CASE REPORT

Coexistence of allergic bronchopulmonary aspergillosis and allergic aspergillus sinusitis in a patient without clinical asthma

Gopal Ghosh, Brijesh Sharma, Ajay Chauhan, M P S Chawla

Department of Internal Medicine, PGIMER & DR. RML Hospital, New Delhi, India

Correspondence to
Dr Gopal Chandra Ghosh,
gcghosh86@gmail.com

SUMMARY

All patients with prolonged cough with a history of atopy, even if not clinically asthmatic, should be evaluated for allergic bronchopulmonary aspergillosis (ABPA); also, we suspect that we may miss the early diagnosis of ABPA if bronchial asthma is considered as a major criteria for the diagnosis of ABPA

BACKGROUND

Allergic bronchopulmonary aspergillosis (ABPA) is a complex hypersensitivity reaction, which occurs predominantly in patients with asthma and cystic fibrosis. ABPA has been estimated to occur in 1–2% of patients with chronic asthma¹ and in up to 10% of patients with cystic fibrosis.² Its clinical and diagnostic manifestations originate from an allergic response to multiple antigens expressed by fungi, among which the most notable is *Aspergillus fumigatus*.³ ABPA is very rarely diagnosed in patients without a history of asthma and no data on the incidence of the disease in the general population are available.⁴ Association of allergic fungal sinusitis (AFS) and ABPA has been reported rarely in the literature.^{5–6}

We report a case of a 30-year-old non-asthmatic woman with coexisting ABPA and allergic aspergillus sinusitis (AAS).

CASE PRESENTATION

A 30-year-old female resident of New Delhi, working as a clerk in a central government department presented with a 5-month history of dry cough. She had developed a dry cough which was gradually progressing in nature over a 4 month period. For the last 1 month, she had a cough throughout the day and during the night-time and this was not controlled even by a cough syrup. Her dry cough had no postural or diurnal variation or was not associated with any chest pain or breathlessness (dyspnoea) or wheezing, but occasionally associated with scanty expectoration. She had a history of dust allergy. She had a history of recurrent episodes of sneezing and nasal discharge for the past 5–6 years especially when exposed to dust. There was no history of night cough or wheezing on exercise or dyspnoea during childhood. There was no history of asthma, prolonged drug intake or no family history of asthma. A prolonged history of intake of antihistaminic drug, especially cetirizine, was present to control the episodes of sneezing and nasal discharge. The patient did not smoke and had

experienced no previous diseases of this nature or pulmonary tuberculosis. For the last 1 month, she was in consultation with a local doctor who had prescribed her an inhaler containing salmeterol and fluticasone with an oral tablet of cetirizine, but even on taking medicines regularly her symptoms were not controlled.

On examination, she was afebrile with normal vital parameters. General physical examination and systemic examination including the respiratory system were unremarkable. An ear, nose and throat consultation was done for indirect nasal endoscopy, which did not reveal any postnasal drip.

INVESTIGATIONS

Her investigations revealed haemoglobin 12.2 g%, total leucocyte count 10 700/mm³ with eosinophil 36% on differential count, erythrocyte sedimentation rate 46 mm in the first hour, fasting blood sugar 118 mg/dl, liver and kidney function tests were within normal limits. Chest x-ray was done and it was within normal limits. We did pulmonary function test (PFT) on several occasions which was normal, forced vital capacity (FVC) of 2.83 litre (83% of predicted), forced expiratory volume in the first second (FEV₁) of 2.37 litre (86% of predicted) and FEV₁/FVC ratio of 83.7%. Postbronchodilator PFT revealed only 3–4% improvement in FEV₁. Sputum examination for Gram stain and Ziehl-Neelsen test was negative in several occasions, Mantoux test was negative. High-resolution CT (HRCT) of the chest (figure 1) revealed bilateral central bronchiectasis with mucus plugging of

Figure 1 High-resolution CT of the chest revealed bilateral central bronchiectasis with mucus plugging of bronchi giving a finger in glove appearance and bronchocele formation.

To cite: Ghosh G, Sharma B, Chauhan A, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-008683

bronchi giving a finger in glove appearance and bronchocele formation. This finding of central bronchiectasis prompted further investigations in the line of ABPA and then we proceeded for skin test (figures 2 and 3) for immediate hypersensitivity reaction to *A fumigatus* which revealed a positive result with a wheal formation of 6 mm × 5 mm size. Serum IgG (256 IU/l) and IgE specific for *A fumigatus* were positive and serum total IgE level (2500 ng/ml) was markedly elevated. Thus, we established the diagnosis of ABPA in patients with non-asthma. As the patient was complaining of recurrent sneezing and rhinorrhoea, we planned for CECT of paranasal sinus (figure 4) which revealed a right maxillary polyp formation. Nasal mucosal washing revealed the growth of *A fumigatus*.

