

Rhino-orbital-cerebral Black Fungus Infection (Mucormycosis) in a Post-Coronavirus Disease 2019 Pneumonia-Treated Patient: A Case Report

Priyadarshi J Kumar¹, Krittibus Samui²

¹Specialist and Consultant, Department of Pulmonary, Critical care and Sleep Medicine, Jaypee Multi-Speciality Hospital, Noida, Uttar Pradesh, India, ²Specialist in Pulmonary Medicine, Senior Registrar, Department of Critical Care Medicine, Jaypee Multi-Speciality Hospital, Noida, Uttar Pradesh, India

Abstract

Mucormycosis (black fungus disease) is an uncommon opportunistic infection. In coronavirus disease 2019 (COVID-19) era, therapeutic use of steroid and tocilizumab results in immune suppression and high blood sugar level. Ultimately, it augments the chance of fungal infection. In our case, a 58-year-old gentleman with comorbidity of diabetes and hypertension on regular treatment developed COVID-19 infection and recovered with treatment based on current guidelines. After around 5 weeks of first COVID-19 symptom (fever), he developed ophthalmic symptoms. Headache developed later. By multidisciplinary team approach, he was diagnosed as rhino-orbital-cerebral mucormycosis based on imaging, functional endoscopic sinus surgery, microbiology, and histopathological examination. Along with surgical debridement, he was put on intravenous liposomal amphotericin B with regular monitoring of kidney function and serum electrolytes. Early diagnosis and prompt treatment are the key approach to aim the reduction of mortality in such a fatal disease.

Key words: Amphotericin-B, Coronavirus disease 2019, Mucormycosis, Steroid

INTRODUCTION

Black fungus disease or mucormycosis is an uncommon infection. It is an opportunistic pathogen containing non-septate hyaline hyphae. It can be isolated from decomposing vegetation and high fructose fruits, soil, feces, and human orifices such as nasal and oral mucosa.^[1] The key causative species agents in human are *Rhizopus*, *Absidia*, and *Cunninghamella*.^[2] The incidence rate of this black fungus globally ranges from 0.005 to 1.7 per million of population. Whereas, in Indian population, its prevalence rate is 0.14 per 1000, that is, about 80 times higher than developed countries. The fatality rate all over world is 46%.^[3] The infective route of the pathogen as an asexual spore is inhalation. It infects nasal and oral

cavities. Normal immune system removes pathogen by phagocytes. The highest ranked risk factor associated with mucormycosis is diabetes mellitus in India.^[4] Hence, uncontrolled diabetes (particularly diabetic ketoacidosis), cancer (such as lymphoma and leukemia), renal dysfunction, organ transplantation, advanced rheumatologic disorders using immunosuppressive medications (like long-term use of steroids), AIDS, extensive burn, and chronic sinusitis are the key risk factors for this fatal disease. In these conditions, leukocytes are less efficient in killing the hyphae forms of fungi which may proliferate more easily. The pathogen invades the vessel walls of the infected region and causes thrombosis, ischemia, and necrosis. The agent can directly spread into the paranasal sinuses and then attacks orbital and intracranial spaces by direct spread or through the bloodstream.^[5]

More than 3.5 million coronavirus disease 2019 (COVID-19)-related deaths have already been reported worldwide. In the absence of an effective therapy, supportive care is the key role in the management of COVID-19. Glucocorticoids and blood thinners are the only drugs found to be beneficial. Steroids are cheap in cost, widely

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Corresponding Author: Dr. Krittibus Samui, Department of Critical Care Medicine, Jaypee Multi-Speciality Hospital, Noida, Uttar Pradesh, India.

available and have shown to reduce mortality in hypoxemic COVID-19 patients. Thus, steroid can increase the risk of secondary infections by suppressing immune system. Moreover, the immune dysregulation caused by the COVID-19 virus and the use of tocilizumab further augment the risk in such patients.^[6]

