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Middle lobe syndrome: a rare presentation of allergic bronchopulmonary aspergillosis

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Key words

Allergic bronchopulmonary aspergillosis; Aspergillus*; bronchial asthma; central bronchiectasis; middle lobe syndrome*

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Summary

Allergic bronchopulmonary aspergillosis (ABPA) is a disease predominantly seen in susceptible asthmatic subjects, due to a hypersensitivity phenomenon caused by colonisation of the airways by Aspergillus *species. Although collapse, both lobar and segmental due to mucoid impaction, is not uncommon in ABPA, a middle lobe syndrome (MLS) secondary to ABPA is rather an uncommon association. We report this rare and unusual clinical presentation in a 36-year-old male, who presented for evaluation of a "non resolving pneumonia". Imaging suggested the presence of a MLS and central bronchiectasis. Further investigations revealed that the patient met 6/8 of the essential diagnostic criteria for ABPA. Appropriate therapy with oral corticosteroids resulted in remarkable symptomatic improvement.*

Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is an immunologically-mediated lung disease occurring in susceptible patients with asthma and cystic fibrosis who develop hypersensitivity to the colonised *Aspergillus* species in the airways, especially *A. fumigatus*. This potentially destructive lung disease has a worldwide distribution and affects approximately 2% of patients with asthma (1). A middle lobe syndrome (MLS) is a clinical entity characterised by chronic or recurrent collapse of the right middle lobe. This term was coined by Graham et al. (2) in 1948, when they described 12 patients with middle lobe atelectasis due to enlarged lymph nodes of non-tuberculous origin. This description followed the original report by Brock and colleagues (3) in 1937, who described eight patients with recurrent atelectasis of the right middle lobe due to extrinsic compression by enlarged tuberculous lymph nodes. Even today, MLS caused by tuberculous lymph nodes is popularly called a "Brock's syndrome".

Radiologically, ABPA is a very "picturesque" disease and has protean manifestations (4). Collapse, both lobar and segmental (5), caused by proximal occlusion of the bronchi by mucoid impaction is not uncommon in ABPA, but a MLS caused by this clinical entity is rather rare and to our knowledge has been documented only twice before (6,7). We report a young man with ABPA who presented with a MLS.

Case Report

A 36-year-old man, a never smoker, was referred for evaluation of a "non-resolving pneumonia". He had a childhood history of episodic wheezing dyspnoea and productive cough, which was associated with recurrent sneezing along with rhinorrhoea. In spite of stains and cultures being negative for *Mycobacterium tu-*

berculosis, the patient had received two complete courses of antituberculous therapy based on his clinical profile. Despite this, there was no resolution of either the symptoms or the opacity for which he was referred. On presentation, he complained of chest pain for the last 15 days along with aggravation of other symptoms. No co-morbidities were reported by the patient and there was no significant family history. Physical examination revealed a young man in no acute distress with no cyanosis or clubbing. Bilateral polyphonic rhonchi with bibasilar coarse crepitations were audible on auscultation. The haemoglobin level was 15.8 gm/dl, along with a total leucocyte count of 11,200 cells/mm^3, with a differential count of neutrophils 70%, lymphocytes 17%, monocytes 1% and eosinophils 1.5%. The absolute eosinophil count was 200 cells/mm^3. On pulmonary function testing, FVC was 3.34 L (76% predicted), FEV_1 was 1.44 L (39% predicted) and FEV_1/FVC ratio was 43% (51% predicted). The total lung capacity was 5.84 L (99% of predicted), residual volume was 2.42 L (157% of predicted) and RV/TLC was 41% (164% of predicted). After inhalation of 400 µg of salbutamol, the FVC was 3.49 L (80% of predicted) and FEV_1 was 1.66 L (45% of predicted). This was indicative of severe airflow limitation with moderate air trapping, and significant reversibility was observed with bronchodilators. Chest radiograph showed an ill-defined opacity abutting the right cardiac border with loss of cardiac silhouette, which appeared as a MLS on the lateral view (**figure 1A** and **1B**). Computed tomography (CT) of the thorax with high resolution cuts (HRCT) confirmed the MLS and, in addition, revealed central bronchiectasis characterised by a 'string of pearls' appearance (**figure 2A** and **2B**), a feature pathognomonic of ABPA (8) prompting further investigations. Skin prick test with antigens of *A. fumigatus* and *A. flavus* elicited a strong type I reaction, whilst strong bands of serum precipitins were detected against the same antigens. Total serum IgE levels were elevated (1,708 kU/L) while specific IgE and IgG were positive for *A. fumigatus*. However, sputum for pathogenic fungi, *M. tuberculosis* and other aerobic organisms were negative. CT of the paranasal sinuses showed left sided anterior, posterior ethmoidal, maxillary and sphenoidal polypoidal sinusitis, but allergic *Aspergillus* sinusitis (AAS) could not be confirmed as the patient refused to undergo functional endoscopic sinus surgery for the diagnosis.

