A Case of Obstructing Bronchial Aspergillosis in a Patient Receiving Cytotoxic Chemotherapy and Inhaled Corticoid Therapy

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Case Report

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Abstract

**Background:** Among various types of aspergillosis, the clinical feature of patients with obstructive bronchial aspergillosis is still unclear. Originally it was reported it occurs not in severe immunocompromised patients such as acquired immunodeficiency syndrome (AIDS) or post organ transplantation, while recent reports have suggested that this disease could afflict patients seen in daily practice of pulmonary medicine.

**Case presentation:** We describe a case of 76 years old woman with obstructing bronchial aspergillosis. This patient presented to the hospital with a productive cough during treatment for asthma and advanced lung cancer. Chest CT showed stenosis of the bronchial lumen. Bronchoscopy showed no recurrence of lung cancer, and aspergillus were found in the granulation tissue. Cough improved with debridement of the lesion by bronchoscopy and oral antifungal medication treatment.

**Conclusion:** Our review of previous case reports as well as this case revealed that obstructing bronchial aspergillosis might occur when patients hold several backgrounds inducing immunosuppression such as solid tumors under anticancer treatment, inhaled corticosteroids and aging. As such patients may have risk to progress to invasive aspergillosis, physicians need to keep in mind obstructing bronchial aspergillosis should be properly diagnosed for delivering them appropriate treatment.

Background

Aspergillus is a ubiquitous fungus that causes a variety of clinical syndromes in the lung, depending on the patient's immune status and underlying lung disease. Obstructing bronchial aspergillosis is known as one type of tracheobronchial aspergillosis that affects immunosuppressed patients [1] [2] [3]. However, the clinical spectrum of this disease remains unclear as the morbidity is very rare and was not described in the classification of pulmonary aspergillosis [1]. We here report a case of obstructing bronchial aspergillosis that developed in a patient with advanced lung cancer undertaken cytotoxic chemotherapy and also with asthma using inhaled corticoid steroids. This case shows the typical clinical course of endotracheal aspergillosis and is considered as useful for understanding this disease.

Case Presentation

A 77-year-old woman with asthma visited our hospital with chronic cough and was diagnosed with lung cancer in the left lower lobe (adenocarcinoma, cT2aN1M0 stage IIA) in year X-5. Though she decided to receive radical radiotherapy, in year X-2 her lung cancer relapse. She took standard combination immunotherapy (cisplatin plus pemetrexed with pembrolizumab), and had been taken maintenance therapy (pemetrexed + pembrolizumab) for a year.

She had a worsening cough since January year X. On auscultation of her chest, her left lung was attenuated in peripheral breath sounds and airway constriction sounds were heard during her mid-to-end inspiration. We suspected exacerbation of bronchial asthma and intensified her inhaled corticosteroid
therapy, but her symptoms tended to worsen. A laboratory test showed WBC count of 9150/µL, neutrophils of 75%, LDH of 246 IU/L, CRP of 4.8 mg/dL, Anti-Aspergillus antibody positive, and no elevation of IgE and eosinophils. Chest CT scan showed stenosis of the bronchial lumen (Fig. 1a), suggesting that lung cancer was exacerbating within the bronchi. Bronchoscopy revealed a white lesion in the upper lobe branch of left bronchus, and the mucosa obstructed bronchi (Fig. 1b). No findings of vascular distension or mucosal irregularity, which are typical findings of lung cancer, were observed. When we performed biopsy of the white lesion in the trachea, the lesion could be collected without resistance but bleeding occurred easily. Histopathological diagnosis did not reveal tumor cells. We diagnosed with obstructing bronchial aspergillosis because of the presence of aspergillus in the white lichen by biopsy (Fig. 1c). We then performed a second bronchoscopy and debridement of the endotracheal white lesion. In addition, she started oral voriconazole in March. Then her cough gradually improved, and WBC and CRP were normalized at a laboratory test. Six months later, we re-examined bronchoscopy and we observed slight white lichen remained in the left upper lobe branch (Fig. 1d), but no aspergillus hyphae were found in the biopsy tissue. We decided to finish voriconazole in 6 months.

