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CASE REPORT

Pseudomembranous Aspergillus tracheobronchitis: A Rare Manifestation of Invasive Aspergillosis in a Immunocompetent Patient

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Purpose: Pseudomembranous Aspergillus tracheobronchitis (PMATB), an uncommon clinical form of invasive aspergillosis, is mainly occurs in patients who are moderate to severely immunocompromised. There are some case reports of immunocompetent individuals developing invasive aspergillosis after occupational exposure (Primarily observed in farmers, sawmill workers, waste collectors, mushroom processing workers, or those who handle grain, hay, or straw), including allergic bronchopulmonary aspergillosis (ABPA), severe asthma with fungal sensitization, hypersensitivity pneumonitis, and invasive pulmonary aspergillosis. To our knowledge, there are no published case reports in the literature with PMATB as the main presentation in construction worker after occupational exposure.

Case Presentation: We report a case of a 45-year-old construction worker who was previously healthy, presented with cough for one weak and dyspnea and wheezing for two days. Computed tomography (CT) of the chest was normal. He was misdiagnosed with severe asthma, and started on intravenous corticosteroids, together with an inhaled short-acting beta2 agonist and inhaled muscarinic antagonist and empirical anti-infective therapy. However, his symptoms were still progressing. Bronchoscopy revealed cream-colored plaques throughout the trachea and bronchial mucosa. Photomicrograph of tissue and culture of post-bronchoscopy sputum and bronchial aspirate showed aspergillus with branching and septate hyphae.

Results: The patient recovered quickly when treated systemically with voriconazole.

Conclusion: Our report presents an immunocompetent construction worker with no chronic diseases who developed invasive aspergillosis primarily manifesting as PMATB due to occupational exposure. This presentation is rare and has not been previously documented in the literature. Early diagnosis and prompt initiation of antifungal therapy may improve the outcome and decrease mortality rate.

Keywords: Pseudomembranous Aspergillus tracheobronchitis, bronchoscopy, immunocompetent, occupation exposure

Introduction

Invasive tracheobronchial aspergillosis (ITBA) is an infrequent but severe form of invasive pulmonary aspergillosis, in which the fungal infection is entirely or predominantly confined to the tracheobronchial tree. Pseudomembranous Aspergillus tracheobronchitis (PMATB) is the most severe form of ITBA.[1] *Aspergillus* conidia can be found almost everywhere and are easily disseminated in the air. Therefore, exposure to them may occur at home, during hospitalization, during specific leisure activities, or at the workplace. The severity of the *Aspergillus* infection depends on the fungal load in the air, but it also depends on the exposed person's immune system. ITBA mainly occurs in immunocompromised patients, such as individuals infected with HIV, cancer patients undergoing radiotherapy or chemotherapy, and recipients of organ transplants, the most common form is invasive pulmonary aspergillosis (IPA).[2–7] Although an increasing number of reports indicates that non-immunocompromised populations, such as patients with COPD,[8,9] diabetes,[10,11] and those in septic shock,[12] liver failure, alcoholism, and after influenza or COVID-19 infection,[13–15] can also develop

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invasive pulmonary aspergillosis. Healthy individuals with intact immune systems are generally resistant to *Aspergillus* infections, as their immune defenses effectively prevent the fungus from colonizing and causing disease. However, if they are exposed to high concentrations of *Aspergillus* spores in their work environment, they may potentially develop invasive aspergillosis too, Invasive aspergillosis can manifest in various forms, including allergic bronchopulmonary aspergillosis (ABPA), severe asthma with fungal sensitization, hypersensitivity pneumonitis, and invasive pulmonary aspergillosis.[16]

Pilaniya et al reported acute invasive pulmonary aspergillosis shortly after occupational exposure to polluted muddy water in a previously healthy subject.[17] A few cases of pulmonary aspergillosis in healthy subjects after exposure to vegetal dust or moldy hay have been described.[18] However, to our knowledge, there have been no reports in the literature of PMATB occurring in construction workers during their work activities.

