



Complications in Severe Covid 19 Infected Individuals: A Case Report and Review of the Literature

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Abstract

Prolonged usage of high-dose steroids in the management of severe COVID 19 infection is one of the major factors for severe post-recovery complications. Immune suppression due to prolonged steroid overdose results in opportunistic infections. COVID 19 associated mucormycosis is one of the most commonly reported opportunistic invasive fungal infections. We describe a case of a 52-year-old diabetic male patient who had developed rhinocerebralmucormycosis along with multisystem complications due to immune suppression during the recovery phase of COVID 19 infection. He received liposomal amphotericin B 200mg/day and syrup posaconazole 21mg/day for 90 days. Regardless of the extensive antifungal drug therapy, the grievousness of the disease couldn't be controlled.

Keywords:

INTRODUCTION

Opportunistic invasive fungal infections (IFI) are more common in immune compromised patients. The common predisposing factors for IFI include neutropenia <500 neutrophils/ml for more than 10 days, hematological malignancies, organ transplantation, corticosteroid treatment more than 4 weeks, chemotherapy, prolonged ICU stay, HIV infection, invasive medical procedures, and the newer immune-suppressive agents[1,2]. The management of novel coronavirus infection (COVID 19) includes prolonged usage of corticosteroids.

CASE REPORT

A 52-year-old male with a known history of controlled type 2 diabetes, presented with cold, shortness of breath, and an intermediate grade fever of 102 F. With a CORAD 5 score on HRCT, the patient was admitted to the hospital for management of COVID 19 infection. Tab. Prednisone 20mg twice

daily for 30 days as a part of COVID treatment protocol. The patient was discharged from the hospital with improved stable oxygen saturation.

The patient had multiple complaints post-discharge; he presented with multiple non-indurated erosive lesions on the tongue and Candida Albicans on buccal mucosa with submandibular lymphadenopathy, right infraorbital nerve paraesthesia, ophthalmalgia, and forehead heaviness suggestive of sinusitis. Mucosal perforation (2mm diameter) in the palate with pus discharge on palpation (fig.1) and no underlying bony changes were observed. Gingival abscess corresponding to maxillary right canine, first premolar along with grade II mobility of maxillary left first premolar and molars was recorded. On CT, mucosal thickenings were observed in the maxillary sinus and other paranasal sinuses concluding pan-sinusitis (fig.2).

with episodes of headache and, the patient was advised for MRI. Endoscopic examination of paranasal sinuses revealed scabs of brownish-black in color indicative of mucormycosis, FESS was done and patency of sinuses was achieved. Culture and sensitivity of the pus from palate revealed Mucormycosis. Liposomal amphotericin B (LAMB) 200mg/day IV was initiated along with the syrup posaconazole 21mg/day.

After episodes of headache in the right temporal as well as vertex region and decreased cognition, MRI brain was done. Right middle cerebral artery (MCA) infarct was diagnosed (fig.3). Anti-edema measures were taken for the management of the right MCA infarct along with neuroprotective, antiplatelets, statins, antiepileptics, Clexane 40mg OD (LMWH), and other supportive care. The patient developed upper motor neuron facial palsy, left homonymous hemianopia, left upper and lower limb paresis. With worsening of paresis and drowsiness, CT brain was done suggesting a large MCA infarct, compressing right lateral ventricle with midline shift. Right fronto-temporo-parietal decompressive emergency craniotomy was performed.

A 2 week post-operative MRI brain (plain and contrast) showed multifocal thin-walled abscesses extending from scalp through cerebral parenchyma into right basal ganglionic structures with the largest collection measuring 12x5cm (fig.4), reexploration and drainage were performed. 150ml of pus was drained and sent for the examination which revealed *Rhizopus Oryzae*, concluding to Rhino-cerebral mucormycosis. Amphotericin B 200mg/day and posaconazole syrup was continued.

