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Paranasal Mucormycosis: A Literature Review

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Abstract

Mucormycosis has wreaked havoc amongst the COVID-19 pandemic, crippling the patients already battling the virus. It is therefore of utmost importance that the facts be separated from the myths in order to tackle this problem from the roots. The basis of this current review article to compile all the information regarding the facts about mucormycosis in one place so as to get a better understanding of the disease process and hence work towards reducing patient morbidity and mortality.

Keywords: COVID-19, Facts, Mucormycosis, Opprotunistic Infection

1. Introduction

Even as our country battles the devastating second wave of coronavirus pandemic, mucormycosis has emerged as a fatal enemy. Although not entirely unknown, it was a rare finding in the pre COVID era. Although a variety of complications have been reported during and post COVID infection, mucormycosis remains the most serious opportunistic fungal infection, rapidly spreading and causing necrosis and infarction of the host tissue[1]. The prevalence of mucormycosis in India is approximately 0. 14 cases per 1000 population, about 80 times the prevalence in developed countries[2]. As the cases of mucormycosis are on a rise, we must be equipped with the right knowledge about the different aspects of mucormycosis. Hence the objective of this current review is to compile and present the facts related to mucormycosis which will aid in dispelling myths and present factual information.

Various clinical forms of mucormycosis have been reported with pulmonary, cutaneous, gastrointestinal, rhinocerebral, central nervous system, and disseminated to name a few. The commonest site for occurrence of oral mucormycosis is usually in the paranasal sinuses or nasal areas. Serious involvement of paranasal sinuses may lead to palatal necrosis and/or ulceration[3,4].

2. Etiology and Predisposing Factors

Mucormycosis can be identified on bread mold, soil, decaying vegetation, or animal manure. Cultures of swabs obtained from the oral cavity, nasal cavity, throat, and stools of healthy persons may show mucormycosis. The fungal spore germinates to form hyphae in the host system upon entering tissues. A host of saprophytic fungi like Rhizopus, Mucor, Cunninghamella, Rhizomucor, Saksenaea, Apophysomyces, or Lichtheimia contribute to the etiology of mucormycosis. Rhizopus is the chief pathogenic mycotic organism in cases with rhinocerebral mucormycosis[5]. Mucormycosis infection of the sinuses typically affects immunocompromised individuals with an impaired neutrophilic response like those with uncontrolled diabetes mellitus, acquired immunodeficiency syndrome, iatrogenic immunosuppression, and hematological malignancies, and those who have undergone organ transplantation[14].

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3. Mucormycosis Spurt Post COVID

In the absence of an effective vaccine or antiviral therapy for the treatment of covid 19, supportive care has played a vital role. Glucocorticoids have been shown to reduce mortality in hypoxemic patients with COVID-19[6]. Steroids have proven to be a double-edged sword in the treatment of COVID-19. Where on one hand it has helped immensely get the cytokine storm under control on the other hand it has wreaked havoc on the sugar levels and immune system, triggering a cascade of untoward events. Moreover, the immune dysregulation caused by the virus and the use of concurrent immunomodulatory drugs such as tocilizumab has further increased the risk of opportunistic infections in COVID-19 patients[7,8]. Inappropriate glucocorticoid use has become one of the contributing factors which have led to an increase in mucormycosis cases in India[9].

The prevalence of paranasal mucormycosis is also on the rise post COVID probably due to systemic immune alterations due to Coronavirus infection[10]. It is hypothesized that SARS- CoV-2 infection may affect CD4+ and CD8+ T- cells, which are highly involved in the pathological process of COVID-19 infection. Severe COVID-19 cases present with a reduction in the absolute number of lymphocytes and T- cells, which is also associated with the worst outcomes. Mucorales- specific T- cells (CD4+ and CD8+) produce cytokines such as interleukin (IL) 4, IL-10, IL-17, and interferon-gamma (IFN-γ) that damage the fungal hyphae[11]. Such specific T- cells were seen only in patients affected by invasive mucormycosis, and they concluded that they could be a useful surrogate diagnostic marker of invasive fungal disease. While it may be speculated that lymphopenia could increase the risk of developing invasive mucormycosis, however, the recovery of lymphocyte count could improve the adaptive immune system and induce the production of Mucorales-specific T-cells, which might have a role in controlling the invasive infection[12]. Impaired phagocytic functions increase the hyphae levels in the blood vessels, which results in ischemia, thrombosis, and finally infarction and tissue necrosis. In diabetic patients with ketoacidosis, the binding of iron to transferrin is inhibited and results in elevated iron levels, which promotes the growth of mucormycosis[13].

