

Educational &
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Case Report



Allergic bronchopulmonary aspergillosis misdiagnosed as recurrent pneumonia

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Conflict of Interest

The authors have no financial conflicts of interest.

Author Contributions

Conceptualization: Li Xiang. Data curation: Nannan Jiang. Formal analysis: Nannan Jiang. Funding acquisition: Li Xiang. Methodology: Nannan Jiang. Project administration: Li Xiang. Visualization: Nannan Jiang. Writing - original draft: Nannan Jiang. Writing - review & editing: Li Xiang.

ABSTRACT

Allergic bronchopulmonary aspergillosis (ABPA) is a disease of the lungs resulting from a hypersensitivity reaction to *Aspergillus fumigatus*. The disease remains underdiagnosed and as many as 57% of patients are misdiagnosed as pulmonary tuberculosis, pneumonia, pulmonary abscess in China. Here we report the case of a 13-year-old girl with ABPA who presented with productive cough, wheezing, bronchiectasis and decline in lung function, total IgE was 25,180 KU/L, *Aspergillus*-specific IgE was 34.7 kUA/L. Chest high-resolution computed tomography (CT) showed infiltration, central bronchiectasis, and high-attenuation mucus in the left lower lobe and lingula. On bronchoscopy, a large amount of purulent material and brownish sputum plugs were seen. This case has been diagnosed as pneumonia 3 times before the ABPA diagnosis. For the treatment, corticosteroid (prednisone 0.5 mg/kg/day) plus itraconazole (200 mg, twice a day) were initiated. The girl responded well to the therapy. Two weeks later, she was free of symptoms. Lung function nearly improved to normal. One month later, peripheral eosinophil percentage and IgE decreased to 0.7% and 1,3451 KU/L (46% reduction), respectively. However, the trend of *A. fumigatus*-specific IgE persistently increased during treatment (from 34.7 KU/L to above 100 KU/L). Chest CT showed improvement in pulmonary infiltration. The present case emphasizes the importance of considering the diagnosis of ABPA in children with uncontrolled pneumonia, hypereosinophilia, and bronchiectasis with a previous history of asthma. Total serum IgE is a useful marker of disease activity and success of therapy while the serum *A. fumigatus*-specific IgE has limited utility in the follow-up of patients with ABPA.

Keywords: Allergic bronchopulmonary aspergillosis; Asthma; *Aspergillus fumigatus*

INTRODUCTION

Allergic bronchopulmonary aspergillosis (ABPA) is an allergic lung disease usually caused by *Aspergillus fumigatus* that complicates the course of patients with asthma and cystic fibrosis (CF). It presents with varied clinical and radiological manifestations usually with uncontrolled asthma, recurrent pulmonary infiltrates with or without bronchiectasis [1]. The disease remains underdiagnosed and as many as 57% of patients are misdiagnosed as pulmonary tuberculosis, pneumonia, pulmonary abscess in China [2]. The prevalence of ABPA is estimated

to be approximately 2.5% in adult patients with asthma [3] and 2%–15% in patients with CF [4]. In the pediatric population, ABPA has mostly been observed in CF [5], but only a few reports have documented the occurrence of ABPA in asthmatic children [6, 7]. Here we report the case of a 13-year-old girl with ABPA who presented with recurrent “pneumonia.”

