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Uncontrolled Asthma Associated with Allergic Bronchopulmonary Aspergillosis: A Case Report

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Abstract

Allergic Bronchopulmonary Aspergillosis (ABPA) is an underdiagnosed disease, leading to delayed treatment and major complications such as pulmonary fibrosis, exacerbated bronchiectasis, and severe persistent asthma with loss of lung function.

We present the case of a 45-year-old woman, with a history of uncontrolled bronchial asthma, who was admitted to hospital with the initial diagnosis of infected bronchiectasis, which in hospitalization showed persistent bronchospasm associated with eosinophilia, elevated IgE, positive galactomannan antigen (*Aspergillus*). In TACAR there was evidence of bronchiectasis of bilateral central location. The patient was treated with corticosteroids and antifungal agents, showing clinical improvement in his outpatient controls.

Serological detection tests for *Aspergillus fumigatus*, together with TACAR, are important in asthmatic patients, particularly in uncontrolled patients, since a timely diagnosis and treatment will improve the prognosis and quality of life of these patients.

Keywords: Asthma; Allergic bronchopulmonary aspergillosis; Aspergillosis

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Introduction

Allergic Bronchopulmonary Aspergillosis (ABPA) is an inflammatory lung disease caused by infection with *Aspergillus fumigatus*, giving a type 1 hypersensitivity response [1]. Its worldwide prevalence is unknown, however, there are epidemiological reports that consider that *Aspergillus fumigatus* colonizes the respiratory tree of 25% of asthmatics; however, only 2% of patients go on to develop ABPA. Currently, worldwide, the global burden of ABPA exceeds 4.8 million, being an underdiagnosed entity that affects the quality of life of patients [2,3].

Although the disease is acquired by inhaling the microscopic spores of *Aspergillus*, most people do not contract it, and there is a higher risk of infection in patients with any immunosuppressive condition or presence of pulmonary disease [4].

For its diagnosis, predisposing factors such as a history of asthma or fibrosis should be taken into account, in addition to laboratory tests, such as a positive *Aspergillus* test, high IgE levels and eosinophil counts. It should be clarified that in most patients with uncontrolled asthma, despite receiving adequate standard treatment, it is recommended that ABPA be suspected [5].

We present the case of a 45-year-old female patient with a history of uncontrolled bronchial asthma, who was admitted to hospital with the initial diagnosis of infected bronchiectasis, laboratory revealed increased IgE, eosinophilia and positive galactomannan antigen, confirming the diagnosis to ABPA.

Case Presentation

Female patient, 45 years old, from Lima-Peru, with family history of bronchial asthma. Allergic to penicillins. With medical history of bronchial asthma 5 years ago, whose usual treatment consists of fluticasone-salmeterol 250/50 µg (2 inhalations every 12 h) and salbutamol on demand, adherent to treatment; with history of asthmatic crises of mild to moderate intensity several times a year in the last 3 years despite regular treatment. No history of previous hospitalizations. She was admitted to the emergency department of Hospital Dos de Mayo on January 21st, 2020 due to 5 days of illness

characterized by increased respiratory frequency and consistency of expectoration, with mucopurulent features, associated with progressive dyspnea. On the day of admission, she presented a fever of 38°C associated with dyspnea on moderate exertion, which was the reason why she went to the emergency department.

At the time of evaluation, the patient presented tachycardia 140 bpm, tachypnea 24 rpm, oxygen saturation 92% (FiO_2 21%), body temperature 38.5°C and blood pressure 110/80 mmHg. On preferential physical examination there were diffuse wheezing in both lung fields and fine crackles in lung bases. The rest of the evaluation was unaltered. Subsequently the patient was referred to the hospitalization area of the Pneumology service.

Among the laboratory findings on the first day of admission to that service, the hemogram showed mild anemia (Hb: 10.5 g/dL), leukocytosis (leukocytes: 19670 mm^3 and abastonates: 393.4 mm^3) with mild eosinophilia (750 mm^3) and a value of C-reactive protein of 185 mg/dL. The electrolytes, urine and sputum GenXpert tests showed no other alterations.

Pulmonary CT (HRCT) showed pulmonary parenchyma with multiple bronchiectasis of cylindrical and varicose appearance of bilateral central location (Figure 1).

