Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.8771-16
Intern Med 57: 243-246, 2018
http://internmed.jp

【 CASE REPORT 】

Spontaneous Regression of Allergic Bronchopulmonary Mycosis Due to *Curvularia lunata*

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Abstract:

Allergic bronchopulmonary mycosis (ABPM) is a pulmonary hypersensitivity disease mainly caused by *Aspergillus fumigatus*. The mainstay treatment for ABPM is systemic corticosteroid therapy. A 25-year-old man presented with pulmonary infiltrates. His peripheral eosinophil, total serum IgE, and serum *Aspergillus*-specific IgE levels were elevated. The patient tested positive in a skin test for *Aspergillus*. However, sputum cultures revealed a *Curvularia lunata* infection. We therefore diagnosed ABPM possibly caused by *C. lunata*, which is rare in Japan. The clinical state of the patient improved under observation. Identification of the causative fungus is an important aspect of the ABPM diagnosis.

Key words: *Curvularia lunata*, allergic bronchopulmonary mycosis, spontaneous regression

(Intern Med 57: 243-246, 2018)
(DOI: 10.2169/internalmedicine.8771-16)

Introduction

Allergic bronchopulmonary mycosis (ABPM) is a pulmonary hypersensitivity disease caused by environmental fungi. The most common of these fungi is *Aspergillus fumigatus*, in which case the condition is termed allergic bronchopulmonary aspergillosis (ABPA). Other fungi include *Candida albicans*, *Schizophyllum commune*, species of *Alternaria*, *Bipolaris*, *Cladosporium*, *Curvularia*, *Fusarium*, *Penicillium*, *Pseudallescheria*, *Rhizopus*, *Saccharomyces*, *Stemphylium*, and *Trichosporon* (1). The prevalence of ABPM without ABPA is most likely underestimated because the causative fungus is not identified in some cases. While systemic corticosteroid therapy is the main treatment for ABPM, antifungal therapy can also be useful. We encountered a case of ABPM caused by *Curvularia lunata*, where the clinical state of the patient improved without administering either systemic corticosteroid or antifungal therapy.

Case Report

A 25-year-old man was admitted to our hospital because of a productive cough that had persisted for 4 months. The patient occasionally expectorated brown plugs and had a history of bronchial asthma since childhood and asthma symptoms approximately once a year following an upper respiratory tract infection. He had not received any maintenance treatment for asthma. The patient exhibited a forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) of 3.00 L and 1.33 L, respectively. The percentage of predicted FEV_1 was 31.0%. The FVC and FEV_1 increased to 3.74 L and 3.42 L, respectively, upon the inhalation of a bronchodilator. It is possible that the FEV_1 before inhalation of the bronchodilator was underestimated because the patient had a strong cough before inhalation; the cough decreased after inhalation. Asthma could be controlled by treatment according to Step 1 or 2 of the Global Initiative for Asthma (2) and was, therefore, considered to be mild. The patient was engaged in landscape gardening. The chest X-ray findings

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Received: December 26, 2016; Accepted: May 9, 2017; Advance Publication by J-STAGE: October 16, 2017
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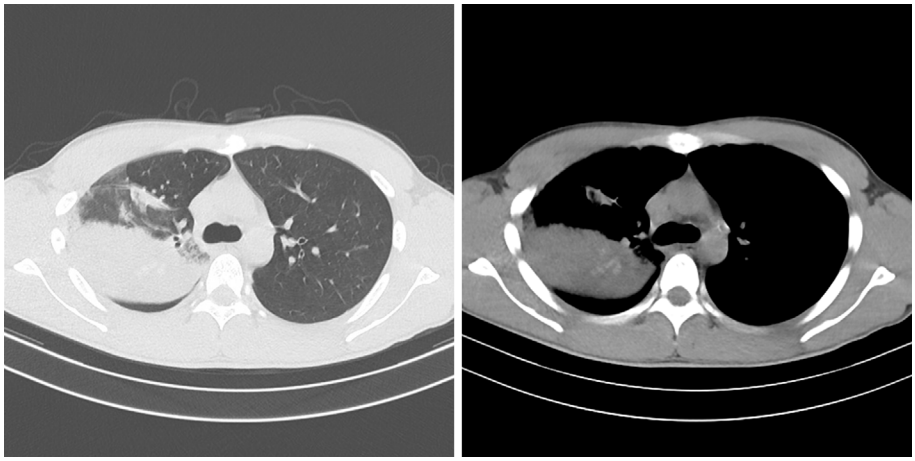

Figure 1. High-resolution chest computed tomography image revealed central bronchiectasis with a mucus plug in the right upper lobe.

Table 1. Laboratory Findings.

