Case Report

Mucormycosis and aspergillosis: The deadly duo in COVID-19—a case report

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Abstract

COVID-19 disease has been associated with fungal infections such as aspergillosis and mucormycosis, especially in diabetic patients who have suffered from a moderately severe form of COVID-19 infection and are treated with steroids. Though there are multiple case reports describing co-infection with mucormycosis during the second wave of the COVID outbreak, the report of a dual fungal infection along with superadded bacterial infection is rare. Here we report a case where the same patient had a fungal storm with aspergillosis and mucormycosis and superadded *Klebsiella*. She was treated aggressively with antifungal agents, antibiotics, surgical debridement, and other supportive care. She improved and was discharged from the hospital after a long stay. She is being followed up regularly in the outpatient department and doing well.

Keywords: Aspergillosis, COVID-19, liposomal amphotericin, mucormycosis, posaconazole

Introduction

The most common fungal infections in patients with COVID-19 include aspergillosis or invasive candidiasis.[1] It is also associated with a wide range of opportunistic bacterial infections.[2] Cases of mucormycosis in COVID-19 have been reported worldwide. However, reports of dual fungal infection in the same patient with superadded bacterial infection are extremely rare.

We report a case of aspergillosis and mucormycosis a deadly duo along with superadded bacterial infection. She was treated with voriconazole and later on switched over to liposomal amphotericin B along with posaconazole. Her nasal sample culture grew multidrug-resistant *Klebsiella* species that was treated with injection colistin. Management of this patient was challenging, but early diagnosis and aggressive management led to a positive outcome in this case. A high degree of clinical suspicion by the family physicians and timely referral to a higher center are rewarding.

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Case Summary

A 67-year-old woman, a known diabetic, was admitted with complaints of swelling in the right cheek associated with pain and redness along with black nasal discharge for 5 to 6 days. She had suffered from a moderately severe COVID-19 infection with a computed tomography severity score (CTSS) of 15/25 2 weeks ago.

On examination, she was conscious, alert, and afebrile. There was no pallor, icterus, cyanosis, limb edema, or axillary or cervical lymphadenopathy. Her blood pressure was 118/70 mm Hg, pulse rate was 100/min. Her respiratory rate was 17/min and oxygen saturation was 97% on room air. Systemic examination revealed no abnormality. The fundoscopic examination was normal. The right cheek was swollen and tender. There was mild proptosis and chemosis of the right eye. Her baseline investigations showed mild anaemia (Hb: 9.8 gm/dL), neutrophilic leucocytosis (TLC: 19,200/mm^3 with N-92%), and normal platelet count

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(130,000/mm^3). Her erythrocyte sedimentation rate (ESR) was raised (65 mm at the end of first hour (AEFH)) and her C reactive protein (CRP) was 18. Her liver function tests and renal function tests were within normal limits. Chest X-ray revealed bilateral hilar prominence. CT paranasal sinus (PNS) showed diffuse mucosal thickening in all paranasal sinuses. T2 coronal scan of magnetic resonance imaging (MRI) of paranasal sinuses showed hyperintense mucosal thickening in both maxillary and ethmoid sinuses [Figure 1]. T1 axial contrast scan showed enhancing sinus mucosal thickening with left intra-orbital extension [Figure 2]. The nasal bone was intact with no fracture or erosions. The visible portion of the orbit, maxilla, mandible and other bones were normal. Screening of the brain revealed no abnormality.

She was suspected to have fungal sinusitis in the background of post-COVID-19 status. A nasal swab was sent for potassium hydroxide (KOH) mount and culture sensitivity. She underwent functional endoscopic sinus surgery (FESS) under general anesthesia. Endoscopic debridement and anterior nasal packing were done. KOH mount revealed plenty of hyaline septate hyphae with acute angle branching and a possible diagnosis of aspergillosis [Figure 3] was made. The lactophenol cotton blue (LPCB) mount confirmed the presence of *Aspergillus* [Figure 4]. Along with broad-spectrum antibiotics inj. voriconazole was added in a dose of 400 mg intravenous (IV) BD on the first day followed by 200 mg IV BD. After 2 days, the mount revealed few non-septate hyphae suggesting infection with *Mucor* too [Figure 5]. The histopathology from bilateral nasal and maxillary sinuses showed broad aseptate fungal hyphae of *Mucor* [Figure 6]. There was the presence of fungal spores and angioinvasion and the periodic acid schiff stain (PAS) staining was positive for the fungus [Figure 7].

