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Case Report

"Mucormycosis" and coronavirus disease 2019: An epidemic within the larger pandemic

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ABSTRACT

India is passing through a significant impact of Wuhan origin coronavirus disease 2019 (COVID-19) pandemic in the second wave. Mucormycosis is emerging as a larger problem for our patients as compared to the first wave. Several plausible explanations have been put forth –but none has been proven as yet. We herein report eight cases of COVID-19-associated rhino-orbital mucormycosis diagnosed and managed at our center. We observed a higher risk among middle-aged men, with known or covert diabetes who received high-dose steroids and/or prolonged oxygen for COVID-19 management.

Keywords: Diabetes, Rhino-Ocular, Steroid, Second wave

INTRODUCTION

The coronavirus disease 2019 (COVID-19) has rampantly spread across the globe and was declared a pandemic on March 11, 2020.[1] Among several treatment options explored, steroids have shown to improve survival in moderate-to-severe COVID-19 pneumonia cases.[2] In a recently published prospective meta-analysis of critically ill patients with COVID-19, administration of systemic corticosteroids, compared with usual care or placebo, was associated with lower 28-day all-cause mortality.[2] Nevertheless, steroid use is associated with complications such as compromised immunity, hypertension, predisposition to bacterial or fungal infections, muscle weakness, and weight gain.[3] There is evidence that these drugs reduce organ dysfunction score, lung injury score, ventilator requirement, and intensive care unit stay.[3]

In addition, secondary infection or coinfection is a well-known complication of respiratory illnesses, for example, severe acute respiratory syndrome, Middle East respiratory syndrome, and influenza.[4] COVID-19-associated secondary infections are still under research.[5] According to the available data, opportunistic infection, predominantly fungal, is observed in 10–30% of cases hospitalized with COVID-19 pneumonia.[6] Among these, mucormycosis caused by *Mucorales* species of the phylum *Zygomycota*, is a potentially lethal infection, complicating the disease course in those with compromised immunity, such as diabetes mellitus.[7] People with pre-existing illnesses, like type 2 diabetes, seem to be more susceptible to the current coronavirus pandemic. Until recently, there were reports of increasing psychological stress and compromised glycemic control among those living with type 2 diabetes amidst coronavirus outbreak.[8] Nowadays, such patients are also facing an upsurge in the incidence of mucormycosis. Injudicious use of steroids is also implicated as a potential causative factor for this opportunistic fungal infection.[3]

Herein, we report eight cases of COVID-19-associated rhino-orbital mucormycosis diagnosed and managed at our center. We observed a higher risk among middle-aged men, with known or covert diabetes who received high-dose steroids and/or prolonged oxygen for COVID-19 management. The experiences gained would likely enable early identification and management of the condition.

CASE REPORT

Case 1

A 60-year-aged female diabetic patient presented 23 days after the onset of COVID symptoms, with headache, retro-orbital pain, running nose with thin black secretion, and facial pain. She required intensive care unit (ICU) care throughout this period, where she was managed with high -dose intravenous steroids and oxygen support by high-flow nasal cannula. She

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also received subcutaneous insulin (as per sliding scale) to manage rising blood sugar levels. Further, there is a history of carcinoma breast for which she had received sixteen cycles of chemotherapy 2 years back.

On examination, maxillary sinus tenderness was present. On ocular examination, only perception of light was present with the left eye conjunctival chemosis, black pigmented nasal crusts were observed in the left periorbital region, nasal cavity, and upper part of nose. A clinical diagnosis of mucormycosis was made and she was put on intravenous liposomal amphotericin B therapy.

Case 2

A 54-year-old male diabetic patient presented on day 24 of COVID-19 symptoms onset, with loss of vision in the left eye and, pain and swelling over nose for 4 days. During this duration, he was being managed at home and received intravenous steroid for nearly 2 weeks (documents unavailable). On examination, visual acuity in the right eye was 6/6 while perception of light was absent in the left eye along with restricted ocular movements. The left eye ptosis with absent pupillary light reflex was also noticed. Magnetic resonance imaging (MRI) paranasal sinuses revealed pansinusitis with the left orbital cellulitis. His glycemic control was poor as indicated by HBA1C of 10.7%. Nasal swab and tissue were taken for potassium hydroxide (KOH) mount to look for fungal growth, which was suggestive of mucormycosis. He was started on intravenous liposomal amphotericin B therapy and underwent debridement surgery.

