

Case report

Endobronchial mucosal nodular lesions in allergic bronchopulmonary aspergillosis

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ABSTRACT

Bronchoscopic findings often show mucoid impaction in patients with allergic bronchopulmonary aspergillosis (ABPA); however, endobronchial mucosal nodular lesions have not been reported. We herein present the first such case of a 52-year-old woman with ABPA with endobronchial mucosal nodular lesions. The endobronchial lesions were located in the orifice of the mucoid impaction, and disappeared after 4 weeks of treatment with prednisolone and itraconazole. *Aspergillus fumigatus* was cultured from bronchial lavage fluid collected from the site of mucoid impaction. Based on these clinical findings, we speculate that the bronchial lesions were caused by an inflammatory and allergic reaction to *Aspergillus* antigens.

1. Introduction

In some patients with eosinophilic pneumonia or eosinophilic granulomatosis with polyangiitis, bronchoscopic findings show mucosal nodular lesions in the trachea and main bronchus [1–3]. The pathologic findings in such patients usually comprise eosinophilic inflammation, edematous changes, and/or necrotizing bronchial inflammation [1–3]. However, these bronchial nodular lesions have not been reported in patients with allergic bronchopulmonary aspergillosis (ABPA). We herein report the case of a patient with ABPA with endobronchial mucosal nodular lesions that disappeared after treatment with prednisolone and itraconazole.

2. Case report

A 52-year-old woman was referred for evaluation of abnormal chest shadows. She had a history of rheumatoid arthritis (RA) that had been treated with low-dose prednisolone and salazosulfapyridine. She also had a history of breast cancer. The patient had never smoked, and had no history of bronchial asthma. Chest computed tomography showed highly attenuated, mucus-filled, dilated bronchi (Fig. 1). Laboratory examination revealed an eosinophil count of 821.5/μL, a total IgE level of 1656 IU/ml, and positivity for *Aspergillus*-specific IgE and precipitating antibody. An immediate skin test for *Aspergillus* yielded a positive

reaction. MPO-ANCA and PR3-ANCA were negative. Fractional exhaled nitric oxide level was elevated to 48 ppb. A lung function test revealed as follows: FVC 2.40 (L), %FVC 90.2%, FEV1 2.03 (L), %FEV1 86.4%, and FEV1/FVC 84.6%. Threshold of methacholine was 20,000 μg/ml. Bronchoscopy revealed multiple nodular mucosal lesions in the orifice of the right B⁹ bronchus (Fig. 2a). Histopathologic examination showed edematous changes and bronchial inflammation with eosinophils (Fig. 3a and b). Mucoid impaction was noted in the distal aspect of the right bronchus (Fig. 2b), and *Aspergillus fumigatus* (*A. fumigatus*) was cultured from the bronchial lavage fluid. There were no clinical findings of vasculitis. The patient was diagnosed with ABPA [4], and treated with oral prednisolone (30mg/day) and itraconazole (400mg/day). Four weeks of treatment resulted in resolution of the endobronchial lesions and the mucoid impaction (Fig. 2c). Prednisolone was slowly tapered off and itraconazole was continued for 16 weeks. A 4-month follow up chest computed tomography scan showed almost complete resolution of the highly attenuated intrabronchial mucus, and bronchiectasis was noted (Fig. 4). Peripheral eosinophil count and total IgE level were decreased to 70.0/μL and 93 IU/ml, respectively.

3. Discussion

In patients with ABPA, bronchoscopy usually show intraluminal retention of inspissated mucoid secretions, which is known as mucoid

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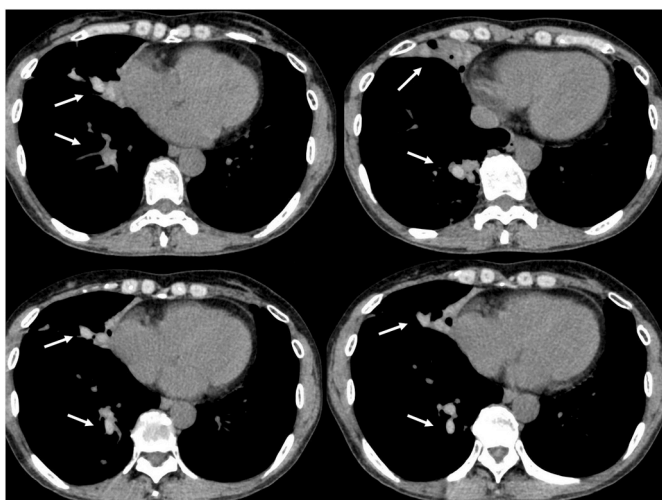


Fig. 1. Chest computed tomography findings obtained at various levels (soft tissue windows) showing highly attenuated, mucus-filled, dilated bronchi in the right middle and lower lobes (arrows).

impaction [5]. The airway walls around this area of mucoïd impaction often has inflammatory and edematous changes [5]. In addition to these findings, our patient had multiple nodular mucosal lesions in the orifice. This is the first report of these bronchoscopic findings in a patient with ABPA.

A few previous reports have described similar endobronchial mucosal nodular lesions in patients with eosinophilic pneumonia and eosinophilic granulomatosis with polyangiitis [1–3]. The pathologic findings in these previous cases were necrotizing bronchial inflammation with eosinophils and thickening of the basement membrane [1–3]. In our case, histologic examinations of the bronchial nodular lesions revealed edematous change and eosinophilic infiltrations. Epithelial cells were denuded, but there were no tissue necrosis. *Aspergillus* hyphae were not detected in this specimens. These pathological findings were nonspecific, but may suggest that these bronchial mucosal lesion represent a localized accentuation of edema associated with eosinophilic inflammation.

