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# Allergic bronchopulmonary aspergillosis complicating Swyer-James-Macleod's syndrome: case report and review of literature

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**Key words**

*abpa; abpm; allergic bronchopulmonary mycosis; asthma; cystic fibrosis; Aspergillus*

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***Summary***

*Allergic bronchopulmonary aspergillosis (ABPA) is a pulmonary disorder that results from immune responses mounted against antigens of* Aspergillus fumigatus*, resulting in non-specific respiratory symptoms and structural lung damage. Classically defined in individuals suffering from bronchial asthma and cystic fibrosis, ABPA has recently been described in other lung diseases including COPD, pulmonary tuberculosis, idiopathic bronchiectasis and others. Herein, we report the first case of ABPA complicating Swyer-James-Macleod's syndrome that was successfully treated with oral antifungal therapy.*

## Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a complex immunologic pulmonary disorder caused by hypersensitivity responses targeted against *Aspergillus fumigatus* colonizing the tracheobronchial tree. It clinically manifests with non-specific symptoms such as low grade fever, wheezing, hemoptysis, productive cough and others (1). The estimated global burden of ABPA is about 4.8 million cases (2), with about 1.38 million cases in India alone (3). The diagnosis of ABPA is based on a combination of clinical, radiological and immunological findings (4). Allergic aspergillosis usually complicates the course of airway disorders like bronchial asthma and cystic fibrosis. Recently, ABPA has also been described in other structural lungs disorders like COPD, post tubercular fibrocavitary disease and others (5-8). Herein, we describe a case of ABPA in a patient with Macleod's syndrome. We also systematically review the literature on this association.

## Case report

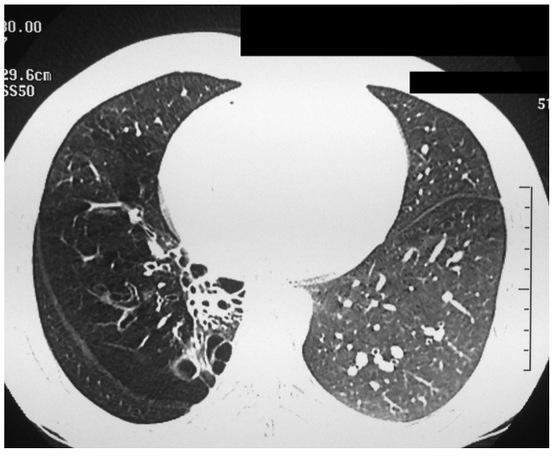
A 21-year old male presented with history of dry cough, breathlessness and wheezing of three months duration. The symptoms were worse during nighttime and were relieved with inhaled salbutamol. The patient denied any history of hemoptysis, chest pain, fever, weight loss, inhalation of foreign body and recurrent childhood infections. Auscultation of the chest revealed bilateral polyphonic wheeze. A provisional diagnosis of bronchial asthma was made. Subsequently the patient was investigated for ABPA. Complete blood count revealed peripheral eosinophilia with elevated serum IgE levels, both total and *A. fumigatus* specific (**table 1**). Spirometry revealed an obstructive pattern without bronchodilator reversibility. Work up for parasitic infestation was negative (normal stool examination and absent filarial antigen in serum). High resolution computed tomography (HRCT) of the thorax revealed bronchiectasis in the right lower

***Table 1*** *- Baseline and follow up investigations.*

| Parameter | Baseline | 8 weeks | 6 months | 9 months |
|---|---|---|---|---|
| Hemoglobin, gm/dL | 12.3 | 14 | 14.6 | |
| Total leukocyte count, cells/µL | 9500 | 8800 | 8000 | |
| Absolute eosinophil count, cells/µL | 2090 | 670 | 560 | |
| Serum filarial antigen | Negative | | | |
| Serum total IgE, IU/mL | 12712 | 8668 | 3628 | 2930 |
| Specific IgE against *A. fumigatus*, kUA/L | 0.62 | 0.61 | 0.5 | |
| Serum precipitins against *A. fumigatus* | Negative | | | |
| Skin test against *A. fumigatus* | Negative | | | |
| FVC (L) | 3.89 | 4.16 | 3.9 | |
| FEV1 (L) | 2.61 | 2.71 | 2.74 | |
| FEV1/FVC ratio | 67.1 | 65.1 | 70.3 | |

