Aspergillus tracheobronchitis is a form of invasive pulmonary aspergillosis in which the Aspergillus infection is limited predominantly to the tracheobronchial tree. It occurs primarily in severely immunocompromised patients such as lung transplant recipients. Here, we report a case of Aspergillus tracheobronchitis in a 42-year-old man with diabetes mellitus, who presented with intractable cough, lack of expectoration of sputum, and chest discomfort. The patient did not respond to conventional treatment with antibiotics and antitussive agents, and he underwent bronchoscopy that showed multiple, discrete, gelatinous whitish plaques mainly involving the trachea and the left bronchus. On the basis of the bronchoscopic and microbiologic findings, we made the diagnosis of Aspergillus tracheobronchitis and initiated antifungal therapy. He showed gradual improvement in his symptoms and continued taking oral itraconazole for 6 months. Physicians should consider Aspergillus tracheobronchitis as a probable diagnosis in immunocompromised patients presenting with atypical respiratory symptoms and should try to establish a prompt diagnosis.

Keywords: Aspergillosis, Allergic Bronchopulmonary; Itraconazole; Bronchoscopy
Laboratory work-up revealed the following: leukocyte count, 12,160 cells/mm$^3$ (neutrophils 75%, lymphocytes 16.5%, monocytes 5.7%, eosinophils 2.5%, and basophils 0.2%); hemoglobin level, 12.3 g/dL; glycosylated hemoglobin, 10.1%; platelet count, 422,000 cells/μL; C-reactive protein level, 3.95 mg/dL; and pro-calcitonin quantitative level, <0.05. The other blood chemistry values were within normal limits, and the human immunodeficiency virus test and serum galactomannan index were negative. Three sputum acid-fast bacilli (AFB) tests were also negative.

A chest radiograph revealed a destroyed tuberculosis scar in the left and right middle lung fields, and this finding showed no interval change compared to that in a chest radiograph obtained a year ago (Figure 1A, B). A chest computed tomography scan showed a fibrotic cavity, traction bronchiectasis, and multiple small nodules with destructive changes in both lungs (Figure 1C).

Empirical antibiotic therapy was initiated immediately on suspicion of community-acquired pneumonia; the patient did not show any improvement with this treatment.

On the seventh hospital day, the patient underwent a flexible bronchoscopy for an evaluation of causality. The bronchoscopic examination demonstrated multiple, discrete, gelatinous whitish plaques involving mainly the trachea and left bronchus (Figure 2A–C). We performed a biopsy of the tracheal lesions, which revealed only chronic active inflammation with necrotic tissues. The AFB, periodic acid–Schiff, and Grocott's methenamine silver stains of the biopsy tissue were all negative.

The patient's symptoms did not improve in spite of empirical antibiotic treatment. On the 14th hospital day, he underwent a second bronchoscopic examination. There was no interval change compared to previous bronchoscopic findings. Another biopsy performed at this time revealed the same findings as the previous biopsy. Although the pathology was not confirmed, we made a presumptive diagnosis of *Aspergillus* tracheobronchitis on the basis of his symptoms, discriminative bronchoscopic findings, and unresponsiveness to antibiotics. On the 16th hospital day, empirical antifungal therapy with intravenous amphotericin B was initiated, and antibiotic administration was discontinued. However, 5 days later, we changed the drug to itraconazole owing to drug fever and renal insufficiency related to amphotericin B administration. After 7 days of intravenous itraconazole administration, the intractable cough, unexpectorated sputum, and chest discomfort symptoms started showing improvement. On the 35th hospital day, he underwent a follow-up bronchoscopic examination, which revealed a significant improvement in the numerous gelatinous whitish plaques in the trachea and left bronchus (Figure 2D–F). On the 44th hospital day, the patient was discharged on oral itraconazole with significant improvement of his symptoms. After 2 months, the *Aspergillus* species was isolated upon microbiological assessments of the sputum, washing fluid, and biopsy specimens. We finally confirmed the diagnosis of *Aspergillus* tracheobronchitis and continued treatment with oral itraconazole for 6 months. Oral itraconazole was discontinued after the patient demonstrated clinical improvement, bronchoscopic resolution, and confirmation of
Invasive tracheobronchitis in diabetic patient