CASE REPORT

A 13-year-old girl referred to our hospital with a 15 months history of productive cough and 4 months of intermittent wheezing in November 2015. Fifteen months ago, she complained of cough and occasionally cough up purulent sputum, then she was admitted to local hospital, her chest x-ray showed opacities, she was diagnosed pneumonia and treated with cephalosporin for 8 days and discharged after cough improving. However, she still suffered from intermittent cough after discharge, and symptoms were aggravated after exercise or cold. Eight months ago, her symptoms were exacerbated after cold, and purulent sputum occasionally contained brown particle, the routine blood test showed white blood cell (WBC) $7.59 \times 10^9/L$, N 55.3%, E 3.6%, CRP 0.5 mg/L, her chest x-ray showed multiple opacities in left lung, she was diagnosed mycoplasmal pneumonia and received treatment by azithromycin (3 courses), her symptoms had slight remission. Four months ago, she experienced wheezing, short of breath, and chest tightness when she traveled abroad, the symptoms relieved after oral glucocorticoid and in the following months she often felt short of breath especially after exercise and gradually exercise intolerance. One month ago, her symptoms got worse, she presented productive cough, wheezing and expectorated an amount of brown black sputum, and referred to local hospital, the routine blood test showed WBC $10.06 \times 10^9/L$, N 60.2%, L 23.3%, E 10.51%, CRP 6.9 mg/L, total IgE > 3,000 IU/mL, pulmonary function test showed mild obstructive ventilatory functional disturbance (forced expiratory volume in 1 second 67.3% predicted), bronchial dilation test(+), chest x-ray showed right upper lung opacities, she was still treated as pneumonia and received cephalosporin with no obvious improvement. Then she referred to our hospital, further investigation was done and the laboratory results were as follows: total IgE and serum IgE were both detected using ImmunoCAP system (Phadia, Uppsala, Sweden). total IgE was 25,180 KU/L (positive, >60 KU/L), *Aspergillus*-specific IgE was 34.7 kUA/L (positive, >0.35 kUA/L). The percentage of T-cell subsets (CD3+ T cell, CD4+T cell, CD8+T cell) and the serum level of IgA, IgG, IgM was relatively normal. Chest high-resolution computed tomography (CT) showed infiltration, bronchiectasis, and high-attenuation mucus in the right lower lobe (**Fig. 1**). On bronchoscopy a large amount of purulent material and brownish sputum plugs within the posterior and anterior segment of the right upper lobe, anterior basal segment of right lower lobe and lingual segment airways were seen (**Fig. 2A**). *Aspergillus fumigatus* were cultured from bronchoalveolar lavage (**Fig. 2B**). The inflammatory cells in the mucus plug were predominantly eosinophils with some histioid cells (**Fig. 2C**). She had a family history of atopic disease and her father suffered from allergic rhinitis.

The diagnosis of ABPA (stage I) was considered. Corticosteroid (prednisone 0.5 mg/kg/day) plus itraconazole (200 mg, twice a day) was initiated. The girl responded well to the therapy. Two weeks later, she was free of symptoms. Lung function nearly improved to normal. One month later, peripheral eosinophil percentage and IgE decreased to 0.7% and 13,451 KU/L (46% reduction), respectively (**Fig. 3**). However, the trend of *A. fumigatus*-specific IgE persistently increased during treatment (from 34.7 KU/L to above 100 KU/L). Chest CT showed improvement in pulmonary infiltration.

