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【 CASE REPORT 】

Obstructive Pneumonia Associated with Endobronchial Aspergilloma: Successful Treatment with Interventional Bronchoscopy and Antifungals

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Abstract:
Endobronchial aspergilloma is a rare disease. A 64-year-old man with severe diabetes mellitus developed a cough and fever and was referred to our hospital. He was diagnosed with obstructive pneumonia associated with endobronchial aspergilloma, underwent interventional bronchoscopy, and was treated with antifungals. While the optimal treatment has not been established, interventional bronchoscopy along with systemic antifungals may improve the outcome in such cases.

Key words: endobronchial aspergilloma, interventional bronchoscopy, aspergillus

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Introduction

Central airway stenosis is caused by various diseases, such as postintubation tracheal stenosis, post-tuberculosis infection, tracheobronchomalacia and lung cancer, or mediastinal malignancy (1). Central airway stenosis is seldom caused by fungal infections. Endobronchial aspergilloma, a rare type of fungal infection, is characterized by the growth of *Aspergillus* species in the bronchial lumen (2). The management of endobronchial aspergilloma with central airway stenosis remains unclear.

We herein report a patient diagnosed with obstructive pneumonia due to right main bronchial stenosis associated with endobronchial aspergilloma. The patient was successfully treated with interventional bronchoscopy and antifungal treatment.

Case Report

A 64-year-old man presented to a hospital with a progressive cough and fever. He had a 12-pack-year smoking history. The patient was diagnosed with hypertension and was being treated for atrial fibrillation. He had also been diagnosed with alcoholic hepatitis one year previously. He had stopped drinking, and his hepatic functions were almost within the normal range.

After admission to the previous medical institution, a chest radiograph revealed infiltrative opacities in the right upper lung zone (Fig. 1A). Laboratory findings showed a white blood cell count of 11,870/μL, hemoglobin level of 10.3 g/dL, albumin level of 1.5 g/dL, and C-reactive protein level of 8.05 mg/dL. The patient was diagnosed with pneumonia. In addition, he had a blood sugar level of 670 mg/dL and hemoglobin A1c level of 15.5%; he was thus diagnosed with type 2 diabetes mellitus on admission. The results of his interferon-γ release assay and human immunodeficiency

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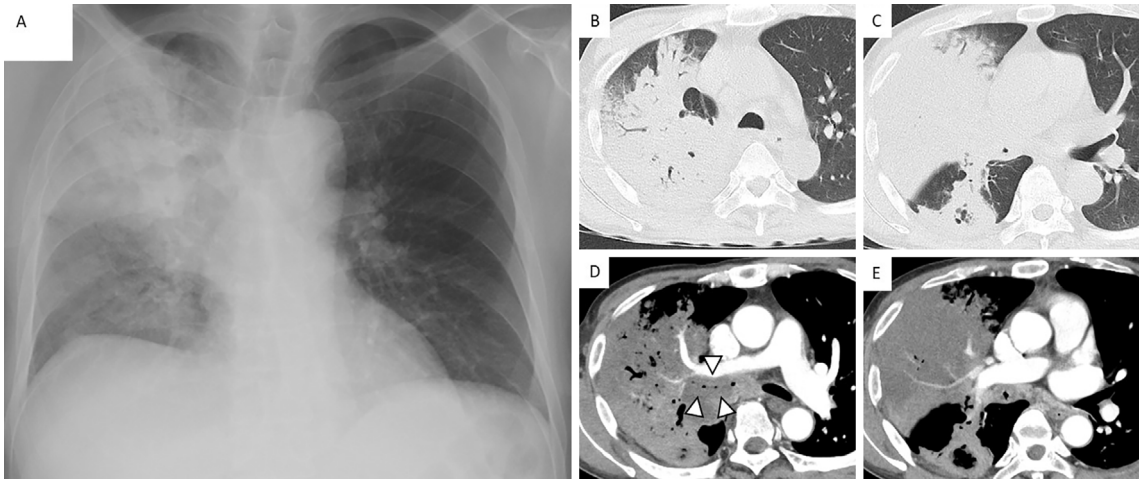

Figure 1. Chest radiograph and computed tomography (CT) at admission. (A) Chest radiograph showing infiltrative opacity in the right upper lung zone. (B-E) Chest CT showing consolidation in the right upper lobe (B, C) and cavity in the right lower lobe (C, E). (D) Narrowing of the right main bronchus with wall thickening and secretions (arrows).

virus infection screening tests were negative. Both the acid-fast bacilli smear and sputum culture were negative. He received antibiotic treatment with piperacillin-tazobactam, and insulin therapy. However, his symptoms deteriorated. Chest computed tomography (CT) revealed a narrowed right main bronchus and thickened right main bronchial wall. The stenosis did not improve despite four weeks of antibiotic treatment, so the patient was transferred to our hospital.