The pathogenesis of ABPA is not completely understood, but the condition is thought to occur due to abnormal exaggerated local and systemic immune response to *Aspergillus* antigens [4]. Recently, Muniz VS et al. reported that eosinophil extracellular DNA trap (EET) have been noted in the airway mucus in patients with ABPA [6]. They also demonstrated that human eosinophils release EETs in response to *A. fumigatus* [6]. EETs are derived from eosinophil extracellular DNA trap cell death (EETosis) [7] and provide adhesive surface that can

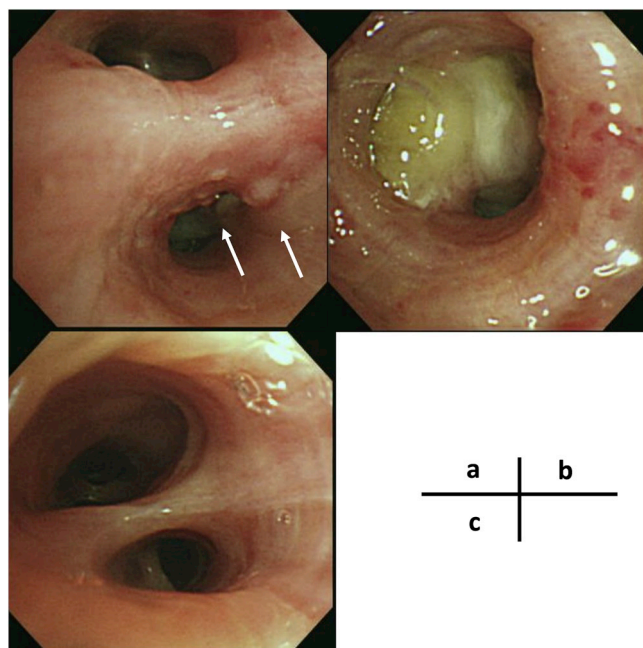


Fig. 2. (a) Fiberoptic bronchoscopic findings showing multiple nodular mucosal lesions (arrows) and edematous changes in the orifice of the right B⁹ bronchus. (b) Mucoïd impaction in the distal aspect of the right B⁹ bronchus. (c) Fiberoptic bronchoscopic findings showing the resolution of these mucosal lesions and edematous changes after 4 weeks of treatment with a systemic corticosteroid and itraconazole.

entrap intact eosinophil granules and microorganisms [7], but lack the killing or fungistatic activities against *A. fumigatus* [6]. In our case, the lesions of interest were located only near the mucoïd impaction, from which *A. fumigatus* was cultured. Therefore, we speculate that these endobronchial mucosal nodular lesions may have been caused by an inflammatory and allergic reaction to *Aspergillus* antigens. Free granules entrapped in EETs may cause long-lasting bronchial wall inflammation leading to epithelial cell damage. However, the precise mechanisms are unclear and require further investigation.

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Declaration of competing interest

I declare on behalf of my co-authors and myself that we do not have

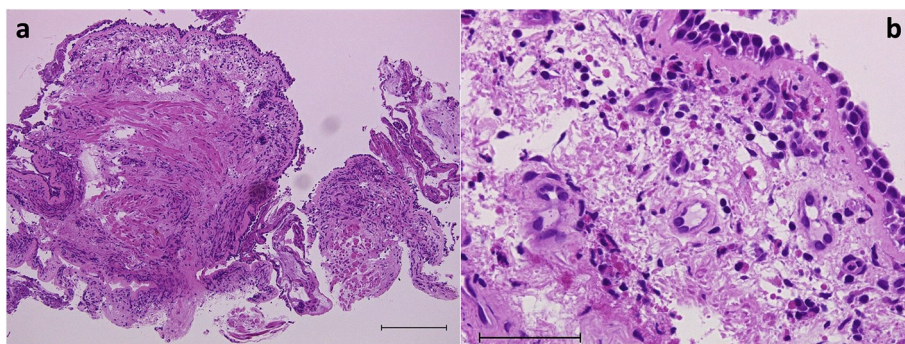


Fig. 3. Biopsy specimens of the mucosal nodular lesions. (a) At low magnification showing denudation of bronchial epithelial cells, subepithelial fibrosis, muscular thickening, and submucosal edematous changes with inflammatory cell infiltration. Bar indicate 200µm. (b) At higher magnification showing submucosal edematous changes and infiltration of eosinophils. Bar indicate 50 µm.

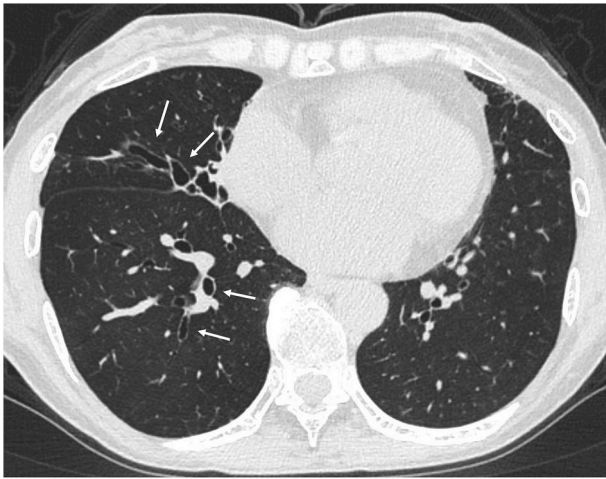


Fig. 4. Chest CT findings after 16-week treatment of prednisolone and itraconazole, showing bronchiectasis with disappearance of mucoid impactions (arrows).

any conflict of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmcr.2019.100975>.

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