Pulmonary Mucormycosis secondary to Severe Acute Respiratory Illness due to Covid 19 Infection: A Case Report.

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ABSTRACT

Patients diagnosed and hospitalized with SARS COV-2 are managed with corticosteroids due to its known benefits for the prevention of airway inflammation secondary to acute respiratory distress syndrome seen commonly in viral pneumonia. However, these patients carry a high risk of developing secondary bacterial and fungal infection. We present a case of 60-year-old male with COVID-19 pneumonia. The patient was diagnosed with pulmonary mucormycosis 18 days following admission. The patient was treated with broad-spectrum antibiotics, remdesivir and corticosteroids along with antifungals including voriconazole and amphotericin B with no significant improvement. However, even after extensive medical management patient was eventually intubated and succumbed to its complications. Mucormycosis although an uncommon infection should be considered due to extensive use of glucocorticoid therapy and concurrent comorbidities present among COVID-19 patients.

Keyword: Pulmonary mucormycosis, Severe acute respiratory illness, Mortality

INTRODUCTION

With the ongoing pandemic and devastating waves of coronavirus disease COVID-19 has left a disastrous effect throughout the globe. Amongst many therapies that have been tried systemic glucocorticoids have found to improve the outcome of patients. Due to the nature of illness, prolonged hospital stay, preexisting medical condition and glucocorticoid use patients diagnosed with severe COVID-19 pneumonia are prone for secondary fungal infection. COVID-19 pneumonia with secondary aspergillus infection has been reported in literature since beginning of the pandemic[1]. However mucormycosis is usually not suspected or diagnosed as it is a rare opportunistic fungal infection and found commonly in patients with stem cell transplant, hematologic malignancies, uncontrolled diabetes mellitus, neutropenia, immunocompromised state[2,3]. Here we present a case of pulmonary mucormycosis in a case of severe COVID-19.

CASE REPORT

A 60 year old man with no known comorbidities presented at our institution with chief complaint of shortness of breath. Patient was transferred from community level hospital where he was diagnosed as a case of COVID-19 (SARS COV-2 RT PCR positive) and was treated accordingly with remdesivir (five doses), antibiotics, steroid and thromboprophylaxis. His symptoms during his first admission was Fever (Temperature 102^0 F) with productive cough. Upon admission, at our emergency patient was received in tachypnea with respiratory rate of 24/min and saturation was maintained at 96% via nasal cannula at 4L/min. Complete Blood Count (CBC) was 22,190/mm^3 with neutrophil predominance. Chest CT scan showed multifocal central and peripheral ground glass opacities and fibrotic changes in both lungs, focal bronchiectatic changes within the consolidation in left lungs, preexisting cyst within the consolidated area in lingula and apical segment of left lower lobe. CT (CO-RADS) severity score was 18/25 (severe). COVID panel for inflammatory marker was sent with findings of elevated IL-6 of 64.4 pg/ml, C-Reactive Protein of 84.1 mg/L and LDH of 394 U/L. Patient was started on Piperacillin and Tazobactam 4.5gm/iv TDS, Azithromycin 500mg OD ,Dexamethasone 6mg/iv OD, Voriconazole 200mg/tab BID and low molecular weight heparin (LMWH). Sputum examination showed Klebsiella Pneumonia with Sputum KOH budding yeast cells with pseudohypae. On the third day of admission, patient had one episode of hemoptysis and LMWH was stopped temporarily. Repeat CBC was done with Hemoglobin of 13.5 gm/dl. RT PCR test was also repeated which was still positive with CT Value of 24.95. Patient was still under oxygen requirement with saturation level at 92% maintained with oxygen at 2L/min. On the fifth day of admission CBC, RFT and LFT was repeated with significant decrease in leukocyte count 16,140 cu/mm3 with rest of the parameters being normal.

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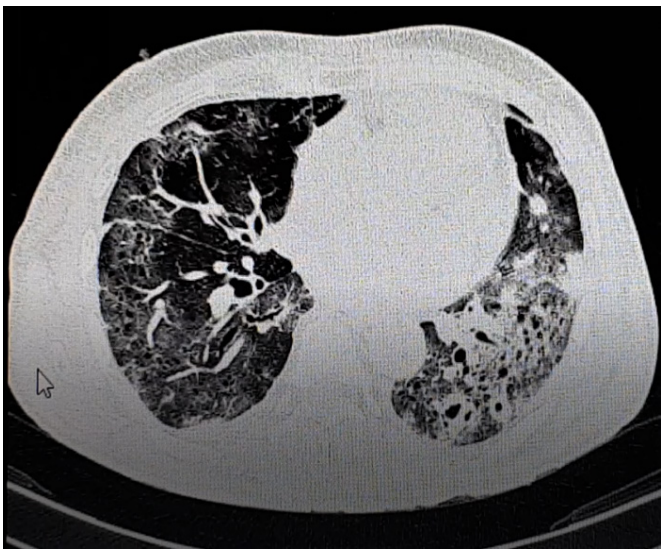