Peripheral blood count		Serology	
White blood cells	13,300 /μL	C-reactive protein	7.02 mg/dL
Neutrophils	66.50 %	IgE	7,451 IU/mL
Eosinophils	14.00 %	RAST for *A. fumigatus*	7.93 Ua/mL
Lymphocytes	12.00 %	Precipitin test for *A. fumigatus*	negative
Monocytes	7.00 %	Skin test for *A. fumigatus*	positive
Basophils	0.50 %	immediate reactivity	
Hemoglobin	14.2 g/dL	Arthus reactivity	false positive
Platelets	36.0×10^4 /μL		
Blood chemistry			
Total protein	6.8 g/dL		
Albumin	3.5 g/dL		
Sodium	139 mEq/L		
Potassium	4.3 mEq/L		
Chloride	100 mEq/L		
Urea nitrogen	13.3 mg/dL		
Creatinine	0.71 mg/dL		
AST	28 IU/L		
ALT	37 IU/L		
LDH	354 IU/L		

AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, RAST: radioallergosorbent test, *A. fumigatus*: *Aspergillus fumigatus*

from 3 years prior to presentation were normal. Chest X-ray images acquired upon admission at our hospital revealed infiltration in the right upper lung field. High-resolution chest computed tomography (CT) images revealed central bronchiectasis, with a mucus plug in the right upper lobe (Fig. 1). The results of laboratory tests (Table 1) revealed total blood eosinophil and serum IgE levels of 1,862/μL and 7,451 IU/mL, respectively. His serum *Aspergillus*-specific IgE levels were elevated, and the skin prick test with *Aspergillus* antigen revealed positive results. The patient was negative for serum *Aspergillus*-specific IgG. Although the patient fulfilled six of the seven primary criteria for diagnosis of ABPA, we performed bronchoscopy to identify the fungus (3). A yellow mucus plug, recognized in the right B^2 (Fig. 2), was submitted for smear test, fungal culture, and pathological examination. Histological findings revealed a large population of mold in the mucus, along with eosinophils. Microscopic evaluation revealed dematiaceous fungi with conidia containing four cells (Fig. 3). The sequence of the internal transcribed spacer region of ribosomal RNA of the isolate was determined and compared with sequences in the basic local alignment search tool database (http://blast.ncbi.nlm.nih.gov/Blast.cgi). Based on the morphological and phylogenetic findings, the fungus was identified to be *C. lunata*. Antifungal susceptibility tests were performed by the broth microdilution method in accordance with the Clinical and Laboratory Standards Institute (CLSI) document M38-A2 (4). The minimum inhibitory concentrations (MICs) and

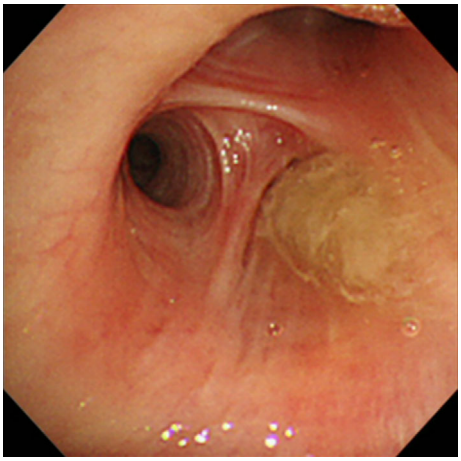

Figure 2. **Bronchoscopy revealed a yellow mucus plug in the lumen of B^2.**

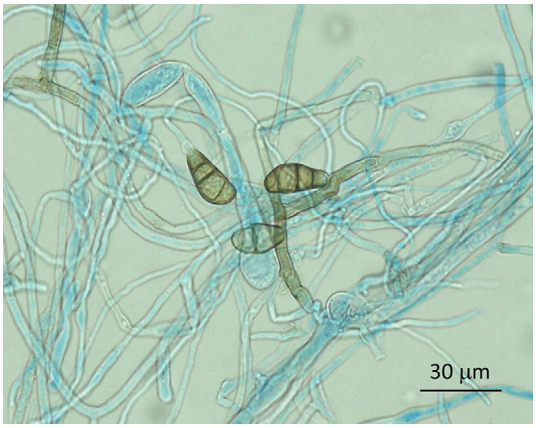

Figure 3. **Microscopic image of *Curvularia lunata* isolated from culture.**

minimum effective concentration (MEC) of different antifungal agents are presented in Table 2. The results revealed several anti-fungal agents to be ineffective against this strain, as expected. In addition, we were concerned about the side effects of long-term corticosteroid administration. However, since the symptoms became mild after admission, we decided to manage the patient by watchful waiting. Although we considered treatment with inhaled corticosteroids based on the FEV_1 findings, this treatment was not introduced because the FEV_1 improved to 3.85 L in the follow-up evaluation.

After 9 months without systemic corticosteroid or antifungal therapy, the patient exhibited an improvement in his symptoms, laboratory diagnostic features, and imaging findings and has remained asymptomatic without any worsening of the condition up to the present time.

Discussion

We herein report a case of ABPM caused by *C. lunata*, in which we identified two important clinical issues. First, the

Table 2. **Results of Antifungal Susceptibility Test for *Curvularia lunata*.**

Antifungal agent	MIC (μg/mL)
Micafungin	2*
Amphotericin	1
Flucytosine	>64
Fluconazole	>64
Itraconazole	>8
Voriconazole	>8
Miconazole	4

MIC: minimal inhibitory concentration
*Diagnosed according to minimum effective concentration (MEC).

causative fungus of ABPM in this case was not *A. fumigatus*, but *C. lunata*. Second, the clinical state of the patient improved without systemic corticosteroid or antifungal therapy. *C. lunata*, a saprobic dematiaceous mold, resides primarily in soil and is pathogenic to plants. Our patient was engaged in the landscape gardening business, where he could have easily been exposed to *C. lunata*. This organism causes endocarditis, brain abscess, skin infection, onychomycosis, keratitis, pneumonia, disseminated disease, mycetoma, allergic bronchopulmonary disease, and sinusitis (5). Chowdhary et al. reported *C. lunata* to be the causative pathogen in 8% of cases of ABPM excluding ABPA; however, cases of ABPM caused by *C. lunata* are rare in Japan (1, 6). Although *A. fumigatus* is the most common cause of ABPM, it should be considered that the causative fungi are not identified in some cases. The most commonly accepted criteria for the diagnosis of ABPA are those proposed by Rosenberg et al. (3). However, these primary criteria do not include the identification of fungi. Because our patient fulfilled six of the seven primary criteria for diagnosis of ABPA, we initially considered ABPA as the diagnosis. However, based on the results of fungal culture and genetic testing, we diagnosed ABPM due to *C. lunata*. Serum *Aspergillus*- and *Candida*-specific IgE levels were elevated, and the result of the serum *Aspergillus*-specific IgG test was negative. The result of the skin prick test with *Aspergillus* antigen was positive. Cur l 3 is, a major allergen of *C. lunata*, is cross-reactive among different fungi and grasses (7). The possibility that the serological findings for *Aspergillus* were positive because of cross reactivity with *Curvularia* seems unlikely, although the existence of significant allergenic cross-reactivity among proteins of *C. lunata*, *Alternaria alternata*, and *Epicoccum nigrum* has been reported (8, 9). Therefore, the patient was considered as having allergy to *Aspergillus* by chance. Although the patient exhibited an allergic reaction to *Aspergillus*, it did not appear to have caused ABPM, because *C. lunata*, and not *A. fumigatus*, was detected in fungal culture. Pathogen identification is very important for accurate diagnosis. Although systemic corticosteroid therapy is the mainstay treatment for ABPM, and the administration of appropriate antifungal

therapy might sometimes be necessary, our patient experienced a spontaneous regression of his symptoms. There are three previous case reports of ABPM due to *C. lunata*, all of which reported a morphological diagnosis. In one case, intracutaneous skin testing for *C. lunata* produced positive results, and enzyme-linked immunosorbent assay for antibody activity against *C. lunata* revealed elevated IgE and IgG levels. Treatment was administered by surgical resection in two cases and systemic corticosteroid therapy in one case. There were no instances of a spontaneous regression (10-12). Kamei et al. reported ABPM caused by *S. commune* as exhibiting spontaneous regression and mild alleviation of symptoms (13). Amitani et al. reported repeat bronchoscopy for bronchial toilet as being effective for removal of mucus plugs and symptom relief (14). In the present case, we only collected a part of the mucus plug for evaluation, which might not have been sufficient to elucidate the drainage effect. Based on the results of antifungal susceptibility testing, we expected several anti-fungal agents to be ineffective against the pathogen. It has been reported that ABPA can progress into invasive pulmonary aspergillosis (15). Sometimes corticosteroid therapy results in compromised immunity and fungal dissemination, as a result, we determined that anti-fungal therapy might not be effective in this case. On the other hand, inhaled corticosteroids are associated with fewer side effects, although they might be ineffective in controlling immunological activity in ABPA (16). Fortunately, the symptoms of the patient were not severe, and, therefore, we did not perform corticosteroid treatment. Because the symptoms had begun to resolve, and the FEV_1 had recovered to the normal level at the follow-up evaluation, we did not introduce inhaled corticosteroid treatment. Although systemic corticosteroid therapy is the mainstay treatment for ABPM, management by watchful waiting might be an alternative treatment based on patient background, clinical course of the disease, and laboratory findings. In conclusion, we encountered a case of ABPM possibly caused by *C. lunata*, where the clinical state of the patient improved based on a conservative follow-up without systemic corticosteroid or antifungal therapy.

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

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