CASE REPORT

Sinobronchial allergic aspergillosis with allergic bronchopulmonary aspergillosis: a less common co-existence

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SUMMARY

Allergic bronchopulmonary aspergillosis (ABPA) is an immunological pulmonary disorder that is characterised by a hyper-responsiveness of the airways to *Aspergillus fumigatus*. Although several other fungi may also present with similar clinical conditions, *Aspergillus* remains the most common fungal pathogen causing airway infections. Co-existence of ABPA with allergic *Aspergillus* sinusitis (AAS) is an uncommon presentation. The concept of one airway/one disease justifies the co-existence of ABPA with AAS, but it does not always hold true. We report a case of a 35-year-old woman who presented with symptoms suggestive of bronchial asthma. On further investigation, the radiological pattern showed fleeting shadows and CT scan showed central cystic bronchiectatic changes characteristic of ABPA. The nasal secretions were investigated for the presence of *Aspergillus* and were found to be positive. Hence a diagnosis of ABPA with AAS was established. The patient was treated with oral steroids and antifungal drugs.

BACKGROUND

Allergic bronchopulmonary aspergillosis (ABPA) is a clinicopathological, immunological pulmonary disorder characterised by a spectrum of clinical manifestations caused by hyper-responsiveness of respiratory epithelium to *Aspergillus fumigatus*. Varied presentations may be attributed to the diverse immunological response depending on the host factors and virulence of organisms. The clinical condition may manifest itself depending on type I, type II or type IVb hypersensitivity reaction.^{1–2} ABPA was first described by Hinson *et al*³ (UK). It was first studied in detail by Pepys *et al*.^{4–5} The prevalence of ABPA is 1–2% in patients with asthma, 7–14% in patients with steroid-dependent asthma and 2–15% in patients with cystic fibrosis.^{6–9} Millar *et al*¹⁰ described the first case of ABPA of maxillary sinuses in 1981. In 2002, Venarske and deShazo¹¹ gave the term sinobronchial allergic mycosis syndrome for fungus-related hypersensitivity in the upper and lower airways.¹²

CASE PRESENTATION

A 35-year-old woman without diabetes presented to our department of pulmonary medicine with symptoms of breathlessness, rhinorrhoea, tenderness over the maxillary areas, fever and cough with purulent expectoration for the past 8 years. To begin with, the symptoms were not troublesome and aggravated on change of seasons or exposure to cold but for the past 1.5 years these symptoms were persistent and

severely affecting her daily activities. She reported episodes of continuous fever with cough and yellowish green expectoration and persistent pain over the bilateral maxillary areas persisting for a week; these symptoms subsided on treatment with macrolides. The patient had simultaneous symptoms of breathlessness progressively worsening for the past 1.5 years, for which she had to be kept on steroids for short durations. Her modified Medical Research Council (mMRC) score had deteriorated from 1 to 3 in the past 6 months. She did not report of purulent or blood-mixed nasal secretions or stridor. She did not report of haematuria or symptoms suggestive of renal disease. On auscultation, bilateral diffuse rhonchi were heard along with bilateral coarse crepitations.

Her blood investigations showed total leucocyte count of 14 000/mm³ with 16% eosinophils (absolute eosinophil count 2240/mm³) and serum IgE 1000 (0–100 IU/mL). An antineutrophilic antibody test was performed and was found to be inconclusive. Serum ACE was performed and the values were found to be <60.24 h urinary calcium and blood calcium levels were within normal limits. Her clinical history did not suggest immunocompromised status and her ELISA for HIV was also found to be negative. She had not undergone any surgical procedure and had no episode of prolonged immobilisation in the course of her illness. Purulent sputum was sent for bacteriological evaluation; Gram positive, Gram negative and acid-fast bacilli (AFB) showed predominant Gram-negative organisms. Culture reports did not show growth of AFB. The patient's radiological investigations revealed bilateral bronchiectatic changes with fleeting opacities in serial X-rays (figure 1). High resolution CT (HRCT) of the thorax showed bilateral central cystic bronchiectatic changes and high attenuation mucous impaction (figures 2 and 3). Skin prick test was strongly positive for *A. fumigatus* and serum precipitins against *Aspergillus*-specific IgE and IgG were 43 and 72 IU, respectively (normal <0.35 kUA/L). Spirometry could not be performed due to persistent cough and breathlessness. The patient had been on steroids and her blood investigations did not suggest suppressed immune response. The patient also gave a history of sinus surgery performed 2 years earlier for nasal congestion. X-ray of the paranasal sinuses showed haziness of the maxillary sinuses (figure 4). On consulting her surgeon it was found that she had undergone a nasal polypectomy because of her sinus problems. Histopathology of

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Figure 1 High resolution CT of the lung window showing right-sided mucous-filled dilated bronchi and central bronchiectatic changes.

the polyp showed *Aspergillus* (figure 5). She had remained asymptomatic for a brief period after which her symptoms resurged and worsened. From the histopathological examination it was found that the fungus invading the airways was the same as that in the sinuses, thus proving it to be ABPA with allergic *Aspergillus* sinusitis (AAS).