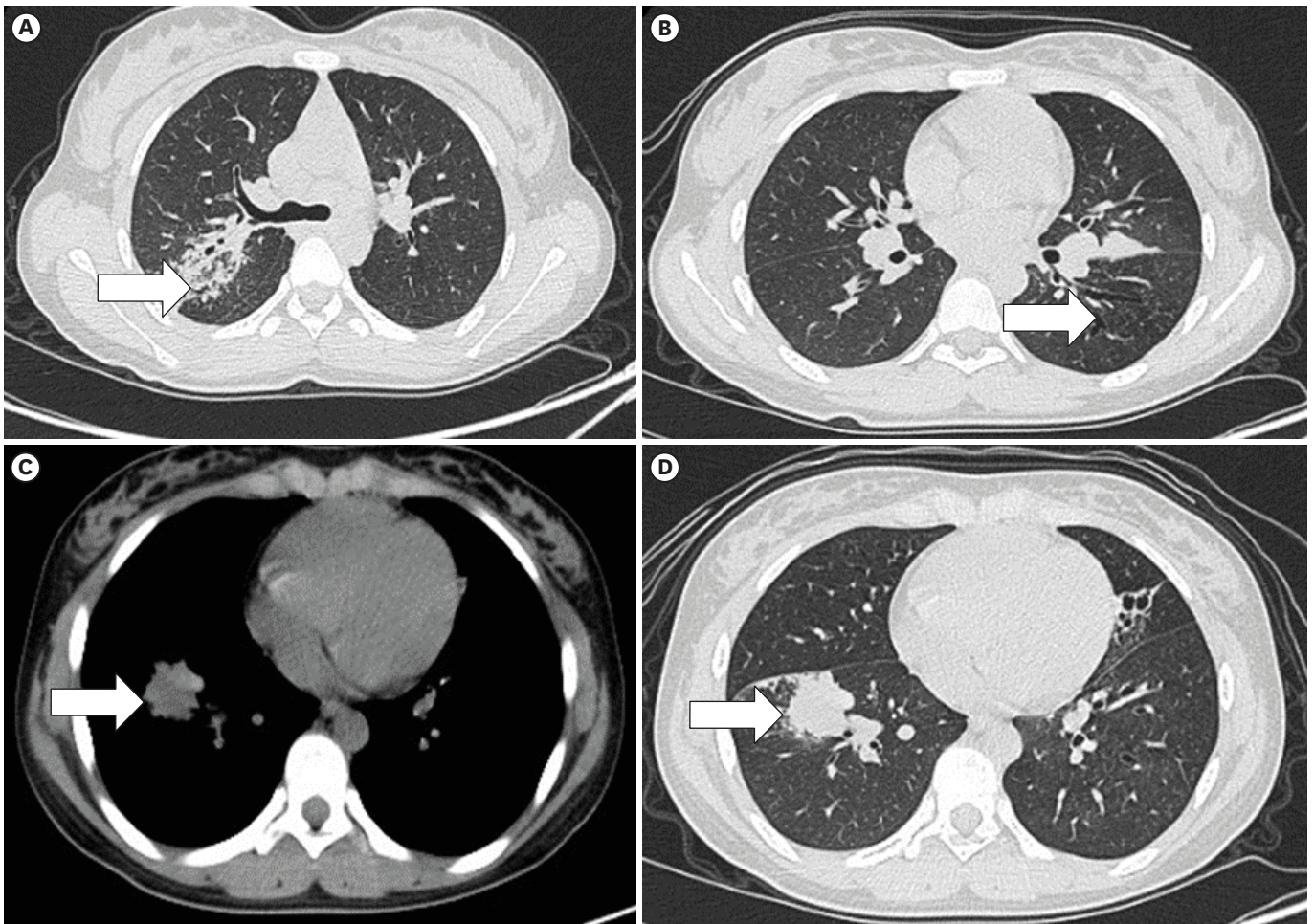


Fig. 1. High-resolution computed tomography chest showed infiltration (A), bronchiectasis (B), and high-attenuation mucus in the right lower lobe (C, mediastinal windows; D, lung windows) .