Voriconazole was stopped and liposomal amphotericin B was started in a dose of 300 mg per day as an infusion along with tab. posaconazole 300 mg twice a day (BD) on day 1, followed by one tab once a day (OD) from the next day. On the eighth day, crust removal was done from both nasal cavities. Repeat sinus endoscopy showed mucopurulent secretions from maxillary ostium and sphenopalatine recess. Her nasal sample culture grew multidrug-resistant (MDR) *Klebsiella* species that was treated with inj. colistin six million intravenous boluses, followed by two

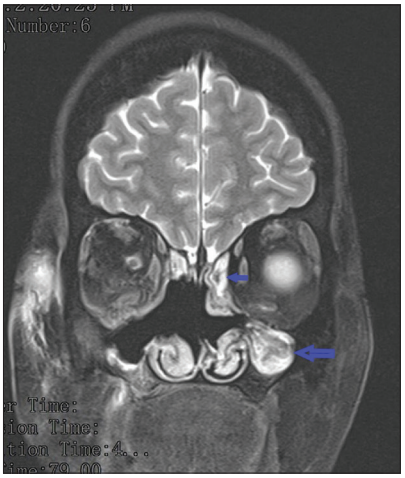

Figure 1: T2 coronal scan showing hyperintense mucosal thickening in both maxillary and ethmoid sinuses

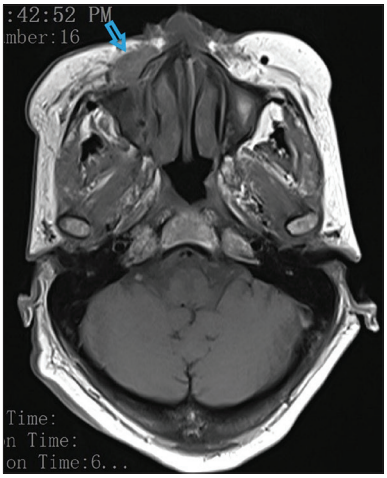

Figure 2: Axial contrast scan showing enhancing sinus mucosal thickening with left intraorbital extension