Due to the lack of typical clinical symptoms and signs, as well as the sensitivity and specificity deficiencies in laboratory testing methods, timely diagnosis and treatment of such diseases are often delayed, leading to a poor prognosis. A case series and review found that the mortality rate of invasive bronchial aspergillosis is approximately 40%, and 23.7% of invasive bronchial aspergillosis patients require mechanical ventilator management.[19]

Case Report

A 49-year-old man presented to our emergency room with cough for one weak and dyspnea and wheezing for two days. His medical history was not significant, he has no history of COVID-19 infection, and he denied tobacco or alcohol use. He was a construction worker who lived in a simple housing made from a container renovation at the construction site; the environment was humid and stuffy. On examination, he was conscious but showed an acutely ill-looking appearance. Initial vital signs were as follows: blood pressure, 180/100mmHg; heart rate, 150 beats/min; respiratory rate, 28 breaths/min; body temperature 37.1°C; and the oxygen saturation 95% while breathing high-flow oxygen (33%). On auscultation of the chest, coarse breathing sounds with wheezing in both lung fields were heard. The patient was suspected of having acute severe asthma by an emergency physician, and he was admitted to our department. Complete blood count results were white blood cell 10.05 x 10^9/L (neutrophils 86.5%, lymphocytes 5.9%, monocytes 7.4%, and eosinophils 0.1%), hemoglobin 147 g/L, and platelet 186 x 10^9/L; and routine blood chemistry results were within normal limits. The human immunodeficiency virus antibody test was negative. The nucleic acids of both the influenza virus and SARS-CoV-2, as detected from pharyngeal sampling, were also negative. Computed tomography (CT) of the chest was normal. He was started on intravenous methylprednisolone (40mg Q12h), together with an inhaled short-acting beta 2 agonist and inhaled muscarinic antagonist and empirical anti-infective therapy. Despite three days of treatment, his symptoms is persisted, with progressive dyspnea, cough, wheezing, and fever. The second chest CT revealed thickening of the peribronchial wall in both lungs (Figure 1). Arterial blood gas showed type I respiratory failure. Bronchoscopy revealed diffuse tracheobronchitis and cream-colored plaques throughout the trachea, left middle stream bronchus, and left upper lobe bronchial mucosa (Figure 2). Cultures of post-bronchoscopy sputum and bronchial aspirate showed heavy growth of *Aspergillus fumigatus*. Photomicrograph of tissue from bronchial biopsies showing A*spergillus* with branching and septate hyphae (Figure 3). The diagnosis of pseudomembranous invasive tracheobronchial aspergillosis was made based on the patient's failure to respond to empirical treatment for asthma, imaging findings, laboratory values, and culture-positive *A. fumigatus*. An antifungal drug regimen of voriconazole was initiated immediately (voriconazole is administered at a dosage of 6 mg/kg every 12 hours. After 24 hours, the maintenance dose is reduced to 4 mg/kg twice daily). The patient's general appearance, dyspnea and fever remarkably improved throughout antifungal treatment. Bronchoscopy showed marked resolution of the lesions. The patient was switched to oral voriconazole at a dosage of 250 mg twice a day for two months and was discharged home. At this writing, the patient is largely asymptomatic.

Discussion and Conclusion

Aspergillus tracheobronchitis, an uncommon form of invasive pulmonary aspergillosis, is characterized by the development of a pseudomembrane, ulcers,or obstruction that is predominantly confined to the tracheobronchial tree. PMATB is the most severe and fatal form of Aspergillus tracheobronchitis.[1] It primarily occurs in immunocompromised hosts, such as patients receiving solid organ transplants, patients with hematologic malignancies, or patients undergoing

