Case Report

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TANAFFOS

Invasive Pulmonary Aspergillosis and Tuberculosis after COVID-19

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Background: Pulmonary tuberculosis (TB) and invasive aspergillosis are distinct infectious diseases that rarely coexist in the same patient. The concurrent occurrence of these infections presents diagnostic and therapeutic challenges, resulting in complex clinical presentations and potentially adverse outcomes. We present a case report highlighting the diagnostic process, management strategies, and pertinent literature regarding the simultaneous occurrence of pulmonary TB and aspergillosis in a patient following COVID-19 infection.

Case Presentation: A 55-year-old male with a history of occupational exposure as a farmer and welder presented with a complex medical condition. He had a previous COVID-19 infection and was hospitalized for three weeks, receiving appropriate treatment. Subsequently, he developed dyspnea and bilateral pleural effusion and underwent treatment with broad-spectrum antibiotics. Further investigations revealed consolidation in the left upper lobe, and biopsy confirmed the presence of Aspergillus species. The patient received voriconazole treatment for several months, but minimal improvement was observed. Recurrent hemoptysis prompted bronchoscopy, which showed positive results for acid-fast bacilli smear and TB PCR testing, indicating concomitant pulmonary TB. Anti-tuberculosis treatment was initiated alongside ongoing management for aspergillosis.

Conclusion: This case report illustrates the diagnostic and therapeutic complexities associated with the simultaneous occurrence of pulmonary TB and aspergillosis in a patient following COVID-19 infection. Clinicians should maintain a high index of suspicion for dual infections in similar clinical scenarios. Prompt recognition, accurate diagnosis, and individualized treatment strategies are crucial for optimal patient management. Further research is warranted to enhance our understanding of this unique clinical entity and improve patient outcomes.

Keywords: COVID-19; Pulmonary Aspergillosis; Pulmonary Tuberculosis

INTRODUCTION

Pulmonary tuberculosis (TB) and invasive aspergillosis are two distinct infectious diseases that affect the respiratory system (1, 2). While each condition has its unique clinical features, the occurrence of both pulmonary tuberculosis and aspergillosis in the same patient is relatively rare and presents a diagnostic and therapeutic challenge (3). The coexistence of these two infections can lead to complex clinical presentations, delayed diagnosis, and potentially adverse outcomes (3, 4).

Pulmonary tuberculosis, caused by *Mycobacterium tuberculosis*, remains a significant global health concern, particularly in resource-limited settings. It is characterized by chronic granulomatous inflammation and can affect various organs, most commonly the lungs. On the other hand, invasive aspergillosis, primarily caused by Aspergillus species, is an opportunistic fungal infection that typically affects immunocompromised individuals, including those with underlying lung diseases, organ transplant recipients, or those receiving immunosuppressive therapy (4, 5).

While both pulmonary tuberculosis and aspergillosis have distinct risk factors and diagnostic criteria, the simultaneous occurrence of these two infections in an individual poses several challenges (5, 6). The overlapping clinical manifestations, radiological findings, and laboratory parameters can complicate the accurate diagnosis and appropriate management of the patient. Additionally, the immunomodulatory effects of tuberculosis and the immunosuppressive consequences of aspergillosis can further complicate the clinical course and treatment outcomes (1, 4, 6).

To date, only a limited number of case reports have documented the coexistence of pulmonary tuberculosis and aspergillosis in the literature. These reports have highlighted the importance of early recognition, prompt diagnosis, and tailored therapeutic strategies to effectively manage these dual infections. However, there remains a need for further exploration and understanding of this unique clinical entity to optimize patient care and outcomes.

In this case report, we present a detailed clinical description of a patient diagnosed with pulmonary tuberculosis and concomitant aspergillosis. We aim to highlight the challenges encountered in the diagnostic process, discuss the management strategies employed, and discuss the pertinent literature surrounding the simultaneous occurrence of these two infections. By sharing this case, we hope to contribute to the existing knowledge base and raise awareness about this uncommon clinical scenario.

CASE SUMMARIES

A 55-year-old male with a history of working as a farmer for 13 years, as well as 13 years of experience as a welder and 2 years as a carpet weaver, presented with a complex medical condition. His past medical history was unremarkable, and his social history was negative for smoking. There was no significant family history of note. Because of fever, cough, sore throat, and positive test for COVID-19 (RT-PCR) in February 2021, he was hospitalized for three weeks at Abhar Hospital (Zanjan province, Iran), receiving appropriate treatment including dexamethasone 6mg daily intravenously for 5 days.

Two weeks after discharge, the patient returned to the hospital due to dyspnea and was readmitted for two months, including a one-week stay in the ICU. During this period, the patient was diagnosed with bilateral pleural effusion, and bilateral chest tubes were inserted. According to the patient, the left-sided pleural effusion was hemorrhagic (unfortunately, the hospital records are not available for verification). With a suspected bacterial infection, the patient was treated with broad-spectrum antibiotics (meropenem, ciprofloxacin, and linezolid).

