pISSN 2454-5929 | eISSN 2454-5937

Case Report

DOI: https://dx.doi.org/10.18203/issn.2454-5929.ijohns20211194

Mucormycosis complicating diabetes mellitus and COVID-19: a diagnostic and therapeutic threat

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Received: 18 January 2021 Accepted: 03 March 2021

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ABSTRACT

COVID-19 infections is known to have a multitude of clinical presentations, and newer clinical complications continue to be reported from all over the world. It is now widely known that the diabetic patients with poor glycemic control are associated with a higher risk of developing severe COVID-19 infection. They are also at a high risk for developing secondary bacterial or fungal, co infections because of the complex interplay of multiple risk factors , necessitating an intensive medical care and monitoring in them. We are presenting a case of mucormycosis in a diabetic patient with moderate COVID pneumonia that presented to us as orbital cellulitis and the events that followed. There have been very few documented cases of mucormycosis in COVID infected diabetic patients so far during this pandemic and we also present a literature review of the same.

Keywords: COVID-19, Diabetes mellitus, Orbital cellulitis, Mucormycosis

INTRODUCTION

India is currently tolling under the wave of Corona Virus Disease-2019 (COVID-19) pandemic, ever since March 2020 until now, 96 lakh Indian population have been affected with COVID-19 and up until November 2020 there have been 1.45 lakh COVID deaths that have been reported across India. Till date there are no definite therapeutics found to be effective for this infection, although Vaccines are In clinical trial phase and is speculated to be for public use in the near future. 1.2

COVID-19 infections can scale from being an asymptomatic carrier state to mild to severe life-threatening pneumonia, while the recent data indicate that it should be regarded as systemic illness that involves multiple systems, like cardiovascular, respiratory, gastrointestinal, neurological, hematopoietic,

hematological and immune system.^{2,3} Certain risk factors have been identified to be associated with increased morbidity and mortality in COVID 19 infection like older age, uncontrolled sugars in diabetic patients, use of corticosteroids, immunosuppression, renal failure and cardiovascular status of the patient.⁴

Currently India is a home for about 61.3 million population with diabetes mellitus making it as the diabetes capital of the world and so, the number of COVID affected diabetics presenting with systemic complications forms a significantly large group. 5.6 Song et al in their meta analysis, found that severely ill COVID patients with uncontrolled sugars have higher probability of harbouring systemic fungal co infections and have identified invasive aspergillosis, candidiasis and mucormycosis as the causative organisms. 7

We report a case of Mucormycosis that presented to us as orbital cellulitis similar to the case reported by Salil et al from Mumbai, India and Amanda et al from New York, America.^{8,9}

CASE REPORT

A 44 year old diabetic lady diagnosed as COVID positive was admitted in our COVID designated hospital in early August of 2020 for uncontrolled sugars. On the 2nd day of admission she complained of left eye pain and inability to open the left eye, Ophthalmology opinion was sought and was diagnosed to have left total ophthalmoplegia, due to orbital cellulitis, however her visual acuity could not be documented. Broad spectrum Intra venous antibiotics were started, and was requiring high doses of short and long acting insulin for the control of sugars. Emergency Computerised tomography (CT) scan of the nose and Para nasal sinus (PNS) showed extensive ethmoidal sinusitis, left preseptal cellulitis with adjacent subcutaneous fat plane thickening and proptosis, CT scan of the chest showed moderate COVID viral interstitial pneumonia pattern (Figure 1 and 2).



Figure 1: Plain CT scan (axial and coronal sections) of nose and para nasal sinus showing extensive mucosal thickening involving the left maxillary, ethmoidal, sphenoidaland frontal sinuses with Osteomeatal complex obstruction and presence of hyperdense areas noted. Left preseptal cellulitis and adjacent subcutaneous plane thickening and proptosis.

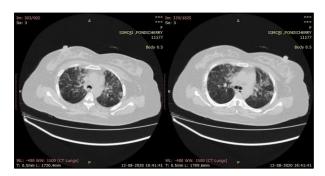


Figure 2: Plain CT scan (axial section) of chest showing ground glass opacities involving all the lobes suggesting moderate COVID viral pneumonia pattern.

COVID pneumonia protocol was intensified, low molecular weight heparin and intravenous steroids were started. The following day, she was found to be in Diabetic Keto acidosis and was shifted to ICU, subsequently her blood sugar levels were controlled, on 2nd day of ICU stay she became hypoxic and had to be intubated by now she had developed acute renal failure. On the subsequent day of ventilation her left eye and the skin surrounding the left side of the nose started showing black discoloration (Figure 3), ENT opinion was sought and we made the clinical diagnosis of Mucormycosis, we took biopsy of the necrosed skin and advised on systemic antifungals.

