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Mucormycosis with Covid-19: A Review on Clinical Manifestations and Treatment

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Abstract

Mucormycosis is a dangerous fungal disease caused by a group of moulds identified as mucormycetes. Mucormycosis is more commonly observed in patients with underlying medical conditions such as; diabetic acidosis, acute leukemia and patients under corticosteroids or cytotoxic drugs. Depending on the patient's, mortality rates can be up to 100%. Initial diagnosis and rapid treatment can decrease the mortality and morbidity of this dangerous fungal disease.

Keywords: Covid-19; diagnosis; management; Mucormycosis.

Introduction

COVID-19 infection is a new infection affecting globally with systemic and oral manifestations at various levels. World Health Organization (WHO) on February 11, 2020, stated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as coronavirus disease (COVID-19). Lungs being the primary site of infection, the morbidity and mortality of COVID-19 disease are rising with opportunistic infections of fungi, viruses and bacteria. The symptoms range from flu-like symptoms to pneumonia. SARS-CoV-2 is spread via naso oral cavity to lungs by means of droplets and aerosols. After inhalation, the S protein of the SARS-CoV-2 binds with the ACE2 receptor, causing the virus entry into the host cell.[1,2] Severe corona virus disease (COVID-19) is presently managed with systemic glucocorticoids. However, glucocorticoids in covid patients can increase the risk of secondary infections, such as fungal infection.[3]

Recently secondary to this infection seen is Mucormycosis, which is observed in few patients with covid-19 and recognized throughout the world. Many

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patients who have recovered from COVID-19 have in recent times diagnosed with black fungus, yellow fungus or mucormycosis disease. Mucormycosis being a fungal infection earlier known as zygomycosis is caused by mucormycetes, affecting the lungs, sinuses, or skin, spreading through inhalation of spores from the air or via penetration of skin through a burn or cut. Mucormycosis even though rare disease but is overwhelming and more frequently seen in uncontrolled diabetic patients.[1] If the disease progresses unchecked, 50-80 percent of patients will die.[4] According to Brown, after candidiasis and aspergillosis infections, mucormycosis ranked as 3rd common opportunistic fungal disease.[5]

In 1885 Paltauf first defined zygomycosis or Phycomycosis and later it was called mucormycosis by R.D. Baker. by definition Mucormycosis is "an insidious fungal infection caused by members of Mucorales and zygomycotic specie". [5,6,7] This fungal disease falls under the common saprobes that are establish in rotten matter or soils.[6,8] Since the last few months, there is continuous raising of mucormycosis cases in patients with COVID-19. Mucormycosis can also involve skin, lungs, gastrointestinal tract, heart, kidney, and mediastinum.[9]

Prevalence

Mucormycosis affects all age groups and both the genders with the prevalence varying from 0.005-1.7 per million populations worldwide .[7]pre-existing medical/systemic condition of the individual decides its clinical appearance. The most communal form is Rhino-orbito-cerebral Mucormycosis (44–49%) which being subsequently cutaneous (10 to 16%), pulmonary (10 to 11%) types. The incidence of Mucormycosis is ranges from 0.2 to 1.2%. in patients with renal transplants.[1]

Etio-pathogenesis

Inhalation or ingestion of spores, and percutaneous injection of spores, are most commonly deep tissues involved by mucorales. In a healthy individual its ear entry to lung or coetaneous tissues is eliminated by means of oxidative metabolites and cationic peptides as a first line of defense mechanism. Due to decreased defense mechanisms and increased availability of micronutrients in diabetic patients, mucormycosis can damage tissues and possibly serious illness.[6]the infarction of the vessels is caused by invasion of the organism to the blood vessel there by initiating clotting, leading to infarction and ultimately tissue death. Growth of organisms is facilitated by tissue necrosis with raise in pH. [1]

Predisposing factors

Common predisposing factors for Mucormycosis are; diabetes mellitus (uncontrolled), acute leukaemia and those taking corticosteroids or cytotoxic drugs, post-transplant/malignancy, ketoacidosis, neutropenia, on chemotherapy, Voriconazole therapy.[4,7,11,12]