The patient was discharged with a right-sided pigtail catheter in place and remained relatively stable until July 2021, when the catheter was removed. In March 2022, the patient presented to a pulmonologist with mild to moderate hemoptysis. A chest CT scan revealed consolidation in the anterior segment of the left upper lobe (LUL), prompting a CT-guided biopsy. The biopsy confirmed the presence of Aspergillus, and the patient was started on voriconazole treatment for several months. Two sputum smears for acid-fast bacilli (AFB) were negative. A follow-up CT scan performed in September 2022 demonstrated minimal change in the lesion despite treatment.

In November 2022, the patient returned due to recurrent hemoptysis. On November 26, 2022, a

bronchoscopy was performed, revealing normal findings. BAL analysis showed negative cytology and galactomannan. Direct acid-fast smear on bronchoalveolar lavage (BAL) was positive at 1+, and TB PCR testing was also positive. Gram staining revealed both Gram-positive and Gram-negative cocci, along with the growth of non-pathogenic Streptococcus and Neisseria species. Fungal culture was negative. Anti-tuberculosis treatment with fixed-dose combination tablets was initiated (isoniazid, rifampin, pyrazinamide, and ethambutol). TB culture was reported positive 6 weeks later.

After one month from the start of the treatment, the clinical symptoms improved. Six months after the end of the tuberculosis treatment, the patient had completely recovered.

Figure 1. Chest CT of the patient on July 6th, 2022

Figure 2. Chest CT of the patient on September 7th, 2022

DISCUSSION

The outcome of COVID-19-associated pulmonary aspergillosis is poor. The simultaneous occurrence of pulmonary tuberculosis and Aspergillus infection in this patient presents several challenges. First, the patient's history of occupational exposure, including farming and welding, may have contributed to increased susceptibility to these infections. Additionally, the patient's prior COVID-19 infection may have compromised his respiratory system, increasing susceptibility to opportunistic infections. COVID-19 increases the risk of certain infections due to associated immune dysfunction, as well as the use of high-dose steroids or IL-6 inhibitors (e.g., tocilizumab).(7).

Coinfection between SARS-CoV-2 and other respiratory pathogens has been reported. Co-fungal infections with COVID-19 were also reported, and the reported pathogens included Aspergillus, Cryptococcus, and Mucorales (8). Zhu et al. showed that pulmonary aspergillosis could develop in patients with asymptomatic, mild, moderate, severe, and critical COVID-19 (8).

Wang et al. found that 8 (7.7%) of 104 COVID-19 patients had invasive pulmonary aspergillosis at the same time. The mean age of these patients was 73±13 years, and all were male. Seven (87.5%) patients had several underlying diseases, including hypertension, diabetes mellitus, chronic obstructive pulmonary disease, chronic kidney disease, and heart disease. Six patients got corticosteroid treatment (9).

Reactivation of pulmonary tuberculosis is known in the context of diabetes mellitus, HIV/AIDS, steroid use, and kidney disease. COVID-19 can weaken the immune system, which could predispose a patient to reactivation of latent tuberculosis infection (LTBI) (10). Our patient demonstrated that, similar to other cases of immune deficiency, multiple diseases can coexist in a single individual. Al-Kayali et al. reported two cases of pulmonary tuberculosis following COVID-19 (11). They support the notion that respiratory viral infections can increase the incidence of TB, as was observed during the

1918–1920 Spanish flu pandemic (5,11). COVID-19 infection may contribute to TB reactivation through several mechanisms, including corticosteroid-induced immunosuppression, cytokine storm, and T-cell lymphocyte depletion. A significant depletion in T-cell lymphocyte counts was recorded in 76% of COVID-19 patients in a study by Diao et al. This depletion may stimulate the development of active TB in patients with LTBI (12).

The management of dual infections requires a comprehensive and tailored approach (4). Antifungal therapy with voriconazole was initiated based on the biopsy results confirming Aspergillus infection. However, the minimal response observed on the follow-up CT scan raises concerns regarding the effectiveness of the chosen treatment regimen. The positive TB culture highlights the importance of considering tuberculosis as a comorbidity and the need for appropriate anti-tuberculosis treatment.

CONCLUSION

In conclusion, this case highlights the unique presentation of concurrent pulmonary tuberculosis and aspergillus infection in a patient with a history of occupational exposure and previous COVID-19 infection. COVID-19 infection promotes weakening of the immune system, leaving the patient susceptible to infections occurring at the same time (6). The diagnostic challenges and suboptimal response to antifungal therapy emphasize the need for a multidisciplinary approach to managing such complex cases. Further research and clinical experience are crucial to improve our understanding of the underlying mechanisms, optimal treatment strategies, and outcomes associated with these dual infections.

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