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Severe asthma revealing an Allergic Bronchopulmonary Mycosis (ABPM)

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Abstract

ABPA/ABPM is an inflammatory disease caused by immune reactions triggered against *Aspergillus fumigatus* or other *Aspergillus* species that colonize the airways of patients, particularly those with asthma or cystic fibrosis. It is a rare, severe, and underdiagnosed condition. We report the clinical case of a 47-year-old female patient being followed for Fernand Widal syndrome, with repeated asthma exacerbations over the past two years and a history of bronchial cast expectoration. Three months ago, she developed progressive exertional dyspnea, associated with a dry cough and respiratory discomfort, which were resistant to maintenance therapy and required frequent courses of systemic corticosteroids. Pulmonary examination revealed bilateral, diffuse wheezing. Chest CT scan showed a proximal bronchiectatic focus in the right upper and middle lobes, with spontaneously hyperdense mucoid impaction and peribronchial thickening, forming a "gloved finger" appearance. Biological workup revealed peripheral blood eosinophilia. Total serum IgE levels were elevated at 688.8 IU/ml. Specific anti-*Aspergillus fumigatus* IgE levels were below 0.10 KUA/L. Recombinant *A. fumigatus* antigenic protein testing could not be performed due to the patient's financial constraints. Serum anti-A. fumigatus IgG levels were negative. According to the ASANO 2021 criteria, our patient meets 6 out of the 10 criteria, thus supporting the diagnosis of allergic bronchopulmonary mycosis (ABPM). The patient was treated with systemic corticosteroids combined with an adjuvant therapy, resulting in good clinical improvement.

Keywords: Aspergillosis; Mycosis; Bronchopulmonary; Allergic; ABPA; ABPM; Asthma; Bronchiectasis.

Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is an inflammatory airway disease characterized by a complex immunological reaction directed against *Aspergillus fumigatus*, a saprophytic fungus of the respiratory tract. In addition to *A. fumigatus*, other species of Aspergillus, such as *A. flavus, A. niger*, and other filamentous fungi like *Penicillium* and *Schizophyllum commune,* can cause similar conditions known as allergic bronchopulmonary mycoses (ABPM). These typically occur in the context of chronic airway diseases, most often asthma and cystic fibrosis, more rarely in chronic obstructive pulmonary disease (COPD), and exceptionally in healthy individuals [1]. We report the case of a 47-year-old female patient, followed for Fernand Widal syndrome, whose asthma, known since adolescence, had become severe and resistant to standard maintenance therapy, thereby revealing an ABPM.

Case presentation

Mrs. A.M, a 47-year-old woman with no toxic habits, followed for Fernand Widal syndrome consisting of asthma known since adolescence, treated with a maintenance therapy combining inhaled Formoterol and Budesonide (200 µg / 6 µg, 2 puffs twice daily), intolerance to NSAIDs, and nasal polyposis for which she underwent surgery 4 years ago. She had been experiencing recurrent asthma exacerbations for the past 2 years, with a history of expectorating a bronchial cast and a hospitalization one year ago for a severe exacerbation requiring intensive care, during which a chest CT scan was performed (Figure 1).

Three months prior to her hospitalization in the pulmonology department, she progressively developed exertional dyspnea, associated with a dry cough and respiratory discomfort, refractory to maintenance therapy, requiring frequent courses of systemic corticosteroids. These symptoms evolved without fever and with preserved general condition. Upon further history-taking, the patient reported that she had moved 4 years ago because she had been exposed to mold in her previous residence.

On clinical examination, the patient was stable hemodynamically and respiratorily, with an oxygen saturation of 98% in ambient air. She was eupneic at 16 breaths per minute, normocardic at 78 beats per minute, and afebrile at 36.8°C, with a performance status of 1. The pleuropulmonary examination revealed bilateral, diffuse wheezing. Nasofibroscopy was unremarkable.

The chest X-ray showed a right bronchial syndrome with thoracic hyperinflation (Figure 2). The chest CT scan revealed a proximal bronchiectasis in the right upper and middle lobes, with mucoid impaction that was spontaneously hyperdense, associated with peribronchial thickening, producing the characteristic "gloved finger" appearance (Figure 3).

Biological workup showed leukocytosis with neutrophilia (WBC = 16590/µL and neutrophils = 13790/µL) associated with blood eosinophilia (eosinophils = 830/µL), while C-reactive protein (CRP) was negative. The total serum IgE level was elevated at 688.8 IU/mL. Specific anti-Aspergillus fumigatus IgE was below 0.10 KUA/L. Testing for recombinant antigenic proteins of A. fumigatus could not be performed due to financial constraints. Anti-A. fumigatus IgG was negative. According to the ASANO 2021 criteria, our patient fulfilled 6 out of the 10 criteria, thus establishing the diagnosis of allergic bronchopulmonary mycosis (ABPM) (Table 1). The patient was treated with systemic corticosteroids: Prednisolone 0.5 mg/kg/day, equivalent to 40 mg/day for 2 weeks, then tapered by 5 mg per week over 6 weeks, combined with adjuvant therapy consisting of calcium, vitamin D, and potassium supplementation, as well as dietary counseling. She also received influenza, pneumococcal, and SARS-CoV-2 vaccinations. The clinical outcome was favorable.

