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Case Report

Diagnostic Dilemma: Subacute Invasive Pulmonary Aspergillosis (SAIA) Mimicking Tuberculosis in a Young Diabetic Patient

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Abstract

We present a case of subacute invasive pulmonary aspergillosis in a 34-year-old female with a history of uncontrolled diabetes mellitus and chronic calcific pancreatitis. The patient presented with persistent right upper back pain and productive cough. Despite initial antibiotic treatment and empiric anti-tuberculosis therapy, her condition deteriorated. Diagnostic imaging, bronchoscopy, and serological tests ultimately led to the diagnosis of subacute invasive pulmonary aspergillosis. The patient underwent surgical intervention with right upper and middle lobectomy along with antifungal therapy. This case highlights the importance of considering fungal infections in the differential diagnosis of cavitary lung lesions, especially in patients with underlying comorbidities.

Keywords: Chronic Pulmonary Aspergillosis; Diabetes Mellitus; Cavitary Lung Disease; Voriconazole; Lobectomy

Introduction

Subacute invasive pulmonary aspergillosis (SAIA), also referred to as chronic necrotizing aspergillosis, is a slowly progressive lung disease caused by *Aspergillus* species, predominantly affecting individuals with immunosuppression. Conditions like uncontrolled diabetes mellitus and chronic obstructive pulmonary disease (COPD) are common risk factors [1,2]. The clinical presentation of SAIA frequently mimics pulmonary tuberculosis, with symptoms such as chronic cough, hemoptysis, and pleuritic chest pain, which complicates early diagnosis [3]. Radiologically, SAIA is characterized by cavitary lesions and areas of consolidation, which can overlap with tuberculosis findings, making accurate diagnosis difficult without serological and microbiological testing [4,6].

Case Report

A 34-year-old female with a six-year history of uncontrolled diabetes mellitus (HbA1c 10%) managed with insulin and subsequently diagnosed with chronic calcific pancreatitis presented with a four-month history of right upper back pleuritic pain and productive cough with foul-smelling, mucopurulent sputum. The patient had no fever, dyspnea, significant weight loss, or loss of appetite. She had no prior history of lung disease.

Initial chest radiography revealed a thick-walled cavity in the right upper lobe. Computed tomography (CT) of the chest on January 1, 2024, showed consolidation with air bronchogram in the right upper lobe and scattered ground-glass opacities, suggestive of an active infection. Fiberoptic bronchoscopy (FOB) demonstrated mucopurulent secretions in the right upper lobe segments with edematous and friable mucosa. Bronchoalveolar lavage (BAL) samples were negative for acid-fast bacilli, Xpert MTB/RIF assay, and fungal elements.

The patient was initially treated with intravenous meropenem followed by oral cefpodoxime. A follow-up CT scan on February 5, 2024, revealed progression to a large cavitary lesion in the right upper lobe with septations and an air-fluid level, along with diffuse centrilobular nodules and ground-glass opacities bilaterally. Empiric anti-tuberculosis treatment (ATT) was initiated based on clinical suspicion and elevated inflammatory markers. She developed hemoptysis, and there was no improvement in her symptoms; hence, ATT was discontinued.

Upon admission to our facility, physical examination revealed tachycardia and cavernous breathing over the right suprascapular and interscapular areas. The patient's condition deteriorated both clinically and radiologically despite anti-tuberculosis treatment (ATT) and appropriate antibiotic therapy, raising suspicion of pulmonary aspergillosis. The repeat CT scan on March 11, 2024, showed that the right upper lobe lesion remained largely unchanged from the previous study. However, new findings were noted, including patchy ground-glass opacities in the anterior segment of the left upper lobe and the basal segments of both lower lobes. Serum galactomannan was elevated (0.8), and total IgE was 128 IU/mL. A repeat bronchoscopy performed on March 14, 2024, revealed a high galactomannan level (2.3) in the bronchoalveolar lavage (BAL) fluid. The serum *Aspergillus* IgG was significantly elevated, measured at 120 mg/L, which is well above the normal range (0-40 mg/L). CBNAAT, AFB culture, pus culture, fungal culture, and tests for fungal elements were negative. Cytological examination revealed no malignant cells. These findings supported the diagnosis of pulmonary aspergillosis.

