Medical Sciences 2021 Vol. 10 (1), p. 150-156, https://doi.org/10.53453/ms.2022.03.17

e-ISSN: 2345-0592
Online issue
Indexed in *Index Copernicus*

Medical Sciences

Official website:
www.medicsciences.com

Pneumonia mimicking invasive pulmonary aspergillosis in patient with lung adenocarcinoma: a case report

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Abstract

Background. Invasive pulmonary aspergillosis is a life-threatening fungal disease and usually affects immunocompromised patients. Clinical symptoms and radiological findings are nonspecific and may be indistinguishable from other pulmonary conditions such as pneumonia or pulmonary tuberculosis. Invasive pulmonary aspergillosis is a rare condition in patients with solid tumours and is usually not considered.

Case report. In this case a 58-year-old man was misdiagnosed with pneumonia. After he failed to respond to antibiotic treatment, pulmonary tuberculosis was suspected. Final diagnosis was invasive pulmonary aspergillosis and lung adenocarcinoma. This case illustrates the challenges of recognizing invasive pulmonary aspergillosis.

Discussion. Diagnosis of invasive pulmonary aspergillosis is challenging and requires a combination of clinical, radiological and microbiological features. Diagnostic methods and accuracy in recognizing invasive pulmonary aspergillosis can differ and depend on patients clinical features.

Keywords. Aspergillus, invasive pulmonary aspergillosis, tuberculosis, lung adenocarcinoma.

Introduction

Invasive aspergillosis is a life-threatening fungal disease which usually affects immunocompromised patients. It's mostly reported in patients with hematologic malignancies, stem cell and solid organ transplant recipients, other risk factors include prolonged therapy with high-dose corticosteroids, cytotoxic therapy, advanced AIDS, chronic granulomatous disease (1-3). Clinical symptoms of invasive pulmonary aspergillosis (IPA) and radiological findings are nonspecific and may be indistinguishable from pneumonia which can lead to delay in diagnosis and potentially worse outcomes (4). IPA is often not considered in patients with solid tumours (5) and this clinical case illustrates that IPA should be considered in oncological patients, particularly those with lung cancer and having pneumonia symptoms.

Case report

A 58-year-old man went to the primary care physician with complaints of cough, fever, left side chest pain and arthralgias lasting for one week. Patient has about thirty pack-year smoking history and is without any underlying diseases. On physical examination the patient presented with fever 38,5 °C, auscultation of the chest revealed left-sided coarse crackles in the upper zone, other vital signs were normal. White blood cell count (WBC) was 19×10^9/L (4 - 10 $\times 10^9$/L), C-reactive protein (CRP) 90 mg/l (< 5mg/l). Chest X-ray revealed infiltrative changes in the left upper lobe pulling left lung root upward (Fig.1). Patient was diagnosed with pneumonia and discharged home with prescribed oral antibiotic treatment (amoxiclav 875/125mg). Ten days later with no clinical improvement the patient was referred to a pulmonologist for consultation suspecting a pulmonary tuberculosis (PTB). On examination the patient presented with fever (38.5 °C), fatigue and worsening left side chest pain. WBC 34×10^9/L (4 - 10 $\times 10^9$/L), CRP 90mg/l (< 5mg/l). Chest X-ray without essential dynamics. The patient was suspected of having PTB, though microscopical, cytological and molecular (Xpert MTB/RIF) test of sputum smear for TB was negative. Chest computed tomography revealed a thick walled cavity (66 × 45 mm) in the left upper lobe and mediastinal lymphadenopathy (Fig.2). Fibrobronchoscopy was performed and showed bloody-purulent secretion in the left upper lobe. Bronchial aspirate sample was taken for *Tuberculosis mycobacterium* exclusion and all tests were negative. Diagnostic biochemical test revealed a positive galactomannan (GM) test (index >3.5) from broncho-alveolar lavage (BAL) also microbiological culture for *Aspergillus fumigatus* was positive. Patient was diagnosed with invasive pulmonary aspergillosis (IPA) and treated with Voriconazole 200mg twice a day for two weeks and then underwent surgical treatment - left lung upper lobe S1 - S2 resection. Histological examination of resected tissues was classified as a poorly differentiated G3 lung adenocarcinoma pT1b pN1.

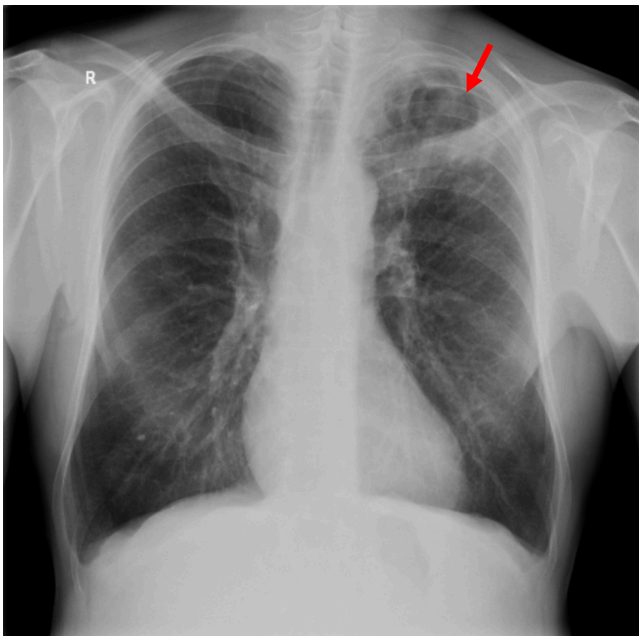

Figure 1. Linear chest X-ray. Infiltrative changes in the left upper lobe.