Table 1: Modified 2020 ISHAM diagnostic criteria for ABPA.

Modified 2020 ISHAM
Predisposing condition (mandatory)
Asthma, cystic fibrosis, COPD
Major criteria (all must be present)
1. Specific IgE > 0.35 kUA/L or positive immediate skin test to A. fumigatus
2. Total IgE ≥ 500 kUI/L
Minor criteria (at least 2 must be present)
1. Positive A. fumigatus precipitins or IgG > 27 mgA/L
2. Bronchiectasis on chest CT scan
3. Blood eosinophilia > 0.5 G/L

Table 2: ASANO 2021 diagnostic criteria for ABPM met by our patient (marked in red).

ASANO 2021	
Criteria (at least 6 must be present)	
1	Asthma or history of asthma
2	Blood eosinophilia > 0.5 G/L
3	Total IgE ≥ 417 kUI/L
4	Positive immediate skin test or specific IgE ≥ 0.35 kUA/L for a filamentous mold
5	Precipitins or specific IgG against a filamentous mold
6	Positive culture from mycological examination of sputum or bronchial lavage
7	Presence of fungal hyphae in bronchial casts
8	Central bronchiectasis on CT scan
9	Presence or history of bronchial casts in the proximal bronchi seen on CT scan or bronchial endoscopy, and/or expectoration of bronchial casts
10	Hyperdense mucus within the bronchial lumen on CT scan

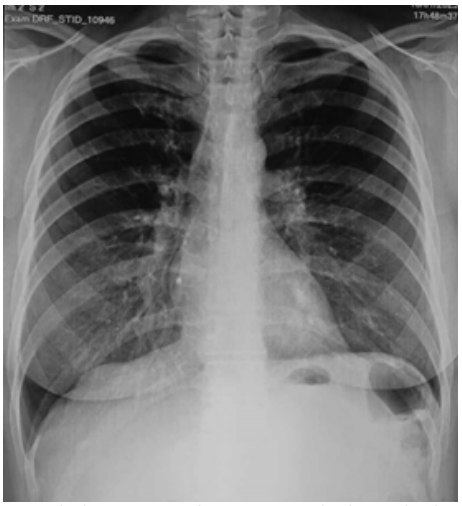

Figure 2: Frontal chest X-ray showing a right bronchial syndrome associated with thoracic hyperinflation.

Discussion

ABPA/ABPM is an inflammatory disease caused by immune reactions triggered against Aspergillus fumigatus or other Aspergillus species that colonize the airways of patients, particularly those with asthma or cystic fibrosis [1,2], as was the case with our patient, who suffered from asthma. Several factors promote the onset of the disease: genetic predisposition, mucus abnormalities, biochemical properties of Aspergillus antigens, as well as the extent of bronchial and tissue destruction. These factors are interdependent, and their relative importance varies among patient populations [3]. The clinical presentation resembles that of poorly controlled, corticosteroid-dependent asthma, although the disease can also affect 19% of well-controlled asthmatics. A history or presence of mucus plugs or

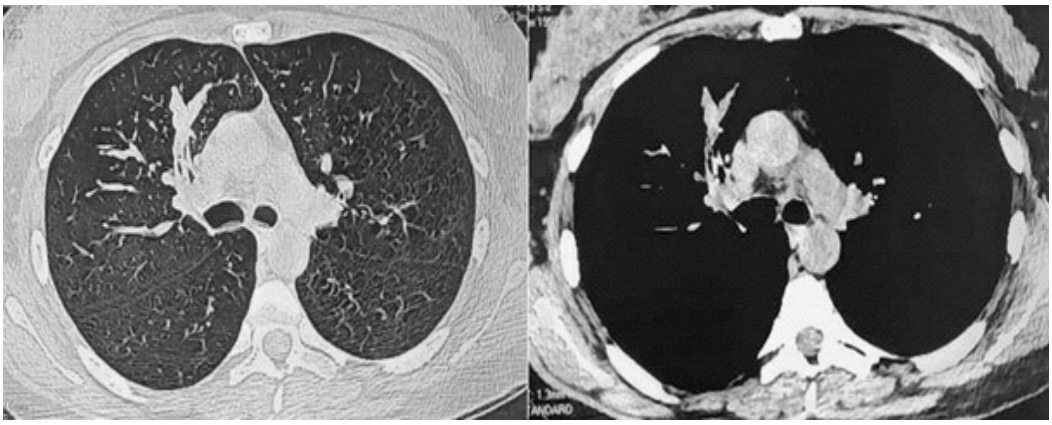

Figure 1: Chest CT scan performed one year ago during the patient's admission to the intensive care unit for a severe asthma exacerbation, showing proximal bronchiectasis of the right upper lobe with a "gloved finger" appearance.