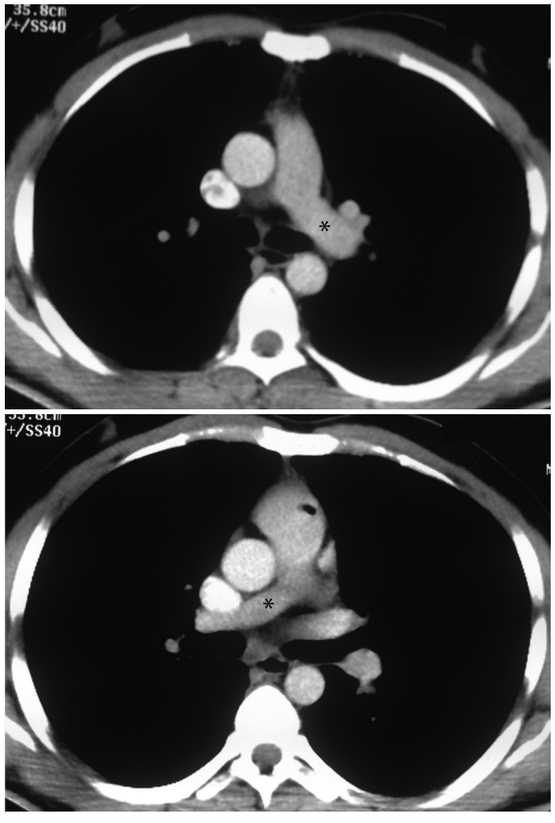
lobe along with mosaic attenuation of right middle lobe bronchus, with small right pulmonary artery suggestive of Macleod's syndrome (**figure 1** and **2**). The size of the pulmonary artery was confirmed on a contrast-enhanced CT scan. A diagnosis of ABPA was made based on fulfillment of both the obligatory criteria (elevated total and aspergillus specific IgE) and two of the three minor criteria (elevated eosinophil count and bronchiectasis) (4).

***Figure 1*** *- High resolution computed tomography (HRCT) of thorax revealing bronchiectasis of right lower lobe with mosaic attenuation.*



Patient was started on oral itraconazole 400 mg/day for the treatment of ABPA. For asthma, he was treated with inhaled

***Figure 2*** *- Contrast enhanced CT of thorax showing small right pulmonary artery as compared to left pulmonary artery. *Right and left pulmonary artery.*



long-acting beta-2 agonist and corticosteroid combination inhaler (formoterol 24 µg/day and fluticasone 500 µg/day) in a single inhaler, both for maintenance and reliever therapy. There was considerable improvement in the patient's symptoms and serum IgE done after six months showed a declining trend. He continues to do well on follow up with significant improvement in his symptoms, lung function and decline in IgE levels.

## Discussion

Allergic bronchopulmonary aspergillosis is a well-described clinical disorder complicating the course of patients with asthma and cystic fibrosis. In normal individuals, inhaled spores of *A. fumigatus* germinate in the airways and activate the Th1 CD4+ responses that clears the fungi, and prevents further infection. On the other hand, in predisposed individuals with structural lung abnormality (asthma and cystic fibrosis), persistence of fungal hyphae along with release of certain proteins (proteases) activates the immune mechanisms with subsequent recruitment of CD4+ Th2 helper cells to the airways. This skewed Th2 cell response causes propagation of inflammation and leads to influx of neutrophils, eosinophils along with excess production of elevated IgE (total and *A. fumigatus* specific). The diagnostic criteria for ABPA has recently been updated. The presence of two obligatory (elevated *A. fumigatus* specific IgE levels and elevated total serum IgE level) and two of the three other criteria (presence of precipitating antibodies against *A. fumigatus* in serum, radiographic pulmonary opacities consistent with ABPA and total eosinophil count > 500 cells/µL) in an asthmatic patient makes a firm diagnosis of ABPA (4).