The following day patient's general condition worsened, she had multi organ organ failure probably due to septicaemia and had persistent hypoxia, that same day she had cardiac arrest and expired. The clinical diagnosis of mucormycosis was confirmed histopathologically.

The biopsy revealed lining epithelium by stratified squamous epithelium with extensive areas of ulceration and necrosis. Subepithelium showed dense acute on chronic inflammatory cell infiltrate including eosinophils. There were presence of thick broad nonseptate hyphae with right angle branching seen in hematoxylin and eosin (H and E) stain. The further confirmation was carried out by Per-iodic Acid Schiff (PAS) stain and Grocotte-Gomori's Methenamine Silver (GMS) stains (Figure 4). The diagnosis of Mucormycosis was offered.



Figure 3: Black discolouration of skin around left eye and nose.

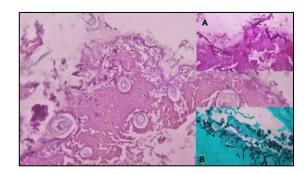


Figure 4: Biopsy showing presence of thick broad nonseptate hyphae with right angle branching suggesting Mucormycosis (H and E stain, inset A-PAS stain and inset B-GMS stain: 40× magnification).

DISCUSSION

COVID-19 is now being increasingly recognized as a systemic illness because of the cascade of immunoregulatory cytokines impacting several organ systems. There seems to be a multi system response to the over expression of inflammatory cytokine storm initiated by the COVID infection. The national treatment guidelines for COVID-19 infection suggest Broad spectrum antibiotics and intravenous delivery of corticosteroids to combat the cytokine storm. However, this can be the cause to dysregulation of the glycemic control and predisposes them to secondary bacterial and fungal infections especially the severely ill diabetic patients with COVID infection. 8,9,12

Recently diabetes mellitus and COVID 19 infection have attracted a lot of attention from many researchers all over the world. The interaction of these two pandemics is another reason for the high mortality rate in the diabetics with poor glycemic control.⁶ Guo et at in their meta analysis, report that these patients with poor glycemic control, are at a high risk of developing severe form of COVID-19 infection, they also found that the mortality rate among them without other comorbidities was 16%.¹³

Song et al in their metaanalysis have stated that with the ongoing pandemic more and more health care experts from all over the world are becoming aware of fungal coinfections in COVID19 infected diabetic patients. They also have suggested the clinical algorithm for diagnosing and treatment of invasive Aspergillus sp, Candida sp, Mucormycosis and cryptococcosis. In New delhi, India Thakar et al have reported candid infection in the blood stream of covid infected diabetic patients and Aspergillosis was reported authors farooqi et al from Pakistan and Bartoletti et al from Italy.

Our patient with COVID pneumonia and uncontrolled diabetes presented to us with orbital cellulitis that turned out to be mucormycosis. Mucormycosis is known to be an aggressive fungal infection with high mortality and are predisposed in diabetic patients with uncontrolled sugars, and in steroid dependent patients. ¹⁴ Total duration of hospital stay in our patient was seven days and she deteriorated very rapidly and this again points to the multiple factors interacting together in the progression of the underlying pathologic condition.

20-60% of mucormycosis patients present with orbital symptoms like orbital pain as in our case and also with the case described by Mehta and by Amanda et al.^{8,9,15} Very few case reports have been reported about mucormycosis from all over the world, as song et al suggests we may be underdiagnosing or misdiagnosing these fungal co infections.

The gold standard treatment for mucormycosis is surgical debridement and systemic antifungals such as Amphotericin B and azoles, in our case the patient's

general condition was poor and was not medically fit for surgical treatment and her renal failure was not suitable for Amphotercin B.⁷

We suggest that physicians should be primed about the occurrence of these fungal co infections in these high risk groups and should plan and initiate treatment specific protocols. We also recommend urgent diagnostic imaging modality in these patients when they present with nasal and or with ophthalmic symptoms. Systemic antifungals should be started immediately and such patients should be closely monitored for other systemic complications. 8,9,12

CONCLUSION

India is now dealing with two pandemics COVID 19 and diabetes mellitus, the interaction these two entities are known to have significantly low outcome. COVID infected diabetic patients presenting with systemic complications are high with uncontrolled sugars so we need to promptly initiate the specific management protocol in these patients. Although mucormycosis is an aggressive disease with high mortality rate early identification, investigation and initiating the treatment protocol may have improved outcomes however we have little knowledge about this at the current situation.

Funding: No funding sources Conflict of interest: None declared Ethical approval: Not required

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Cite this article as: Amalanathan S, Colbert KR, Chockalingam SK, Sinhasan SP, Jadhav C. Mucormycosis complicating diabetes mellitus and COVID-19: a diagnostic and therapeutic threat. Int J Otorhinolaryngol Head Neck Surg 2021;7:679-82.