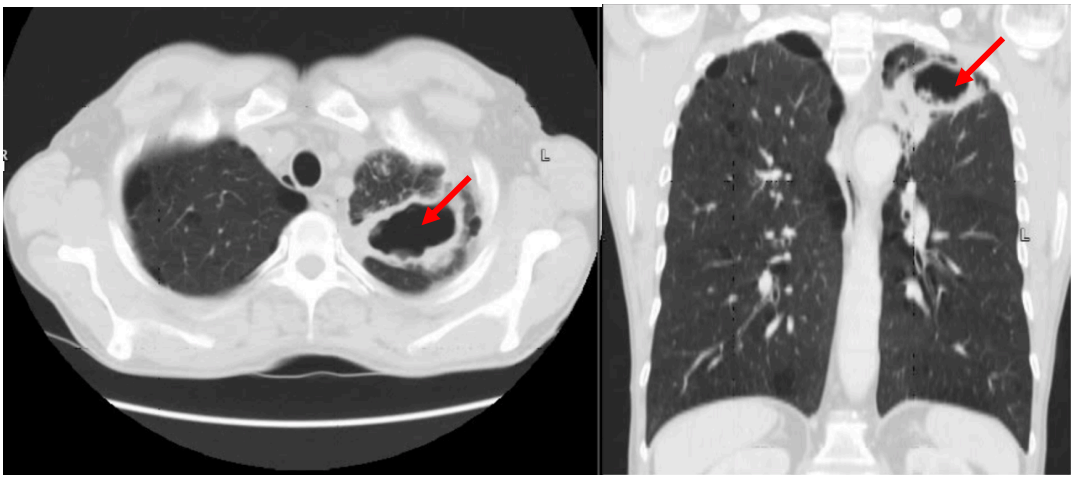

Figure 2. Axial and coronary chest CT. A thick walled cavity in the left upper lobe.

Discussion

The incidence of Aspergillus growth in patients with lung carcinoma has been reported as being 14.2 %, but only a few cases of combined aspergilloma and lung cancer have been reported in the literature (6). The incidence and severity of invasive aspergillosis are strongly related to a patient's immunosuppression. Individuals with prolonged neutropenia are particularly at risk, with reports of an incidence up to 70% in patients with neutropenia lasting more than 30 days (7). In this discussion I want to emphasize the most important diagnostic features of IPA as diagnosis still remains challenging and requires a combination of clinical, radiological and microbiological features (5, 8, 9). Because of

atypical clinical and radiographic characteristics of infection, a significant part of IPA cases are still undetectable using current criteria (10, 11). The clinical and radiographic characteristics of IPA are nonspecific and appear late in the dissease's progression (12). Low-grade fever may accompany IPA, which may be followed by a mild, non-productive cough. As a clinical symptom of angioinvasion and tissue necrosis caused by invasive fungal growth, pleuritic chest pain and pneumonia develop. Cavitation, which is caused by a substantial necrosis of the lung parenchyma, is more likely to develop in non-immunocompromised patients (5, 13). During the early stages of the disease, cough and sputum production are non-existent or minor and in patients with respiratory disease who have failed to respond to broad-spectrum antibiotics, IPA should be seriously considered (14). While chest X-rays are not sensitive enough to detect early stages of disease, CT chest scans are recommended for IPA detection. A halo sign, which can be seen on CT scans is a highly indicative of acute IPA (9, 17). Later after neutrophils recovery these lesions, which indicate a halo sign cavitates and creates a "air crescent" sign, a characteristic indication of a late filamentous invasive mold disease (18). Microbiological diagnosis of IPA remains a challenge as respiratory cultures of *Aspergillus* has less than 30% diagnostic sensitivity but more than 60% predictive value in immunocompromised patients (9). Serological tests can be used only for immunocompetent patients as immunocompromised patients do not produce anti-*Aspergillus* antibodies. High concentration of antibodies indicates the presence of noninvasive form of Aspergillus infection and radiographical evaluation should be considered (14). Galactomannan (GM) is one of the most important antigen for IPA diagnosis and this test is most often used in clinics (5, 8, 9). GM values can also be used to monitor treatment efficacy (19). GM serum assay has a high sensitivity 67% − 100% and high specificity 86% − 99% in neutropenic patients, though low sensitivity rates – 30% can be seen in patients receiving antifungal therapy, pediatric patients and nonneutropenic patients (20, 21, 23). Other studies showed that in most cases lesions on CT scans almost matched with the detection of the GM antigen in the serum and in other cases CT scans even preceded it (20). Studies showed that in high-rsik patiens with IPA, including nonneutropenic individuals, BAL fluid GM has a higher sensitivity than serum GM (24). Obtaining specimens for histopathologic diagnosis is difficult in many patients. Although histopathologic evidence of fungus is critical for determining the importance of Aspergillus growing in culture, its diagnostic accuracy is low and these techniques are also time-consuming and insensitive. (25– 27).

Conclusion

- IPA is a life-threatening condition and early diagnosis is the cornerstone for preventing serious complications.
- IPA has a high potential to be overlooked due to it's nonspecific clinical symptoms and radiological findings.
- Clinicians should suspect IPA not only in immunocompromised patients but also in oncological patients presenting with pneumonia symptoms, especially those with lung cancer.
- Diagnostic methods and accuracy depend on patients clinical features.
- Diagnosis of IPA requires a combination of diagnostic features. CT chest

scans combined with BAL fluid GM assay should be considered as having the highest predictive value in patients with lung cancer, though results should be considered in conjuction with other diagnostic tests and the clinical context.

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