The patient received antibiotic therapy with ceftazidime 2 gr/24 h for 14 days, prior sputum culture which was positive for *Pseudomonas aeruginosa*, in addition to inhaler therapy (salbutamol 2 PUFF/6 h and Ipatropium bromide 2 PUFF/6 h). On the fifth day of treatment there is evidence of persistent bronchospasm, the results of the control laboratory tests show a slight leukocytosis (10,140 mm^3 - abastonates: 0 mm^3) with a slight eosinophilia (750 mm^3) and a decrease in c-reactive protein (58.7 mg/dl).

Due to the persistence of bronchospasm, eosinophilia and the distribution of bronchiectasis in the pulmonary HRCT, it was decided to expand the laboratories, obtaining a value of immunoglobulin E greater than 2500 IU/ml and a positive result of galactomannan antigen (*Aspergillus*).

With these results a diagnosis of Allergic Bronchopulmonary Aspergillosis (ABPA) was made and she was discharged with Itraconazole 200 mg c/12 h and prednisone 20 mg c/24 h.

The patient continues to attend her check-ups at the hospital, with clinical improvement and absence of bronchospasm episodes.

Discussion

ABPA is an inflammatory lung disease produced by an infection of the *Aspergillus* fungus, as a response to the antigens of this infection, with immune responses mediated by antibodies (IgE and IgG) and by cells, release of cytokines and interleukins, among others. These responses, combined with the toxic effects of the fungus, cause airway damage such as epithelial rupture and activation of immune responses, which can lead to bronchiectasis and fibrosis [1,6].

The International Society for Human and Animal Mycology (ISHAM) has proposed diagnostic criteria, grouping them into 3 blocks: Predisposing conditions, mandatory criteria and other criteria. For diagnosis, one of the predisposing conditions must be present: Asthma or cystic fibrosis; both mandatory criteria: Positive *Aspergillus* skin test with elevated serum IgE levels >1000 IU/mL; and at least 2 of 3 of the other criteria: Total eosinophil count >500 cells/µL, presence of IgG antibodies to *Aspergillus fumigatus* or chest

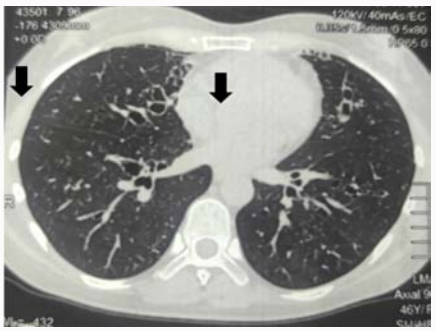

Figure 1: This is a Computed Tomography (CT) scan of the thorax showing centrally located cystic bronchiectasis.

radiograph consistent with ABPA [7]. In the present case, the patient reported a history of asthma and at the laboratory level presented IgE concentrations greater than 2500 IU/mL, eosinophilia and a positive galactomannan test, which corroborated the diagnosis of ABPA.

With the development of ABPA, there is a poor control of asthma, so they may worsen and manifest with cough or increased expectoration, considering that some patients may have brownish black expectoration, secondary to the accumulation of degenerated eosinophils, desquamated epithelial cells and mucin [1,6,8]. They may also present hemoptysis, fever or febrile fever, weight loss, general malaise, wheezing and bronchial hyperresponsiveness [9].

At the imaging level, chest radiography usually shows the presence of fugitive opacities as indicative of ABPA, and is useful in follow-up, avoiding the need for repeated CT scans. For patients with ABPA, High-Resolution Computed Tomography (HRCT) of the chest is the most sensitive test, as it allows better evaluation of the distribution of bronchiectasis and other findings that are not apparent on radiography. Bronchiectasis and mucoid impaction are the classic ABPA findings on CT [5,10]. In this patient, bronchiectasis was evidenced in the middle lobe and lingula, which, in the context of a patient with a history of asthma, increases the clinical suspicion of ABPA.

Regarding treatment, itraconazole and voriconazole are used in the treatment of ABPA and only for patients who cannot taper oral corticosteroid or have an exacerbation of ABPA. The use of other drugs such as Omalizumab, itraconazole and voriconazole are still being investigated10. In this case the patient was prescribed Itraconazole and Prednisone.

In conclusion, we report a case of ABPA with a clinical presentation of uncontrolled asthma. It is recommended that serological screening tests for *Aspergillus fumigatus* be routinely performed, together with high-resolution chest CT, in asthmatic patients, particularly in those with uncontrolled and/or difficult to treat asthma, since a timely diagnosis and treatment will improve the prognosis and quality of life of these patients.

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