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CASE REPORT

Coexistence of Asymptomatic Allergic Bronchopulmonary Aspergillosis and Active Pulmonary Tuberculosis: Case Report

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Abstract: We present a rare case of asymptomatic allergic bronchopulmonary aspergillosis (ABPA) concurrent with active pulmonary tuberculosis. Allergic bronchopulmonary aspergillosis is an immunological pulmonary disorder characterized by hypersensitivity to Aspergillus fumigatus, while pulmonary tuberculosis (PTB) is a complex infection caused by Mycobacterium tuberculosis (MTB). The association between pulmonary tuberculosis infections and Aspergillus infections remains a fascinating area of inquiry. A 26-year-old female patient exhibited no symptoms. However, her initial chest computed tomography revealed bronchiectasis with high-attenuation mucus plugs in the upper lobes, peripheral lung atelectasis, and a tree-in-bud pattern. To obtain a clear diagnosis, she visited multiple hospitals and incurred substantial time and financial costs. Active tuberculosis was initially confirmed using specialized detection methods, including metagenomic next-generation sequencing and Xpert MTB/RIF analysis of bronchoalveolar lavage fluid. Subsequent pathological biopsy and Aspergillus-specific antibody tests further confirmed the diagnosis of allergic bronchopulmonary aspergillosis combined with active tuberculosis. Following twelve months of antituberculosis therapy, an avoidable surgery, and three months of oral glucocorticoid treatment, the patient's lung lesions showed significant resolution. This case provides valuable insights into the clinical diagnosis and management of these two distinct infectious diseases.

Keywords: allergic bronchopulmonary aspergillosis, tuberculosis, coexistence, asymptomatic, case report

Introduction

Allergic bronchopulmonary aspergillosis is an immunological pulmonary disorder characterized by hypersensitivity to Aspergillus fumigatus, which colonizes the airways primarily in patients with chronic lung disease, notably asthma or cystic fibrosis.[1] Pulmonary tuberculosis is a complex pulmonary infection caused by Mycobacterium tuberculosis. Patients with a history of PTB often develop various complications, including bronchiectasis and chronic pulmonary aspergillosis, collectively termed post-tubercular lung diseases (PTLD).[2] The prevalence of ABPA in PTLD patients is approximately 2.37%.[3] However, simultaneous diagnosis of active PTB and ABPA is much more seldom documented.

Case Report

A 26-year-old woman presented with incidental findings of bilateral lung lesions on a Chest X-ray during a health examination. She remained asymptomatic, with no fever, dry cough, wheezing, or weight loss, and denied any previous respiratory diseases. A CT scan showed bronchiectasis with intraluminal high-attenuation mucus plugs in the right upper lobe, accompanied by peripheral lung atelectasis and tree-in-bud appearance. Additionally, a solid nodule was noted in the lingual segment of the left upper lobe (Figure 1A).

Laboratory findings previously in the local hospital revealed an elevated eosinophil count (EOS, $0.91x10^9$/L) and EOS% (17.6%), along with a total serum immunoglobulin E (IgE) level exceeding 6000 ng/mL (normal <165 IU/mL).

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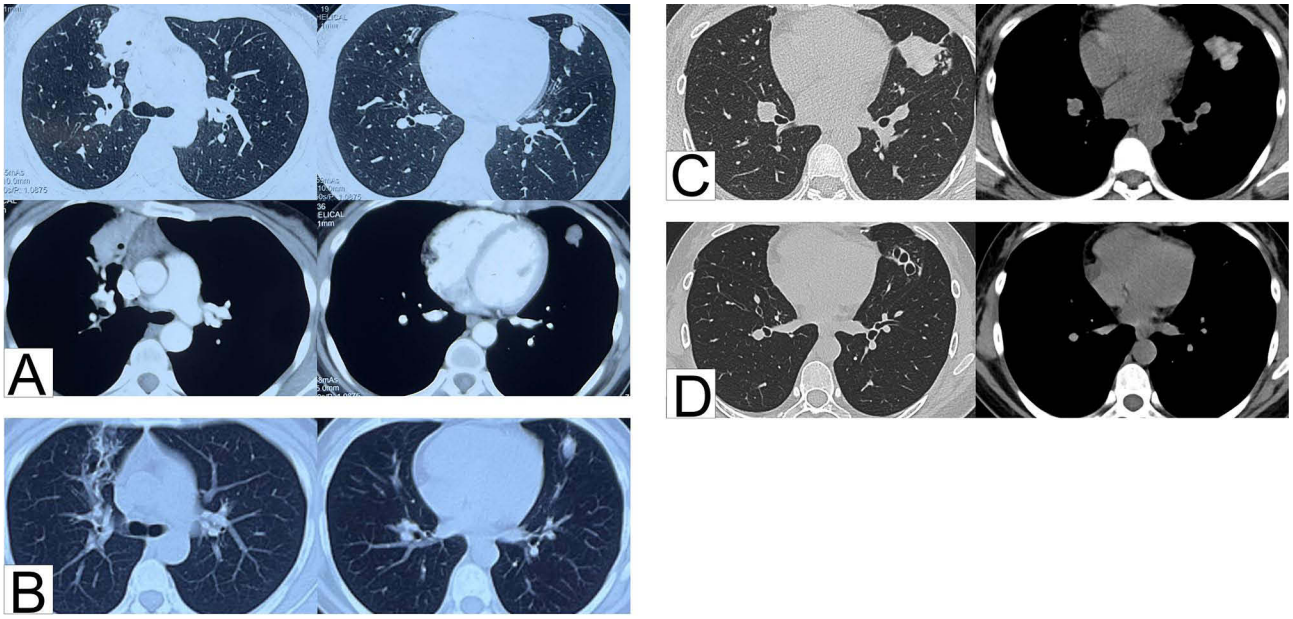