A search of the PubMed and EmBase databases using the following search terms: ("Macleod's syndrome" OR "Macleods syndrome" OR "Macleod syndrome" OR "Swyer-James syndrome" OR "Swyer James syndrome") AND ("abpa" OR "allergic bronchopulmonary aspergillosis" OR "abpm" OR "allergic bronchopulmonary mycosis" OR "aspergillosis") did not yield any citation on the association of Macleod's syndrome with ABPA, making the index case the first report on this association. Swyer-James-Macleod syndrome (SJMS) is a rare clinical entity (9,10), and is considered a pulmonary injury, secondary to viral lower respiratory tract infections, inflicted during lung development (less than eight years) (11,12). Morphologically, there is bronchiolar destruction and obliteration, with air trapping and hypoperfusion of the involved segment or lobe or the entire lung. If reduction of pulmonary blood flow occurs during the developing period of the lung, then there can be hypoplasia of the pulmonary artery of the affected side. Bronchiectasis is an invariable finding and is usually the result of recurrent infections of the involved area (9,10). Patients with SJMS present with variable symptoms such as cough, dyspnea, hemoptysis, recurrent pulmonary infections and others. Occasionally, patients may be asymptomatic for several years and present only during adulthood (13). The index case denied any history of childhood or recurrent lower respiratory tract infections and was asymptomatic till the current presentation. The diagnosis of SJMS is clinical and is confirmed by radionuclide ventilation perfusion scintigraphy and pulmonary angiography (CT) (13). On chest radiograph, it manifests as unilateral hyperlucency, while on HRCT thorax, there is evidence of air trapping with mosaic perfusion in the involved segment, lobe or the entire lung. The lung volumes on HRCT thorax are normal or reduced on the affected side (14). Pulmonary angiogram reveals a hypoplastic pulmonary artery on the involved side with normal bronchial circulation (15,16). With the advent of CECT thorax, the need for invasive investigations has become less important. The index case had typical radiologic findings with air trapping and a hypoplastic right pulmonary artery. The lung function tests usually reveals restrictive pattern, although there may be obstructive pattern in the presence of bronchiectasis, as seen in the index case (11).

Apart from asthma and cystic fibrosis, ABPA has been also described in other conditions including chronic obstructive pulmonary disease (17), Kartagener's syndrome (8), fibrocavitary disease following pulmonary tuberculosis (7,18), idiopathic bronchiectasis (19), and others. The index case fulfilled the criteria for ABPA, both obligatory criteria (elevated *A. fumigatus* specific and total serum IgE levels) and two other criteria (elevated eosinophil count and bronchiectasis). It is likely that some patients with other pulmonary disorders due to structural abnormality (scarring and loss of cilia) are predisposed to develop *Aspergillus* colonization and subsequently ABPA. Although there is no previous report of ABPA in SJMS, a case of semi-invasive aspergillosis has been previously described in an immunocompetent adult male, indicating that SJMS may predispose an individual to colonization with *Aspergillus* and its complications (20). The response to oral itraconazole with a documented fall in serum IgE levels, significant improvement in clinical symptoms and stabilization of lung function further supports the diagnosis of ABPA in the index case. Also, due to the rarity of SJMS, such an association may have been previously overlooked.

In conclusion, the understanding of ABPA is still evolving with an ever-growing list of conditions (asthma, cystic fibrosis, COPD, pulmonary tuberculosis, Kartagener's syndrome and others) that predispose individuals to develop this disease. The possibility of ABPA should be kept in those with SJMS as treatment of ABPA prevents progression of further lung damage, thereby improving clinical outcomes.

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