Case 3

A 58-year-old male diabetic patient presented 20 days after the COVID-19 symptom onset with bilateral ocular pain and restricted eye movements. He was receiving intravenous steroids at home along with supportive care for COVID-19 disease (dose of steroid not known). On ocular examination, black pigmentation and swelling were observed over the right lower lid, with no other significant ocular finding. On evaluation, random blood sugar was 397 mg/dl. Contrast MRI imaging of paranasal sinuses revealed invasive fungal sinusitis? Mucormycosis. The patient underwent right endoscopic nasal crust debridement under general anesthesia. He also received intravenous liposomal amphotericin B coverage along with basal and short-acting insulin (as per the sliding scale).

Case 4

A 40-year-old female diabetic patient presented on 7th day of COVID-19 illness with complaints of redness in the right eye with painful and restricted eye movements. On evaluation, her random blood sugar was 423 mg/dl. Ocular examination revealed right eye congestion with exposure keratitis with corneal haze. On further evaluation, perception of light was present in the right eye whereas in the left eye, visual acuity was 6/9 (aided). Corneal scrapping was done. Post-scrapping visual acuity improved in the right eye with finger counting present at one foot. Corneal scrapping showed fungal growth on KOH media. She received intravenous liposomal amphotericin B therapy.

Case 5

A non-diabetic 45-year-old male patient was admitted in ICU for the management of COVID-19 pneumonia. High-dose steroids (dexamethasone at 16 mg twice per day) along with oxygen supplementation using high-flow nasal cannula at 16 l/min were required to maintain target oxygen saturation. A week later, rise in blood sugar levels was noted which was managed by regular insulin (as per the sliding scale). On further evaluation, HbA1C was found to be 7.6%. On day 20 of hospital stay, he developed painful black nasal crusting, retro-orbital pain, and ulceration over nape of neck and upper part of nose. On skin examination, ulceration with granulomatous tissue was present which was likely to be secondary to steam inhalation or pressure of the oxygen mask. The patient was advised topical clotrimazole (1%), fluticasone propionate (0.05%), and fusidic acid (2%). He also received intravenous liposomal amphotericin B coverage.

Case 6

A 44-year-old male diabetic patient was admitted 1 week after negative COVID-19 reverse transcription polymerase chain reaction (RT-PCR) report with complaints of nasal blockage, low appetite, and severe weakness. On examination, visual acuity right eye was 6/9, left eye was 6/9, near vision defective, with no other significant ocular findings. For his diabetes management, he was on oral antidiabetic drugs (sulfonylurea, DPP4 inhibitors, and metformin). Subsequently, he received intravenous liposomal amphotericin B therapy and underwent debridement surgery to remove nasal crust under general anesthesia.

Case 7

A 56-year-old diabetic male patient presented 8 days after negative COVID-19 RT-PCR report, with nasal stuffiness, severe headache, and retro-orbital pain. He received intravenous steroid (dose not known) at home for initial 5–6 days of the illness. Subsequently, he was admitted to a nearby hospital ICU for 20 days. On evaluation, MRI scan with contrast brain, paranasal sinus, and orbit revealed extensive nodular soft-tissue thickening with non-enhancing area in bilateral maxillary sinuses, left-sided ethmoidal air cell, left inferior turbinate, and bilateral frontoethmoidal recesses.

During hospital stay, he received intravenous liposomal amphotericin B and blood sugars were managed using regular insulin as per the sliding scale.

Case 8

A 58-year-old diabetic female patient presented with swelling over right cheek and difficulty in opening the mouth, 4 days after testing negative for COVID-19 RT-PCR. On examination, multiple nodular swellings were visible over right cheek. It was non-tender on palpation. Ocular examination was unremarkable. She received intravenous steroids and oxygen treatment at home for around 10 days for COVID-19 management. On investigation, HbA1c was 14.2% and she was on oral antidiabetic drugs for diabetes management. MRI paranasal sinuses and brain showed involvement of maxillary and ethmoidal sinuses with intracranial spread. She was referred to higher center for the management of intracranial extension. Figure 1 depicts the spectrum of clinical manifestations of our patients.

