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Original Research Paper

Pulmonary Medicine

" A CASE REPORT OF PULMONARY MUCORMYCOSIS IN COVID 19 POSITIVE PATIENT: TSUNAMI AFTER EARTHQUAKE"

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ABSTRACT Pulmonary Mucormycosis is a rare invasive fungal infection (IFI) due to several species of saprophytic fungi, occurring most often in immunocompromised patients (including organ transplantation). During the ongoing Coronavirus disease 2019 (COVID-19) pandemic, there have been increasing reports of bacterial and fungal co-infections occurring in COVID-19 patients due to various reasons including underlying co-morbidities, usage of steroids and other immunomodulators and covid infection itself. Here, I describe a case of pulmonary mucormycosis occurring in a 60 years old male diabetic patient who had history of COVID -19 infection 2 months back. For that, he was managed with oral antiviral, injectable antibiotics, steroids and other supportive care based on telecommunication at home. Approximately two months after COVID-19 diagnosis, he developed left sided chest pain, cough with expectoration and hoarseness of voice. After confirmation of diagnosis with TBLB (trans bronchial lung biopsy), he was given broad-spectrum antifungal therapy Amphotericin –B and other supportive treatment. After aggressive therapeutic measures, he was discharged after a prolonged hospital stay. Pulmonary mucormycosis with COVID-19 may need to be evaluated as an emerging disease association and clinicians should be vigilant to evaluate for the same.

KEYWORDS : Amphotericin B injection, Coronavirus disease 2019 (COVID-19) and Mucormycosis, trans bronchial lung biopsy.

INTRODUCTION

Mucormycosis (previously called Zygomycosis) is the term used for invasive fungal infections (IFIs) occurring due to saprophytic environmental fungi–*Rhizopus arrhizus* (most common), *Mucor*, *Cunninghamella*, *Aposphysomyces*, *Licitheimia* (*Absidia*), *Saksenaea*, *Rhizomucor*] [1]. Mucormycosis can have at least six different clinical presentations–rhino cerebral, pulmonary, cutaneous, gastrointestinal, disseminated and miscellaneous [2]. Pulmonary mucormycosis is the 2nd most common manifestation (after rhino cerebral) and often seen in patients with haematological disorders and transplant recipients[3,4].

The common risk factors for mucormycosis include hematologic malignancies, solid organ transplant recipients (SOTRs), stem cell transplantation, prolonged and severe neutropenia, poorly controlled diabetes mellitus (DM), iron overload, deferoxamine therapy, major trauma, prolonged corticosteroid use, illicit intravenous drug use, neonatal prematurity, malnutrition and potential nosocomial sources (including bandages and intravascular devices) [1], [5], [6]. Mucormycosis comprises 2–6% of IFIs [6],[7].

Life-threatening fungal infections have risen sharply in recent years, owing to advances and intensity of medical care in this ongoing Coronavirus disease 2019 (COVID-19) pandemic, due to the novel severe-acute-respiratory-syndrome-coronavirus-2 (SARS-CoV-2) which can be associated to significant and sustained lymphopenia compromising the immune system, especially in the most severe cases.[8]These insights create a foundation for the development of new immune-based strategies for prevention or enhanced clearance of fungal diseases.

Here I describe a case of diabetic patient who developed pulmonary mucormycosis infection after COVID-19 which is rare as compare to other site involved by mucormycosis.

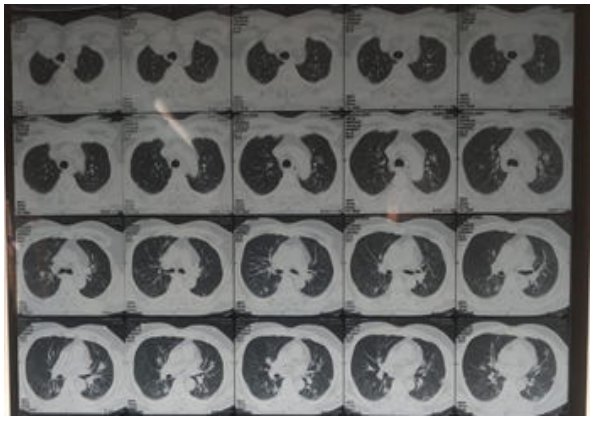
CASE REPORT:

A 60-year-old male patient was admitted to our hospital with chief complain of weight loss around 10kg in last 2 months, left sided chest pain, cough with expectoration since last 10 days. He was known case of diabetes mellitus since last 15 years for that he was on regular oral hypoglycaemic agents. He had habit of tobacco chewing and smoking since 30 years.