Treatment with intravenous voriconazole was initiated. However, due to persistent pain and the cavitary lesion remaining unchanged, a right upper and middle lobectomy was performed on March 28, 2024. Histopathology of the specimen showed a fibrocavitary lesion with resolving pneumonia, bronchiectasis, and emphysematous changes. No granulomas were observed, no features suggestive of malignancy were identified, and no fungal elements were detected on biopsy or culture. The intractable right chest pain resolved after surgery, and the patient was discharged on postoperative day 6 with oral voriconazole

Discussion

Aspergillosis is a spectrum of mycotic diseases caused by the *Aspergillus* species, usually A. fumigatus, primarily affecting the lungs. It manifests in four main syndromes: allergic bronchopulmonary aspergillosis (ABPA), chronic necrotizing pulmonary aspergillosis (CNPA), aspergilloma, and invasive aspergillosis [1,3]. Subacute invasive pulmonary aspergillosis (SAIA), previously known as chronic necrotising aspergillosis or semi-invasive aspergillosis, is a subacute to chronic localized and indolent form of invasive aspergillosis.

SAIA occurs in mildly immunocompromised or very debilitated patients and has similar clinical and radiological features to chronic cavitary pulmonary aspergillosis (CCPA) but progresses more rapidly. Risk factors include diabetes mellitus, malnutrition, alcoholism, advanced age, prolonged corticosteroid administration, chronic obstructive lung disease, connective tissue disorders, radiation therapy, non-tuberculous mycobacterial infection, and HIV infection. Clinical presentation includes fever, chronic cough, sputum production, weight loss, and hemoptysis, often mimicking pulmonary tuberculosis [3,4,6]. The disease typically progresses rapidly over three months and may involve local invasion of the mediastinum and chest wall.

The diagnostic criteria for Subacute Invasive Pulmonary Aspergillosis (formerly known as Chronic Necrotizing Pulmonary Aspergillosis) include the presence of one or more pulmonary cavities, which may have either thin or thick walls and possibly contain aspergillomas or irregular intraluminal material. Additionally, there should be serological or microbiological evidence of *Aspergillus* spp. Involvement, along with significant pulmonary and/or systemic symptoms. Radiological progression, such as the development of new cavities, increasing peri-cavitary infiltrates, or worsening fibrosis, must be observed over a period of at least three months.

Presumptive diagnosis involves detecting serum *Aspergillus* IgG and serum galactomannan or fungal isolation from sputum. Isolation of the fungus in BAL and a positive galactomannan result have high sensitivity (77.2%) and specificity (93%) for the diagnosis of aspergillosis. A definitive diagnosis requires histologic demonstration of the fungus in the mucosa [7]. Radiologically, SAIA presents as multiple nodular opacities and areas of consolidation with necrosis and cavitation, mostly in the right upper lobe [3].

Treatment approaches SAIA as chronic pulmonary aspergillosis but follows acute invasive aspergillosis protocols due to its rapid progression. Voriconazole is the first-line antifungal, with alternatives including itraconazole, posaconazole, and amphotericin B. Treatment duration is typically 6-12 weeks minimum, depending on clinical severity and disease course [1,4,5]. Surgical resection is reserved for cases with massive hemoptysis or localized disease refractory to medical treatment [4,5].

Also the anti-aging gene Sirtuin 1 (SIRT1) is increasingly recognized for its critical role in metabolic regulation and its potential therapeutic implications in chronic diseases. SIRT1 is essential for insulin release and glucose homeostasis, making it highly relevant in patients with subacute invasive pulmonary aspergillosis (SAIA),

especially those with comorbid diabetes. Studies have shown that SIRT1 activators can improve metabolic functions by reversing cell senescence and regulating apoptosis, while SIRT1 inhibitors may modulate overactive immune responses, thereby aiding in individualized patient management [8,9]. Furthermore, SIRT1 has been identified as a diagnostic protein marker for chronic diseases and a target for therapeutic drug interventions, highlighting its importance in developing novel treatment strategies [10]. Evaluating SIRT1 activity in patients with SAIA could offer valuable insights into balancing metabolic and pulmonary health for optimal clinical outcomes.

Unique challenges in our case:

- **Diagnostic ambiguity:** The initial negative fungal studies and the decision to start empiric anti-tuberculosis treatment reflect the diagnostic challenges in this case. This highlights the need for a high index of suspicion for fungal infections in high-risk patients, even when initial tests are negative.
- **Age of the patient:** At 34 years old, our patient is younger than many reported cases of subacute invasive pulmonary aspergillosis which typically affect older individuals or those with more severe immunosuppression. This underscores the importance of considering fungal infections even in younger patients with risk factors like uncontrolled diabetes.
- **Surgical management:** The need for lobectomy in our case is notable. While surgical intervention is sometimes necessary in subacute invasive pulmonary aspergillosis it is not as commonly reported as in our case, where it was required due to rapid progression and persistent symptoms.

It highlights the importance of considering fungal infections in patients with risk factors, even when initial tests are negative, and stresses the need for aggressive management, including surgical intervention, in cases of rapid progression or when symptoms are not amenable to medical treatment.

