CASE REPORT

Invasive Pulmonary Aspergillosis in an Apparently Immunocompetent Host: A Diagnostic Challenge

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Abstract

Invasive pulmonary aspergillosis (IPA) is classically associated with immunocompromised states; however, it is increasingly recognized in individuals without overt immunodeficiency. We report a case of IPA in an apparently immunocompetent adult male who presented with acute respiratory symptoms and progressive radiological consolidation. The diagnosis was established through bronchoscopy and histopathological confirmation following clinical deterioration despite empirical antimicrobial therapy. This case highlights the importance of maintaining a high index of suspicion for invasive fungal infections even in immunocompetent hosts and emphasizes the role of early tissue diagnosis.

Keywords: Acute respiratory distress syndrome, Bronchoscopy, Case report, Galactomannan, Invasive pulmonary aspergillosis.

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Introduction

Aspergillus species are ubiquitous environmental fungi that primarily cause invasive disease in patients with impaired host immunity, including those with hematological malignancies, prolonged neutropenia, solid organ transplantation, or long-term immunosuppressive therapy.[1,2] Invasive pulmonary aspergillosis in immunocompetent individuals is traditionally considered uncommon and is frequently under-recognized due to nonspecific clinical and radiological features.[3]

Over the past two decades, increasing reports have documented invasive aspergillosis in patients without classical immunosuppressive conditions, particularly in critically ill individuals and those with transient pulmonary or systemic immune dysfunction.[4–6] Delayed diagnosis in this population is common and is associated with inappropriate antimicrobial escalation and worse outcomes. We report a case of invasive pulmonary aspergillosis in an apparently immunocompetent adult male, highlighting the diagnostic challenges and reviewing the relevant literature.

Case Presentation

A 45-year-old male presented with an acute onset of fever, productive cough, and progressive dyspnea for 1 week duration. He had no prior diagnosis of chronic respiratory disease, including chronic obstructive pulmonary disease, bronchiectasis, or asthma. There was no history of diabetes mellitus, chronic kidney disease, chronic liver disease, malignancy, connective tissue disease, or prior pulmonary tuberculosis. There was no history of frequent oral corticosteroid use or long-term inhaled corticosteroid therapy. The patient had a smoking history of approximately 10 pack-years, predominantly cigarette smoking, and had quit smoking 2 years ago. He denied alcohol and other substance abuse and had no significant occupational or environmental exposure. There was no history suggestive of any recent viral infection.

On examination, the patient was febrile (101° F), with a pulse rate of 120/min, BP—140/90 mm Hg, SpO_2—80% on room air, and bilateral inspiratory crackles on auscultation. Initial laboratory evaluation revealed a total leukocyte count of 23,000 cells/mm3 (normal 4,000–11,000 cells/mm^3), with neutrophilic predominance (88%) and elevated CRP—315 mg/L (0–6 mg/L). Renal and hepatic function tests were within normal limits. Human immunodeficiency virus 1 and 2 serology was negative. Chest radiograph showed bilateral multilobar consolidatory changes on presentation, with worsening of the consolidatory changes after 48 hours (Figs 1A and B).

The patient was initiated on empirical broad-spectrum antimicrobial therapy at admission. After 48 hours of hospitalization, there was persistent fever, worsening hypoxemia, and radiological progression with increasing bilateral consolidations (Fig. 1B), prompting further diagnostic evaluations. High-resolution computed tomography (HRCT) of the thorax was performed, which demonstrated innumerable nodules involving both lungs, distributed along bronchovascular, perilymphatic, centriacinar, and subpleural regions, with a few nodules exhibiting a tree-in-bud pattern suggestive of endobronchial spread. Multiple coalescent air-space opacities were noted along the bronchovascular bundles, displaying both solid and ground-glass attenuation. Areas of mosaic attenuation were present, along with patchy ground-glass opacities involving the right middle lobe and bilateral lower lobes. Subpleural fibrosis in the right lower lobe and patchy peripheral

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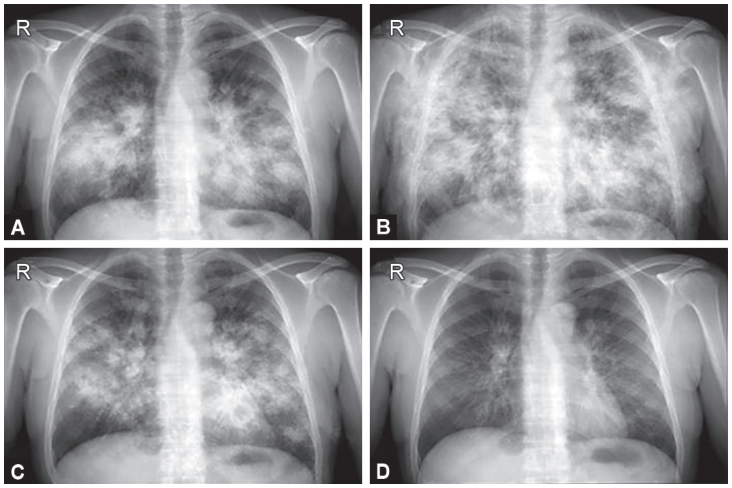