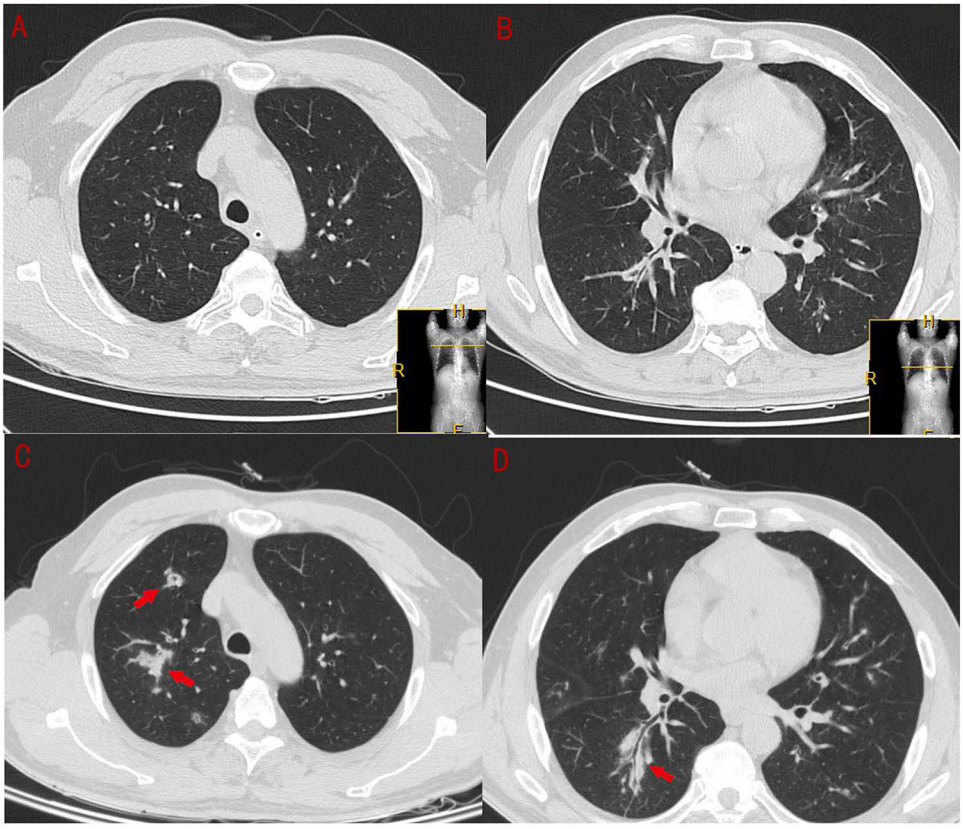

Figure 1 (**A** and **B**) show the patient's CT scans at the time of admission, with no significant abnormalities observed. (**C** and **D**) depict the chest CT after 7 days, revealing thickened bronchial walls and surrounding exudative lesions (the area indicated by the red arrow).

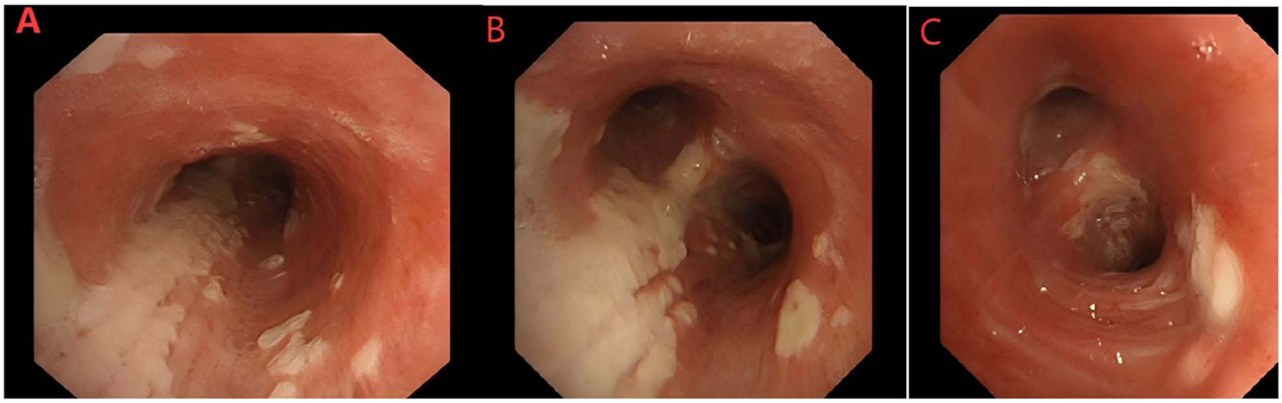

Figure 2 Bronchoscopy revealed diffuse tracheobronchitis and cream-colored plaques throughout the trachea (**A** and **B**), left middle stream bronchus, left upper lobe bronchus mucosa (**C**).