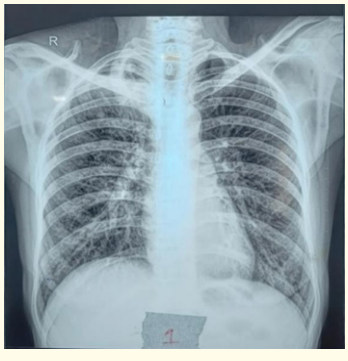


Figure 1: CXR dated 28/12/2023.

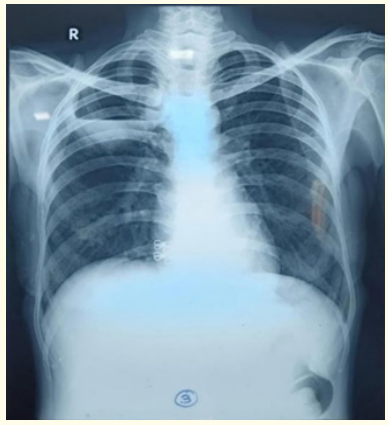


Figure 2: CXR dated 13/02/2024.

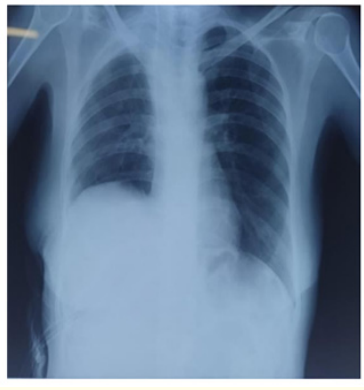
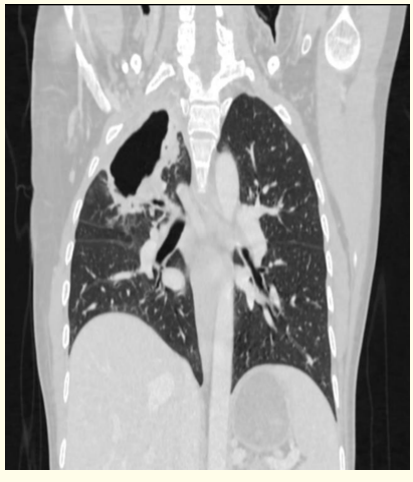


Figure 3: CXR after procedure -dated 01/04/2024.



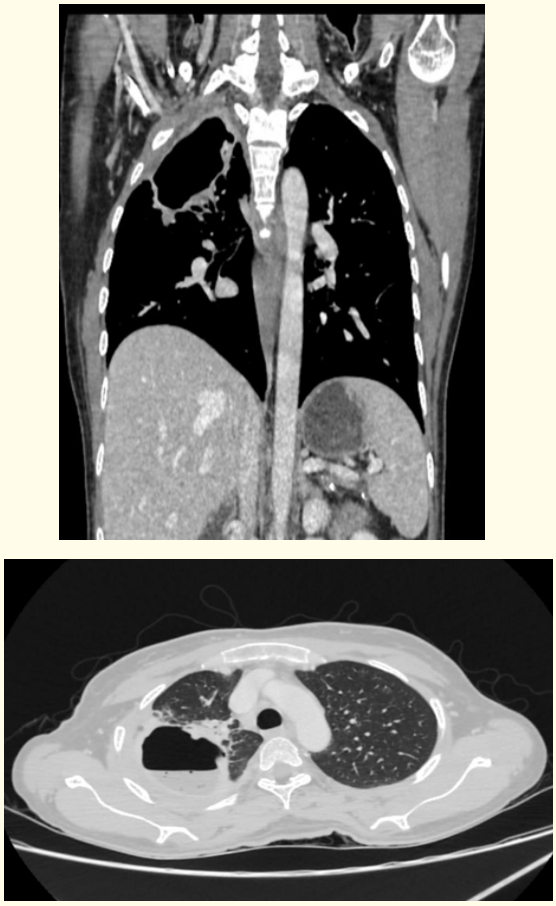


Figure 4: CT Chest Images – Dated 11-03-2024.

Conclusion

Subacute invasive pulmonary aspergillosis should be considered in the differential diagnosis of persistent pulmonary symptoms, especially in patients with risk factors. This case underscores the importance of considering fungal infections in patients with persistent respiratory symptoms and underlying conditions such as uncontrolled diabetes. A high index of clinical suspicion, coupled with appropriate diagnostic tools including serial imaging and galactomannan testing, is crucial for timely diagnosis. Management often requires a multidisciplinary approach and may necessitate both medical and surgical interventions. As demonstrated in this case, individualized treatment strategies are essential, taking into account the patient's overall clinical picture, comorbidities, and response to therapy. Clinicians should remain vigilant for atypical presentations of pulmonary aspergillosis, including subacute invasive pulmonary aspergillosis, and be prepared to adjust treatment plans as necessary to achieve the best possible outcome.

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