CASE REPORT

In our case study, a 58-year-old gentleman, previously a known case of type II diabetes and hypertension on regular treatment with oral drugs, had a history of intermittent episodes of fever for 13 days along with cough and progressive increased breathlessness for 3 days. On clinical examination, he was conscious and co-operative. His pulse was 88/m. Blood pressure was 140/78. Respiratory rate was 30/min. Temperature was 98.8 degree F. His oxygen saturation was 84% on room air. On chest auscultation, inspiratory crackles were audible on multiple areas of chest. On routine investigation, he had hemoglobin level of 10.5 gm%, total leukocyte count of 6200 per mm³ (Neutrophil-70%), platelet count of 2.63 lakh per mm³, HbA1c of 9.9%, CRP of 10 mg/Lt, D-dimer of 720 ng/ml, IL6 of 14.03 pg/ml, urea of 81 mg/dl, creatinine of 1.12 mg/dl, sodium of 129 mEq/Lt, potassium of 6.69 mmol/Lt. Arterial blood gas showed type I respiratory failure. Chest X-ray revealed bilateral interstitial opacity, more on peripheral lung side [Figure 1a]. Throat swab for severe acute respiratory syndrome corona virus reverse transcription-polymerase chain reaction (SARS COVID19 RT-PCR) was positive. He was managed with antiviral, antibiotic, steroid, blood thinner, nebulization, oxygen by non-rebreathing facemask, intermittent non-invasive ventilation support, and other best supportive cares. After 3 weeks of treatment, he became COVID negative, improved clinically, and was shifted to general ward from ICU. High-resolution computed tomography (CT) thorax showed diffuse parenchymal lung changes [Figure 1b]. After about 5 weeks of onset of first COVID

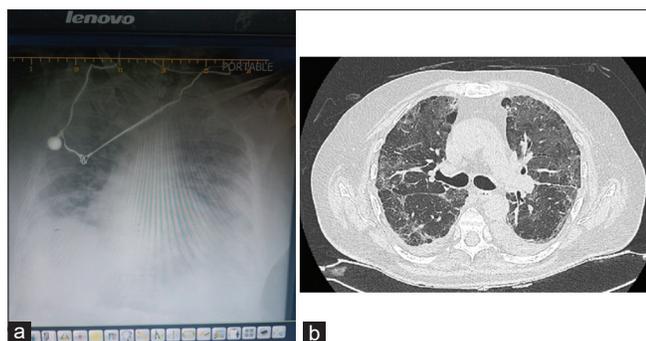


Figure 1 (a) Chest X-ray showing bilateral reticular opacity, more in periphery. (b) High-resolution computed tomography thorax showing diffuse parenchymal lung changes

symptom, he developed left eye swelling, watering, and drooping of left eyelid diagnosed as left orbital cellulitis by Ophthalmologist. He had no nasal discharge, pain in nose, and loss of vision. Nasal puffiness was found on examination. Magnetic resonance imaging (MRI) of orbit and paranasal sinuses [Figure 2] was suggestive of likely infective fungal sinusitis with the left orbit, paranasal sinuses, and brain involvement. Headache started after 1 week of these ophthalmic symptoms. After surgical debridement, multiple punch biopsy of ethmoid and maxillary sinus was done by functional endoscopic sinus surgery approach. Histopathology was suggestive of invasive mucormycosis. Fungal culture of nasal tissue showed growth of *Rhizopus* species [Figure 3]. He was started treatment with intravenous liposomal amphotericin B with regular monitoring of kidney function and serum electrolyte. He is still with only little ptosis which is improving.

DISCUSSION

Diagnosis of black fungus is an emergency. Because the pathogen invades blood vessels and progresses fast. Imaging shows the extension of the damage. Surgical debridement actually helps to confirm diagnosis by histopathological findings and increases the possibility of being cured.^[1] COVID-19 pneumonia results extensive pulmonary disease and the subsequent alveolo-interstitial pathology that increases the risk of invasive fungal infections.

