

## Case Report



# Coinfections in Intensive Care Unit with pulmonary tuberculosis and mucormycosis: A clinical dilemma

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### Abstract

Herein, we present the case report of an adult male diabetic patient who had coinfection with *Mycobacterium tuberculosis* and mucormycosis, which otherwise is a rare clinical entity. Diabetes mellitus may predispose a patient to tuberculosis (TB) infection which further weakens immune system thus making him susceptible to other fungal or bacterial infections which may pose various treatment difficulties. Therefore, there is a need for mycological and bacteriological investigations in patients with pulmonary TB to rule out secondary coinfections thus contributing to better management.

**Keywords:** Coinfection, diabetes mellitus, mucormycosis, pulmonary tuberculosis

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## Introduction

Dual infections in intensive care might be encountered, especially in immunocompromised patients. Most of the dual infections cause a diagnostic dilemma and require a high degree of suspicion in susceptible individuals. However, dual infections with mucormycosis may follow a fulminant course and may be associated with higher mortality and morbidity.<sup>[1]</sup> We hereby report coinfection of pulmonary tuberculosis (TB) with mucormycosis in a diabetic male that worsened rapidly in spite of the antimicrobial therapy targeted toward the same.

## Case Report

Patient relatives have consented to the publication of the medical records for academic purpose. A 72-year-old nonsmoker male, known case of diabetes mellitus type II since 10 years, on oral hypoglycemic agents, presented with the complaints of altered sensorium with low-grade fever associated with pain abdomen and vomiting and was diagnosed to have severe urinary tract infection. He

was being managed in the ward for diabetic ketoacidosis for the same and was doing well until the 9<sup>th</sup> day of admission when he developed cough, expectoration, and difficulty in breathing. Subsequently, the patient was intubated and transferred to Intensive Care Unit (ICU) for mechanical ventilation with Synchronized Intermittent Mandatory Ventilation mode and further managed according to the institutional protocol. All routine biochemical and hematological investigations including the chest X-ray (CXR) were sent. Blood sugar levels were found to be 460 mg% and total lymphocyte count was 1200 mm<sup>3</sup>, and urine ketones were found to be positive. Arterial blood gas on the day of admission at FiO<sub>2</sub> of 0.6 had a PaO<sub>2</sub>/FiO<sub>2</sub> (PF) ratio of 261. Empirical antibiotic therapy and vasopressor support with noradrenaline (0.5 µg/kg/min) was started as per protocol. Sputum examination undertaken in the ward itself was negative for acid fast-*Bacilli* (AFB). The CXR

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showed bilateral cavitory lesions in all the zones on the very 1<sup>st</sup> day of ICU admission. With a high index of suspicion for fungal pneumonia based on the clinical and radiological findings and negative sputum for AFB, antifungal (caspofungin 70 mg intravenous [IV] loading dose followed by 50 mg IV once daily) was started as a part of treatment. HIV and other viral markers were found to be negative on further investigation. However, no clinical improvement was noticed over 5 days, and radiological deterioration was evident by the appearance of new cavitory lesions developing over every 24 h [Figure 1]. The PF ratio also started deteriorating consistently with the values of 161 on the 3<sup>rd</sup> day falling to 114.5 on the 9<sup>th</sup> day with FiO<sub>2</sub> going up to 0.9. With patient condition deteriorating as evidenced by higher inotropic support and decreasing PF ratio, bronchoalveolar lavage (BAL) was performed, and washings were sent for AFB staining, pyogenic culture, and fungal culture. AFB staining revealed positive results for AFB. Subsequently, antitubercular treatment was also initiated as per the Revised National Tuberculosis Control Program guidelines for the same. Although the potassium hydroxide wet mount revealed no fungal elements, fungal culture showed growth of *Rhizopus* species on the 2<sup>nd</sup> day of inoculation [Figure 2], following which amphotericin B (in the dose of 0.5 mg/kg IV loading dose followed by 1 mg/kg once daily) was introduced as per culture sensitivity. On the 11<sup>th</sup> day, the PF ratio had further fallen to 71 on FiO<sub>2</sub> of 1.0. However, the patient failed to improve and succumbed on the 12<sup>th</sup> day of admission to ICU.

