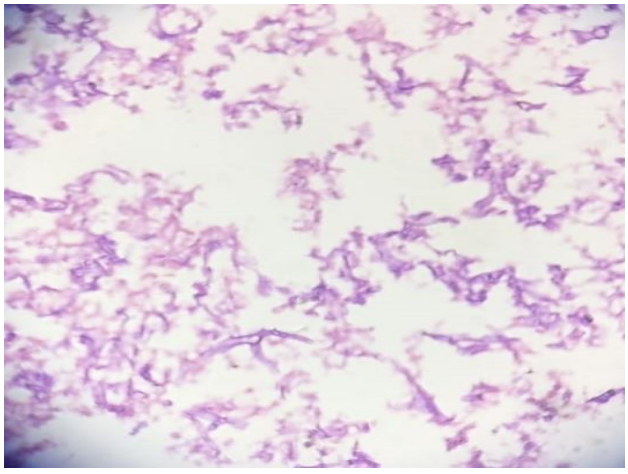

Figure 2: Tissue section, showing mucor on hematoxylin and eosin stain (H and E) with broad aseptate hyphae (original magnification-160).

Microbiological and histopathological studies were performed on tissue biopsies. Microbiological specimen was inoculated on Sabouraud's agar, incubated at 30 °C and the sample was examined microscopically. Fungal growth was studied macroscopically at 37 °C.

Lactophenol cotton blue stain was used for the examination preparing a wet mount. It was composed of two most important components such as methyl blue and lactophenol. Methyl blue is a histological stain which stains collagen blue in tissue sections, and lactophenol is a mixer of four components such as phenol, lactic acid, and glycerol in water. Where phenol helps to kill any microorganisms, lactic acid preserves fungal structures and glycerol inhibits the cellulolytic activity of the fungus. When preparing the microscopic slide, methyl blue stains the chitin in the fungal cell walls, as a bright cerulean colour and lactophenol acts as a mountant.

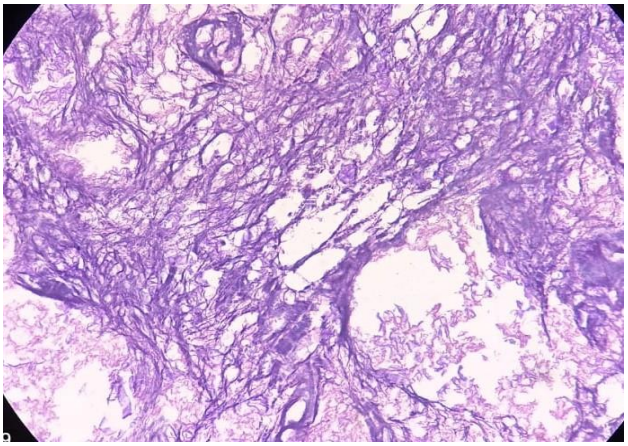

Figure 3: Tissue section, showing mucor on hematoxylin and eosin stain (H and E) with broad aseptate hyphae (original magnification-40).

On microscopic examination colonies of *Rhizopus oryzae* was identified, which was aseptate, branching broad based fungal hyphae and having tendency of haem invasion.

Histopathological examination of tissue on H and E staining also confirmed the presence of fungal filaments against the background of necrotic tissues and inflammatory cells.

DISCUSSION

Mucormycosis is a fungal infection caused by fungi in the order *Mucorales*. Once deposited, the fungus grows branch-like filaments which invade blood vessels, causing clots to form and surrounding tissues to die.[12] Mucorales are ubiquitous thermotolerant saprophytic fungi found in decaying organic matter (like bread), hospital wards, dust and soil samples.[13,14] An ecological study on *Mucorales* in Indian soils documented the isolation of pathogenic species such as *Rhizopus*, *Lichtheimia*, *Cunninghamella*, *Rhizomucor* and *Apophysomyces*.[13] Similarly, aeromycological analysis in a community and hospital setting from India reported the isolation of pathogenic *Mucorales* in air samples.[14]

Without population-based estimates, it was difficult to determine the exact incidence and prevalence of mucormycosis in the Indian population.

The mold usually gains entry into the host through the respiratory tract and exhibits a remarkable affinity for arteries and grows along internal elastic lamina causing thrombosis and infarction.[15,16] The progression of the disease from nose and sinuses is either direct or through vascular occlusion. Intracranial involvement also occurs by invasion through superior orbital fissure, ophthalmic vessels, cribriform plate, carotid artery or possibly via a perineural route.[17,18] Studies have shown an increased incidence with fairly severe course of mucormycosis, in patient with history of COVID-19. The most common site was sinuses, introrbital involvement and intracranial involvement. Mortality rate is very high varying with types of mucormycosis, pulmonary mucormycosis: 50-70%, rhinocerebral: 30-70%, CNS involvement: >80%, disseminated: >90%, AIDS: almost 100%.

CONCLUSION

The exact prevalence of mucormycosis in India is undetermined, though the exact prevalence is much higher than the developed countries. Factor contributing to exposure to co-infections is treatment with mechanical ventilation, antibiotic therapy, monoclonal antibodies and the use of corticosteroids. Especially corticosteroids which act as a double-edged sword are commonly used to treat serious form of COVID-19 disease and reduce the damage caused by the own body's immune system during SARS-CoV-2 infection. Unfortunately, corticosteroids are also immunosuppressive and increases blood sugar levels in both diabetic and non-diabetic patients. Both of these effects are now believed to contribute to mucormycosis. In Indian context a considerable number of patients are ignorant of their diabetes status till they acquire mucormycosis. Though uncontrolled diabetes is a common risk factor in all types of mucormycosis, it is significantly associated with ROCM type. Other emerging risk factors of mucormycosis are pulmonary tuberculosis, chronic kidney disease, and critically ill patients.

Health care professionals should pay special attention and be more vigilant for the probability of invasive mucormycosis in COVID-19 patients. More research is needed for better prevention and management of opportunistic infections in COVID-19 patients and review of the current treatment protocol, so that the number of active cases can be reduced. The prophylactic treatment protocols need to be assessed and guidelines need to established in order to reduce morbidity.

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