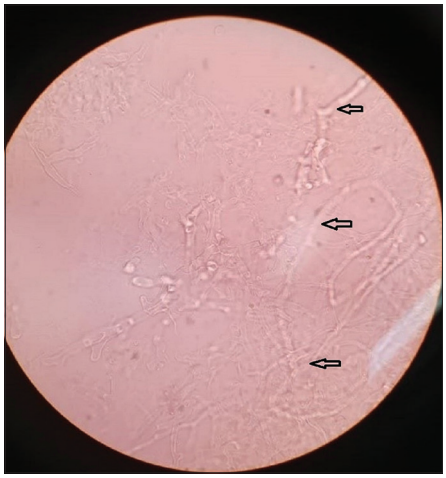

Figure 3: Acute angle branching of aspergillus

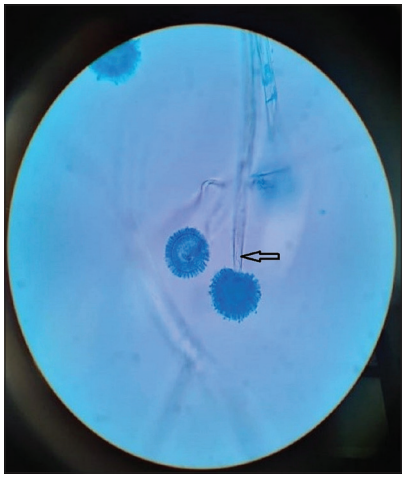

Figure 4: LPCB mount showing Aspergillus niger

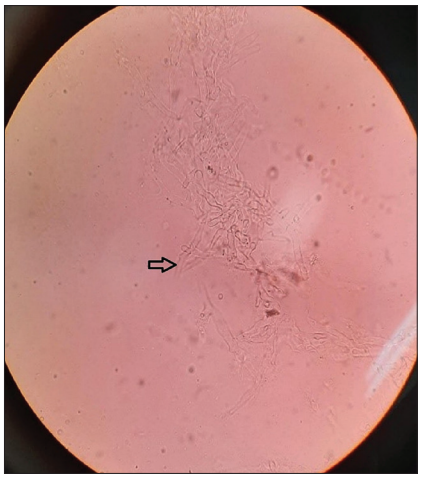

Figure 5: Broad aseptate hyphae of *Mucor*

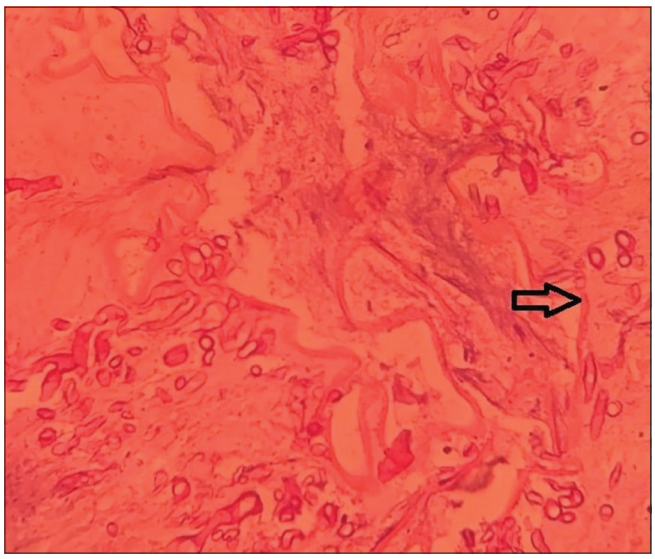

Figure 6: Wide angled branching aseptate fungal hyphae of mucor (Hematoxylin and Eosin)

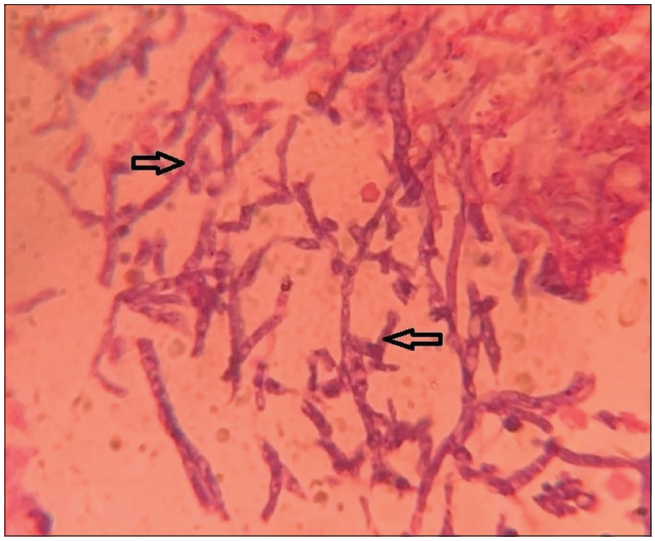

Figure 7: Periodic acid schiff stain positive mucor

million twice-daily doses for 1 week. Subsequent KOH mounts were negative for the fungus and the culture was sterile. She improved and her repeat contrast enhanced magnetic resonance imaging (CEMRI) of paranasal sinuses, orbit, and brain did not show any extension. She was discharged on oral hypoglycemic agents and posaconazole. She took posaconazole for 45 days. She is being followed up regularly and doing well.

Discussion

An increasing number of COVID-19 cases with superadded bacterial or fungal infections pose a challenge to the healthcare system. The exact pathogenesis is not known. Immune dysregulation, thrombotic angiopathy, and pleiotropic alterations of glucose metabolism probably play a vital role.[3] Diabetes is the most common co-morbidity associated with 47.5% of cases.[2,3] In a systemic review by Singh *et al.*,[4] 101 cases of *Mucor* were reported in people with COVID-19. These secondary infections can be seen during the active reverse transcription polymerase chain reaction (RT-PCR)-positive COVID-19 cases or may come up in the recovering phase. Singh *et al.*[4] found *Mucor* in 59.4% of active COVID cases and 40.6% of recovered cases. Our patient developed a fungal infection during the recovery period. Involvement of the nose and sinuses is common (88.9%), followed by rhino-orbital in 56.7% of cases. Roden *et al.*,[5] also, in their review, found the sinuses as the most common (39%) site involved. Co-infection with fungus is associated with high mortality. Study by Sarkar *et al.*[6] showed a mortality rate of 40% vs. 87.5% by Gerg *et al.*[7]In a series by Sharma *et al.*,[8] all patients had a positive outcome.

Mixed invasive fungal infections in the pre-COVID-19 era have been reported.[9,10] In previous studies, mixed invasive fungal infections were found in 1 out of 16 and 3 out of 36 cases.[11,12] Dual infection by *Aspergillus* and *Mucor* along with superadded *Pseudomonas* was reported.[13] Nephrotoxicity needs to be kept in mind in patients receiving liposomal amphotericin along with colistin[14], which also shows a synergic effect on fungicidal potency.[15]

Awareness among family physicians plays a key role in early diagnosis and referral of these cases to appropriate centers, leading to a positive outcome.

Conclusion

A high degree of clinical suspicion of fungal infections in COVID-19 patients, especially in diabetic patients helps in early diagnosis and appropriate care, leading to a fruitful outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients

understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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