The patient was treated with oral steroids prednisolone 30 mg once daily and antifungal itraconazole 200 mg twice daily for 6 weeks; the steroid was tapered over the next 6 months. The patient was started on inhaled medications in the form of indacaterol 150 µg once daily. She did not show the expected response with these medications so we started her on omalizumab, a humanised monoclonal antibody against serum IgE,

300 mg every 2 weeks for 6 weeks. The patient showed marked improvement and her symptoms attenuated. Serum IgE measured after 6 weeks was 645 IU.

INVESTIGATIONS

HRCT, CT, total leucocyte count, absolute eosinophil count, differential percentage leucocyte count and X-ray of the posterior nasal sinus.

DIFFERENTIAL DIAGNOSIS

- ▶ Postinfective fibrocavitary disease
- ▶ Wegener's granulomatosis
- ▶ Sarcoidosis

Figure 2 Signet ring appearance and high attenuation mucous impaction in the patient of allergic bronchopulmonary aspergillosis.

Figure 3 Coronal section showing central bronchiectatic changes with mucous impaction.

TREATMENT

- ▶ Indacaterol 150 µg once daily in inhaled form
- ▶ Prednisolone 30 mg once daily
- ▶ Itraconazole 200 mg twice daily
- ▶ Omalizumab (humanised monoclonal antibody against serum IgE) 300 mg every weeks for 6 weeks.

OUTCOME AND FOLLOW-UP

The patient responded well to the treatment and showed a marked improvement of symptoms.

Figure 4 Maxillary sinusitis in the patient with nasal polyps and allergic *Aspergillus* sinusitis.

Figure 5 Microscopic view of *Aspergillus fumigatus*.

DISCUSSION

Fungal infections of the rhinosinusal passages have been well known. Allergic fungal sinusitis (AFS) may present as invasive/non-invasive lesions depending on the immune status of the patient. In patients with an intact immune system fungal infections may limit themselves to AFS, fungal colonisation or fungal ball, whereas in patients with diabetes or carcinoma, invasive granulomatous forms may be present. AFS usually presents with chronic rhinosinusitis with discharge of eosinophil-rich mucin. The offending organisms are usually *Alternaria*, *Curvularia*, *Bipolaris*, *Cladosporium*, *Exserohilum* and *Dreschsler*.^{13–15} Safirstein¹⁶ first described a case of ABPA with nasal polyposis with a history of passage of nasal plugs. Millar *et al*¹⁰ described the first case of allergic aspergillosis of maxillary sinuses. *Aspergillus* hypersensitivity is defined by the presence of immediate cutaneous hypersensitivity to *A. fumigatus* as proven by a skin prick test. However, only few patients with *Aspergillus* hypersensitivity develop the clinical picture of ABPA.^{17–18} It is a common observation that ABPA commonly occurs in patients with asthma and cystic fibrosis. The susceptibility of patients with asthma to develop ABPA is not yet explored, though the pathogenesis may hint towards a strong association. Inhaled conidia of the fungus (2–3µ) get deposited in the alveoli, may persist there or germinate into hyphae under favourable conditions, releasing proteases, toxins, sabotaging the mucociliary clearance and leading to inflammatory response. Increased mucous impaction initiates a never ending inflammatory process.^{19–20} In patients with pre-existing cavitary lesions, saprophytic *Aspergillus* growth may occur, which in circumstances of immune suppression may invade surrounding blood vessels leading to invasive aspergillosis causing haemoptysis. Several humoral factors play a significant role in immunopathogenesis of ABPA. Downregulation of type 1 CD4 T helper cells, mutations in CFTR, and human leucocyte antigen (HLA) phenotypes HLA DR2 and DR5 predispose to this condition. In our patient, all criteria for ABPA and AAS were verified. The patient had no diabetes and had no signs of invasive disease. The presentation was typically that of allergic rhinosinusitis with bronchial asthma. Serum IgE was raised with peripheral eosinophilia. Serum IgE and IgG against *A. fumigatus* were raised. The radiographic pattern as deduced from serial chest

X-ray was characteristic of ABPA with AAS. The nasal discharge was evaluated for fungal elements and was found to be positive.