DISCUSSION

India has recently gone through the second wave of COVID-19 pandemic and now seems to be controlling it well.[9] However, the nation continues to face an onslaught of adverse publicity based on fake, doctored, incorrect, and biased journalism.[10] At the same time, we are also struggling with a genuine medical problem – significant increase in mucormycosis among our coronavirus cases.

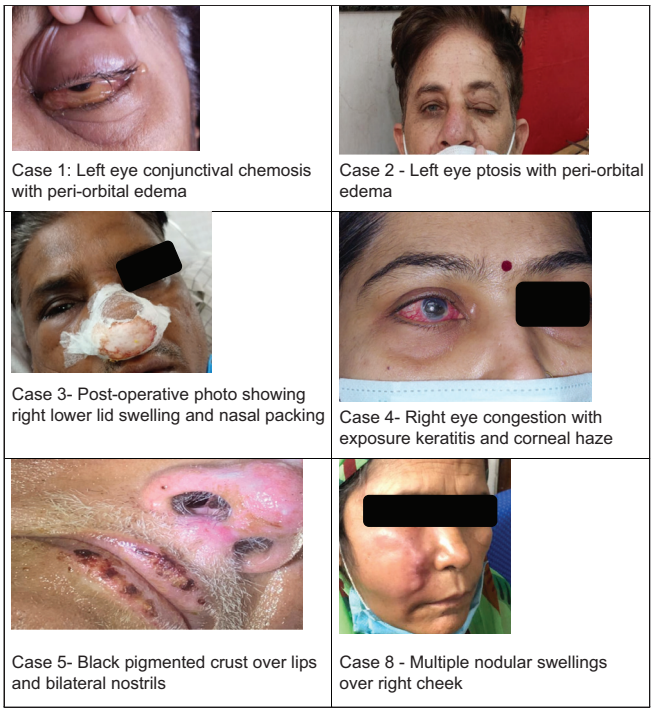

Figure 1: Spectrum of clinical manifestation of mucormycosis infection in patients with coronavirus disease 2019.

Some of the immune alterations by COVID-19 infection, immunosuppressive therapy, pre-existing comorbidities such as diabetes mellitus or lung pathology, hospital-acquired infections, and widespread use of antibiotics could account for the rising number of cases with mucormycosis.[7,11] Mucormycosis, simply known as "Black Fungus," develops in the nasal tract (including paranasal sinuses) and has the potential to spread towards the eyes and the brain. If diagnosis is delayed, it leads to poor outcome. Majority of our patients had unilateral spread of the disease.

In our cases, seven out of eight had diabetes mellitus and four patients were receiving intravenous steroids (unsupervised) in high doses or for prolonged duration. Moreover, the on-going pandemic has adversely affected diabetes care in those living with type 2 diabetes, as shown in recent studies.[8]

The mainstay of treatment for mucormycosis is amphotericin B along with surgical debridement.[12] All our patients were started on intravenous amphotericin B treatment and underwent surgical debridement. Amphotericin B being a fungi-static drug, needs to be continued for prolonged duration. Hence, our patients are currently still admitted in hospital and receiving treatment. We believe that development of community immunity against COVID-19 (natural immunity by being exposed to the virus or induced immunity following vaccination) will help our country emerge quickly from this pandemic.[13]

CONCLUSION

A high index of suspicion for early diagnosis of mucormycosis in patients with coronavirus and its aggressive management is essential, particularly in the second wave of the pandemic. This will allow for prompt treatment and a better outcome, especially in high-risk patients. We observed a higher risk among middle-aged men, with known or covert diabetes who received high-dose steroids and/or prolonged oxygen for COVID-19 management. Our series of eight cases document the spectrum of the clinical presentation and have the potential to help colleagues tackle this infection more efficiently.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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