Figs 1A to D: Chest X-rays. (A) On admission—showing bilateral consolidatory changes; (B) Worsening of consolidatory changes; (C) Resolving consolidatory changes after treatment with IV Voriconazole; (D) Chest X-ray after 2 weeks showing significant resolution of consolidatory changes

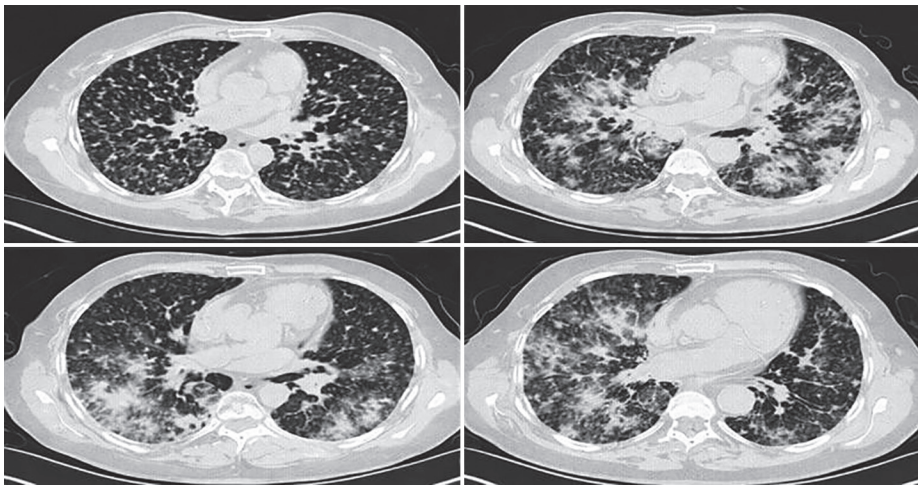


Fig. 2: HRCT thorax demonstrating widespread bilateral centrilobular and peribronchovascular nodules with areas of ground-glass attenuation and confluent consolidation, reflecting progressive diffuse pulmonary involvement

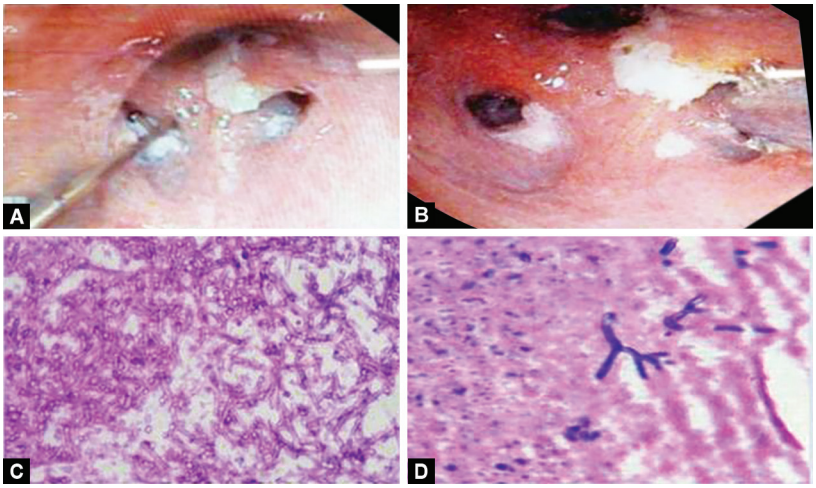
fibrosis in the right middle lobe were also noted, likely representing postinfectious changes. Overall, the imaging features favored an infectious etiology (Fig. 2).

A flexible bronchoscopy was then performed. Bronchoscopic examination revealed inflamed bronchial mucosa with purulent secretions. Necrotic material was visualized in the carina, the right upper and middle lobes, and the left lower lobe. Bronchoalveolar lavage and endobronchial lung biopsy were obtained during the same procedure, and adequate tissue samples were secured (Figs 3A and B). The specimens were sent for bacterial, mycobacterial, and fungal evaluation.

Histopathological examination of the endobronchial biopsies demonstrated septate hyphae with acute-angle branching consistent with *Aspergillus* species (Figs 3C and D). Fungal cultures subsequently confirmed *Aspergillus* growth. Bronchoalveolar lavage samples were negative for acid-fast bacilli, GeneXpert MTB/RIF, and pyogenic organisms. Cytological analysis showed no evidence of malignancy.

A comprehensive evaluation was then undertaken to exclude an underlying immunodeficiency state. Lymphocyte subset analyses were normal, which ruled out idiopathic CD4 lymphocytopenia. Dihydrorhodamine (DHR) flow cytometry assay was done and was found to be normal, hence ruling out chronic granulomatous disease. Serum immunoglobulin levels (IgG, IgA, and IgM) were normal. Glycated hemoglobin was within normal range, excluding occult diabetes mellitus. Renal and hepatic function tests were normal. There was no history of immunosuppressive medication use, chemotherapy, or prolonged corticosteroid therapy. Based on clinical history and laboratory evaluation, the patient was considered apparently immunocompetent.