Figure 1 High-resolution CT scan images showing various stages of pulmonary changes. (**A**) Bronchiectasis with intraluminal high-attenuation mucus in the right upper lobe, associated with peripheral lung atelectasis and a tree-in-bud appearance, along with a solid nodule in the lingual segment of the left upper lobe. (**B**) Partial absorption of bilateral upper lung lesions after 8 months of anti-tuberculosis therapy, with a reduction in the size of the lesions. (**C**) A newly developed solid mass in the lingual segment of the left upper lobe, observed 4 months post-surgery, indicating possible post-surgical changes or recurrence. (**D**) Marked reduction in the size of the solid mass in the left upper lobe lingual segment after six weeks of steroid treatment, suggesting a significant therapeutic response.

The purified protein derivative (PPD) skin test was positive (++). The sputum smear, acid-fast staining, and sputum culture were negative. Further assessments excluded malignancies and autoimmune disorders such as ANCA-associated vasculitis. Ultimately, metagenomic next-generation sequencing (mNGS) of bronchoalveolar lavage fluid (BALF) collected from the right upper lobe revealed the presence of Mycobacterium tuberculosis (reads of 23). Additionally, the Xpert MTB/RIF analysis of BALF yielded a positive result, indicating sensitivity to rifampicin, streptomycin, ethambutol, and second-line injectable drugs, confirming the diagnosis of active pulmonary tuberculosis, though both the acid-fast stain and MTB culture of the BALF were negative.

Consequently, the patient underwent a 12-month course of standard anti-tuberculosis therapy (RPT/INH/EMB/PZA with an initial phase for 2 months, followed by a maintenance phase for 10 months with RPT/INH). Follow-up radiological assessments demonstrated gradual partial absorption of bilateral upper lung lesions (Figure 1B). Due to concerns about incomplete lesion resolution and the risk of tuberculosis recurrence, bilateral upper lung segmentectomy surgery was performed following a thorough evaluation. Histopathological examination of the excised lung tissue from both lobes revealed chronic inflammation with widespread hemorrhage and deposition of erythematous exudate within certain alveolar regions, accompanied by focal accumulation of eosinophils, aggregated mononuclear macrophages, and scattered multinucleated giant cell reactions in localized areas (Figure 2A). Significant necrotic material and eosinophil accumulation, along with Charcot-Leyden crystal formation, were observed in some bronchial lumens (Figure 2B). Both acid-fast staining, MTB culture, and TB-DNA testing yielded negative results, with no evidence of fungal hyphae detected.

Four months post-surgery, the follow-up chest CT scans revealed a newly solid mass in the lingual segment of the left upper lobe (Figure 1C). Subsequently, the patient presented to our institution. Upon review of the patient's medical history, we noted prior elevations in EOS and total serum IgE. Considering the diagnosis of PTB may have overshadowed the identification of potential comorbidities, we reassessed the patient's condition. The EOS count and total serum IgE level remained elevated. Sputum samples subjected to acid-fast staining and culture, as well as BALF subjected to mNGS, returned negative results. Additionally, serum IgG specific to Aspergillus fumigatus tested positive (2398 AU/mL), with a moderately sensitive A.fumigatus-specific IgE level (6.94 kUA/L, normal <0.35 kUA/L). Pulmonary function testing was normal, while the bronchial provocation test suggested a potential positive response.