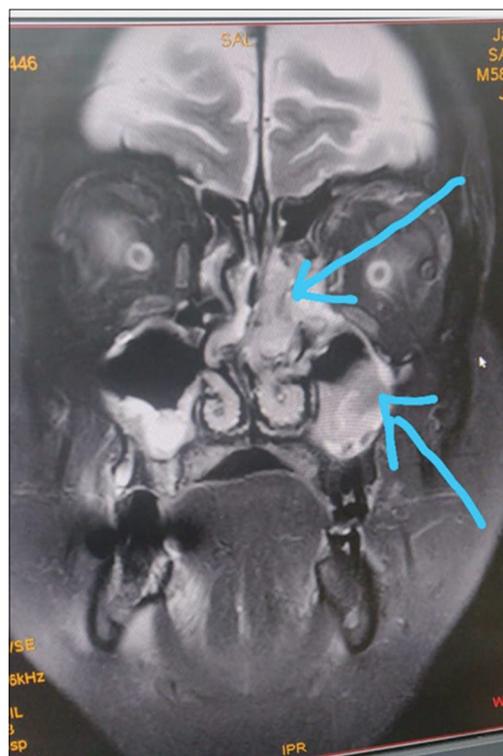


Figure 2: Magnetic resonance imaging showing lesion in nose and paranasal sinus



Figure 3: Microbiology slide showing black fungus in KOH mount stain (P.C.-Dr. Roopjyoti and Dr. Priyanka, Department of Microbiology)

In addition, the immune system dysregulation associated with COVID-19 along with reduced numbers of T lymphocytes, CD4+T, and CD8+T cells changes innate immunity.^[7] Alterations in innate along with cell-mediated immunity, such as chemotaxis, phagocytosis, and cytokine secretion in diabetics are being reported too many times. Natural killer cell activity is decreased in these individuals and more pro-inflammatory M1 macrophages are present. Disease severity in COVID-19 patients is due to both viral infection and the host response. Poor glucose control also suppresses the antiviral response. In COVID-19 patients, delay in IFN response with a prolonged hyperinflammatory state and lower CD4 and CD8 cell numbers causes severe disease progression by exacerbating cytokine storm. Change of vascular tone toward more vasoconstriction results subsequent organ ischemia, tissue edema, and a procoagulant state.^[4]

Rhino-orbital-cerebral mucormycosis presents with symptoms such as facial pain and paresthesia, headache, periorbital and nasal swelling, eyelid drooping, proptosis, external and internal ophthalmoplegia, visual loss, and blackish necrosis of palate and nasal mucosa. In our patient, first presentation was ophthalmic symptoms. Nasal puffiness was found on examination. After 1 week of these findings, headache was started. The disease usually begins in the nasal and oral mucosa and spreads to paranasal sinuses. It progresses into the orbital space through the lamina

papyracea. Vision loss happens due to the involvement of optic nerve or retinal supplying vessels. It involves intracranial space directly through the orbital orifices and sinus walls, or through the bloodstream. One deadly complication like cavernous sinus thrombosis results in damage to the cranial nerves III, IV, V1, V2, and VI. Regular clinical examination and imaging (CT and MRI) are very important to detect the progression of the mucormycosis. It is confirmed by the detection of blackish necrotic tissues in the involved region and histopathological examinations. Systemic amphotericin B (liposomal formulation) is the first drug of choice for the treatment and significantly improves the survival rate. Posaconazole is an oral antifungal drug used as step-down therapy after initial control of disease. Regular daily debridement of necrotic tissues from paranasal sinuses helps to prevent the propagation of mucormycosis.^[5]

CONCLUSION

Mucormycosis is a life-threatening infection with very high mortality rate even after best possible medical management. Hence, once patient is suspected clinically, all physicians should be aware of quick diagnosis and prompt treatment to try to reduce the progression of disease followed by mortality.

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