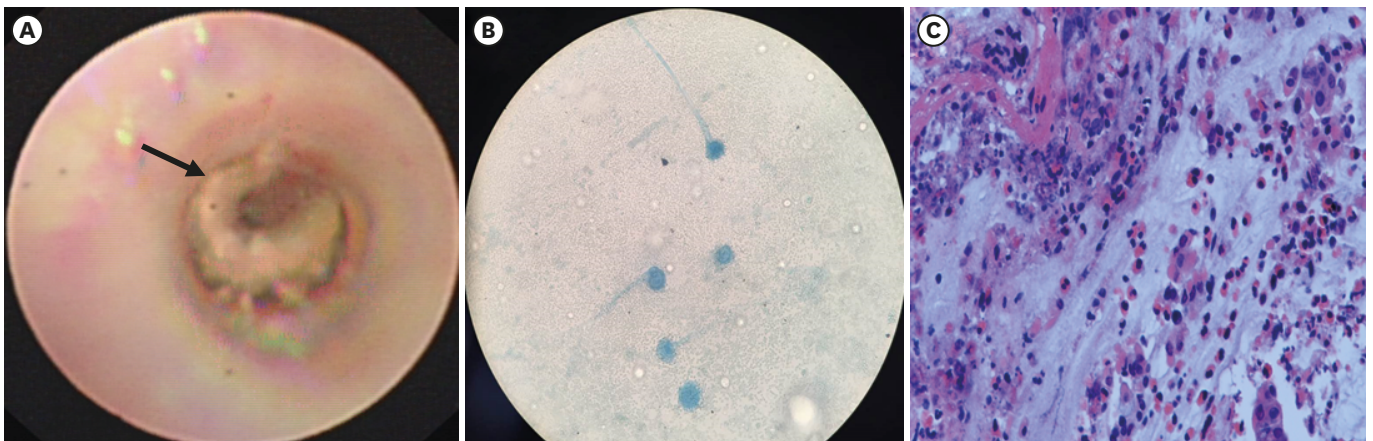


Fig. 2. Bronchoscopy showed mucus plugs (black arrow; A), and *Aspergillus fumigatus* cultured from bronchoalveolar lavage (B), the inflammatory cells in the mucus plug were predominantly eosinophils with some histioid cells (C; H&E, ×200).