After admission to our hospital, chest CT revealed consolidation in the right upper and middle lobes, right main bronchus narrowing with wall thickening, secretions, and a right lower lobe cavity (Fig. 1B-E). Bronchoscopy demonstrated a nearly obstructed right main bronchus with bronchial wall edema and endoluminal masses (Fig. 2A, B). Based on these findings, the patient was diagnosed with obstructive pneumonia due to endoluminal masses in the right main bronchus.

We performed an interventional bronchoscopy for the endobronchial mass at the orifice of the right main bronchus to the orifice of the right upper bronchus to release the bronchial stenosis. Balloon bronchoplasty was performed with a flexible bronchoscope, but the stenosis did not resolve. Subsequently, we performed argon plasma coagulation (APC) with a flexible bronchoscope (Fig. 2C) (3). The right main bronchus was gradually dilated, and APC was repeated to remove the devitalized tissue. Since the response to antibiotic treatment was poor, administration of antifungals was started after bronchoscopy. The initial therapy consisted of micafungin (150 mg/day, intravenously).

A histopathologic examination of the biopsy specimens obtained from the endoluminal mass showed the infiltration of inflammatory cells, mainly consisting of lymphocytes, under the epithelium. In addition, a small amount of fungus-like structure was also found (Fig. 3A, B). A bronchoscopic biopsy of the right main bronchus and right upper lobe revealed no malignancy. A microscopic examination of the specimen obtained from bronchial washing showed Y-shaped branching septate hyphae (Fig. 3C), indicative of an *Aspergillus* fungi infection. However, *Aspergillus* species were not detected in the culture of the bronchial lavage fluid and specimen. A serological panel revealed a β-D glucan level of 29.6 pg/mL (reference range <11.0 pg/mL). The aspergillus antigen level in serum was 0.7 (reference range <0.5), and the *Candida albicans* antigen was not detected in the serum. Although the morphology was not clearly revealed in the septate hyphae in the tissue sample, a comprehensive diagnosis of endobronchial aspergilloma was made based on the bronchial washing cytology. The cavity in the right lower lobe was judged to be pulmonary aspergilloma based on the CT findings.

The fever and cough improved after interventional bronchoscopy and antifungal treatment. Chest radiograph revealed improvement in consolidation at the right upper lung zone. Bronchoscopic findings two weeks after the administration of antifungals showed improvement in the edema. The endoluminal mass in the right main bronchus had disappeared, and the stenosis of the right main bronchus was resolved. Antifungal treatment was then switched to voriconazole (200 mg every 12 hours orally), and the patient was discharged from our hospital.

He was treated with voriconazole for another six months. Chest radiograph and CT revealed improvement in the consolidation (Fig. 4B-E). Bronchial stenosis of the right main bronchus persisted but improved (Fig. 2D). One year has passed since the completion of antifungal treatment, and the patient has not developed restenosis of the right main bronchus.

Discussion

We encountered a case of obstructive pneumonia associated with endobronchial aspergilloma. The patient was suc-

