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Case report

Direct transbronchial administration of liposomal amphotericin B into a pulmonary aspergilloma

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ABSTRACT

Pulmonary aspergillomas usually occur in pre-existing lung cavities exhibiting local immunodeficiency. As pulmonary aspergillomas only partially touch the walls of the cavities containing them, they rarely come into contact with the bloodstream, which makes it difficult for antifungal agents to reach them. Although surgical treatment is the optimal strategy for curing the condition, most patients also have pulmonary complications such as tuberculosis and pulmonary fibrosis, which makes this strategy difficult. A 72-year-old male patient complained of recurrent hemoptysis and dyspnea, and a chest X-ray and CT scan demonstrated the existence of a fungus ball in a pulmonary cavity exhibiting fibrosis. Although an examination of the patient's sputum was inconclusive, his increased 1-3-beta-D-glucan level and Aspergillus galactomannan antigen index were suggestive of pulmonary aspergilloma. Since the systemic administration of voriconazole for two months followed by itraconazole for one month was ineffective and surgical treatment was not possible due to the patient's poor respiratory function, liposomal amphotericin B was transbronchially administered directly into the aspergilloma. The patient underwent fiberoptic bronchoscopy, and a yellow fungus ball was observed in the cavity connecting to the right B^2bi-beta, a biopsy sample of which was found to contain *Aspergillus fumigatus*. Nine transbronchial administrations of liposomal amphotericin B were conducted using a transbronchial aspiration cytology needle, which resulted in the aspergilloma disappearing by seven and a half months after the first treatment. This strategy could be suitable for aspergilloma patients with complications because it is safe and rarely causes further complications.

Introduction

Aspergillus is commonly found in all environments and causes a variety of diseases depending on the immunological status of the host and the local condition of the lung [1,2]. Pulmonary aspergillomas usually occur in pre-existing lung cavities exhibiting localized immune deficiency [3]. As pulmonary aspergillomas only partially touch the walls of the cavities containing them, they rarely come into contact with the bloodstream, which is the major reason why the systemic administration of antifungal agents is ineffective at eradicating the condition [4]. Most patients with pulmonary aspergillomas exhibit complications such as tuberculosis and pulmonary fibrosis, which makes curative surgical treatment difficult. We report a case of aspergilloma that was successfully treated via the transbronchial administration of liposomal amphotericin B (L-AMB) directly into the aspergilloma using a transbronchial aspiration cytology (TBAC) needle.

Case report

A 72-year-old male patient complained of recurrent hemoptysis and dyspnea, and a chest X-ray and CT scan (Fig. 1) demonstrated the existence of a fungus ball (longest diameter: 28 mm) in a pulmonary cavity exhibiting idiopathic pulmonary fibrosis (IPF)-induced traction bronchiectasis. Although an examination of the patient's sputum was inconclusive, he exhibited a high 1-3-beta-D-glucan level (53.8 pg/mL) and an Aspergillus galactomannan

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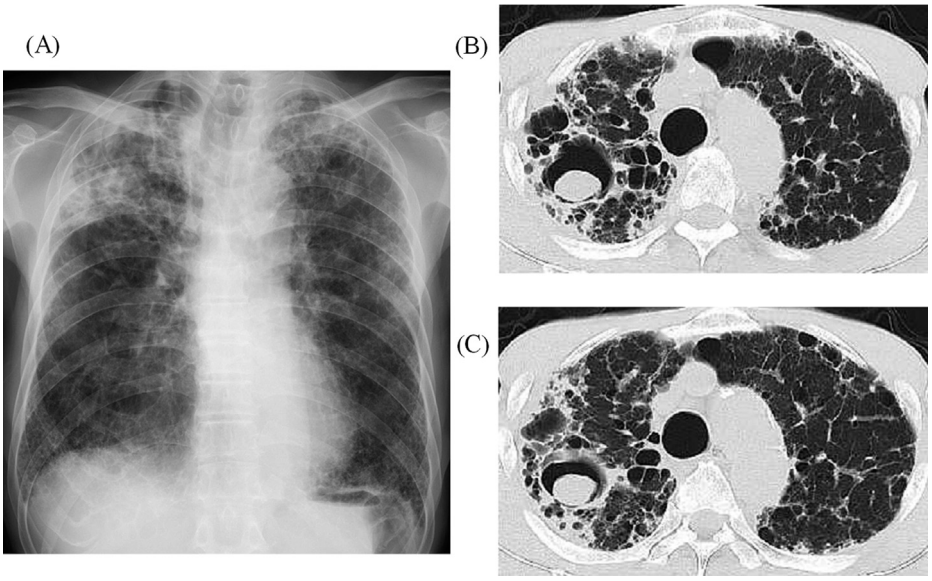