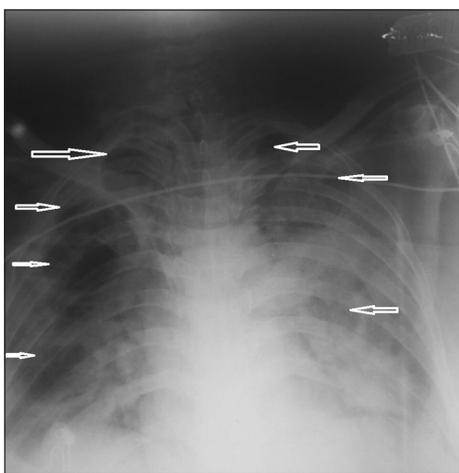
## Discussion

Opportunistic fungal organisms such as *Candida* species, *Aspergillus* species, *Mucor* species, and *Cryptococcus neoformans* may be encountered in diabetic patients

who are usually immunocompromised by virtue of the disease itself. Diabetes mellitus may predispose to mucormycosis in 36–88% of patients which is a serious, potentially fatal fungal infection that needs a high degree of suspicion for the diagnosis.<sup>[2,3]</sup> Patients with uncontrolled hyperglycemia, particularly those with ketoacidosis, are the most susceptible and it may be the first manifestation in patients with undiagnosed diabetes mellitus.<sup>[3]</sup> The most common presentation is rhino-orbital-cerebral involvement followed by pulmonary infection.<sup>[4]</sup>

Patients with diabetes are prone to develop TB and have high chances of treatment failure. There is also a higher risk of progressing from latent to active TB. A large proportion of people with diabetes further developing TB are not diagnosed, or diagnosed too late, may be due to lack of awareness on the part of the patient to report early for any development of chest symptoms.<sup>[5]</sup>

Coinfection with pulmonary TB and mucormycosis in immunocompromised patients may present a diagnostic dilemma owing to similar clinical presentation and need a high degree of clinical suspicion and early aggressive treatment.<sup>[6]</sup> Both clinical entities may present with cough, fever, hemoptysis, and/or chest pain. TB being endemic always forms the first diagnosis. In addition, the radiological features of consolidation, cavitation, infiltrates, and effusion are common to both the diseases and, therefore, histopathological examination or culture sensitivity should be undertaken at the earliest to make definitive diagnosis. Clinical and radiological presentations alone are inconclusive toward a particular disease.<sup>[7]</sup> It is possible that the high relapse cases, treatment failures, resistance, and high mortality



**Figure 1:** Multiple cavitory lesions on day 5



**Figure 2:** Lactophenol cotton blue mount showing *Rhizopus Microsporus* species (LCB ×200)

associated with TB infection are partly attributed to coinfection with opportunistic fungal pathogens and drug-resistant non-TB bacteria.<sup>[2]</sup>

In the present case, an immunocompromised state prevailing as a result of diabetes and TB made the patient prone to acquire coinfection with mucormycosis. Although cavitation was evidenced on the very 1<sup>st</sup> day of admission to ICU, negative sputum examination in the ward made TB an unlikely diagnosis. An antifungal was started empirically to contain the opportunistic fungal infection. However, conclusive diagnosis was made only after BAL which demonstrated the presence of AFB on smear and ubiquitous filamentous fungus *Rhizopus* species, of *Mucorale* order, colonization on culture.

There are isolated reports of coinfection of mucormycosis and TB in immunocompromised patient where the patients were successfully treated.<sup>[8,9]</sup> In the present case, the unfavorable outcome may be the result of delayed diagnosis which was probably missed for the first 8 days in a ward where primarily the focus was on treating diabetic ketoacidosis. Meanwhile, the hyperglycemic environment that favors immune dysfunction (e.g., damage to the neutrophil function, depression of the antioxidant system, and humoral immunity) flared up coinfection of mucormycosis with latent TB progressing to active TB and followed a fulminant course.<sup>[10]</sup>

## Conclusion

Latent TB and drug-resistant TB in patient with diabetes make them susceptible to opportunistic infections with potentially fatal fungal infections. Simultaneous infection with *Mycobacterium tuberculosis* and mucormycosis is a rare finding and requires high clinical vigilance. Now-a-days, it is imperative to consider fungal infections as an important differential

diagnosis. Early and aggressive treatment targeting the isolated organisms may help reduce the mortality and morbidity. Meanwhile, screening the patients with diabetes for coinfections, especially in nonresolving pneumonias are imperative and should be practiced in a protocolized form in early stages of diabetes.

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## Conflicts of interest

There are no conflicts of interest.

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