immunosuppressive therapy, including corticosteroid therapy.[20–22] It is less commonly observed in immunocompetent patients with no underlying lung diseases. In recent years, the incidence of invasive aspergillosis (IA) among non-immunocompromised patients has increased. Previous studies have reported of 38 cases of tracheobronchitis in non-immunocompromised patients. Patients were elderly (89.5% patients were ≥65 years), presented advanced COPD (GOLD III+IV in 81.3%) and heart insufficiency (55.3%), with higher APACHE II score in those with invasive tracheobronchitis.[23]

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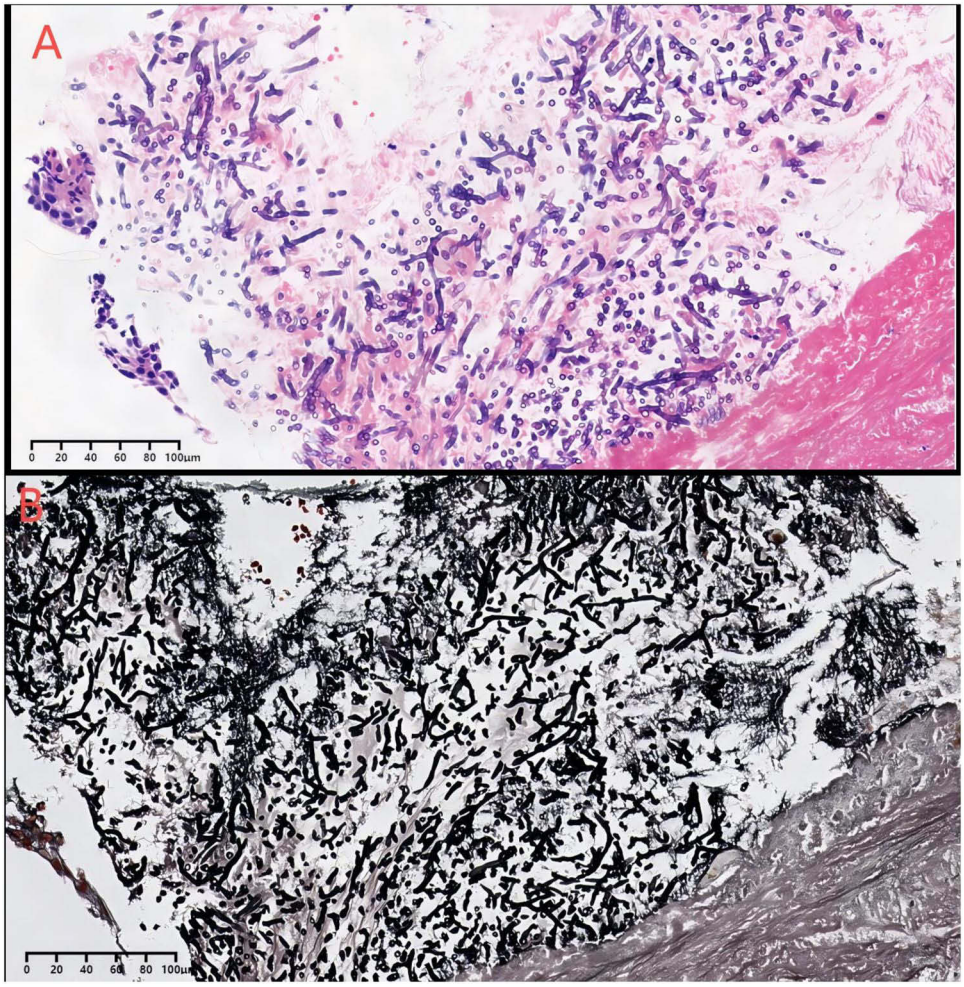

Figure 3 Histopathological findings of the bronchoscopy biopsy specimen demonstrate extensive tissue necrosis associated with infiltration of the fungal hyphae on hematoxylin and eosin stain (× 20), (**A**) and periodic acid-Schiff stain (× 20), (**B**).