The patient was advised prednisolone 30 mg along with macrolide antibiotics and antihistamines for 6 weeks followed by 20 mg for 8 weeks and then tapered 5 mg every week. Itraconazole 200 mg twice daily was also added to the regimen 2 weeks after the steroid therapy. An inhaled form of the longest acting β_2 agonist was added for breathlessness throughout the duration of treatment and the patient was asked to continue it even after the course was completed. The patient was considered for omalizumab therapy as she still had trouble with her nasal symptoms and breathlessness. Serum IgE was repeated after 2 months and was found to be 645 IU. The patient was very compliant with treatment and had a good response by the fifth month of therapy.

Learning points

- ▶ Allergic bronchopulmonary aspergillosis and allergic *Aspergillus* sinusitis may co-exist.
- ▶ Steroids and itraconazole are the first line of therapy once the diagnosis has been made.
- ▶ Patients not responding to first-line drugs may be planned for anti-IgE antibody treatment omalizumab; a good outcome has been shown to occur in several cases.

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REFERENCES

- 1 Rajan TV. The Gell-Coombs classification of hypersensitivity reactions: a reinterpretation. *Trends Immunol* 2003;24:376–9.
- 2 Geha RS, Sampson HA, Askenase PW, *et al.* Allergy and hypersensitivity. In: Janeway CA, Travers P, Walport M, *et al.* eds. *Immunobiology*. New York, NY: Garland, 2001:517–56.
- 3 Hinson KFW, Moon AJ, Plummer NS. Broncho-pulmonary aspergillosis; a review and a report of eight new cases. *Thorax* 1952;7:317–33.
- 4 Pepys J, Riddell RW, Ciron KM, *et al.* Clinical and immunologic significance of *Aspergillus fumigatus* in the sputum. *Am Rev Respir Dis* 1959;80:167–80.
- 5 McCarthy DS, Pepys J. Allergic bronchopulmonary aspergillosis: clinical immunology: 1 Clinical features. *Clin Allergy* 1971;1:261–86.
- 6 Schwartz HJ, Greenberger PA. The prevalence of allergic bronchopulmonary aspergillosis in patients with asthma, determined by serologic and radiologic criteria in patients at risk. *J Lab Clin Med* 1991;117:138–42.
- 7 Greenberger PA, Patterson R Jr. Allergic bronchopulmonary aspergillosis and the evaluation of the patient with asthma. *J Allergy Clin Immunol* 1988;81:646–50.
- 8 Becker JW, Burke W, McDonald G, *et al.* Prevalence of allergic bronchopulmonary aspergillosis and atopy in adult patients with cystic fibrosis. *Chest* 1996;109:1536–40.
- 9 Basich JE, Graves TS, Baz MN, *et al.* Allergic bronchopulmonary aspergillosis in corticosteroid-dependent asthmatics. *J Allergy Clin Immunol* 1981;68:98–102.
- 10 Millar JW, Johnston A, Lamb D. Allergic aspergillosis of the maxillary sinuses. *Thorax* 1981;36:710.
- 11 Venarske DL, deShazo RD. Sinobronchial allergic mycosis. The SAM syndrome. *Chest* 2002;121:1670–6.
- 12 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.
- 13 Corey JP, Delsupehe KG, Ferguson BJ. Allergic fungal sinusitis: allergic, infectious or both? *Otolaryngol Head Neck Surg* 1995;113:110.
- 14 Manning SC, Schafer SD, Close LG, *et al.* Culture positive allergic fungal sinusitis. *Arch Otolaryngol Head Neck Surg* 1991;117:174–8.
- 15 Bartynski JM, Mc Caffrey TV, Frigas E. Allergic fungal sinusitis secondary to dematiaceous fungi: *Curvularia lunata* and *Alternaria*. *Otolaryngol Head Neck Surg* 1990;103:32–9.
- 16 Safirstein BH. Allergic bronchopulmonary aspergillosis with obstruction of the upper respiratory tract. *Chest* 1976;70:788–90.
- 17 Agarwal R, Chakrabarti A. Epidemiology of allergic bronchopulmonary aspergillosis. In: Pasqualotto A. ed. *Aspergillosis: from diagnosis to prevention*. New York, NY: Springer, 2010:671–88.
- 18 Bateman ED. A new look at the natural history of *Aspergillus* hypersensitivity in asthmatics. *Respir Med* 1994;88:325–7.
- 19 Kauffman HK, Tomee JFC. Inflammatory cells and airway defense against *Aspergillus fumigatus*. *Immunol Allergy Clin North Am* 1998;18:619–40.
- 20 Kauffman HF, Tomee JF, Van de Riet MA, *et al.* Protease dependent activation of epithelial cells by fungal allergens leads to morphologic changes and cytokine production. *J Allergy Clin Immunol* 2000;105:1185–93.

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