Figure 1 Chest CT Scan showing ground glass appearance on right lower lobe with cavitary lesion on left lower lobe

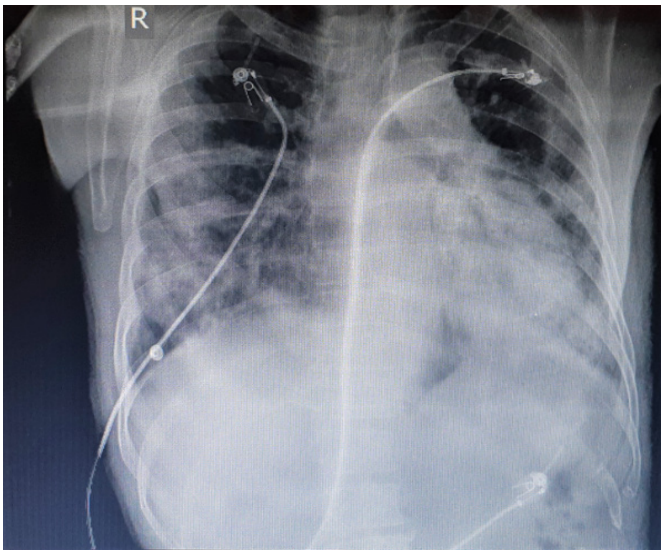

Figure 2 Chest Xray showing Bilateral Consolidation

Repeat chest x-ray was noted with bilateral consolidation and ground glass appearance. Patient's blood sugar was monitored six hourly and was treated with insulin as per the correction scale. On the eighth day of his hospital stay his oxygen requirement was gradually tapered to 1L/min which patient was able to tolerate. Repeat CBC showed decrease in leukocyte count at 14,950 cu/mm3, electrolytes were normal, ALT was elevated at 150 and sputum still showed growth of Klebsiella Pneumonia but sputum KOH showed no fungal elements. Chest Xray showed increase in infiltrates with bilateral consolidation. Repeat RT PCR was still positive with CT value of 35.0. On the tenth day of admission inflammatory markers were repeated Ferritin was elevated at 863 ng/ml, IL-6 was elevated 67.0pg/ml, CRP was elevated at 77.0 mg/L while procalcitonin was normal. Repeat sputum culture showed growth of Aspergillus flavus so Voriconazole was continued. On the 13th day of his admission patient had another episode of Hemoptysis. PT/INR was sent which came out normal with slight elevation of ALT(63.0). Tranexamic Acid 500mg/tab was added which decreased hemoptysis. Chest x-ray was repeated on the 14th day of admission which showed bilateral progression of consolidation with new cavitary lesions. Repeat CBC showed increase of leukocyte count at 20,120 cu/mm3. Antibiotics were escalated to Meropenem and Clindamycin, Since patient was breathless dexamethasone was changed to methylprednisolone. HRCT was repeated which showed multifocal central and peripheral ground glass opacities and fibrotic changes in both lungs, cavitary lesions in bilateral lung fields predominantly in peripheral aspect of bilateral lower lobes secondary to fungal infection and small cystic lesions.

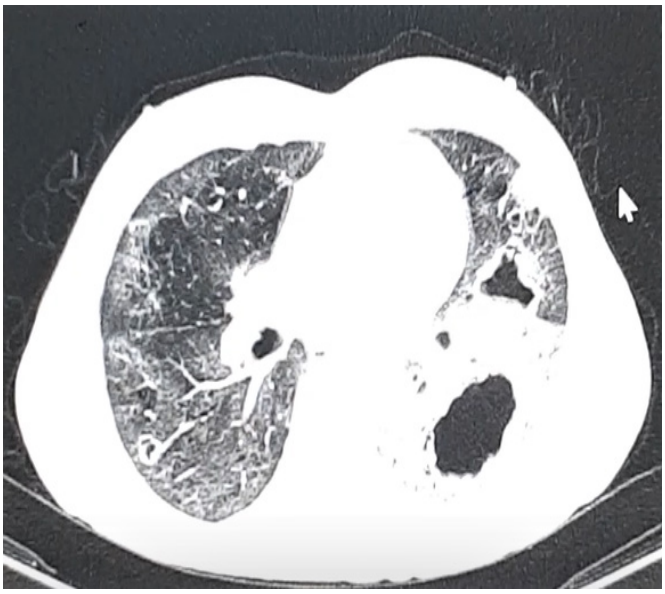

Figure 3 Repeat Chest CT showing cavity at the left lower lobe with ground glass opacities.