The diagnosis of ABPA was based on: a) presence of asthma; b) type I hypersensitivity to extracts of *A. fumigatus* and *A. flavus* as evidenced by a positive skin prick test; c) elevated total serum IgE levels; d) presence of serum precipitins against *A. fumigatus* and *A. flavus*; e) presence of specific IgE against *A. fumigatus*; f) presence of specific IgG against *A. fumigatus*; and g) central/proximal bronchiectasis on the HRCT scan of the thorax. Our patient met 6/8 of the major diagnostic criteria (**table 1**). A diagnosis of ABPA presenting as a MLS was made, and the patient was initiated on oral prednisolone in the dosage of 0.5 mg/kg daily, which was further tapered at the rate of 5 mg per month over the next 4 months, as the patient improved steadily. In addition, for the management of asthma and rhinosinusitis, he received combination of inhaled budesonide and formoterol, along with intranasal mometasone. Within a fortnight he was, to a large extent, relieved of his symptoms. His complaints of cough and breathlessness had decreased significantly, while wheezing was abolished. Spirometry after 4 months of initiation of therapy with oral corticosteroids for ABPA showed an improvement of 300 mL in FEV_1, and the total IgE levels had reduced by 43% to 976 kU/L. However, the chest radiograph continued to depict the middle lobe opacity despite the patient being asymptomatic on tapering doses of oral prednisolone.

Figure 1A *- Chest radiograph PA view showing an ill-defined opacity abutting the right cardiac border, with loss of cardiac silhouette suggestive of a middle lobe syndrome.*

Figure 1B *- Lateral view showing wedge shaped antero-inferior opacity confirming a middle lobe syndrome.*

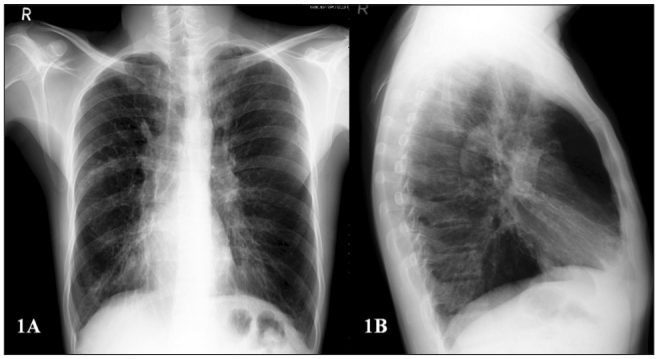

Figure 2A *- Computed tomography of the thorax (mediastinal window) showing collapse of the right middle lobe.*

Figure 2B *- High resolution computed tomography of the thorax, showing central bronchiectasis.*

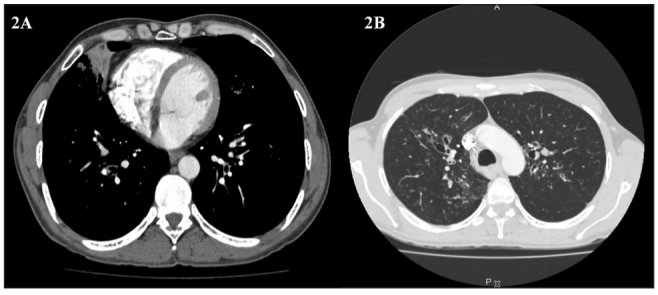

Table 1 *- Comparison of the two previously documented patients, along with the current patient with ABPA presenting with middle lobe syndrome (MLS).*

Authors, Reference **Year of publication, Country**	**Eisenberg RS and Valdesuso C (6)** **1980, USA**	**Shah A et al. (7)** **1993, India**	**Current patient**
Age / Gender	16 years / Female	55 years / Male	36 years / Male
Duration of asthma	No information	2 years	Since childhood
Duration of present illness	5 days	2 weeks	2 weeks
Current symptoms Chest pain Cough Fever	 Yes No Yes	 Yes Yes Yes	 Yes Yes No
Received antituberculous therapy for radiographic appearances	No	Yes	Yes
Peripheral blood eosinophilia	Yes	Yes	No
Transient pulmonary infiltrates (chest radiograph)	Yes	Yes	Serial radiographs not available
Immediate cutaneous reactivity to *Aspergillus*	Yes	Yes	Yes
Elevated total serum IgE	Yes	No information	Yes
Elevated specific IgE and IgG against *A. fumigatus*	No information	No information	Yes
Precipitating antibodies against *A. fumigatus*	Yes	Yes	Yes
Central bronchiectasis with normal tapering of distal bronchi	Yes	Yes	Yes
Expectoration of golden brownish sputum plugs	No	Yes	No
Positive sputum culture for *A. fumigatus*	No	No	No
Late (Arthus type) skin reactivity to *A. fumigatus*	Yes	Yes	No
Concomitant allergic *Aspergillus* sinusitis	No	Yes	No
Response to oral prednisolone	- Marked clearing of the opacity within 2 months	- Symptoms abolished within 2 weeks - Reinflated middle lobe after 1 month	- Significant symptomatic improvement at 2 weeks - Spirometry: improvement at 4 months - Total IgE: 43% reduction at 4 months - MLS persisting at 4 months

