

Clinical Communications

Repeated exacerbation by environmental exposure and spontaneous resolution of allergic bronchopulmonary mycosis

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Clinical Implications

- Acute exacerbation of allergic bronchopulmonary mycosis can occur in response to an acute exposure to environmental fungi, for example, from a contaminated air conditioner. Environmental control to avoid further fungal exposure can induce spontaneous resolution of the flare.

Allergic bronchopulmonary mycosis (ABPM) is characterized by type I and type III hypersensitivity to fungi colonized in the eosinophil-rich mucus plugs in the airways.¹ *Aspergillus* spp., especially *A. fumigatus*, is most frequently isolated from the airways of patients with ABPM, but other fungi such as *Penicillium* spp. and *Schizophyllum commune* can cause a similar pathology in the airways.² Unfortunately, most patients who achieve clinical remission often relapse repeatedly,³ possibly due to reoccurring exposure to environmental fungi. However, there has been little evidence regarding the association between exacerbation of ABPM and exposure to environmental fungi. Here, we present a patient whose ABPM manifestations repeatedly deteriorated from acute fungi exposure and then subsequently resolved spontaneously once the environmental trigger was removed, without the need for any pharmacotherapy.

A 27-year-old man presented to a clinic with a fever and was referred to us due to abnormal shadows on his chest radiograph (Figure 1, A). His job involved the maintenance and replacement of air conditioning systems in buildings. He had a history of atopic dermatitis and asthma that had been treated with inhaled corticosteroids for 2 years. He had experienced temporal fever and expectoration of mucus plugs 10 months ago, treated with oral clarithromycin.

He had a fever of 38.0°C (100.4°F) 2 days after cleaning a mold-laden air conditioner at his own home by himself. Peripheral blood tests showed eosinophilia (1400/μL) without neutrophilia and an increase in both C-reactive proteins (CRP) (4.61 mg/dL). Total and *A. fumigatus* specific IgE was 17,691 and 19.0 IU/mL, respectively, and a precipitin test was positive for *A. fumigatus* antibodies. A sputum culture was negative for bacteria but showed *S. commune* on a potato-dextrose-agar plate. Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁) was 78.0% and 74.5% of the predicted value,

respectively, and FEV₁/FVC was 84.5%. A chest radiograph showed opacity in the middle field of the right lung and in the upper field of the left lung (Figure 1, A). Thoracic computed tomography showed opacification, central bronchiectasis, and mucus plugs in the bronchi, with some areas featuring high attenuation mucus (Figure 1, B-D). Abundant eosinophils and Charcot-Leyden crystals (Figure E1, A, available in this article's Online Repository at www.jaci-inpractice.org), with some fungal hyphae (Figure E1, B, available in this article's Online Repository at www.jaci-inpractice.org), were observed in the mucous plug obtained by bronchoscopy.

Mycobiome analysis using polymerase chain reaction (PCR) amplification of the internal transcribed spacer 1 region of the fungal ribosomal RNA gene, followed by next-generation sequencing, demonstrated that *S. commune* and *A. fumigatus* accounted for 74% and 10% of the fungal burden (110,256 reads of the total reads [119,040]) from the mucus plugs, respectively. The diagnosis of ABPM was confirmed, based on the criteria proposed by the International Society of Human and Animal Mycology: serum IgE levels >1000 IU/mL, *A. fumigatus* specific IgE and precipitin, peripheral blood eosinophilia, and radiographic findings. In addition, serum tests for *S. commune* specific IgE and IgG using the previously reported enzyme-linked immunosorbent assay were both positive.⁴ The patient abandoned the contaminated air conditioner, and his symptoms spontaneously improved in 2 weeks, without the need for pharmacotherapy. The pulmonary opacities and mucus plugs in the lungs disappeared followed by a gradual decrease in the total IgE levels in serum and peripheral eosinophil counts, and FEV₁ improved to 79.9% of the predicted value (Figure 2).

Nine months later, the patient experienced another episode of fever, expectoration of mucus plugs, and pulmonary opacities after exposure to contaminated air conditioners. He again recovered after 2 weeks of fungi avoidance and did not require pharmacotherapy.

In this case, there are 2 important clinical issues raised with regard to the pathogenesis of ABPM: first, ABPM can be acutely exacerbated by environmental factors, but can also be spontaneously resolved by removal of the triggering environmental factor. Second, multiple fungi, *A. fumigatus*, and *S. commune* can be associated with the pathogenesis of ABPM.

In the present case, acute exacerbation of ABPM occurred, with peripheral blood eosinophilia, increased serum IgE, and mucus plugs in the bronchi. Accompanying symptoms included fever and an increase of serum CRP levels, which are relatively rare (5%-15%) during ABPM flare (unpublished data). We speculate that massive exposure to fungal antigens from an air conditioner caused the acute inflammatory symptoms in the present case. A similar phenomenon is observed in hypersensitivity pneumonia, an allergic pulmonary disease characterized by type III and type IV hypersensitivity to inhaled antigens including fungi.⁵ Acute hypersensitivity pneumonia develops from exposure to a large dose of antigens and exhibits acute symptoms such as fever, acute respiratory failure, peripheral blood neutrophilia, and elevated serum CRP levels.⁵ Although the standard treatment for ABPM consists of systemic corticosteroids and/or antifungal agents,³ the patient in the present case

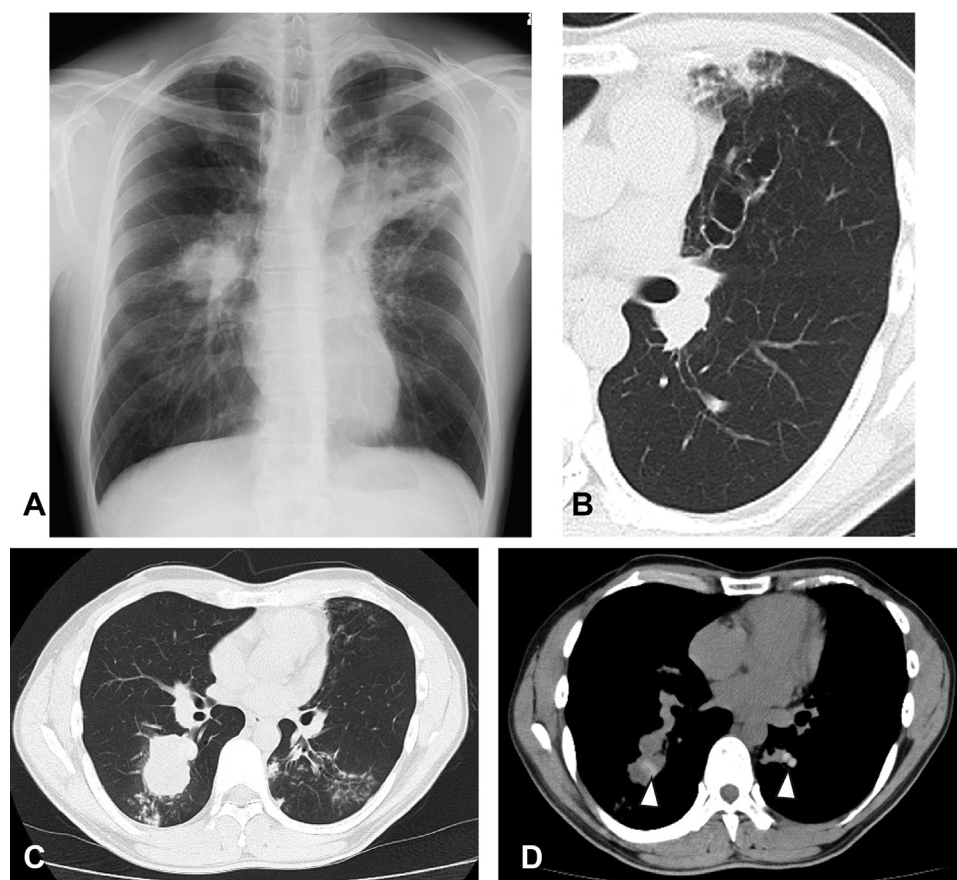


FIGURE 1. Chest radiograph findings on the first visit to the clinic. A chest X-ray showed consolidation in the left upper lung fields and a tumor-like shadow in the right middle lung field (A). Chest computed tomography showed central bronchiectasis (B) and mucoid impaction with high attenuation mucus (arrowhead) in both the lower lung fields (C, D).

improved without any pharmacological intervention; rather he eliminated the source of the fungal exposure, the contaminated air conditioner. It is well known that acute hypersensitivity pneumonia can be ameliorated by antigen avoidance alone,⁵ and this could also be the case for acute exacerbation of ABPM. Evaluation and modification of environmental factors should be considered in all cases of ABPM.⁶

The patient's serum in the present case was positive for *Aspergillus* and *S. commune* specific IgE and IgG/precipitated antibodies, whereas only *S. commune* was isolated in a sputum culture. A mycobiome analysis of the mucus plugs, obtained by bronchoscopy, detected both *A. fumigatus* and *S. commune*. *A. fumigatus* is a filamentous fungus present indoors and is often detected in the filters of air conditioners.⁷ *S. commune* is a basidiomycete, which is ubiquitous in the environment and has been reported as one of the causative fungi of ABPM.⁸ ABPM, associated with both *A. fumigatus* and *S. commune*, diagnosed by serological tests, fungal culture, and/or PCR, has been reported previously; however, to the best of our knowledge, this is the first case to identify *A. fumigatus* and *S. commune* simultaneously, using next-generation sequencing mycobiome analysis of mucus plugs.⁹ Unfortunately, we did not have the opportunity to examine the fungus in the air conditioner that caused acute exacerbation of ABPM in the present case.

In conclusion, we were presented with a case of acute exacerbation of ABPM, potentially due to the exposure to a contaminated air conditioner, which naturally resolved once the exposure stopped. It is necessary to evaluate the possible source of fungal antigen exposure in the external environment in patients with ABPM, especially for those with acute symptoms, allowing environmental alterations to avoid further fungal antigen exposure.

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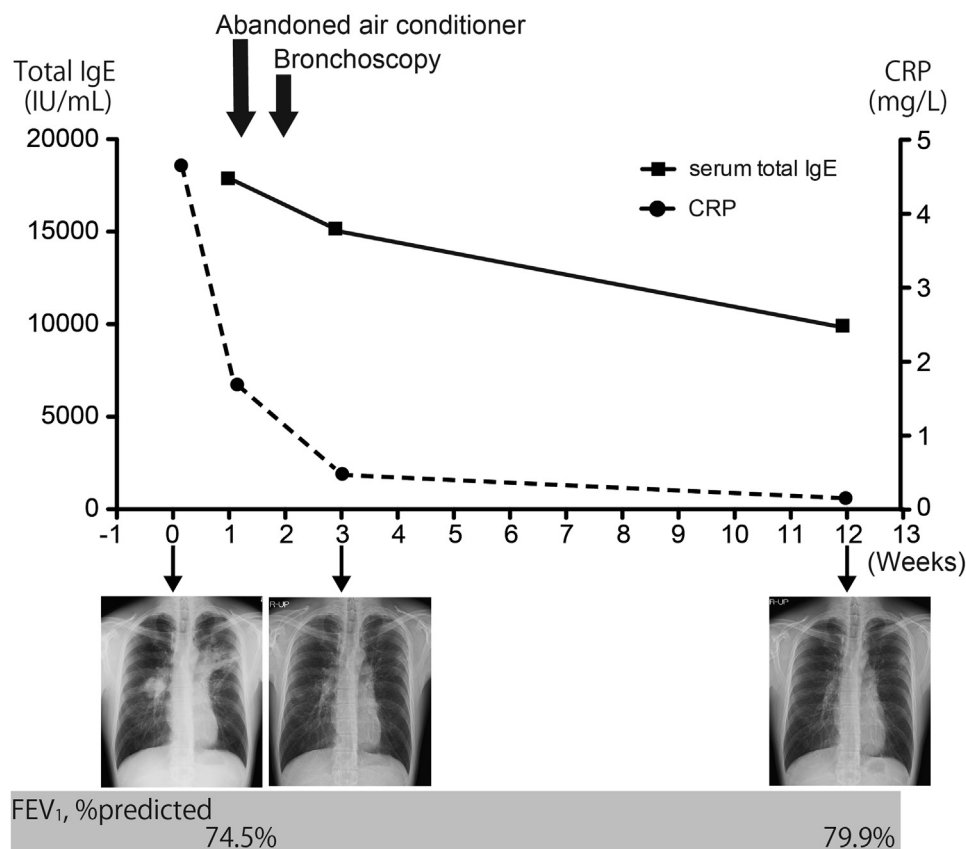


FIGURE 2. The clinical course of the patient, showing his IgE, C-reactive protein (CRP) levels, percentage forced expiratory volume (FEV₁, %predicted), and pulmonary opacities once the contaminated air conditioner was abandoned.

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REFERENCES

- O'Driscoll BR, Hopkinson LC, Denning DW. Mold sensitization is common amongst patients with severe asthma requiring multiple hospital admissions. *BMC Pulm Med* 2005;5:1209-10.
- Kamei K, Unno H, Nagao K, Kuriyama T, Nishimura K, Miyaji M. Allergic bronchopulmonary mycosis caused by the basidiomycetous fungus *Schizophyllum commune*. *Clin Infect Dis* 1994;18:305-9.
- Agarwal R, Chakrabarti A, Shah A, Gupta D, Meis JF, Guleria R, et al. Allergic bronchopulmonary aspergillosis: review of literature and proposal of new diagnostic and classification criteria. *Clin Exp Allergy* 2013;43:850-73.
- Toyotome T, Satoh M, Yahiro M, Watanabe A, Nomura F, Kamei K. Glucoamylase is a major allergen of *Schizophyllum commune*. *Clin Exp Allergy* 2014;44:450-7.
- Lacasse Y, Selman M, Costabel U, Dalphin JC, Morell F, Erkinjuntti-Pekkanen R, et al. Classification of hypersensitivity pneumonitis: a hypothesis. *Int Arch Allergy Immunol* 2009;149:161-6.
- Agarwal R, Devi D, Gupta D, Chakrabarti A. A questionnaire-based study on the role of environmental factors in allergic bronchopulmonary aspergillosis. *Lung India* 2014;31:232-6.
- Jo WK, Lee JH. Airborne fungal and bacterial levels associated with the use of automobile air conditioners or heaters, room air conditioners, and humidifiers. *Arch Environ Occup Health* 2008;63:101-7.
- Chowdhary A, Agarwal K, Kathuria S, Gaur SN, Randhawa HS, Meis JF. Allergic bronchopulmonary mycosis due to fungi other than *Aspergillus*: a global overview. *Crit Rev Microbiol* 2014;40:30-48.
- Seki M, Ohno H, Gotoh K, Motooka D, Nakamura S, Iida T, et al. Allergic bronchopulmonary mycosis due to co-infection with *Aspergillus fumigatus* and *Schizophyllum commune*. *IDCases* 2014;1:5-8.

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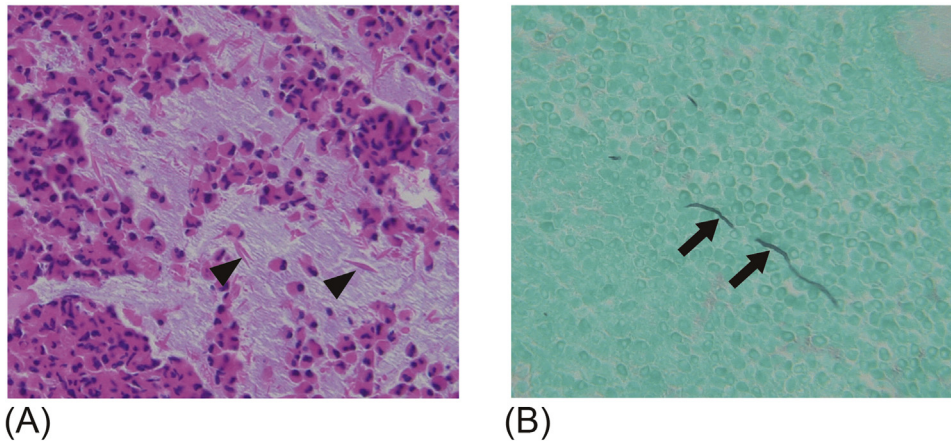


FIGURE E1. Biopsy specimens of the mucus plugs obtained by bronchoscopy showed eosinophils, and Charcot-Leyden crystals (arrowhead), on a hematoxylin and eosin stain **(A)** and fungal hyphae (arrow) on a Grocott's methenamine silver stain **(B)**.