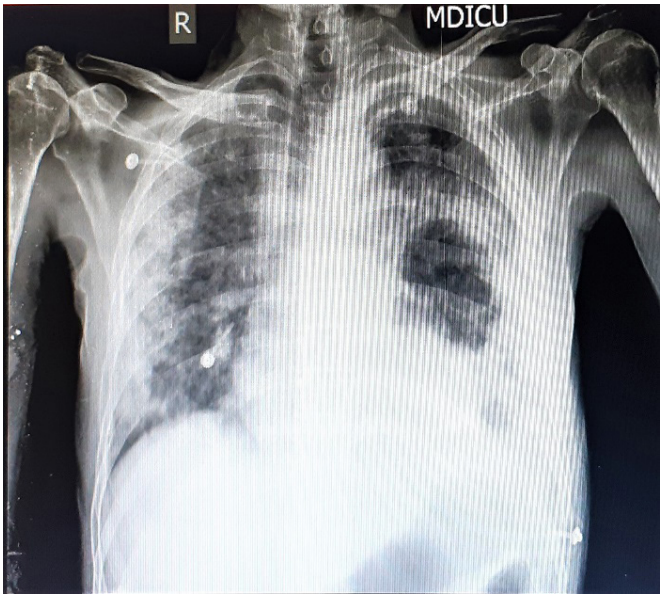

Figure 4 Repeat Chest Xray showing cavitation in left lobe with Bilateral Consolidation

On the 15th day of admission patient complained of generalized body ache with fever and vomiting. Patient's sputum profile showed growth of MRCONS (Methicillin

resistant coagulase negative staphylococcus species) so Clindamycin was changed to Levofloxacin as per the antibiogram. However KOH preparation showed no fungal elements . Patients RT PCR was repeated on his 18th hospital day which came negative, labs were repeated which showed decrease in leukocyte count but repeat sputum profile showed growth of mucor species and patient was shifted to ICU for close monitoring. Inj Amphotericin B was started at 0.25 mg/kg. On the 19th hospital day patients condition deteriorated as oxygen requirement increased. Due to persistent tachycardia and tachypnea with persistent type I respiratory failure, the patient was intubated. On 20th day of hospital stay patient was hypotensive with features of septic shock. Central line was inserted and inotropes were started but patient's vitals were poor with rapid deterioration and the patient succumbed to illness the same day.

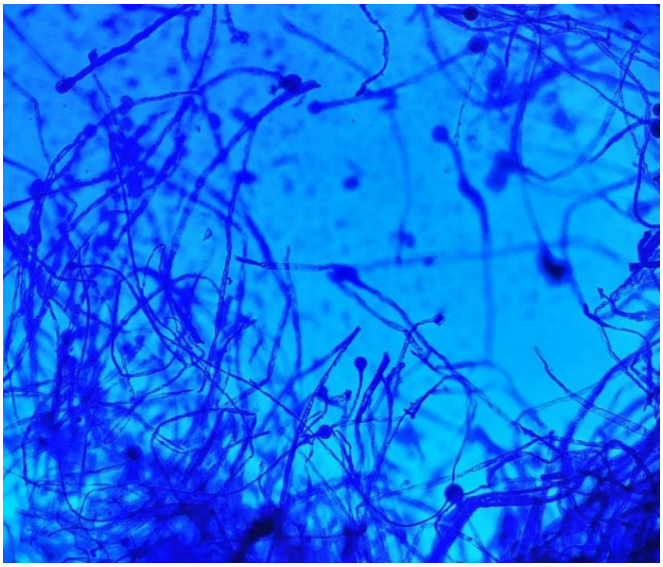

Figure 5 Lactophenol cotton blue mount showing aseptate hyphae with nodal rhizoids and short sporangiophores with terminal spherical sporangiophores

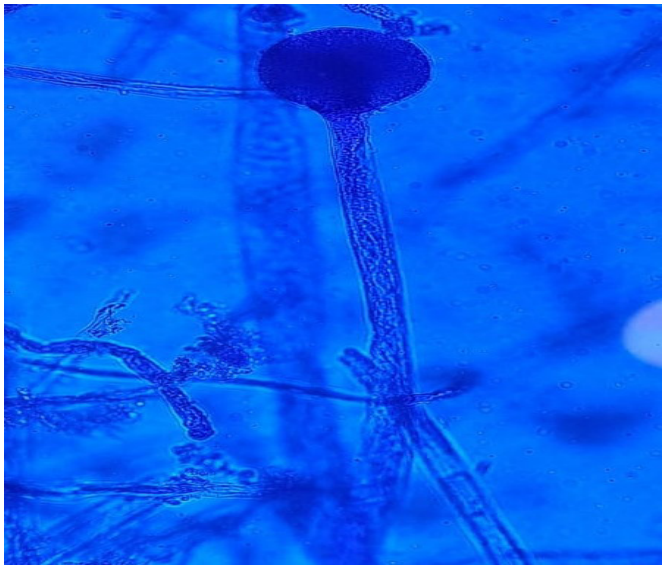

Figure 6 High power photomicrograph showing sporangium (lactophenol cotton blue stain)

DISCUSSION

Mucormycosis is an uncommon but aggressive angioinvasive infection caused by the fungi of the family Mucoraceae and order Mucorales. The term zygomycosis previously included the fungus that caused mucormycosis and entomophthoramycosis. But later with the help of molecular details and re-structuring based on the structure, life cycle and ecology the term zygomycosis was erased[4]. The agent that causes mucormycosis are present as common saprobes on decaying food, agricultural and forest soils and animal excrement[5]. Inhalation of the fungal spore is the known mode of infection with no evidence of human to human transmission[6]. The most common site of infection is rhinocerebral, cutaneous, lung, disseminated and gastrointestinal tract in decreasing order[7]. Prior to the COVID-19 pandemic, based on a systemic review of literature published between 2000 and 2017 diabetes was the most common risk factor (40%) amongst patients and more common in Asia (46%) and Africa (75%). Haematologic malignancy was the next common risk factor (32%) followed by solid organ transplant(14%)[7]. Recently, cases of mucormycosis specially amongst COVID-19 have been reported worldwide and India in particular has burdened the majority of cases as per Singh AK et al (0.14 per 1000)[8]. The main reason that promotes the growth of Mucorales spores in covid-19 patient is a favorable condition of low oxygen (hypoxia), uncontrolled blood sugar (diabetes, new-onset hyperglycemia, steroid induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis), high iron levels (increased ferritins) and decreased phagocytic activity of WBC due to immunosuppressive state (steroid induced, SARS-COV-2) along with several other factors like prolonged hospital stay and mechanical ventilation[8]. Mucorales infection have a tendency for rapid deterioration due to its angioinvasive property which results in thrombosis and tissue necrosis. Mucormycosis without concomitant COVID-19 infection has a mortality rate ranging from 40-80%[9]. Clinical features may present with persistent fever, dyspnea, cough and hemoptysis. Our patient had fever, dyspnea and episodic hemoptysis which prompted for further lab workup.

Radiological finding of pulmonary mucormycosis may present as lobar and segmental consolidation, multilobar distribution, single or multiple nodules which are nonspecific as it may be seen in pulmonary aspergillus. CT findings are variable as well. Ground glass lesion is the earliest imaging seen in PM which might progress to consolidation, nodules or masses, but this is a non-specific sign with repeated frequency between 19% and 53[10]–[12]. Chamilos et al, in order to differentiate aspergillosis from mucormycosis found that images with presence of more than 10 lesions and pleural effusion was more suggestive of pulmonary mucormycosis(PM)[13]. The reverse halo sign which is a ground glass lesion with a peripheral rim of consolidation is so far the most specific sign for mucormycosis seen in 19%-94% patients[10],[11],[14],[15]. Our patient's CT chest initially showed multifocal central and peripheral ground glass opacities and fibrotic changes which were nonspecific for PM.

Bronchoscopy and CT biopsy aided histopathology and direct microscopy can be helpful modalities for mucormycosis. Sputum culture and BAL cytology may show no growth making it unreliable at times[16]. The characteristic histopathology of mucormycosis appear as broad, non septate hyphae with right angle branching. Specific biomarker such as Beta-d-glucan and serum galactomannan antigen can help in diagnosing aspergillosis infection but no such biomarkers are associated with mucormycosis. Our index case had no growth for mucormycosis in its initial sputum culture requiring repeated collection of sputum samples.

Our patient was treated with voriconazole and liposomal amphotericin B based on the sputum culture growth. Surgical debridement of the source is the ideal management in cases who can tolerate surgery. In patients like ours who are unable to undergo surgery due to high surgical mortality risk, patient can benefit form high dose of amphotericin B up to 10mg/kg/daily[17]. However the patient deteriorated very rapidly with subsequent intubation before his treatment could be escalated.

CONCLUSION

With the increase in COVID-19 cases, physicians caring for such patient should keep a high suspicion level for possible secondary fungal infection. Mucormycosis is a progressive and fatal disease usually seen in diabetic ,immunocompromised and hematological malignancy patients. Diagnosis of mucormycosis can be a challenge due to its non-specific presentation. The need for invasive procedure and histopathology report for confirmation makes it even more difficult. Early detection with surgical intervention and aggressive medical treatment can improve the outcome of the patient.

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