The abscess close to the ventricles was not addressed while considering the post-operative risks. Further radiological evaluation was reported with resorption of the sphenoid bone and bilateral maxillary bones beyond the surgical limits. The existing systemic comorbidities, the diffuse spread of infection, and unclear surgical margins accounting for poor prognosis aborted further surgical management.

DISCUSSION

The persistent immune response by pro-inflammatory mediators in the SARS-CoV-2 infection resulting in pulmonary fibrosis is the main cause of life-threatening respiratory disorders [3]. In patients with

high viral load, corticosteroid administration regulates the endogenous pro-inflammatory response thus preventing the post disease pulmonary fibrosis [4]. Duration of corticosteroid therapy is very crucial. Corticosteroids course beyond 10 days is considered only in cases with sustained persistence of ground-glass opacities [5]. Besides anti-inflammatory action, long-term usage results in immune suppression [6]. Exogenous corticosteroids are potential in increasing the clotting factors and fibrinogen concentrations resulting in thrombosis [7]. A hypercoagulable state with endothelial damage associated with SARS-CoV-2 infection has an essential role in thrombosis resulting in infarcts of major organs [8].

Tocilizumab along with steroids was found to improve the mortality in severe stages of SARS-CoV-2 infection [9]. On the contrary, neutropenia is the undesirable effect on prolonged usage of tocilizumab and steroids leading to opportunistic infections [10]. Incidence of opportunistic fungal infections associated with COVID 19 infection accounts for 26.7% [11].

Mucormycosis is a lethal opportunistic fungal infection with a violent course. Along with many other systemic conditions, uncontrolled diabetes with metabolic acidosis, prolonged neutropenia, and long-term usage of corticosteroids account for the major predisposing factors [12]. Stage 1 manifests with nonspecific symptoms like a low-grade fever, sinusitis, invasion of surrounding blood vessels, and their thrombosis and spread into surrounding soft tissue leading to necrosis with a classic eschar formation. In stage 2, the infection spreads to orbit either by direct or vascular spread resulting in ophthalmalgia, ophthalmoplegia, chemosis, proptosis resulting in blindness. Stage 3 involves intracranial invasion with symptoms of confusion, disorientation, comatose, and death [13].

The standard therapy for invasive mucormycosis is intravenous amphotericin-B administration. With an increased circulation time, greater concentrations in the infected tissue, and decreased renal toxicity, lipid-based amphotericin B (LAMB) with a dosage of 5mg/kg/d as 1mg/ml infusion, is the drug of choice over the conventional amphotericin B [14]. The antifungal efficacy of amphotericin-B in mucormycosis is complicated by variability in sensitivity among isolates and spores and hyphal

forms, by unknown penetration of infected tissue, and by poor immunocompetence [15]. In this patient, by the time the disease was suspected, extensive tissue destruction had occurred; besides, the pace of the disease was very rapid, and the patient's general condition was so poor that medical therapy with liposomal amphotericin B 200mg/day, syrup posaconazole 21mg/day supplementation for 90 days failed to control the disease and surgical options were not possible.

CONCLUSION

With our clinical experience and review of the literature on opportunistic infections in COVID 19 patients, we suggest a prophylactic antifungal therapy with drugs like amphotericin B, posaconazole or isavuconazole in patients with long term steroid therapy and prolonged hospital stay with severe SARS-CoV-2 infection to prevent post-COVID-19 opportunistic fungal infections. Further research with a large sample is required to establish a prophylactic antifungal regimen in severe SARS-CoV-2 infection.

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1. Figure1:
 - a. Mucosal perforations in the palate with pus discharge.
 - b. Gingival abscess corresponding to maxillary right canine, first premolar.
2. Figure 2: CT image showing mucosal thickenings in the maxillary sinus and other paranasal sinuses.
3. Figure 3: MRI brain demonstrating Right middle cerebral artery (MCA) infarct.
4. Figure 4: MRI brain displaying thin-walled abscesses.