Occupational exposure to *Aspergillus* spores commonly occurs in the following environments: Construction and Demolition Sites, Agricultural Settings, Healthcare Facilities, Indoor Environments with Poor Ventilation. These environments can release *Aspergillus* spores into the air, increasing the risk of inhalation and potential health issues for workers. Punia reported a case of primary CNS aspergillosis in an immunocompetent person who was working in an area with excessive ongoing construction.[24] A paper describes 2 cases of immunocompetent males with acute community-acquired invasive pulmonary aspergillosis developing shortly after spreading bark chippings.[18] We have not found any literature reporting cases of PMATB in construction workers who has normal immune function and no underlying conditions. In our case, the patient was a construction worker living in a hot and humid environment near the construction site. Considering that our patient was immunocompetent, and does not have any significant immune deficiency or structural lung disease, we conclude that massive exposure to *Aspergillus* conidia leads to acute PMATB in our patient.

Diagnosis may also be delayed due to a low index of clinical suspicion, particularly in a low risk patient.[25] Our patient initially visited the hospital with cough and dyspnea, and upon examination, bilateral wheezing was noted. A chest CT showed no significant abnormalities, and he was initially misdiagnosed with severe asthma. Although he received regular treatment for asthma; his symptoms did not improve and develop respiratory failure. The diagnosis is a dilemma. Therefore, we decided to perform a second chest CT, which revealed bronchial thickening in both lungs, and bronchoscopy revealed the formation of pseudomembranes in the trachea and the main bronchi. Subsequently, culturing of bronchoalveolar lavage fluid indicated *Aspergillus fumigatus* infection; Denning et al proposed that "pseudomembranous Aspergillus tracheobronchitis" is reserved for patients with very extensive involvement of the whole of the tracheobronchial tree, with a membranous slough overlying

the mucosa containing Aspergillus.[1] Definitive diagnosis is made when there is histologic demonstration of invasion of the mucosa by hypha. The treatment was adjusted to antifungal therapy with voriconazole, The patient showed remarkable clinical improvement, and follow-up bronchoscopy showed resolution of the lesions.

Because the mortality rate of ITBA is very high, identification and early treatment might be life-saving. Therefore, pseudomembranous necrotizing tracheobronchial aspergillosis must be considered in immunocompetent patients with dyspnea progressing to severe hypoxemia without invasion of the pulmonary parenchyma. Bronchoscopy can visually identify lesions in the airways and collect valuable specimens for further laboratory examination and should be performed as early as possible when a patient is suspected to have invasive *Aspergillus* infection.

The exposure to *Aspergillus* particles, which is commonly seen in occupations like farming, sawmilling, waste collection, mushroom processing, and handling of grain, hay, or straw. However, our patient is a construction worker, which is an occupational exposure often overlooked by clinicians. Additionally occupational *Aspergillus* infections typically manifest as ABPA, allergic alveolitis, or invasive pulmonary aspergillosis, with clear indications on CT scans or symptoms. In contrast, our patient presented with PMATB, which lacks specific CT or symptomatic signs, making it easily overlooked by clinicians and can even lead to misdiagnosis.

Abbreviations

ITBA, Invasive tracheobronchial aspergillosis; PMATB, Pseudomembranous Aspergillus tracheobronchitis; CT, Computed tomography.

Ethics

This study was approved for publication by Longgang Central Hospital Of Shenzhen. Written informed consent was obtained from the patient for the publication of this case report.

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Disclosure

The authors report no conflicts of interest in this work.

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