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Case Report

Invasive pulmonary and sino-orbital mucor mycosis in patient with SARS-Cov-2 infection with diabetic ketoacidosis

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ABSTRACT

Patients with Severe acute respiratory syndrome coronavirus-2 (SARS-Cov-2) are susceptible for developing fungal infection due to uncontrolled diabetes or immunosuppression. A 46 years male presented with diabetic ketoacidosis, respiratory failure with peri orbital blackish discoloration with SARS-Cov-2 positive report. Computed tomography (CT) chest was suggestive of perihilar ground glass opacity and multiple thick-walled cavities. Left nasal cavity scrapings revealed hyaline aseptate hyphae and growth of *Rhizopus arrhizus*. Patient was initially managed conservatively with liposomal amphotericin B but later underwent orbital exenteration and finally succumbed. We want to emphasize higher mortality and aggressive management of mucor mycosis when it occurs with SARS-Cov-2 as a concurrent illness.

Keywords: Disseminated, Co-infection, Diabetes, COVID-19

INTRODUCTION

Mucormycosis is an invasive fungal infection, frequently acute and enormously severe caused by opportunist and ubiquitous fungi belonging to the class *Phygomycetes*, subclass *Zygomycetes*, order *Mucorales*, family *Mucoraceae* and usually by the following species: *Absidia corymbifera*, *Apophysomyces elegans*, *Cunninghamella bertholletiae*, *Mucor rouxii*, *Rhizomucor pussillus*, *Rhizopus arrhizus*. Mucormycosis is third cause of invasive fungal infection after *Aspergillus* and *Candida* spp in humans.[1]

Coinfection in patients with coronavirus disease 2019 (COVID-19) has been reported on multiple series, being bacterial in origin the most frequent; and fungal infection being reported only in severe cases.

Fungal infections are emerging well in COVID 19 pandemic. Possibly due to widespread use of iv steroids and anti-inflammatory and immunomodulatory drugs. Superimposed aspergillus and candida infection has been well described in the literature, in patient with COVID 19 pneumonia.[2,3] However there is very limited data on co-infection with mucormycosis in critically ill patient. Mucor mycosis is one entity which come across in patient with COVID 19. Only one case report in literature where rhino cerebral mucor mycosis has been described and one case reported of pulmonary mucormycosis but we are presenting a case of mucor mycosis with concurrent Sino-orbital and pulmonary involvement in setting of SARS-Cov-2 and naïve for steroids and immunomodulators.[4,5]

CASE REPORT

A 46 years male presented to medicine emergency with history of fever for 3 days (101 to 103˚ Fahrenheit) intermittent, relieved with antipyretics followed by dry cough and shortness of breath last for 1 day. At presentation he was conscious, oriented with GCS of

E4V5M6, his left eyelid was swollen and periorbital blackish discoloration was present. Hemodynamically, he was unstable, his blood pressure was 90/60 mm of Hg, pulse 92/min, Spo2 90% under venturi mask (Fio2 ~ 0.6) with flow of 8 liter per min. No past history of diabetes mellitus, hypertension or any other co morbidities was reported.

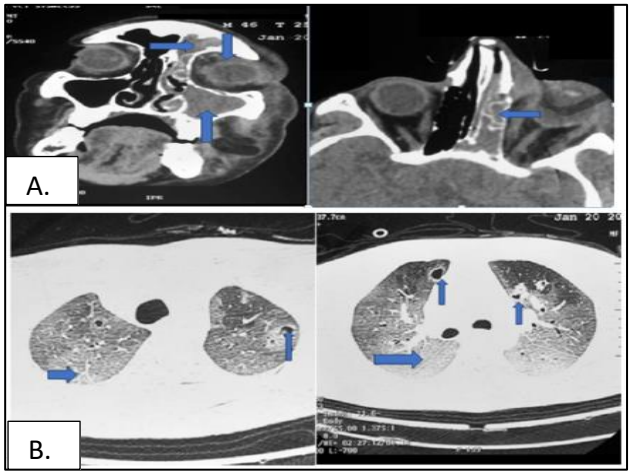

Figure 1: (A) Soft tissue density lesion seen involving left maxillary (upward facing arrow), anterior ethmoidal and frontal sinus with few hyperdense areas in left frontal sinus (horizontal arrow). Mild thinning of walls of ethmoidal air sinuses. Peri ocular thickening of soft tissue and irregularity of eye ball suggesting orbital cellulitis (down ward facing arrows). (B) Ground glass haze (horizontal arrows) with interstitial thickening seen in bilateral lung fields more so in basal lung fields with evidence of few soft tissue density nodules showing cavitation (vertical arrows) within them seen in bilateral upper lobe, right middle lobe and lingula.

On investigations, nasal pharyngeal swab was found to be positive for SARS COV 2 by gene expert test. Random blood glucose was 450 mg/ dl and serum ketones was 6.5 and arterial blood gas analysis was suggestive of high anion gap metabolic acidosis. His complete blood count showed Hb 14.8 gm/dL, TLC 21000/cu mm, platelet count 1 lakh 37 thousand, electrolytes Na 163, K 3.5, His renal and liver functions were normal. Chest roentgenogram was suggestive of peripheral and perihilar patchy areas of consolidation. But patient underwent non contrast CT paranasal sinuses and high resolution CT chest. CT Scan of Para nasal sinuses scan (Figure 1A) was suggestive of left maxillary sinus and nostril areas hyper density and left edematous globe with surrounding hyper density suggestive of per orbital inflammation. CT chest (Figure 1B) revealed multiple thick walled cavities in bilateral upper and lower lobes with peri-hilar and basal ground glass opacity with patchy area of consolidation.