4. Clinical Features

Mucormycosis is characterized by the presence of hyphal invasion of sinus tissue and a time course of fewer than four weeks[15,16]. Clinically, rhinocerebral mucormycosis can present with atypical signs and symptoms similar to complicated sinusitis, such as nasal blockage, crusting, proptosis, facial pain and edema, ptosis, chemosis, and even ophthalmoplegia, with headache and fever and various neurological signs and symptoms of intracranial extension are present[17,18]. A black eschar is often seen in the nasal cavity or over the hard palate region but is not characteristic[19,20]. The oral presenting symptoms of rhino orbito cerebral mucormycosis include nonhealing extraction sockets, mucosal necrosis, buccal, palatal ulcers, and sinuses with no evidence of periapical or periodontal lesions. Some patients may present with unexplained toothache, mobility without significant radiographic evidence of bone loss along with exposed necrotic maxilla.

Without early diagnosis and treatment, there may be a rapid progression of the disease, with reported mortality rates from intra-orbital and intracranial complications of 50–80 percent[21]. Unfortunately even with prompt diagnosis, treatment of underlying diseases, and aggressive medical and surgical intervention, the management is often not effective, leading to an extension of the infection and ultimately death[22].

5. Diagnosis

A lack of clinical suspicion and difficulty isolating the causative fungi might contribute to the underdiagnosis of mucormycosis[23]. Pulmonary mucormycosis is now being increasingly diagnosed, and the case fatality has improved over time[24]. Although a high degree of clinical suspicion is required to diagnose pulmonary mucormycosis[25], confirmation of the clinical diagnosis requires microscopic examination of the biopsied tissue[26,27].

5.1 Histopathology

The histopathological examination of the affected tissue shows a broad, non-septate type of hyphae with the pathognomonic nature of hyphae branching at right angles. The hyphae are observed with a deeper connective tissue invasion. The special staining method, Grocott-

Gomori methylamine silver stain helps in confirmation of the non-septate hyphae. Some other features may also include mycotic infiltration of blood vessels, vasculitis with thrombosis, tissue infarction, hemorrhage, and acute neutrophilic infiltrate[28]. Cases with bony perforations may show the presence of fungal organisms in marrow areas. Sometimes the cytological specimens collected from cases with histological diagnosis of mucormycosis may show the absence of organisms in fungal culture, hence a thorough clinical examination of the oral cavity in invasive lesions is recommended to achieve a clinical diagnosis. All mucormycosis cases don't show the classical diagnostic interpretation in imaging studies like radiographs, computerized tomography (CT), magnetic resonance (MR), culture studies, or serological tests. Thus, a good clinical evaluation and histopathological examination remains the gold standard in diagnosis[29,30,31].

6. Management

Control of hyperglycemia, early treatment with liposomal amphotericin B, and surgery are essential for the successful management of mucormycosis[32,33,34]. Both medication and surgical management strategies are employed in mucormycosis cases. The drug of choice which is most commonly used in the management of mucormycosis is Amphotericin B (liposomal). Combination management of liposomal Amphotericin B and posaconazole showed synergistic effects against fungal hyphae formation[35] Neutropenic patients or individuals with graft-versus-host disease should be recommended for oral posaconazole medication as prophylactic management against mucormycosis, whereas mucormycosis cases in neutropenia or graft-versus-host disease patients should be managed by oral administration of fluconazole, while itraconazole and voriconazole are administered as prophylactic doses[36].

7. Myths *Vs* Facts

1. It's caused by a black fungus
   The name seems to have stuck given its angioinvasisve nature which blocks the blood flow and causes necrosis of the tissue giving it a characteristic black color.
2. Person to person transmission
   Mucormycosis is not contagious and hence cannot be transmitted from person to person. The source of infection is environmental from airborne spores produced by the Fungus.
3. Soiled masks, steam inhalation, and humidifiers as vehicles of transmission of the fungus
   Where the importance of maintaining hygiene could never be more stressed upon, however, there is no strong evidence to suggest that soiled masks or the use of humidifiers or steam inhalation could be a probable cause of infection.
4. Popping immunity boosting pills can avoid mucor infection.
   While having good immunity is one of the benefits but overdoing it is always fatal and so is the case wherein it is being suggested that popping excessive zinc pills aids mucormycosis infection.

8. Conclusion

With an estimated 77 million cases in the adult population, diabetes is India's fastest-growing epidemic. A recent cross-sectional study from all states of India revealed that 47% of Indians are unaware of their diabetic status and only a quarter of all patients achieved adequate glycemic control on treatment[37]. This has made India the world's capital of diabetes and has been one of the prime reasons for the deadly rise in mucormycosis infections with several states even declaring it as an endemic. Our immune system is usually efficient in tackling the fungus but an Unholy trinity of diabetes, COVID-19, and injudicious steroid use can weaken the immune system and give a strong foothold to these opportunistic pathogens. The Safety of the health care workers along with complete patient care is the need of the hour in emergency interventions in cases of COVID-19 which can be managed successfully with adequate precautions[38]. The importance of research comes into play when we face such unknown adversities. As frontline caregivers, we need to be prepared with the right amount of knowledge which helps us in taking wise judgments to the maximum benefit of the patients. The need of the hour is to not spread fear and panic but instead, be equipped with all facts, be aware, act wisely, and more importantly, act timely to prevent a cascade of untoward events hence reducing mortality and morbidity as far as possible.

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