Clinical Manifestations

In humans this infection occurs mainly in Superficial and Visceral forms. The characteristic superficial form is seen in finger nails, external ear and skin. Whereas, visceral forms in gastrointestinal, pulmonary, and rhino cerebral types. The route of entry is through either cutaneous or respiratory route.[6]Mucormycosis can be classified into 6 types: rhinoorbital-cerebral, pulmonary, disseminated, cutaneous, gastrointestinal, and miscellaneous based on anatomic site and clinical appearance.[1]

Mucormycosis commonly presents with a fever, headache, pain, altered mental status, redness around eyes and/or nose, double vision, shortness of breath, coughing, proptosis, nasal discharge, sinusitis, necrotic nasal concha, loosening of teeth, and necrotic ulcers in nasal cavity, palate. Intraorally, large ulceration and necrosis can be seen with most common site of involvement being palate, lip, gingiva, and alveolar ridge.[1,11,13,14]A case of Rhino-Orbital Mucormycosis related with covid-19 was published.[2]

Rhinocerebral Mucormycosis

It infects the paranasal sinuses with consequent inhalation of spores, and later can extend to the brain resulting in successive infection of sinuses, nose and eyes appropriately giving the term Rhinocerebral Mucormycosis. The prevalence ranges from 33 to 50% mostly characterized by palatal and sinus necrosis which further extension in to the orbit. Symptoms like fever, accompanied by blindness, exophthalmos, bleeding from nose, and facial paralysis can be seen.[6]

Diagnosis

The diagnosis of mucormycosis is challenging. Use of Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) imaging is promising to diagnose the features of sinusitis.[1] CT of the chest could recognize infiltrates suggestive of Mucormycosis.[10] Fungal culture and staining are advised for diagnosis mucormycosis.[6]

Histopathological Features

Various laboratory techniques such as; PAS stains, culture, calcofluor, Gomori methenamine silver stain is advised to detect mucor. Histological examination of the affected tissue can show, extensive necrosis along with numerous large branching pale-staining hyphae with branching at right or obtuse angles. The culture frequently shows characteristic ovoid or round shaped sporangia. Necrotic tissue containing hyphae (thin wall/infrequently septae and non - parallel sides) might be seen with signs of angio – invasion and infarction.[6]

Prevention

Regular use of masks, by wearing shoes, long sleeve shirts, long trousers, and maintenance of personal hygiene along with scrub bath is advised.[11]Optimum blood sugar control in COVID-19 patients, especially those on steroids is recommended. Use steroids only for COVID-19 patients with hypoxemia, avoid unproven immunosuppressive agents for treating COVID-19. [13]

Treatment

Treatment requires multidisciplinary approach with Microbiologist, Internal Medicine Specialist, Neurologist, Ophthalmologist, ENT Specialist, Dentist, and Biochemist.[11] Management of mucormycosis should always be directed towards early diagnosis of the disease, a reversal of underlying predisposing factors, and early administration of systemic antifungal therapy and broad surgical debridement of infected tissue.[9]

As an initial therapy includes lipid formulation of amphotericin B (Liposomal amphotericin B) and amphotericin B lipid complex (ABLC). Hyperbaric oxygen (HBO) therapy can be given as an adjuvant remedy, to increase oxygen saturation level and upturn vascularity.[1,6,15] Newer triazoles, namely posaconazole and isavuconazole, have better in vitro activity against Mucorales. Amphotericin B deoxycholate (D-AmB)- 1.0-1.5 mg/kg/day for 3-6 weeks can be advised.[15]

Prognosis

The prognosis largely be influenced by the disease condition and succeeding effective treatment. Survival percentage differs with foci of the infection and rhino cerebral Mucormycosis.[6]

Conclusion

Mucormycosis appearance can be very violent and having a disquieting mortality rate. Hence early and prompt early diagnosis with timely treatment can helps to reduce the morbidity rate. Medical and dental practitioners should be conscious and able to identify about COVID-19 with secondary infection such as Mucormycosis as early as possible.

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