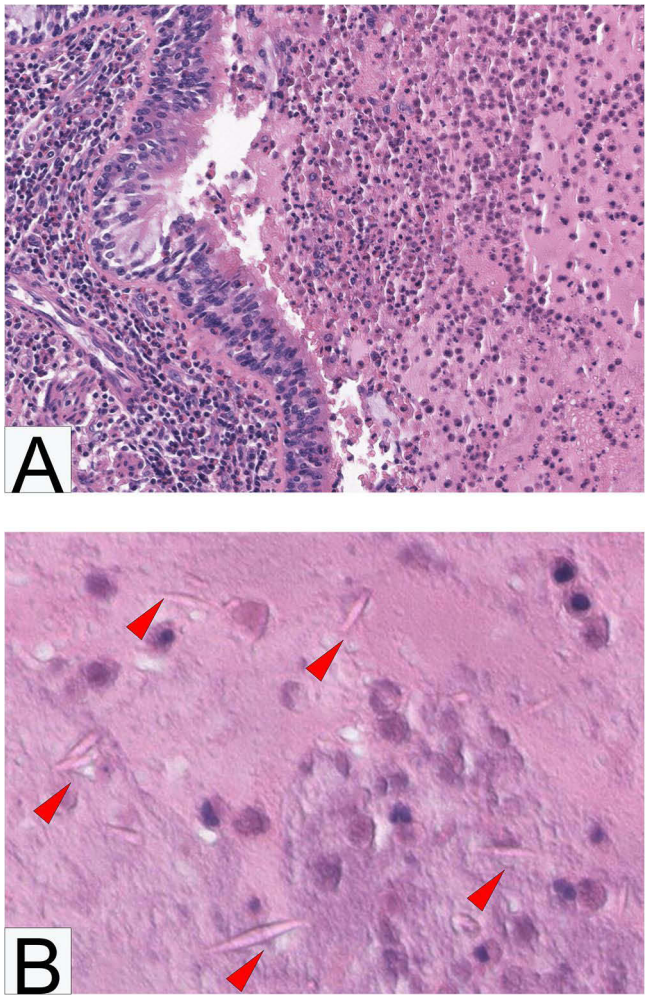

Figure 2 Histopathological examination of the resection specimen showing chronic inflammation. (**A**) Marked infiltration of eosinophils, accumulation of mononuclear macrophages, and a multinucleated giant cell reaction, highlighting the inflammatory response (Hematoxylin and Eosin stain, ×200). (**B**) Significant necrotic material and eosinophil accumulation within some bronchial lumens, with the presence of Charcot-Leyden crystals (highlighted by the red arrow), indicating an ongoing inflammatory process (Hematoxylin and Eosin stain, ×400).

Considering all findings, the patient met the criteria outlined by the International Society for Human and Animal Mycology (ISHAM) for ABPA.[4] Then she received itraconazole therapy for 12 weeks, during which no changes were observed in the lesion. Subsequently, oral corticosteroid therapy was initiated at an initial dose of 30mg qd, and tapered to 20mg qd after two weeks. After six weeks of steroid treatment, a follow-up chest CT scan revealed obvious absorption of the lesion (Figure 1D), along with gradual reductions in serum total IgE and EOS levels. Currently, the patient continues on a maintenance dose of prednisone 5 mg qd, with regular outpatient visits and plans for gradual medication discontinuation.

Discussion

To our knowledge, this is the second reported case of asymptomatic ABPA coexisting with active PTB. Min et al previously reported a similar case.[5] However, unlike our identification of MTB through molecular analysis of bronchoalveolar lavage fluid, they observed both the typical pathological features of ABPA and PTB in the same lung lobe. The association between ABPA and PTB also remains a fascinating area of inquiry. On one hand, bronchial inflammation following tuberculosis infection, along with pulmonary scar cavity formation and bronchiectasis, creates a conducive environment for fungal colonization, thus predisposing individuals with a history of tuberculosis to develop Aspergillus-related pulmonary diseases,[6] including ABPA in some cases. On the other hand, due to similar clinical features and

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radiological manifestations, such as fleeting opacities, central bronchiectasis, mucus plugging, and centrilobular nodules (with a tree-in-bud appearance), patients with ABPA are often misdiagnosed with pulmonary tuberculosis and may receive prolonged anti-tuberculosis therapy, particularly in regions with high prevalence of tuberculosis.[7]

Additionally, some active tuberculosis patients experience symptoms such as dyspnea, wheezing, cough, and sputum production shortly after anti-tuberculosis treatment, leading to a diagnosis of ABPA upon reevaluation.[8] It is conjectured that this could be linked to the suppression of the $CD4^+$/Th1 immune response following anti-tuberculosis therapy, consequently favoring the Th2 type of response associated with asthma development and potentially ABPA.[6,9,10] However, this mechanism has not been thoroughly investigated. As for why not every patient develops ABPA, this may be linked to genetic susceptibility.[11] Notably, this patient has exhibited a high Th2 type of immune response before anti-tuberculosis treatment. Previous reports have documented the potential coexistence of ABPA and active PTB within the same patient, and the confirmation of tuberculosis presence ultimately depended on pathological biopsy or Xpert MTB/RIF analysis.[12] In this case, the presence of Mycobacterium tuberculosis was confirmed through mNGS and Xpert MTB/RIF analysis, with subsequent lesion absorption post-anti-tuberculosis therapy further validating it.

Conclusion

In conclusion, the presence of PTB and ABPA probably exhibits temporal and spatial overlap. This emphasizes the importance of employing comprehensive diagnostic approaches, including pathological biopsy, Xpert MTB/RIF analysis, or mNGS for MTB detection. Additionally, before initiating glucocorticoid therapy for ABPA, particularly in patients from tuberculosis-endemic regions, meticulous assessment and exclusion of PTB are essential.

Abbreviations

RIF, Rifampicin; RPT, Rifapentine; INH, Isoniazid; EMB, Ethambutol; PZA, Pyrazinamide.

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Disclosure

The authors report no conflicts of interest in this work.

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