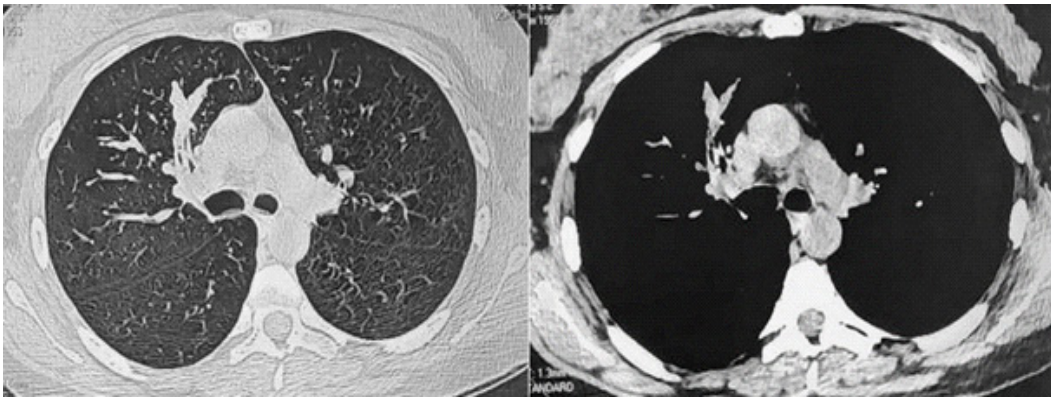

Figure 3: Chest CT scan on admission showing proximal bronchiectasis of the right upper lobe with a "gloved finger" appearance.

bronchial casts remains a highly suggestive sign [1]. The most frequent radiological manifestations are transient and fleeting pulmonary opacities, as well as bronchiectasis [4].

In our patient, the diagnosis was suspected in the presence of poorly controlled asthma, a history of expectoration of a bronchial cast, and proximal bronchiectasis with spontaneously dense mucoid impactions on chest CT scan.

The positive diagnosis of the disease is based on numerous clinical, biological, and radiological criteria, initially described in 1977 by Rosenberg and Patterson. These criteria have since been modified and simplified: the modified ISHAM 2020 criteria (Table 1) [5]. It is estimated that there are about five million cases of ABPA worldwide, with a prevalence of 3 to 13% among asthmatic patients [6]. However, pulmonology/allergology specialists have observed that a significant proportion of clinical ABPA cases are underdiagnosed because they do not meet the strict diagnostic criteria [2,3]. The diagnosis of ABPM not caused by Aspergillus is even more difficult, as traditional criteria are specific to ABPA caused by *A. fumigatus*, and no standardized diagnostic criteria currently exist for ABPM. Laboratory tests for specific IgE/IgG may not be positive for the fungi responsible for ABPM, and its clinical features are often atypical [2].

In 2021, K. Asano proposed new diagnostic criteria for ABPM, using as a gold standard the presence of fungal hyphae in eosinophilic bronchial casts, and tested them in various conditions close to ABPM (such as chronic eosinophilic pneumonia, severe asthma with fungal sensitization, and chronic pulmonary aspergillosis). This study confirmed the good sensitivity of the ISHAM criteria (77.2%) and demonstrated very good sensitivity (89.9%) and specificity (96%) for the presence of 6 out of 10 "Asano" criteria [2]. In applying the ASANO 2021 criteria, our patient met 6 out of 10 criteria, further supporting the diagnosis (Table 2) [5].

The advantage of these criteria, beyond their diagnostic performance, is that they are applicable to other molds besides A. fumigatus and propose a category of probable diagnosis when 5 criteria are present, increasing sensitivity to 96.2% [2,5].

The treatment of ABPA/ABPM is primarily based on oral corticosteroids, which help reduce bronchopulmonary inflammation. The addition of antifungal therapy is indicated as a second-line option in corticosteroid-dependent asthmatic patients and in cases of recurrent exacerbations, notably to reduce the long-term side effects of corticosteroid treatment. The first-line recommended antifungal is Itraconazole [7].

Treatment with Omalizumab has been shown in several case series to improve respiratory function, reduce exacerbation rates, and allow corticosteroid-sparing effects. However, to date, no formal recommendations can be issued [8-10].

The prognosis of ABPA/ABPM depends on the number of exacerbations, treatment dependence (whether corticosteroids or antifungals), and the occurrence of complications such as bronchiectasis, atelectasis, decreased respiratory function, as well as the development of fibrosis and long-term chronic respiratory failure. It also depends on complications related to corticosteroid and/or antifungal treatments, which require close monitoring throughout patient management [5].

Conclusion

ABPA/ABPM remains a rare and underdiagnosed disease that progresses through episodes of exacerbations, which can lead to corticosteroid dependence. It should be considered in any asthmatic patient with poor disease control despite well-conducted maintenance therapy, in order to prevent numerous complications, most of which are irreversible, such as bronchiectasis, fibrosis, and respiratory failure. The new 2021 diagnostic criteria proposed by Asano have made it possible to extend the application of the diagnosis to molds other than A. fumigatus and to introduce a new diagnostic category.

Conflict of interest : The authors declare that they have no conflicts of interest.

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