DIFFERENTIAL DIAGNOSIS

- ▶ Drug-resistant asthma
- ▶ Interstitial lung disease

TREATMENT

Tablet Prednisolone and Tablet Itraconazole

OUTCOME AND FOLLOW-UP

The patient became symptom-free on first follow-up after 2 weeks of starting treatment. At present, she is doing well, free of symptoms.

DISCUSSION

Aspergillosis remains a significant cause of morbidity and mortality. The spectrum of disease is diverse and ranges from non-invasive disease with an excessive immune response, such as in ABPA, to a lack of an immune response as seen in patients with quantitative or qualitative granulocyte deficits and subsequent invasive pulmonary aspergillosis.⁶ ABPA is an important cause of bronchiectasis,⁷ and it may present with any severity of asthma, and occasionally with no asthma or cystic fibrosis.⁸ The diagnosis of ABPA is based on haematological, radiological and immunological criteria along with the presence of long-standing asthma, and occasionally cystic fibrosis.^{9–10} However, ABPA occurring without asthma is very uncommon and such instances have been documented as case reports and deserves reporting.^{11–14} Case reports are present in the literature of co-existent ABPA with AAS in patients with asthma, but our patient was a non-asthmatic, and having coexistent AAS, thus unique in that aspect.

Our patient was fulfilling six of the seven major criteria for the diagnosis of ABPA according to Rosenberg M *et al*,¹⁵ except bronchial asthma, thus diagnosed as a case of ABPA. As she had a history of atopy, thus predispose to become sensitised against aspergillus antigens thus can developed ABPA.¹⁶ According to

Figure 2 Skin testing showing immediate hypersensitivity reaction to *Aspergillus fumigatus*, *Aspergillus niger* and *Aspergillus flavus*.

Figure 3 Skin testing showing immediate hypersensitivity reaction to *Aspergillus fumigatus*, *Aspergillus niger* and *Aspergillus flavus*.

Greenberger's criteria,¹⁷ asthma, immediate cutaneous reactivity to *Aspergillus* species or *A fumigatus*, elevated total serum IgE (>417 kU/l or 1 000 ng/ml), elevated serum *A fumigatus*-specific IgE and/or serum IgG-*A fumigatus*, and proximal or central bronchiectasis are needed for the diagnosis of ABPA. Our patient had immediate cutaneous reactivity to *A fumigatus*, elevated total serum IgE level (2500 mg/ml), positive serum IgE and IgG specific for *A fumigatus* and central bronchiectasis with bronchocele formation in HRCT chest. She also had marked peripheral eosinophilia. Thus, our patient was fulfilling four major Greenberger's criteria.

The association of AFS and ABPA may be concomitant or not, with a possible time lag of several years between the onset of naso-sinal and bronchopulmonary disease, even after recovery from the original episode.¹⁸ Concomitant occurrence of ABPA and AAS seems to be infrequently recognised. Since asthma and sinusitis are often seen by two different specialties, the occurrence of AAS in ABPA and ABPA in AAS may easily be overlooked.¹⁹

Greenberger and Patterson²⁰ considered that patients with ABPA can be classified into five stages, namely acute stage, remission, exacerbation, corticosteroid-dependent asthma and fibrotic-end stage. Severe asthma with fungal sensitisation (SAFS) is not a well-recognised fungal complication of asthma. In ABPA, the total immunoglobulin E (IgE) is usually >1000 IU/ml, whereas in SAFS it is <1000 IU/ml; either skin prick tests or fungus-specific IgE tests are positive. SAFS is a problem in patients with poorly controlled asthma and occasionally presents in the intensive care unit. Production of mucous plugs and

Figure 4 CECT of paranasal sinus revealed right maxillary polyp formation.

coughing paroxysms is more common in ABPA, but both the condition can be managed with high doses of corticosteroids and oral antifungal agents.⁸ Glancy *et al*⁴ reported that 11 of 42 patients with allergic bronchopulmonary fungal disease had no evidence of asthma. But, in those cases, some patients developed bronchial asthma later. These facts suggest that those patients might have been in a stage preceding bronchial asthma. These facts suggest that our patient might have been at a stage preceding bronchial asthma and may develop bronchial asthma later.