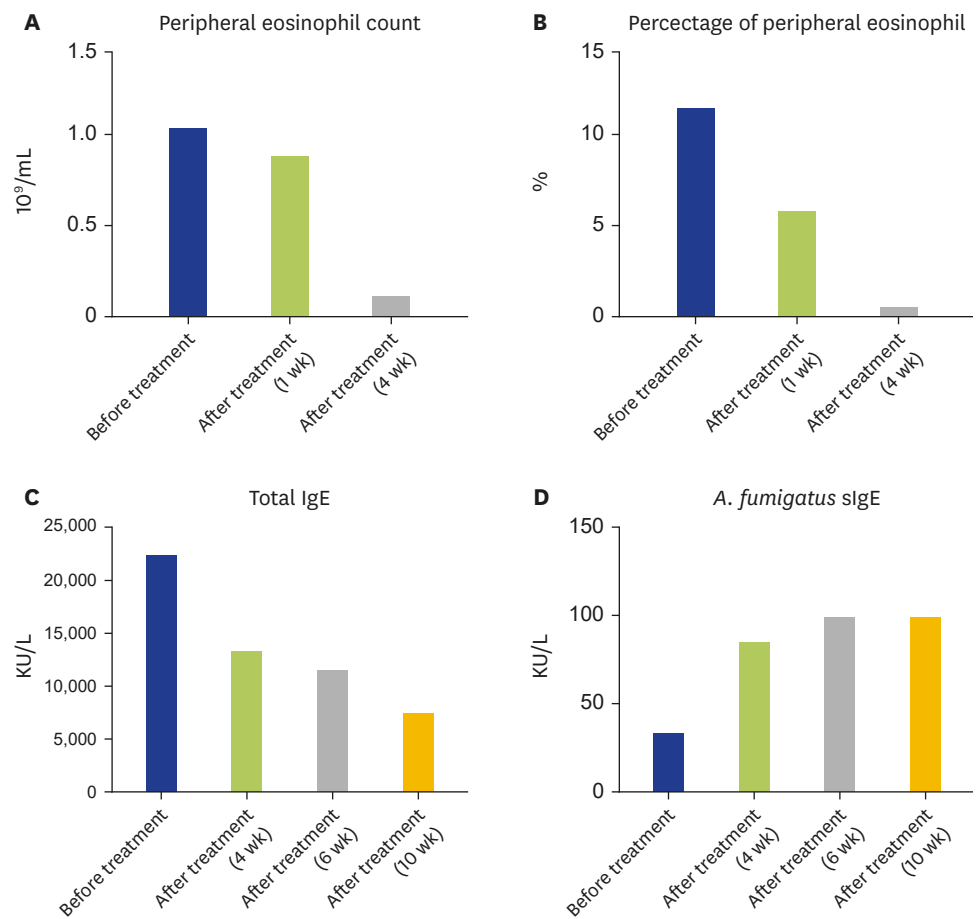


Fig. 3. (A) Peripheral eosinophil count before and after treatment 1 week and 4 weeks. (B) Percentage of peripheral eosinophil before and after treatment 1 week and 4 weeks. (C) Total IgE before and after treatment 4 weeks, 6 weeks, and 10 weeks. (D) *A. fumigatus*-specific IgE before and after treatment 4 weeks, 6 weeks, and 10 weeks. sIgE, specific IgE; *A. fumigatus*, *Aspergillus fumigatus*.

DISCUSSION

As our understanding of ABPA is improving, diagnostic criteria continue to evolve. Based on clinical, radiologic, and laboratory features, the first criteria were proposed in 1977 by Rosenberg et al. [8], which remains the most well acknowledged criteria. However, there was lack of consensus on the number of major and minor criteria required for the diagnosis. The International Society for Human & Animal Mycology (ISHAM) Working Group has proposed a more practical criteria in 2013 [9] and Agarwal et al. [10] proposed a revised version based on ISHAM criteria and new scoring system recently. Although the newly proposed criteria will ensure accurate diagnosis, ABPA can remain surprising silent, and this underscores the need for routinely screening the asthmatic patients for ABPA.

Due to the absence of preexisting asthma, this case has been diagnosed as pneumonia 3 times before the ABPA diagnosis. Differentiating ABPA from more common pulmonary disorders remains a challenge due to similarities in symptoms. Because both pneumonia and ABPA may cause pulmonary infiltrations on chest radiographs [11].

Corticosteroids remain the mainstay in the management of ABPA, by targeting the inflammatory response triggered by *A. fumigatus* [11]. Dosing of oral steroids for ABPA has not been well defined. A common treatment strategy is 2 weeks of daily prednisone 0.5 mg/kg, followed by 6 to 8 weeks of alternate day therapy and then tapering by 5–10 mg every 2 weeks. Antifungals play an important, yet adjunctive role in the management of ABPA, among the antifungals, used to treat ABPA, itraconazole is the most commonly recommended, and the dose is 200 mg twice daily for 4–6 months [12].

The criteria for response to therapy were clinical and/or radiological improvement with 25% decline in IgE levels [9]. The serum total IgE showed a significant decline in this patient, however, the trend of *A. fumigatus*-specific IgE increased after 10 weeks treatment. This discordance between total and specific IgE after treatment has recently demonstrated in a retrospective study of 81 ABPA patients, the *A. fumigatus*-specific IgE increased in 42 subjects (51.9%) after 8-week treatment. The authors suspected that the reason for this discrepancy was due to the fact that IgE against *A. fumigatus* is produced locally (such as the lung) while the production of total IgE in ABPA is in the peripheral immune system [13]. Thus, as the total IgE is a useful test for monitoring treatment response in ABPA while the serum *A. fumigatus*-specific IgE has limited utility in the follow-up of patients with ABPA [13]. However, it remains the most specific investigations in screening and diagnosis of ABPA. *A. fumigatus*-specific IgE of >0.35 kUA/L was found to have a sensitivity and specificity of 100% and 69.3%, respectively, in the diagnosis of ABPA [14].

The present case emphasizes the importance of considering the diagnosis of ABPA in children with uncontrolled pneumonia, hypereosinophilia, and bronchiectasis with a previous history of asthma. Early diagnosis and initiation of systemic corticosteroids are essential to prevent irreversible damage. Total serum IgE is a useful marker of disease activity and success of therapy while the serum *A. fumigatus*-specific IgE has limited utility in the follow-up of patients with ABPA.

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