RISING INCIDENCE OF MUCORMYCOSIS DURING COVID 19: A REVIEW

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Abstract:
During this pandemic of COVID-19, we discover that patients with COVID-19 are at increased menace of fungal infections. As this novel disease spreads worldwide, new challenges arise in the clinical practice with the growing risk of co-infections is a significant threat not only to the health systems but also to patient's lives. Although there is still not enough published statistical data, co-infections in COVID-19 patients found that a significant number of patients hospitalized with COVID-19 developed secondary systemic mycoses that led to sever complications and even death. This review will discuss incidence of rising cases of mucormycosis during pandemic.

Keywords: COVID-19, Gastrointestinal, Mucormycosis, Pandemic & Pneumonia.

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INTRODUCTION:

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is causing the pandemic covid-19. This current global issue is associated with a wide range of disease patterns, ranging from mild to life-threatening pneumonia.[1] The existence of a wide range of fungal co-infections may be related to preexisting morbidity (diabetes mellitus, lung disease) or may develop as a hospital-acquired infection such as ventilator-associated pneumonia.

Pandemic has rapidly spread to 212 countries and caused nearly 5 million laboratory-confirmed cases and more than 310,000 deaths globally.[2] COVID-19 patients always have immunosuppression with a decrease in CD4 +T and CD8 +T cells.[3] Critically ill patients admitted to the intensive care unit (ICU) with more extended stays were more likely to develop fungal co-infections.[4] It is crucial to notice that COVID- 19 patients can develop fungal infections.[5]

Mucormycosis or Zygomycosis, also called Phycomycosis, is an uncommon, aggressive, invasive, rapidly progressive, and life-threatening fungal infection. According to Paltauf (1885), it has a high mortality. Imaging techniques are not typically diagnostic. Even their cultures are not reliable. The histological examination obtains a definitive diagnosis. Treating underlying diseases and aggressive medical and surgical management is insufficient, leading to an extension of the infection and death. [6]

Due to the rich vascularity of anatomy in the maxillofacial region, there are a few incidences of opportunistic infections.[7] Mucormycosis can evade this defense mechanism because of their potential virulence.[8] Attributable risk factors are uncontrolled diabetes mellitus, Acquired Immune Deficiency Syndrome (AIDS), long-term steroid therapy, hematological conditions like leukemia and lymphomas, renal failure.[9] Mucormycosis can gain entry into the body through the nose, breached skin, and tooth extraction sockets. Primary infection sites

include the skin, ears, gastrointestinal tract, and there could be disseminated forms involving multiple locations like pulmonary and rhino -orbito-cerebral.[10] Depending on the site of infection and underlying predisposing factors, mortality rates may vary from 10% to 100%. 7 Early diagnosis and immediate intervention are essential for such patients. Treatment includes control of the underlying risk factors, antifungal therapy, surgical debridement, supportive therapy, and surgical or prosthetic rehabilitation. It is essential to the restoration of quality of life to the premorbid state.11 In this article, we will review the incidence of the rise of mucormycosis cases in covid -19 positive patients.

METHOD:

We did the literature search in PubMed and Google Scholar to analyze the reported cases of mucormycosis during Covid-19. Publications with relevant information based on their abstracts and, or full text are included in this article. Only reported cases of Mucormycosis during pandemic were included. Cases with other fungal infections and case reports before the pandemic were excluded.

RESULTS:

We reviewed literature on the subject (MUCORMYCOSIS COVID -19) over the past one year (December 2019-current date). There were case reports of mucormycosis with orbital compartment syndrome, rhino orbital mucormycosis, gastrointestinal mucormycosis, pneumonia, and a middle cerebral artery infarct.

Salil Mehta, Abha Pandey reported a 60-year-old male patient's history of severe breathlessness, pyrexia, tachypnea, and generalized malaise with longstanding diabetes (> 10 years) on oral anti hypoglycemic tablets. The relevant physical examination revealed bilateral crept at the lung bases with a normal cardiovascular and neurological exam; a positive nasopharyngeal swab was confirmed by chest CT scan. He also presented with Bilateral lid edema with right eye prominence. MRI of the brain showed orbits, paranasal sinuses, a soft tissue swelling in the right malar, premaxillary, and retrobulbar regions, preliminary diagnosis of right orbital cellulitis was made. After ophthalmic evaluation, clinical and MRI findings suggested invasive fungal infection, likely mucormycosis. It started with antifungal therapy, but this ventilated patient continued to deteriorate. Despite all preventive measures, he died on day six of this admission.[11,12]

Epifanio Silvino do Monte Junior et al. have reported a case of an 86-year-old male patient with a history of arterial hypertension who was admitted to the emergency room with acute diarrhea, cough, dyspnea, and fever that started five days before admission. The collected throat swab from the patient confirmed COVID-19. The patient presented melena and severe anemia with mild abdominal tenderness within five days of ICU admission. Two giant gastric ulcers with dirty debris and a deep hemorrhagic base without active bleeding located in the greater and lesser curvature. Pathological examination confirmed mucormycosis. Unfortunately, the patient dies one week following hospitalization, 36 hours after the EGD, and before a diagnosis was established.[13]

Hanley et al. reported a case of a 22-year-old male with COVID-19 pneumonia and a middle cerebral artery infarct. This disseminated mucormycosis involving the lungs and brain was discovered during a postmortem study.[14]

Werthman-Ehrenreich reported the case of a female 33-year-old who showed signs of left-sided ptosis and proptosis with altered sensorium. She also had underlying diabetic ketoacidosis with a positive COVID-19 nasopharyngeal swab. Facial imaging showed maxillary and ethmoidal sinus mucosal thickening. The brain MRI showed multiple areas of infarction and ischemia. The nasal biopsy and subsequent culture showed mucor presence. All findings confirmed the diagnosis of the invasive mucor infection. The author concluded that early identification of fungal co-infections might significantly reduce morbidity and mortality.[15]