Fig. 1. Chest X-ray (A) and CT scan (B, C) obtained at the first visit demonstrated the existence of a fungus ball (longest diameter: 28 mm) in a pulmonary cavity exhibiting idiopathic pulmonary fibrosis-induced traction bronchiectasis.

antigen index of 2.2, which were suggestive of pulmonary aspergilloma. Voriconazole (VRCZ) was systemically administered for two months, before itraconazole (ITCZ) was systemically administered for a further month; however, this did not have any effect on the patient's symptoms or the size of his aspergilloma. Since surgical treatment was not possible due to the patient's poor respiratory function, topical treatment was adopted.

Fiberoptic bronchoscopy (FOB) was performed, and a yellow fungus ball was observed in the cavity connecting to the right B^2bi-beta (Fig. 2(A)), a biopsy examination of which detected *Aspergillus fumigatus*.

Since the fungus ball was visible during the FOB, L-AMB was transbronchially administered directly into the aspergilloma using a TBAC needle. One hundred mg/body (2.5 mg/kg) were administered during each treatment, which was equivalent to the dose that would have been administered during systemic therapy. The L-AMB was dissolved in distilled water at a concentration of 10 mg/mL and was administered through a TBAC needle (Fig. 2(B)) at a dose of 0.5 mL per instillation, with each instillation site being different from the previous sites in order to ensure the diffuse and appropriate permeation of L-AMB into the fungus ball. After the procedure, the patient was asked to adopt a right-sided posture for 1 h. The procedure was conducted once a week in the outpatient department for four weeks, and after its safety had been confirmed the L-AMB dose was increased to 200 mg/body, and the procedure was conducted a further three times. By the sixth round of treatment, the fungus ball had diminished in size and turned brown (Fig. 2(C)), and the breakage of the aspergilloma into several parts was observed due to an increase in the internal pressure of the aspergilloma caused by the direct administration of L-AMB (Fig. 2(D)). Surprisingly, during the subsequent treatment period the aspergilloma fragments re-assembled into a single structured fungus ball. At three months after the seventh treatment round, the diameter of the aspergilloma had decreased to 14 mm (Fig. 3(A, B)). Then, the L-AMB dose was reduced to its initial level due to the shrinkage of the fungus ball, and two further rounds of treatment were performed. In the end, the aspergilloma disappeared at two months after the ninth round of treatment; i.e., seven and a half months after the start of treatment (Fig. 3(C, D)).

The patient's 1-3-beta-D-glucan level gradually decreased to 28.0 pg/mL, and his Aspergillus galactomannan antigen index was 0.4 at three months after the start of treatment.

During the study period, the fibrotic pulmonary cavity enlarged (Figs. 1 and 3), and the patient's pulmonary function deteriorated in accordance with the progression of his IPF. Chemically-induced bronchitis and drug-induced interstitial lung disease were considered to be potential side effects of the abovementioned treatment regimen, but neither of these conditions developed. In addition, no L-AMB-related renal dysfunction or hypokalemia were observed.

The abovementioned treatment was so effective that the patient's hemoptysis disappeared within two weeks and his aspergilloma shrank within three months and had completely disappeared within seven months.

Discussion

Aspergillus is a ubiquitous fungus, and all human beings breath in its conidia during everyday life. However, any conidia that attach to the lower respiratory tract are removed by mucociliary clearance, and those that reach the alveoli are phagocytosed by alveolar macrophages [5]. Furthermore, even when the conidia sprout hyphae they are sterilized by neutrophils [6], resulting in healthy hosts escaping from fungal infection. Aspergillus can cause a variety of diseases depending on both the immunological status of the host and the local condition of the lung [1,2]. Pulmonary aspergillomas usually occur in pre-existing lung cavities exhibiting local immunodeficiency, such as those caused by tuberculosis, bronchiectasis, emphysema, pneumoconiosis, sarcoidosis, and interstitial pneumonia [3].

Pulmonary aspergillomas are classified into simple and complex aspergillomas [7], and the latter type is more prevalent because it is associated with underlying diseases. Surgery such as cavernostomy with muscle transposition, partial resection, segmentectomy, or lobectomy [9–11] is recommended as a curative treatment [8].