Discussion

Aspergillus tracheobronchitis is a rare form of invasive pulmonary aspergillosis in which the Aspergillus infection is limited entirely or predominantly to the tracheobronchial tree. Wheaton first reported Aspergillus tracheobronchitis in a 2.5-year-old girl who died of pneumonia in 1890. The incidence of Aspergillus tracheobronchitis occurs in less than 7% of pulmonary aspergillosis cases. It usually occurs in patients with hematological malignancy with neutropenia, bone marrow or solid organ transplant recipients, and in those receiving corticosteroid therapy. However, it can occur in lesser immunocompromised patients such as those with post-influenza symptoms, chronic obstructive pulmonary disease, and diabetes and in the elderly.

In this case, we think that Aspergillus tracheobronchitis was caused by uncontrolled diabetes and a severely destroyed scar of tuberculosis suitable for Aspergillus colonization.

The clinical manifestations of this infection are usually nonspecific, and includes cough, exertional dyspnea, white or purulent sputum, fever, wheezing, and night sweats. Our patient also had the same clinical manifestations such as intractable cough, unexpectorated sputum, and chest discomfort.

Wu et al. has proposed a classification of the intraluminal lesions, based on bronchoscopic morphology, into four types: the superficial infiltration type, full-layer involvement type, occlusion type, and mixed type. Our case can be classified as the superficial infiltration type.

Aspergillus tracheobronchitis is diagnosed by one of the

Figure 2. (A–C) Bronchoscopic examination images obtained upon admission showing multiple, discrete, gelatinous, whitish plaques mainly involving the trachea and the left bronchus. (D–F) Follow-up bronchoscopic examination images showing significant improvement compared to numerous gelatinous whitish plaques in the trachea and the left bronchus that were seen earlier.
following histologic evidence of tissue invasion by *Aspergillus* on a biopsy, histology suggestive of aspergillosis associated with positive cultures of the *Aspergillus* species, clinical and radiological findings strongly suggestive of invasive aspergillosis associated with microbiologic identification in bronchoalveolar lavage, or a positive galactomannan serum assay. In our case, we did not obtain pathologic confirmation of the *Aspergillus* species. However, the *Aspergillus* species was isolated upon microbiological assessments of the sputum, washing fluid, and biopsy specimens. Tasci et al. reported that microscopic examination of respiratory specimens is also a useful sensitive tool to confirm the diagnosis. In addition, the patient’s bronchoscopic findings improved after antifungal therapy. Moreover, he did not respond to conventional antibiotics. We think that *Aspergillus* hyphae were not visualized on the biopsy specimens because of inappropriate circumstances for proliferation owing to his relatively mild immunocompromised state.

The outcome of antifungal therapy depends largely on the patient’s immune status. Amphotericin B was the treatment of choice for invasive aspergillosis in the past, but recently, voriconazole has been recommended as the primary treatment regimen. However, we were unable to use voriconazole owing to health insurance coverage restrictions. We first initiated antifungal therapy with IV amphotericin B. However, we changed IV amphotericin B to itraconazole owing to the development of drug fever and acute renal insufficiency after 5 days. Kramer et al. reported that oral therapy with itraconazole, administered for 6–12 months, was effective in invasive aspergillosis after lung transplantation. However, the optimal duration of therapy has not been defined. Most experts attempt to treat until resolution or stabilization of all clinical and radiographic manifestations. *Aspergillus* tracheobronchitis is considered a rare disease these days. However, we can predict that the incidence of *Aspergillus* tracheobronchitis may rise owing to the increasing number of immunocompromised hosts such as transplant recipients, and cancer, human immunodeficiency virus-infected, and elderly patients. Physicians should therefore consider *Aspergillus* tracheobronchitis as a possible diagnosis in immunocompromised patients presenting with atypical respiratory symptoms and should attempt a prompt diagnosis with a procedure such as bronchoscopy.

**Conflicts of Interest**

No potential conflict of interest relevant to this article was reported.

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