CASE REPORT

Mycobacterium avium intracellulare infection complicated by allergic bronchopulmonary aspergillosis in a non-asthmatic patient

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SUMMARY

Allergic bronchopulmonary aspergillosis (ABPA) most often develops in patients with asthma or cystic fibrosis. We present a 91-year-old non-asthmatic patient with pre-existing *Mycobacterium avium* complex (MAC) infection who got diagnosed with ABPA. Treatment of the two conditions can be challenging as immunosuppression with steroids for treatment of ABPA may exacerbate the underlying MAC infection. Treatment with steroids and antibiotics resulted in significant improvement in the patient's condition.

BACKGROUND

Allergic bronchopulmonary aspergillosis (ABPA) is a complex hypersensitivity reaction of the airways. It is considered as the response by airways to its colonisation by *Aspergillus* species. This develops almost exclusively in patients with asthma or cystic fibrosis. Rarely, ABPA occurs in patients with bronchiectasis, chronic granulomatous disease, hyper-immunoglobulinemia E and in lung transplant recipients.

CASE PRESENTATION

A 91-year-old non-asthmatic man with a history of active *Mycobacterium avium* complex (MAC) infection and left upper lobe fibrocavitary disease presented with worsening dyspnoea, cough and thick brownish phlegm for 2 weeks. He was being treated with a combination of ethambutol, rifampin and azithromycin for the past 13 months; however, he had poor compliance with the treatment. On presentation, he was haemodynamically stable, afebrile, with decreased breath sounds in bilateral lung fields and scattered rhonchi.

INVESTIGATIONS

Initial blood work revealed eosinophil count elevated to 25%, which increased up to 46.3% with an absolute count of 7000 during the hospital course. CT scan of the chest revealed bronchiectasis and extensive cavitary disease in the left lung apex, which had worsened from the previous study a year before (figure 1). It also showed a new left upper lobe infiltrate and worsening nodularity in the right upper lobe. Meanwhile, sputum acid-fast stain was positive for MAC, but antimycobacterial therapy

was held on suspicion of eosinophilic reaction from ethambutol. No other systemic signs of an allergic reaction were apparent. Stool tests were negative for parasitic infection and sputum cytology showed eosinophilia of 29%. The IgE level was markedly elevated at 1068 kU/L and serology was positive for *Aspergillus fumigatus* precipitins. *Aspergillus* IgE RAST also returned high at 1.29 kU/L, thus confirming the diagnosis of ABPA.

DIFFERENTIAL DIAGNOSIS

Our differential diagnosis included pneumonia, parasitic infection, drug reaction (ethambutol), pulmonary eosinophilic syndrome, acute eosinophilic pneumonia and ABPA. The stool tests for parasites were negative. Both ethambutol and rifampin were held but did not result in improvement of patient's clinical status nor the eosinophil count. The patient also did not respond to initial empirical antibiotics and the response to steroid further confirmed our suspicion of ABPA along with the positive serology and laboratories.

TREATMENT

Initially, he was empirically started on broad-spectrum antibiotics for suspected pneumonia. His clinical condition, however, did not improve. Later, he developed a new right lower lobe infiltrate and was started on 0.75 mg/kg prednisone on the suspicion of ABPA. Concurrently, he was also started on nebulised amikacin and clarithromycin for the management of underlying MAC infection. Antifungals were not used in this case considering the patient's age, comorbidities and the risk of associated side effects. Further, there was a concern for a potential serious drug interaction between triazoles and clarithromycin, limiting the treatment options.

OUTCOME AND FOLLOW-UP

This patient responded very well to steroids and had a significant improvement in dyspnoea and eosinophilia. The eosinophil count decreased to 2% within 24 hours of initiating the steroids and the repeat *Aspergillus* IgE level also dropped to 662 kU/L.

DISCUSSION

ABPA is unlikely to present in very elderly without a history of asthma. Underlying MAC infection,

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Figure 1 CT chest showing left upper lobe cavitary lesion with an infiltrate.

however, may predispose to colonisation with *Aspergillus*. A high index of suspicion is required to diagnose ABPA in patients with pulmonary eosinophilia but without pre-existent asthma. In this case, the *Aspergillus* serum precipitins were positive and IgE levels were above 1000, which is diagnostic for ABPA.^{1–4} Patients with ABPA typically have an elevated absolute total eosinophil count of at least $>500/\text{mm}^3$ and often $>1000/\text{mm}^3$.⁵ There is no upper limit established for the peripheral eosinophilia observed in ABPA, and this patient had up to 7000 without any other systemic signs of an allergic reaction.⁶ Chest CT has become the modality of choice in evaluating patients suspected of having ABPA, and central bronchiectasis mostly affecting the middle and upper lobes is frequently seen as in this case.⁷ The incidence of ABPA in patient's pre-existing MAC infection is unclear. One retrospective study showed an increased incidence of ABPA in patients with MAC infection, but this was not statistically significant.⁸ The concurrence of these entities is discussed in the literature rarely. However, the treatment of the patient with this dual presentation is even more infrequently discussed. Immunosuppression with steroids for treatment of ABPA may exacerbate even a dormant MAC infection. Failure to recognise and treat both entities may be seen as treatment failure rather than a failure of diagnosis, which could lead to progression of the disease and possibly to pulmonary fibrosis.⁹ Treatment in the setting of active MAC infection is complicated since immunosuppression with steroids may cause dissemination of infection. Although there are some data on the use of antifungal agents in ABPA, they are not the first-line treatment and should only be

used as a corticosteroid-sparing agent or when the patient is not responding to steroids alone.^{10 11}

Learning points

- ▶ Allergic bronchopulmonary aspergillosis (ABPA) and *Mycobacterium avium* complex (MAC) infection are rare entities that may coexist.
- ▶ Patients with eosinophilia, worsening respiratory symptoms and CT images showing new infiltrates in the setting of bronchiectasis that do not improve with antibiotics should be investigated for ABPA.
- ▶ Treatment should include steroids and antibiotic to treat both ABPA and MAC infection.
- ▶ Patients need to be closely monitored since steroids may cause dissemination of MAC infection.

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