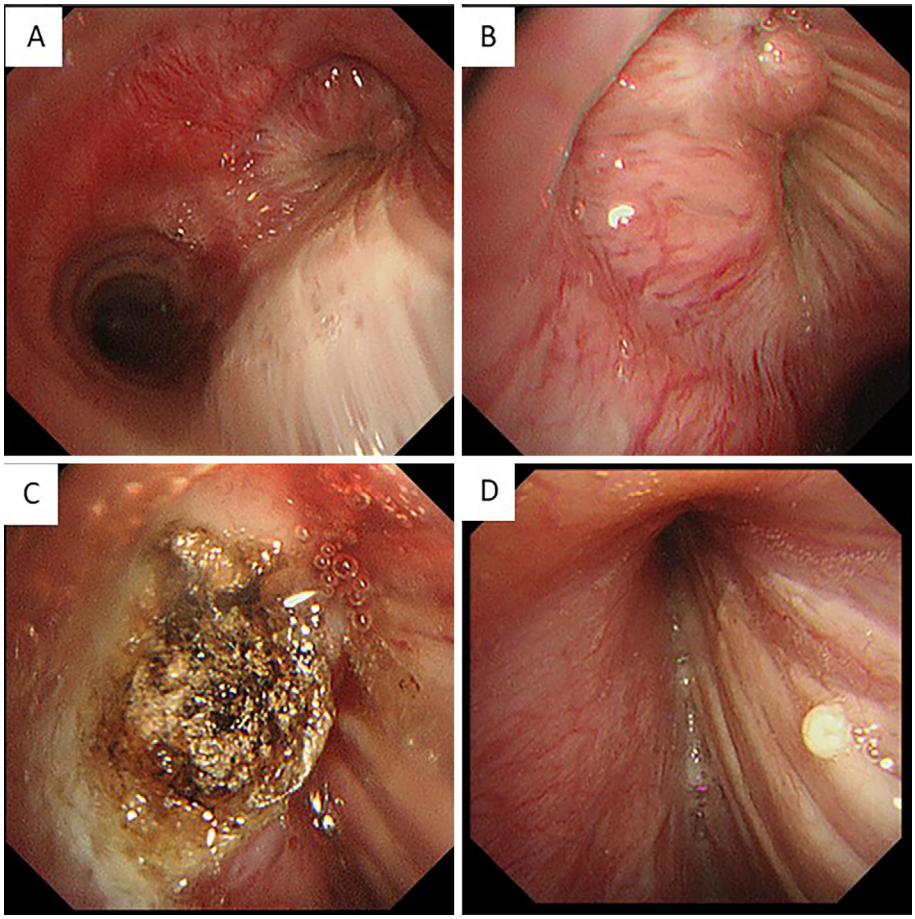

Figure 2. **Bronchoscopic findings of endobronchial aspergilloma. (A, B) Right main bronchus is almost obstructed by bronchial wall edema and endoluminal masses. (C) Right main bronchus after argon plasma coagulation. (D) Improvement in right main bronchial stenosis six months after interventional bronchoscopy and antifungal treatment.**

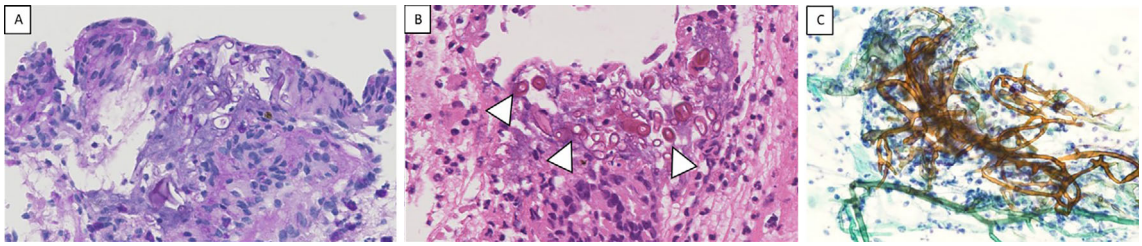

Figure 3. **Histopathology and cytology. (A, B) Histopathology of the biopsy specimens obtained from the endoluminal mass lesion of the right main bronchus showing the infiltration of inflammatory cells, which mainly consist of lymphocytes, under the epithelium. A small fungus-like structure is observed (B, arrows). (A) Hematoxylin and Eosin staining; (B) Periodic acid-Schiff staining (magnification, 40×). (C) A microscopic examination of specimens obtained from bronchial washing showing Y-shaped, branching septate hyphae with numerous neutrophils in the background (Papanicolaou staining; magnification, 40×).**

cessfully treated with interventional bronchoscopy and systemic antifungal treatment.