Given the clinical deterioration, antibiotics were escalated after 48 hours as per institutional protocol. Sputum cultures collected at admission showed no growth on the final report at 48 hours. Following confirmation of invasive pulmonary aspergillosis, antibacterial agents were de-escalated, and antifungals, IV



Figs 3A to D: (A) Bronchoscopic image of necrotic material in the right upper lobe bronchus; (B) Bronchoscopy image (with biopsy forceps) showing necrotic material in the right upper lobe; (C) Histopathology image showing *Aspergillus* species; (D) Histopathology of endobronchial biopsy showing numerous entangled *Aspergillus* fungi

voriconazole was given at a dose of 400 mg IV twice a day on day 1 as a loading dose and then 200 mg IV twice a day for 4 days. The patient showed gradual clinical improvement with resolution of fever, reduction in oxygen requirement, and radiological improvement (Fig. 1C). IV Voriconazole was changed to oral voriconazole-200 mg twice a day, and the patient was discharged on the same. Follow-up imaging was done 2 weeks after discharge, which showed significant resolution (Fig. 1D).

Discussion

Invasive pulmonary aspergillosis is traditionally regarded as a disease confined to profoundly immunocompromised hosts; however, a growing body of literature over the past two decades has clearly demonstrated that invasive pulmonary aspergillosis (IPA) can occur in individuals without classical immunosuppressive risk factors.[3–7] In immunocompetent or apparently immunocompetent patients, the diagnosis is frequently delayed because clinical manifestations are nonspecific and overlap considerably with bacterial pneumonia, tuberculosis, or viral infections, often resulting in inappropriate escalation of antibacterial therapy and delayed antifungal initiation.[4,5]

The pathogenesis of IPA in immunocompetent hosts appears to differ from that in neutropenic patients. Rather than systemic immunodeficiency, localized pulmonary immune dysfunction plays a pivotal role. Structural epithelial injury, impaired mucociliary clearance, and dysfunctional alveolar macrophage responses facilitate fungal invasion and tissue penetration.[6,8] Cigarette smoking, as observed in the present case, is a well-recognized contributor to impaired innate pulmonary immunity. Experimental and clinical studies have demonstrated that smoking reduces macrophage phagocytosis, impairs oxidative burst activity, and alters cytokine signaling, thereby diminishing effective clearance of inhaled *Aspergillus* conidia.[9,10] Importantly, this susceptibility may exist even in the absence of clinically overt COPD.

Another increasingly recognized population at risk comprises critically ill and acutely unwell patients without traditional immunosuppression. Sepsis, severe pneumonia, and systemic inflammatory states can induce a phenomenon termed immunoparalysis, characterized by functional impairment of neutrophils and monocytes despite normal cell counts.[4,7,11] This transient immune dysfunction is sufficient to permit angioinvasive fungal disease and explains the occurrence of IPA in patients with normal baseline immune investigations.

Radiological manifestations of IPA in immunocompetent hosts are often atypical and lack the classical halo sign or air-crescent sign typically seen in neutropenic patients.[3,12] Instead, imaging frequently reveals centrilobular nodules, tree-in-bud opacities, patchy consolidations, or miliary nodules, which closely mimic tuberculosis or atypical bacterial infections.[3–5] Such nonspecific appearances contribute significantly to diagnostic delay, as occurred in the present case.

Microbiological diagnosis of IPA in non-neutropenic hosts remains challenging. Sputum cultures are frequently negative, and serum fungal biomarkers such as galactomannan and β-D-glucan demonstrate reduced sensitivity outside neutropenic populations.[13,14] Consequently, bronchoscopy with bronchoalveolar lavage and tissue biopsy assumes critical diagnostic importance. Histopathological demonstration of tissue invasion by septate hyphae with acute-angle branching remains the gold standard and allows definitive differentiation between colonization and invasive disease.[13]

Timely initiation of antifungal therapy is the most important determinant of outcome. Several studies have demonstrated that delays in antifungal treatment are independently associated with increased mortality in IPA, even among immunocompetent patients.[4,7,15] Voriconazole remains the recommended first-line agent, with alternative therapies reserved for intolerance or resistance. Compared to immunocompromised populations, outcomes in immunocompetent hosts are generally more favorable when diagnosis is established early.[16]

This case underscores several important clinical lessons. First, IPA should be considered in the differential diagnosis of non-resolving or rapidly progressive pneumonia irrespective of immune

status. Second, smoking and acute pulmonary insults may act as sufficient predisposing factors in otherwise immunocompetent individuals. Finally, early bronchoscopy with tissue diagnosis is essential to avoid diagnostic delay, unnecessary antibiotic escalation, and adverse outcomes.

Conclusion

Invasive pulmonary aspergillosis can occur in apparently immunocompetent individuals and may present with nonspecific clinical and radiological features. Early bronchoscopy with tissue diagnosis and prompt antifungal therapy are essential for favorable outcomes.

AI Disclosure

The authors confirm that no AI was used.

Acknowledgment

Nil.

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