Learning points

- ▶ Allergic bronchopulmonary aspergillosis (ABPA) may present without symptoms of clinical asthma.
- ▶ ABPA and allergic aspergillus sinusitis may coexist, but are infrequently detected.
- ▶ We should keep ABPA as a differential diagnosis in patients presented with prolonged dry cough without clinical asthma.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Greenberger PA, Smith LJ, Hsu CC, *et al*. Analysis of bronchoalveolar lavage in allergic bronchopulmonary aspergillosis: divergent responses of antigen-specific antibodies and total IgE. *J Allergy Clin Immunol* 1988;82:164–70.
- 2 Laufer P, Fink JN, Bruns WT, *et al*. Allergic bronchopulmonary aspergillosis in cystic fibrosis. *J Allergy Clin Immunol* 1984;73:44–8.
- 3 Vlahakis NE, Aksamit TR. Diagnosis and treatment of allergic bronchopulmonary aspergillosis. *Mayo Clin Proc* 2001;76:930–8.
- 4 Glancy JJ, Elder JL, McAleer R. Allergic bronchopulmonary fungal diseases without clinical asthma. *Thorax* 1981;36:345–9.
- 5 Braun JJ, Pauli G, Schultz P, *et al*. Allergic fungal sinusitis associated with allergic bronchopulmonary aspergillosis: an uncommon sinobronchial allergic mycosis. *Am J Rhinol* 2007;21:412–16.
- 6 Thompson GR III, Patterson TF. Pulmonary aspergillosis: recent advances. *Semin Respir Crit Care Med* 2011;32:673–81.
- 7 McShane PJ, Naureckas ET, Strek ME. Bronchiectasis in a diverse US population: effects of ethnicity on etiology and sputum culture. *Chest* 2012;42:159–67.
- 8 Hogan C, Denning DW. Allergic bronchopulmonary aspergillosis and related allergic syndromes. *Semin Respir Crit Care Med* 2011;32:682–92.
- 9 Braun JJ, Pauli G, de Blay F. Allergic fungal sinusitis and allergic broncho-pulmonary aspergillosis: a fortuitous association or a nosological rhino-bronchial entity? *Rev Mal Respir* 2005;22:405–11.
- 10 Aggarwal R. Allergic broncho-pulmonary aspergillosis. *Chest* 2009;135:805–26.
- 11 Amin MU, Mahmood R. Multiple bronchoceles in a non-asthmatic patient with allergic bronchopulmonary aspergillosis. *J Pak Med Assoc* 2008;58:514–16.
- 12 Shah A, Maurya V, Panjabi C, *et al*. Allergic bronchopulmonary aspergillosis without clinical asthma caused by *Aspergillus niger*. *Allergy* 2004;59:236–7.
- 13 Hoshino H, Tagaki S, Kon H, *et al*. Allergic bronchopulmonary aspergillosis due to *Aspergillus niger* without bronchial asthma. *Respiration* 1999;66:369–72.
- 14 Berkin KE, Vernon DR, Kerr JW. Lung collapse caused by allergic bronchopulmonary aspergillosis in non-asthmatic patients. *Br Med J* 1982;285:552–3.
- 15 Rosenberg M, Patterson R, Mintzer R, *et al*. Clinical and immunologic criteria for the diagnosis of allergic bronchopulmonary aspergillosis. *Ann Intern Med* 1977;86:405–14.
- 16 Nepomuceno IB, Esrig S, Moss RB. Allergic bronchopulmonary aspergillosis in cystic fibrosis: role of atopy and response to itraconazole. *Chest* 1999;115:364–70.
- 17 Greenberger PA. Allergic bronchopulmonary aspergillosis. *J Allergy Clin Immunol* 2002;110:685–92.
- 18 Braun JJ, Pauli G, de Blay F. Allergic fungal sinusitis and allergic broncho-pulmonary aspergillosis: a fortuitous association or a nosological rhino-bronchial entity. *Rev Mal Respir* 2005;22:405–11.
- 19 Shah A, Panchal N, Agarwal AK. Concomitant allergic bronchopulmonary aspergillosis and allergic *Aspergillus* sinusitis: a review of an uncommon association. *Clin Exp Allergy* 2001;31:1896–905.
- 20 Greenberger PA, Patterson R. Allergic bronchopulmonary aspergillosis and the evaluation of the patient with asthma. *J Allergy Clin Immunol* 1988;81:646–50.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow