Clinical Characteristics of Fifty Patients with Allergic Bronchopulmonary Aspergillosis

Min-Fang Zou[1,2], Yan Yang[3], Lin Liu[1], En-Hua Sun[4], Liang Dong[1]

[1]Department of Respiratory and Critical Care Medicine, Qilu Hospital of Shandong University, Jinan, Shandong 250012, China
[2]Department of General Practice, Qilu Hospital of Shandong University, Jinan, Shandong 250012, China
[3]Department of Otolaryngology, Qilu Hospital of Shandong University, Jinan, Shandong 250012, China
[4]Department of Bacterial Culture Clinical Laboratory, Qilu Hospital of Shandong University, Jinan, Shandong 250012, China

Min-Fang Zou and Yan Yang contributed equally to this work.

To the Editor: Allergic bronchopulmonary aspergillosis (ABPA) is an immunological pulmonary disorder caused by hypersensitivity to *Aspergillus fumigatus*. It occurs almost in patients with bronchial asthma or cystic fibrosis.[1] Its clinical characteristics include repeated attacks of wheezing, transient pulmonary opacity, and bronchiectasis. China is the largest populated country in the world, but studies on ABPA in China are limited. In this article, we described the features of ABPA and the causes of misdiagnosis through analyzing the clinical data of 50 patients.

These data were collected between January 2014 and November 2017 in Qilu Hospital, Shandong University, included the demographic characteristics, clinical manifestation, laboratory parameters, and imaging features. Diagnostic criteria were as follows:[2] (1) Predisposing conditions included asthma, chronic obstructive pulmonary diseases (COPD), and other conditions; (2) the essential criteria included (i) specific IgE against *A. fumigatus* antigens (sIgE) >0.35 kUA/L, and (ii) serum total IgE >1000 U/ml; (3) the other criteria, of which at least two of three were required, included (i) absolute eosinophil count (EOS) >0.5 × 10^9/L, (ii) radiographic pulmonary opacities consistent with ABPA, and (iii) positive specific IgG against *A. fumigatus* (sIgG). If the patient meets all other criteria, a serum total IgE <1000 U/ml could be diagnosed. SPSS software version 22.0 (SPSS Inc., Chicago, IL, USA) was used to analyze all the recorded data. Variables are expressed as the mean ± standard deviation. Abnormal distribution parameters are expressed as median (interquartile range). Classification variables are expressed in frequency (percentage).

There were 23 men and 27 women. The mean age was 48.0 ± 13.3 years, and body mass index was 22.3 ± 3.8 kg/m^2. Duration of symptoms was 4.5 (2.0–20.0) years. Predisposing conditions among 50 patients included 46 patients (92%) with asthma, 2 patients (4%) with COPD, 1 patient (2%) with allergic rhinitis, and 1 patient (2%) with bronchiectasis. The clinical presentation included coughing (96%), sputum (90%), wheezing (82%), chest tightness (46%), fever (30%), and weight loss (18%). Cough and sputum production were the two most common symptoms. *Aspergillus* skin test was performed in 28 patients, and all results were positive. The serum IgE was 2765 (1235–7030) U/ml. EOS was 1.04 (0.50–1.58) × 10^9/L and positive in 76%. sIgE was 10.54 (2–34.35) kUA/L and positive in 100%. sIgG was positive in 88%. Specific IgM (sIgM) was positive in 66%. Bronchiectasis was the most common finding in the high-resolution computed tomography (HRCT) (56%, Figure 1a), followed by transient pulmonary infiltrates (30%) and consolidation (14%, Figure 1b). In addition, mucoid impaction was 16%, including 4 cases of high-attenuation mucus (HAM) [Figure 1c], fibrosis (6%), gloved finger (2%, Figure 1a), and pneumothorax and pyothorax (2% of each). Spirometry was performed in 47 patients. Obstructive ventilatory defects were the most common abnormality, and these were found in 35 of 47 (75%). Mixed defects, restrictive patterns, and normal spirometry were observed in 11%, 4%, and 11% of cases, respectively. Bronchodilator reversibility was observed in all but five of the patients who had obstructive defects. The symptoms improved significantly in all patients after 2 months of treatment. After treatment, the IgE was 1965 (865.2–4200) U/ml and EOS was 0.20 (0.02–0.32) × 10^9/L. The levels of IgE and EOS were lower after treatment relative to baseline. There were some improvements in HRCT after 2 months of treatment [Figure 1d–1f].

ABPA with central bronchiectasis and HAM are important radiological findings associated with ABPA. These have gradually attracted the attention of doctors. ABPA is easily misdiagnosed when the patient has other atypical image features (transient pulmonary infiltrates, consolidation, or fibrosis). Before taking part in our study, some patients were misdiagnosed with bronchiectasis, pneumonia, tuberculosis, or cancer. Five patients had received antituberculous therapy, three patients had undergone

Address for correspondence: Dr. Liang Dong, Department of Respiratory and Critical Care Medicine, Qilu Hospital of Shandong University, Jinan, Shandong 250012, China
E-Mail: dl5506@126.com

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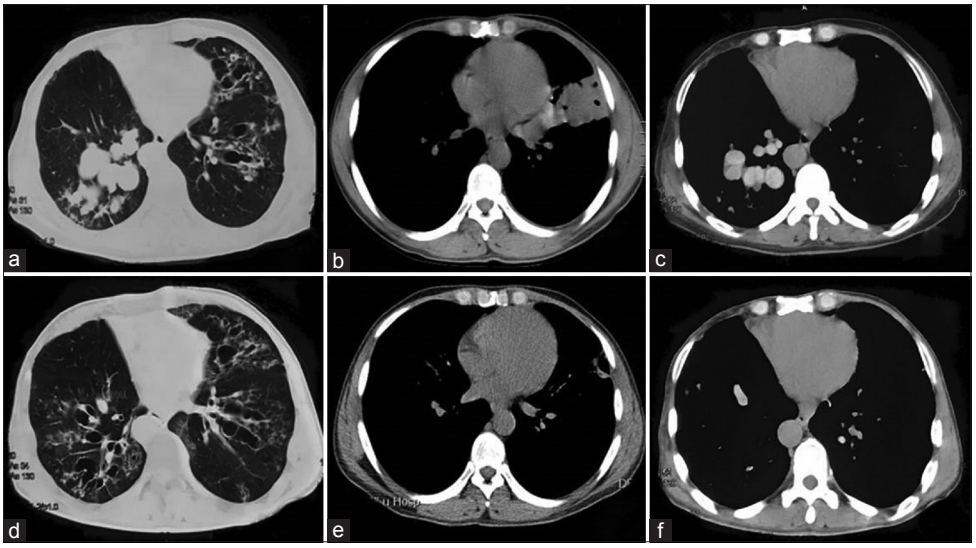

Figure 1: Prior treatment: (a) high-resolution computed tomography of the chest (lung window) showing left-sided bronchiectasis and a right-sided gloved finger. (b) Mediastinal window showing left upper lobe consolidation. (c) Mediastinal window showing high attenuation mucus. After treatment: the imaging showed the patients had improved significantly after 2 months of treatment (d-f). Consolidation and high attenuation mucus disappeared.

surgical treatment, and one patient had received chemotherapy. Most of them had sustained irreversible injury from these treatments. Hence, atypical presentation is one reason for misdiagnosis.

In our study, the strongest predisposing condition of ABPA was found to be asthma. One important cause of misdiagnosis is that clinicians usually do not pay this kind of attention to non-asthmatic patients. In the past, due to lack of clinical experience, clinicians have often diagnosed asthma-related ABPA. In recent years, the number of diagnosed cases of ABPA has gradually increased in our hospital through the increase in physician awareness and the widespread availability of immunological assays for ABPA.

The diagnostic criteria have been updated over the years.[3] However, there are still no consensus criteria. These criteria had a large number of limitations, including lack of unified cutoff value in immune indices.[2] In our study, 24% of patients had an EOS $<0.5 \times 10^9$/L and 20% of patients had a serum IgE <1000 U/ml. Another reason for misdiagnosis is that clinicians usually use increased EOS and serum IgE <1000 U/ml to rule out ABPA. Our findings may help clinicians adjust their concept of ABPA.

In our study, sIgG and sIgM were positive in 84% and 56% of the patients studied. The problem of whether some patients should be diagnosed with ABPA, with invasive pulmonary aspergillosis, or with chronic pulmonary aspergillosis remains troublesome because sIgG are not specific to ABPA and increased values may be other forms of aspergillosis.[4] Clinicians must study the overlap between the symptoms of pulmonary aspergillosis and these other conditions.

We conclude the prime reasons for misdiagnosis of ABPA are limited awareness of ABPA. There is a profound need for better training of physicians, especially pulmonary physicians, to recognize this disease. It is important to diagnose patients early to prevent long-term morbidity associated with the irreversible changes that occur with uncontrolled ABPA.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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