Discussion And Conclusions

In 1991, Kramer and coworkers proposed a classification of tracheobronchial aspergillosis in three types [2, 4]. The authors distinguished allergic, invasive, and saprophytic forms of aspergillus tracheobronchial involvement, similarly to pathogenesis of pulmonary aspergillosis. Allergic bronchopulmonary aspergillosis (ABPA) occurs in patients with normal immune function as antibody reactions (IgE and IgG) or cell-mediated immune responses (types I, III, IV hypersensitivity reactions). Invasive tracheobronchial aspergillosis (ITBA) occurs in patients with severe immunosuppression such as after organ transplantation or hematologic malignancies. Obstructing bronchial aspergillosis was first described by Denning et al. in three patients with AIDS [5]. This pathological feature was defined as the presence of thick mucous plugs containing aspergillus hyphae, with little or no airway inflammation and no evidence of invasion or allergic reaction. Obstructive bronchial aspergillosis is also known as endobronchial aspergillosis (EBA) [3]. It could not only cause obstructive pneumonia but be fatal by progression to invasive pulmonary aspergillosis (IPA) or forming tracheal-mediastinal fistula [3].

Though originally obstructive bronchial aspergillosis was reported to afflict patients with severe immunodeficiency, this time we experienced a case in an elderly outpatient without apparent immunosuppression. To elucidate patients’ backgrounds suffering from this, we performed comprehensive PubMed search for case reports of obstructive bronchial aspergillosis and found 34 cases [2] [4] [5] [6] [7] [8] [9] [10] [11] [12]. Their ages ranged from 28 to 76, but most of them were in their 60s and 70s. Only eight patients had severe immunodeficiency, such as AIDS, hematological malignancies, and post-transplantation. On the contrary, in 7 patients, no obvious backgrounds were described. The remaining 19 had some kind of comorbidity related with immunosuppression, including 4 with diabetes mellitus, 8 with solid tumors such as lung cancer, 7 with a history of tuberculosis, and 1 with rheumatoid arthritis. Among 10 of the 19 patients had multiple such complications. Our review demonstrated that more common patients than previously thought might have a risk of this disease,
though the incidence is very low. In our case, in addition to maintained cytotoxic chemotherapy and old age, inhaled steroid therapy for asthma might have a certain role as it is often reported to cause infection such as oral candidiasis or bacterial pneumonia via direct immunosuppressive effects [13].

Initial symptoms are non-specific and included asymptomatic, cough, hemoptysis, dyspnea, malaise, weight loss, chest pain, and fever [3] [9]. On a chest X-ray or CT, this appears as a nodular shadow or bronchial obstruction. PET-CT seems to be able to exclude the possibility of malignancy such as lung cancer as this shows low upkate of FDG [1] [3]. Bronchoscopy is essential for diagnosis. Typical finding by bronchoscopy is an increased white necrotic material obstructing the bronchi observed in this case, and definitive diagnosis is a presence of hyphae. Currently, no standard treatment for this has not been established, while, as performed in this case, antifungal drugs such as voriconazole (VRCZ), itraconazole (ITCZ), and micafungin (MCFG), and direct debridement of the abscess by bronchoscopy are thought to be two major treatment options [3].

In conclusion, it is likely that obstructing bronchial aspergillosis could occur in much more common patients with pulmonary diseases. When obstructive lesions are found on imaging tests in aged patients along with respiratory symptoms, physicians should consider this disease as one of differential diagnoses, and bronchoscopy should be actively performed for detecting the existence of hyphae.

**Abbreviations**

Allergic bronchopulmonary aspergillosis (ABPA)

Acquired immunodeficiency syndrome (AIDS)

Endobronchial aspergillosis (EBA)

Invasive tracheobronchial aspergillosis (ITBA)

Invasive pulmonary aspergillosis (IPA)

Itraconazole (ITCZ)

Micafungin (MCFG)

Voriconazole (VRCZ)

**Declarations**

Ethics approval and consent to participate: Pathology data were used with patient consent.

Consent for publication: Written informed consent to publish was obtained from the patient
Availability of data and materials: The datasets generated and/or analysed during the current study are not publicly available due to this patient’s will but are available from the corresponding author on reasonable request.

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References


Figures
Figure 1

a. Chest CT scan on admission.
b. The image of first bronchoscopy.
c. Grocot dyeing of the mucosa.
d. The image of bronchoscopy after 6 months voriconazole treatment.

Figure 1

See image above for figure legend