Aspergillus species can cause various pulmonary diseases. Endobronchial aspergilloma is a rare manifestation of pulmonary *Aspergillus* species infection. Endobronchial aspergilloma is characterized by the growth of *Aspergillus* species in the bronchial lumen, with or without parenchymal lesions or cavities (4, 5). The present patient was diagnosed with endobronchial aspergilloma in the right bronchus with a cavity in the right lower lobe. The cavity was resolved with antifungals and was thus diagnosed as pulmonary aspergilloma. Endobronchial aspergilloma with central airway stenosis can cause obstructive pneumonia due to the overgrowth of massive fungus, mucus, and cellular debris. The develop-

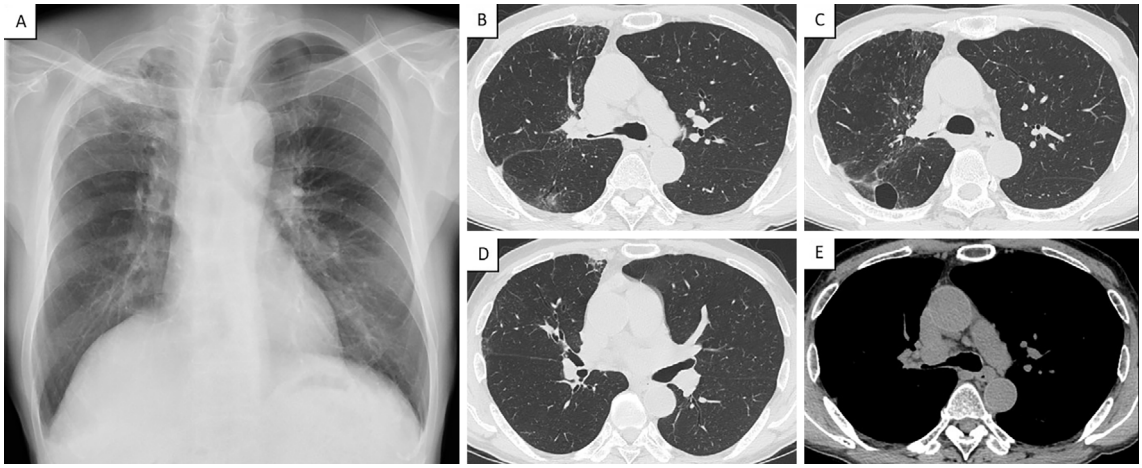

Figure 4. **Chest radiograph and computed tomography (CT) after treatment. (A) Chest radiograph six months after interventional bronchoscopy and antifungal treatment showing improvement in the infiltrative opacity of the right upper lung zone. (B-E) Chest CT six months after interventional bronchoscopy and antifungal treatment showing improvement in consolidation of the right upper and middle lobes, a reduction in the size of the cavity in the right lower lobe, and the release of the stenosis in the right main bronchus.**

ment of *Aspergillus* species infection depends on the individual's immune status and the presence of underlying lung disease (6), such as pulmonary tuberculosis, lung cancer, lung resection for early-stage lung cancer, and foreign body aspiration in the lungs (7, 8). It has not been conclusively associated with immune deficiency. Ngu et al. reported (7) that 8 of 28 endobronchial aspergilloma patients were severely immunocompromised. In a study by Huang et al. (8), none of 17 endobronchial aspergilloma patients exhibited severe immune deficiency. In the present case, no underlying lung disease was present. The patient was not immunocompromised but did have severe diabetes mellitus. Diabetes was recently identified as a risk factor for developing aspergillus infections in non-immunocompromised patients (9).

Wu et al. classified the bronchoscopic findings of airway aspergillosis into four types (10): type I, superficial infiltration type; type II, full-layer involvement type; type III, occlusion type; and type IV, mixed type. The bronchoscopic features of type I include inflammatory infiltration, mucosa hyperemia, and pseudomembrane plaques in the lumen without apparent airway occlusion. The bronchoscopic findings of type II include inflammatory infiltration through the matrix layer of bronchi, substantial and deep ulceration, extensive tissue necrosis, cartilage invasion, and normal airway destruction. The bronchoscopic features of type III include airway obstruction or constriction of over 50% of the original caliber of the involved bronchi caused by extensive pseudomembrane formation, polypoid granulation, or necrotic tissues without definite deeper tissue invasion. In type IV, the bronchoscopic features satisfy at least two distinct types simultaneously. Bronchoscopic findings reflect the extent of disease progression. In the present case, the right main bronchus was almost completely obstructed by wall edema and endoluminal masses, so this case was classified as type III.