Discussion

Middle lobe syndrome is a distinct though uncommon clinical entity, which is rather poorly defined in the literature. Although no consistent clinical definition exists till date, a MLS is often referred to as the chronic or recurrent collapse of the right middle lobe. It is now recognised that several clinical entities can present as MLS (9), a few of them being described as case reports (10,11). One among these uncommon presentations is the occurrence of a MLS in patients with ABPA. Middle lobe syndrome is generally divided into obstructive and non-ob-

structive types. Obstruction of the middle lobe bronchus may be due to an intraluminal or extraluminal obstruction, and is the characteristic feature of MLS (9). There are several causative factors, which include both benign and malignant conditions. Tumours, including primary carcinoma of the lung, account for 24% of patients with MLS and 8 to 10% are secondary to tuberculosis (Brock's syndrome) (12). The non-obstructive form is typically caused by inflammation, commonly as the result of infection in majority of patients with MLS. Benign inflammatory disease accounts for around 62% of cases and has been identified as the most common cause of MLS (12). It can occur in adults and children with recurrent pneumonia, and is often associated with asthma, bronchiectasis and cystic fibrosis (9).

It has been postulated that the middle lobe has a greater tendency to collapse, as the middle lobe bronchus has a narrow origin with an acute angle, which can easily be obstructed. Furthermore, if the surrounding lymph nodes are enlarged either due to inflammation or a tumour, extrinsic compression can occur. In addition, the anatomical separation of the middle lobe from the right upper and lower lobes by fissures can result in poor collateral ventilation from the surrounding areas (13).

Imaging plays a key role in the diagnosis of MLS. It is now recognised that the atelectatic middle lobe is classically seen on a lateral chest roentgenogram as a wedge-shaped density extending from the hilum, anteriorly and inferiorly (14). Though difficult to detect on a posteroanterior radiograph, the volume loss within the right middle lobe is often seen as obscuring the right cardiac border (Silhouette sign) due to the loss of contact of the right middle lobe with the lateral wall of the right atrium (9). However, when the signs of middle lobe collapse are equivocal, a lordotic view could be of help. In this view, the MLS results in a wedge shaped density in the basal central zone of the right lower lung field, due to parenchymal involvement of the middle lobe (15). The advent of HRCT has helped with the diagnostic confirmation of MLS. It presents as a trapezoidal or broad triangular opacity, which has its base towards the hilum and is contiguous with the right cardiac border. CT imaging can also evaluate endobronchial or parenchymal abnormalities (8), as well as demonstrate bronchiectasis, as was seen in our patient. Bronchial patency, lymph node enlargement and calcifications or other causes of extrinsic compression of the right middle lobe airway too can be visualised (9).

Our patient met 6 of the 8 essential diagnostic criteria for ABPA, including central bronchiectasis, a *sine qua non* (16) for the diagnosis. This was detected on HRCT, done to evaluate MLS. Mucous hypersecretion, commonly seen in patients with asthma, is a well recognised feature of ABPA. Secretions and viscid sputum result in the mucoid impaction and consequent collapse. Ineffective clearance of this impacted mucous along with anatomically poor collateral ventilation of the middle lobe contribute to the development of chronic infection and atelectasis. Due to the vicious cycle of recurrent inflammation and obstruction, leading to a greater impairment of the cough mechanism and expectoration of secretions, these patients are at a greater risk for recurrent collapse of the middle lobe bronchus. While reviewing 1340 chest radiographs in 113 patients with ABPA, lobar/segmental collapse was observed in 17% patients (17).

The comparative features of the two published reports of MLS in ABPA along with the current patient are summarised in **table 1**. The duration of the presenting illness was brief in all the three patients. Symptomatic improvement with oral corticosteroids was observed in all. Although radiological clearance was found in the first two patients, the chest radiograph of the current patient continued to show MLS. Both our patients (cases 2 and 3) had received antituberculous therapy prior to being referred to us for evaluation. In high tuberculous prevalence countries, patients with ABPA are often erroneously diagnosed as pulmonary tuberculosis due to the strikingly similar chest radiograph appearances. This often results in initiation of antituberculous drugs while lung damage continues to progress (16).

The middle lobe has a propensity to collapse in isolation while in ABPA, segmental or lobar collapse is not uncommon. It is rather surprising that a search of the literature revealed only two previous reports of ABPA presenting MLS (6,7). Since the MLS is first detected on imaging, a high index of suspicion would obviate the need for invasive diagnostic procedures like fibreoptic bronchoscopy, that these patients often undergo. ABPA should be considered among the differentials while evaluating a MLS, especially in patients with history suggestive of bronchial asthma.

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