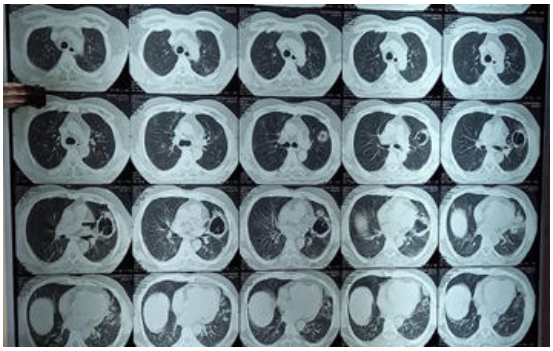
Patient had positive history of COVID -19 infection before 2 months. At that time, he had complained of fever, weakness and dry cough, for that he took treatment at home on basis of telecommunication. He took antiviral tab. Favipiravir for 5 days and Inj.cefosalbactam and methyl-prednisolone for 7 days as per documents available from his treatment part. Patient became relatively asymptomatic after that.

On evaluation at time of admission, patient was maintaing oxygen 86% off air and respiratory examination showed presence of course crepitation in left lower lobe on auscultation. Admission laboratory testing revealed white blood cell count 13.20 × 10^9/L (normal range {N}: 3.8–10.5 × 10^9/L), lymphocyte count 0.7 × 10^9/L (N:/ 1.0–3.0 × 10^9/L) and elevated inflammatory markers–C-reactive protein 16.38 nmol/L (N: 0–3.81 nmol/L), procalcitonin 0.72 μg/L (N: 0.02–0.10 μg/L), lactate dehydrogenase 583.33 nmol/(sL) [N: 833.33–4033.33 nmol/(sL), ferritin 0.15 nmol/L (N: 0.07–0.90 nmol/L) and D-dimer 894 μg/L DDU (N: ≤ 229 μg/L DDU).

In radiological examination, serial CT Thorax showed increase in severity of lesion within 1-month duration. From scattered area of ground glass densities in 1month back CT scan, present CT had 52*46mm thick walled cavitory lesion in left lower lobe with bilateral multiple scattered areas of GGOs and parenchymal bands. [Figure 1] All other investigation to rule out pulmonary tuberculosis, re infection with COVID like 2 sputum AFB, sputum CBNAAT, RT-PCR were negative.



(A)Multiple, scattered areas of ground glass Densities are seen in both lung fields predominantly in Peripheral location



(B) About 52*46mm thick walled cavity lesion with thick internal septa and consolidation seen in left lower lobe.

Figure 1: Ct Thorax Showing Changes Of Pulmonary Mucormycosis After 2 Months Of Covid Positive Treatment:

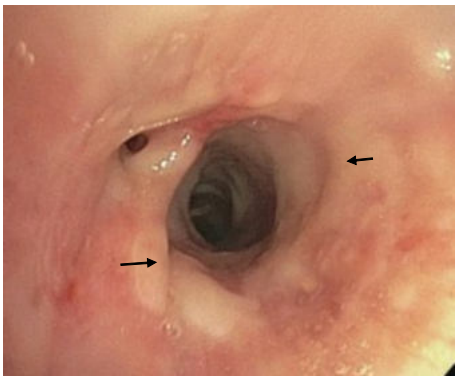


Figure 2: Bronchoscopic View Of Left Lower Lobe Showing Irregular Mucosa With Whitish Patch.

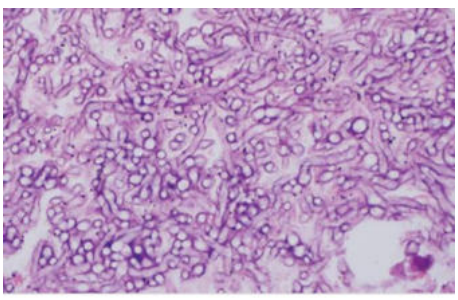


Figure 3: Histopathological Slide Of Tissue Taken Via Trans Bronchial Lung Biopsy Showing Lung Parenchyma With Organising Pneumonia And Abundant Necrotic Material Withnecrosed Tissue And Vessels And Many Aseptate/ pauciseptate Broad, Twisted, Ribbon Like Fungal Hyphae With Angled Branching Resembling Mucor Species.

Then bronchoscopy guided Trans Bronchial Needle Aspiration was done which showed presence of irregular mucosa with whitish patch in superior basal segment of left lower lobe [Figure 2] and sent sample for BAL CBNNAT, BAL cytology and lung tissue for histopathological examination. Amongst, BAL CBNAAT and cytology were negative and we ruled out possibility of pulmonary tuberculosis and malignancy.HPE showed acute necrotising /organizing pneumonia related to invasive fungal infection consistent with MUCORMYCOSIS with tissue and blood vessels invasion present [Figure 3]

Patient was then given Inj.liposomal Amphotericin B 7ml/kg/day for 4 weeks then shifted to maintenance therapy with tablet posaconazole (300) mg one tablet in twice a day dosage for 15 days. Along with antifungal coverage of antibiotics, anticoagulants and other supplementary treatment was given according to his laboratory investigations. Patient was given discharge after 7 weeks of indoor treatment.

DISCUSSION

Pulmonary mucormycosis is the second most common site of involvement in Mucor infection after COVID 19 treatment now a days. The fungus grows on decaying food, soil, and animal excrement. Human usually become infected by inhalation of spores and most often seen in patients with haematological disorders and transplant recipients [3,4]. Haematological malignancy was the major risk factor (32–40%), followed by diabetes mellitus (32–56%), haematopoietic stem cell transplant (1–9.8%) and solid organ transplant (6.5–9%) and renal disease (13–18%) in pulmonary mucormycosis [9,10,11]. A diabetic patient who received high-dose corticosteroids for COVID-19 management and given oxygen for longer duration developed rhino-orbital mucormycosis. An intubated COVID-19 patients develop a new pulmonary lesion, with bronchial aspirate revealing *Rhizopus*. In patients with no classic risk factors for IFIs, severe COVID-19 may have led to lymphopenia and immune system alterations, predisposing to mucormycosis. [9]

The patients often present with high fever (38–70%), persistent cough (50–61%), pleuritic chest pain (22–37%), dyspnoea (19–34%), and haemoptysis (16–28%). The diagnosis of pulmonary mucormycosis remains a challenge. Imaging studies can be non-specific. The patients may present with lung infiltration and consolidation (58–96%), multiple nodules, pleural effusion (6–21%), thickly walled cavities (6–37%), hilar or mediastinal lymphadenopathy (3.3%), air crescent sign (1.1–8%) and pneumothorax (1–3%) on imaging studies. The reverse halo sign, the characteristic sign of mucormycosis, was seen only in 9.8% of the patients [10,11,12].

Pulmonary mucormycosis is usually unilateral (62–75%), occasionally bilateral (16–25%), rarely hilar or mediastinal (3%). In unilateral lung disease, upper lobe is commonly involved (40–45%), followed by lower lobe (16–21%) and middle lobe (1–3%); the multi-lobar disease is seen in 6–12% of the pulmonary mucormycosis cases [10,11].

Both bronchoscopic and percutaneous lung biopsy are effective tools to help diagnose PM. CT-guided lung biopsy of suspicious for fungal pneumonia, laboratory testing results in 80% of patients were shown to be positive for fungal infection by using Calcofluor white staining [13]. Although the process is not widely available, demonstrating circulating Mucorales DNA by using quantitative polymerase chain reaction (qPCR) has been shown to be an effective method for revealing mucormycosis in patients with cutaneous, rhino cerebral, pulmonary, and disseminated forms.

In the treatment part, if feasible, attempts to reverse the underlying predisposing factors for infection should be made. Treatment may include control of blood glucose levels, treatment of metabolic acidosis, or tapering of immunosuppressive agents [14]. Treatment then consists of antifungal therapy and, if possible, surgical debridement of affected tissue. Lipid formulations of amphotericin B are associated with less renal impairment compared with conventional amphotericin B deoxycholate. Most azole antifungal agents have no significant activity against mucormycosis. Posaconazole is a newer broad-spectrum triazole that has shown activity against many species of the order Mucorales [15]. Surgery is recommended for patients with localized disease and results in improved outcomes compared with in those treated with antifungal therapy alone. Surgery is usually reserved for patients with unifocal disease and can consist of wedge resection, lobectomy, or pneumonectomy.

CONCLUSION

Pulmonary Mucormycosis has a high mortality rate, in part because of the underlying risk factors for the disease. The most common risk factors include diabetes mellitus, hematologic malignancy, and solid organ and stem cell transplant. Clinicians should be vigilant to evaluate for mucormycosis in patients with COVID-19 infection. Further research is needed to evaluate the potential link between these two infections. Because of the angioinvasive nature of the disease, pulmonary necrosis is common. It can appear as a reverse halo at CT and correlates with necrosis found at pathologic analysis. Delay in treatment are associated with a greater mortality rate. The treatment of mucormycosis largely depends on early and precise diagnosis followed by long term use of combination of antifungal medications and surgical intervention when necessary.

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