DISCUSSION:

Mucormycosis is a rare opportunistic fungal infection characterized by infarction and necrosis of host tissues resulting from the vasculature invasion by hyphae. This disease usually presents with signs of acute sinusitis, fever, nasal congestion, purulent

nasal discharge, and headache. Sinuses involvement with contiguous spread to adjacent structures such as the palate, orbit, brain results in clinical symptoms. It can spread from the ethmoid sinus to the frontal lobe results in obtundation. Clinical suspicion and early treatment with surgical debridement are vital in preventing the morbidity of this often-fatal condition. The clinical hallmark of mucormycosis is vascular invasion resulting in thrombosis and tissue infarction/necrosis. The most common clinical presentation of mucormycosis is a rhino- orbital-cerebral infection. It is believed to be secondary to inhalation of spores into the paranasal sinuses of a susceptible host. Predisposing mucormycosis factors are diabetes, systemic corticosteroid use, neutropenia, hematologic malignancies, stem cell transplant, and immunocompromised individuals. Seventy percent of rhino-orbital-cerebral mucormycosis cases have been found with diabetes mellitus. They also developed ketoacidosis at the time of presentation. The major diagnostic modalities for mucormycosis are histopathology, direct microscopy, and culture from clinical specimens.8 A complex interplay of factors may lead to an increase in the incidence of secondary infections. Due to their impact on morbidity and mortality is being recognized.[14]

In a recent review, 8% of patients had secondary fungal infections during hospital admission with the widespread use of broad-spectrum antibiotics.[15]

In India, guidelines recommend intravenous methylprednisolone 0.5-1 mg/kg/day for three days in moderate cases. The dose needs to increase up to 1-2 mg/kg/day for three days in severe cases.[16] The National Institute of Health recommends the use of dexamethasone (6 mg per day for a maximum of 10 days) in ventilated patients or require supplemental oxygen, excluding milder cases.[17] There are specific pathophysiologic features of COVID-19 that may permit secondary fungal infections to cause widespread pulmonary disease and the following alveoli-interstitial pathology. That may advance the risk of invasive fungal infections.[18] The immune dysregulation associated with COVID-19 may show reduced numbers of T lymphocytes- CD4+T and CD8+T cells. This leads to alteration in innate immunity.[19] New Delhi (India) reported 15 admitted patients with COVID-19 infection developed bloodstream candida infections. Out of which 10 had a fungal infection.,[20] White et al. screened 135 adults with COVID-19 illness and reported an incidence of invasive fungal infections of 26.7% (commonly aspergillosis (14.1%), or yeast, usually candida (12·6%). Patients with invasive fungal diseases had higher mortality (53% with vs. 31% without). This was significantly reduced by appropriate therapy. Corticosteroid therapy with a history of chronic pulmonary disease was associated with a higher risk of invasive fungal infection.[21] Similarly, high incidences have been noticed in Pakistan (23/147, 15.6%) and Italy (30/108, 27.7%). The authors suggested that the development of invasive fungal infections alters the natural history of the disease.[22, 23] Song et al. have presented a procedure for the early diagnosis and management of common invasive fungal infections (aspergillus, candidiasis, cryptococcosis, and mucormycosis).[24, 25]

The incident rate of mucormycosis varies from 0.005 to 1.7 per million population.[26,27] The global mucormycosis case fatality rate is 46%.[28] Mucormycosis is challenging to diagnose. Early diagnosis and treatment are essential. A delay of even six days is associated with a doubling of 30- day mortality from 35% to 66%. Despite early diagnosis and aggressive combined surgical and medical therapy, the prognosis for recovery from mucormycosis is poor. High suspicion must be considered in immunocompromised patients. It shows unilateral facial pain or swelling, orbital swelling, or proptosis in high-risk individuals. Tissue necrosis is a hallmark of mucormycosis. This may be consequential from angioinvasion and vascular thrombosis. Once the diagnosis is considered, empiric antifungal treatment should be started. A prompt surgical opinion should also be sought. Orbital compartment syndrome (OCS) results from an expansile process within the closed compartment of the orbit leading to increased orbital pressure.

This may result in ischemia and vision loss. It is an ophthalmologic emergency that requires lateral canthotomy and inferior cantholysis to decompress the orbit. Delay in care can lead to permanent blindness. This diagnosis should be suspected in patients presenting with acute proptosis, elevated

intraocular pressure, rapid vision loss, ophthalmoplegia, fixed dilated pupil, or afferent pupillary defect. OCS causes can be retrobulbar hemorrhage (from trauma, vascular malformations, tumors), cellulitis, orbital malignancy, or previous orbital surgery.[29]

SUMMARY AND CONCLUSION:

The COVID-19 is associated with a significant incidence of secondary infections, both bacterial and fungal, probably due to deterioration of immunity. The extensive use of steroids/monoclonal antibodies/broad-spectrum antibiotics as part of COVID-19 treatment may lead to fungal diseases. Clinicians should be aware of the possibility of invasive secondary fungal infections in patients with COVID-19 infection, especially in patients with preexisting risk factors. They should enable early diagnosis and treatment with the subsequent reduction of mortality and morbidity. Monitoring the use of therapeutic agents to achieve a therapeutic effect at the lowest dose and shortest durations. The use of broad-spectrum antibiotics, especially in the absence of infection, should be re-evaluated. This article reviews the data available on various platforms. A further detailed review of the published and unpublished cases should understand better mucormycosis associated with Covid-19

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