

Article

Early the diagnosis, intervention and treatment is key for Covid-19 induced Mucormycosis

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Academic Editor: Augustine Ibegbu

Received: 25 August 2021; Accepted: 28 September 2021; Published: 30 September 2021.

Abstract: The novel corona virus (COVID-19) outbreak declared as a global pandemic. Glucocorticoids are inexpensive, widely available, and have been shown to reduce mortality in hypoxemic patients with COVID-19. With increasing risk of new strains of covid virus infections and now the latest dreadful fungal infection Mucormycosis, the situation is becoming more and more devastating. Survival in mucormycosis depends on early diagnosis, alleviation of basic predisposing factors, aggressive debridement of necrotic tissues, and appropriate systemic antifungal agents.

Keywords: COVID-19 Pandemic; Immunocompromised; Mucormycosis; Amphotericin B.

1. Introduction

The novel corona virus (COVID-19) outbreak declared as a global pandemic [1] on March 11, 2020, which impact a large number of people worldwide. A significant increase in number of COVID-19 cases was observed leading to collapse of local health-care systems [2]. COVID-19 has already claimed more than one million lives worldwide. The severity of the disease ranges from asymptomatic infection to respiratory failure and death [3]. Glucocorticoids are the only drugs proven to be beneficial in COVID-19. Glucocorticoids are inexpensive, widely available, and have been shown to reduce mortality in hypoxemic patients with COVID-19. Nevertheless, glucocorticoids can increase the risk of secondary fungal and bacterial infections. With increasing risk of new strains of covid virus infections and now the latest dreadful fungal infection Mucormycosis, the situation is becoming more and more devastating [4].

Mucormycosis is an opportunistic infection caused by organisms in the order Mucorales [5]. These organisms are ubiquitous in nature but can cause devastating rhino-orbito-cerebral infection in susceptible patients [6]. Mucormycosis is often associated with rapid progression to Orbital apex syndrome with brain infarction in a patient with ketotic diabetes and COVID-19. Early diagnosis and treatment are essential to prevent further end organ damage.

Mucormycosis is usually seen in immunocompromised individuals with diabetes being an independent risk factor. Diabetes has also been identified as an independent variable associated with severity of COVID-19 infection and hospitalization. SARS-CoV-2 virus itself has been implicated in causing an impaired cell mediated immune response with drop in CD4 + T and CD8 + T cell counts [7]. A combination of these factors makes the hospitalized COVID-19 patients a high-risk Group for fungal infections like aspergillosis and mucormycosis. Whereas aspergillosis is associated with Fungus balls of the sinuses without tissue invasion, mucormycosis is an angioinvasive fungal infection which causes ischemic necrosis of the areas involved. The clinical course is rapid with case fatality rate of 46% [8].

With patients on ongoing Covid treatment, it's very essential to take thorough history of any prior drug use especially steroids and other comorbidities like diabetes mellitus. A complete head and neck examination and neurological examination are required.

2. Discussion

Acute invasive rhino- orbital Mucormycosis is rare and life threatening infection with high mortality. It is characterized by direct invasion and necrosis of local structures followed by rapid progression and angioinvasion from the nasal and sinus mucosa into the orbit and brain. While many Fungal species can cause this, it most commonly involves *Aspergillus*, *Rhizopus*, *Mucor*, and *Rhizomucor* [9]. Mortality is high, ranging between 50% and 80%, with factors including Intracranial or orbital involvement, irreversible immune suppression, and mucormycosis leading to poorer outcomes [10].

A complex interplay of factors, including preexisting diseases, such as diabetes mellitus, previous respiratory pathology, use of immunosuppressive therapy, the risk of hospital-acquired infections, and systemic immune alterations of COVID-19 infection itself may lead to secondary infections, which are increasingly being recognized in view of their impact on morbidity and mortality [11].

The symptoms presenting in rhino-orbito-cerebral Mucormycosis are facial pain and paresthesia, headache, periorbital and nasal swelling, inflammation, eyelid drooping, Proptosis, external and internal ophthalmoplegia, visual Loss, and blackish necrosis of palate and nasal mucosa [12]. The Disease usually initiates on the nasal and oral mucosa and spreads to paranasal sinuses. It propagates into the orbital space through the lamina papyracea. Vision loss is due to the involvement of optic nerve or retinal supplying vessels. Intracranial space can be involved directly through the Orbital orifices and sinus walls, or through the bloodstream. Cavernous sinus thrombosis as another complication results In damage to the cranial nerves III, IV, V1, V2, and VI [13]. Regular examination and imaging (CT and MRI) are crucial to detect the propagation of the mucormycosis. Based on the infected region, the imaging findings may include opacifications of involved paranasal sinuses, bone destruction of Sinus walls, alterations of intraorbital tissue signal with or Without focal mass, cavernous sinus filling defect, intracranial focal mass, and/or alteration of the meningeal signal. Mucormycosis is confirmed by the detection of blackish necrotic tissues in the involved region and histopathology. The histological stains that identify the mucor structures include hematoxylin and eosin, Periodic acid-Schiff (PAS), and Gomori methenamine silver (GMS). Histopathologic examinations disclose relatively broad non-septate hyphae with right angle branches, necrotizing granulomatous inflammation, and vasculitis together with the presence of mucor hyphae within the vascular wall and lumen.

Rhinoorbitocerebral mucormycosis is a relatively fatal infection. Survival in mucormycosis depends on early diagnosis, alleviation of basic predisposing factors, aggressive debridement of necrotic tissues, and appropriate systemic antifungal agents [12]. Predisposing factors such as corticosteroid therapy should be discontinued, and blood sugar should be controlled restrictively. Systemic amphotericin B and its liposomal formulation is the first drug of choice for the treatment of mucormycosis and significantly improve the survival rate [14].

Treatment of Mucormycosis requires a multimodal approach involving antifungal therapy, surgical debridement, and reversal of immunosuppression to the degree possible. Hyperglycemia, Diabetic ketoacidosis, and metabolic disturbances provide a favorable environment for fungal growth and should be aggressively addressed with glycemic control and electrolyte repletion [15]. Concurrently, surgical debridement of necrotic tissue and antifungal therapy with liposomal amphotericin B or combination Therapy with amphotericin B and posaconazole or caspofungin has been shown to improve survival. Posaconazole is an oral antifungal agent that has been used as step-down therapy after initial control of the mucormycosis by amphotericin. Regular daily debridement of necrotic tissues from Paranasal sinuses is necessary to prevent the propagation of mucormycosis. Also, irrigation of the sinuses and the involved regions with diluted amphotericin B is recommended. Orbital exenteration in the presence of focal mass or extensive necrotic tissues has been suggested in most studies.

3. Conclusion

COVID-19 patients treated with corticosteroid therapy due to hypoxia have a risk of rhino-orbital and/or rhino-orbitocerebral Mucormycosis, particularly when another risk factor such as Diabetes mellitus is present. In these patients, vision changes, orbital Pain, and orbital inflammation should be promptly evaluated; otherwise, the propagation of the infection into the intracranial space may be fatal. This early the diagnosis is made, early the intervention and treatment, the better will be the result.

Author Contributions: All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

Conflicts of Interest: “The authors declare no conflict of interest.”

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