Although optimal treatment for obstructive pneumonia associated with endobronchial aspergilloma has not been established, treatment with a combination of systemic antifungals and interventional bronchoscopy has been described (8). In particular, interventional bronchoscopy is essential for rapidly relieving obstructive symptoms in cases with central airway obstruction (11). Surgery or stent placement are treatment options (other than APC) to release central airway stenosis. In the present case, right pneumonectomy was considered necessary for treatment. Surgery was not the first choice of treatment because of its invasiveness. Stent placement was avoided due to the presence of active infection. In this case, balloon bronchoplasty was performed initially, but the stenosis did not resolve. Therefore, APC was performed because it has been proven effective for the treatment of endobronchial tuberculosis. In addition, APC has been proven effective for the treatment of endoluminal hemoptysis and benign and malignant airway stenosis (3). It may be more suitable for airway stenosis with obstructive pneumonia, as in this case, because of its immediate effect, with rapid coagulation with minimal manipulation and mechanical trauma to the target tissue (12). We believe that interventional bronchoscopy with systemic antifungals improved the outcome in this case, although the possibility of antifungals alone having been effective cannot be excluded.

Conclusions

We encountered a case of obstructive pneumonia associated with endobronchial aspergilloma, successfully treated with interventional bronchoscopy and antifungal treatment. In endobronchial aspergilloma accompanied by central airway stenosis, interventional bronchoscopy along with systemic antifungal treatment may improve the outcome.

Written informed consent was obtained for the publication of this report and any accompanying images.

The authors state that they have no Conflict of Interest (COI).

References

1. Murgu SD, Egressy K, Laxmanan B, Doblare G, Ortiz-Comino R, Hogarth DK. Central airway obstruction: benign strictures, tracheobronchomalacia, and malignancy-related obstruction. Chest **150**: 426-441, 2016.
2. Sunnetcioglu A, Ekin S, Erten R, Parlak M, Esen R. Endobronchial aspergilloma: a case report. Respir Med Case Rep **18**: 1-3, 2016.
3. Yasuo M, Tanabe T, Tsushima K, et al. Endobronchial argon plasma coagulation for the management of post-intubation tracheal stenosis. Respirology **11**: 659-662, 2006.
4. Ma JE, Yun EY, Kim YE, et al. Endobronchial aspergilloma: report of 10 cases and literature review. Yonsei Med J **52**: 787-792, 2011.
5. Araújo D, Figueiredo M, Monteiro P. Endobronchial aspergilloma: an unusual presentation of pulmonary aspergillosis. Rev Port Pneumol **22**: 61-62, 2016.
6. Hospenthal DR, Kwon-Chung KJ, Bennett JE. Concentrations of airborne *Aspergillus* compared to the incidence of invasive aspergillosis: lack of correlation. Med Mycol **36**: 165-168, 1998.
7. Ngu S, Narula N, Abureesh M, Li JJ, Chalhoub M. Endobronchial aspergilloma - a comprehensive literature review with focus on diagnosis and treatment modalities. Eur J Clin Microbiol Infect Dis **39**: 601-605, 2020.
8. Huang D, Li B, Chu H, et al. Endobronchial aspergilloma: a case report and literature review. Exp Ther Med **14**: 547-554, 2017.
9. Ghanaat F, Tayek JA. Weight loss and diabetes are new risk factor for the development of invasive aspergillosis infection in non-immunocompromized humans. Clinic Pract **14**: 296-301, 2017.
10. Wu N, Huang Y, Li Q, Bai C, Huang HD, Yao XP. Isolated invasive *Aspergillus* tracheobronchitis: a clinical study of 19 cases. Clin Microbiol Infect **16**: 689-695, 2010.
11. Keshishyan S, DeLorenzo L, Hammoud K, Avagyan A, Assallum H, Harris K. Infections causing central airway obstruction: role of bronchoscopy in diagnosis and management. J Thorac Dis **9**: 1707-1724, 2017.
12. Bolliger CT, Sutedja TG, Strausz J, Freitag L. Therapeutic bronchoscopy with immediate effect: laser, electrocautery, argon plasma coagulation and stents. Eur Respir J **27**: 1258-1271, 2006.