Left nasal cavity scrapings were sent to mycology lab. A 20% KOH mount of scraping revealed hyaline broad aseptate hyphae with right angle branching suggestive of sample positive for Mucor group of fungi. (Figure 2 A). The specimen were inoculated on two SDA tubes and incubated at 25°C and 37°C. Cottony mycelium grew in both the tubes after 48 hrs of incubation which was initially white with white to greyish surface and later turns into blackish grey. (Figure 2B) The lactophenol cotton blue (LCB) mount of growth showed hyaline broad, ribbon like aseptate hyphae with sporangiophores bearing angular to lemon shaped sporangiospores with longitudinal striations. Growth was identified as *Rhizopus arrhizus.* (Figure 2 C)

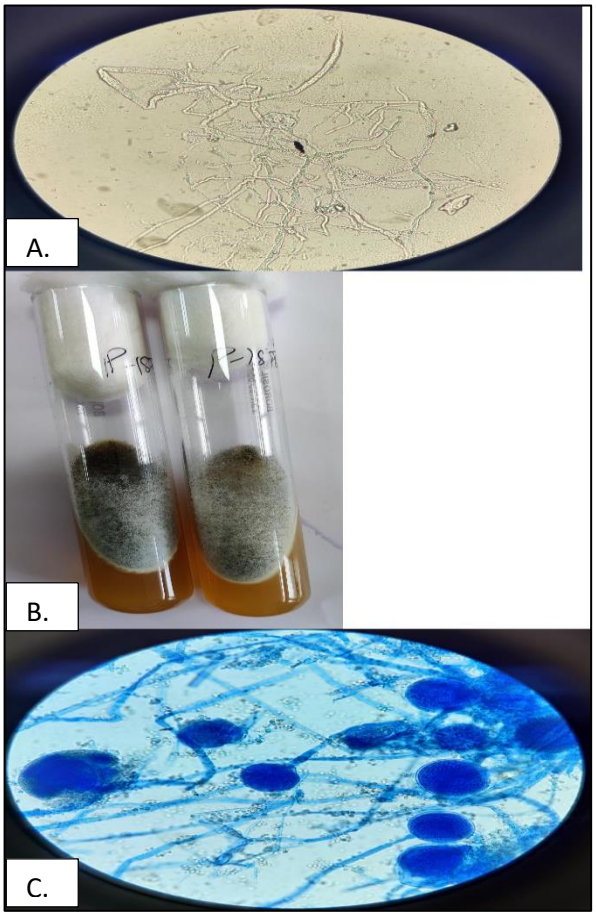

Figure 2: (A) KOH wet mount on 40 x suggestive of aseptate hyphae. (B) Growth of Rhizopus in SDA tubes. (C) LCB mount showing *Rhizopus arrhizus.*

Patient was managed for diabetic ketoacidosis with IV fluids, insulin infusion and iv antibiotics. Periodic blood glucose, blood ketones and arterial blood gas monitoring was done. in view uncontrolled blood sugars with left peri orbital blackish discoloration, there was high suspicion of fungal infection, liposomal amphotericin B was started along with antibiotics.

His blood glucose levels were gradually controlled, and resolution of high anion gap metabolic acidosis. Patient was planned for orbital exenteration by treating surgeons. Patient underwent total maxillectomy and debridement

and clinical specimen was sent for for microbiological and histological examination.

But patient was hemodynamically unstable despite on dual inotropics and mechanical ventilation and subsequently develop cardiac arrest on third post-operative day and could not be resuscitated and expired.

DISCUSSION

COVID-19 related deaths has crossed more than 1.5 lac cases in India. In absence of definitive anti viral treatment.

There are specific pathophysiologic features of COVID-19 that may permit secondary fungal infections, including a propensity to cause extensive pulmonary disease and the subsequent alveolo-interstitial pathology that may enhance the risk of invasive fungal infections. Second, the immune dysregulation associated with COVID-19, with reduced numbers of T lymphocytes, CD4+T, and CD8+T cells, may alter innate immunity.

Mucormycosis is rare opportunistic fungal infection characterized by infarction and necrosis of host tissues that results from invasion of the vasculature by hyphae. The most common clinical presentation of mucormycosis is rhino-orbital-cerebral infection, believed to be secondary to inhalation of spores into the paranasal sinuses of a susceptible host.[6]

Predisposing situations for mucormycosis include diabetes, systemic corticosteroid use, neutropenia, hematologic malignancies, stem cell transplant, and immunocompromised individuals.

Werthman-Ehrenreich reported the case of a 33-year-old female who presented with left-sided ptosis and proptosis with altered sensorium.[7] Investigations revealed diabetic ketoacidosis with COVID-19 infection similar to our index case and imaging was significant for maxillary and ethmoidal sinus mucosal thickening &on culture Mucor was demonstrated. Different organs might be involved, the most frequently affected of which are the lungs, being the second most common manifestation (58%) with a mortality rate up to 80% due to its aggressive clinical course.[8]

The European Confederation of Medical Mycology Mucormycosis Guidelines strongly suggest an early surgical treatment to remove the infected tissue (either through local debridement or complete resection) in addition to systemic antifungal treatment.[9]

Orbital exenteration for life- threatening infection is triaged as a Level A condition or an urgent condition requiring surgery within 4–72 hours as per the preferred practice pattern advised in our country during COVID 19.

CONCLUSION

As COVID 19 cases are increasing day by day, surveillance for fungal co infection should be initiated, in settings of poorly controlled diabetes and underlying immunosuppressive state or persistent fever and respiratory failure, high suspicion for mucor mycosis should be kept and manage aggressively once proven, as it will results in fatal outcome.

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