Figure 1



Figure 2



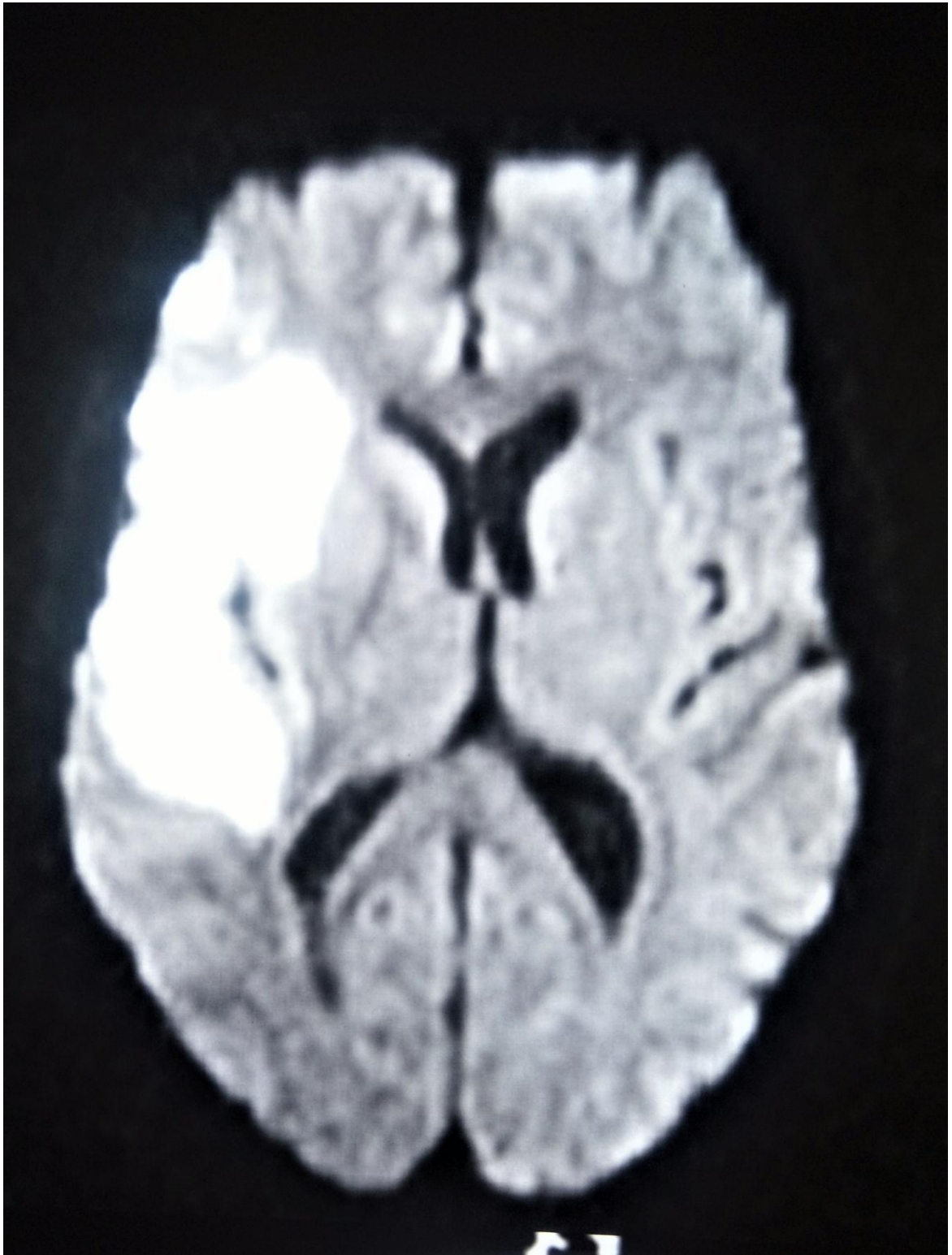


Figure 3

Figure 4

