

A Case Report of *Aspergillus* Hypersensitivity Syndrome with Obstructing Bronchial Aspergillosis

P Lee,*^{MBBS, MRCP (UK), M Med (Int Med)}, S K Goh,**^{FAMS, MRCP (UK), M Med (Int Med)}, W M Yap,***^{FAMS, MBBS, MRCP (UK)},
C C Chan,****^{FAMS, MRCP (UK)}

Abstract

Introduction: A 62-year-old Indian male with diabetes mellitus presented with atypical, overlap features of *Aspergillus* hypersensitivity syndrome and obstructing bronchial aspergillosis. **Clinical Picture:** He was febrile and tachypnoeic with diffuse crepitations and wheezing. Chest X-ray was normal but eosinophil count was 2900/mm³ and Ig E >10,000 IU/ml. **Treatment and Outcome:** He responded initially to high dose steroid therapy but deteriorated subsequently from extensive mucus plugging of the bronchial tree which resulted in respiratory failure and death. He was HIV-negative. **Conclusion:** Culture and histologic examination of bronchoscopically identified tracheobronchial mucus plugs should be performed as early treatment may be life-saving.

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Key words: Diabetes mellitus, HIV-negative, Obstructing bronchial aspergillosis

Introduction

The spectrum of pulmonary aspergillosis includes saprophytic colonisation, hypersensitivity syndromes and invasive lung disease.^{1,2} There has been a tendency to classify these syndromes as separate entities but clinical overlap occurs.³

We report an unusual case with overlap features of *Aspergillus* hypersensitivity syndrome and obstructing bronchial aspergillosis (OBA). This is a case report of OBA, a new entity characterised by bronchial mucoid impaction⁴ in a HIV-negative patient.

Case Report

A 62-year-old Indian male was admitted with productive cough and fever for 5 days. He was a non-smoker and had just returned from a 6-month stay in India. He had diabetes mellitus for 20 years on glibenclamide and metformin; ischaemic heart disease and hypertension for 10 years. He was treated for pulmonary tuberculosis 6 years ago and Tolosa Hunt syndrome which resolved with a short course of steroid therapy 8 years ago.

He denied a history of bronchial asthma or chronic bronchitis and did not complain of recent weight loss, fatigue or night sweats. There was no family history of bronchial asthma.

Upon hospitalisation, he was febrile and tachypnoeic with a respiratory rate of 30 breaths per minute. Diffuse crepitations and wheezing were noted. There were no hepatosplenomegaly, lymphadenopathy or oral candidiasis. The chest X-ray was normal (Fig.1) and the arterial blood gas on intranasal oxygen 2 L/min revealed pH 7.33, PaCO₂ 39.9 mmHg and PaO₂ 132.4 mmHg. The white cell count was 8200/mm³ with absolute neutrophil count (ANC) 2800/mm³, lymphocyte count 1600/mm³ and eosinophil count 2900/mm³. The erythrocyte sedimentation rate was 113 mm/h and blood cultures done on admission were negative for bacterial growth. The Ig E level was more than 10,000 IU/ml and microfilarial Ig G was positive. Stool culture was negative for parasites and the anti-nuclear, anti-dsDNA, anti-neutrophil cytoplasmic antibodies and rheumatoid factor were negative.

He was given clarithromycin (PO) 500 mg bid,

* Registrar

**** Consultant

Department of Respiratory Medicine

** Consultant

Department of General Medicine

*** Consultant

Department of Pathology

Tan Tock Seng Hospital

Address for Reprints: Dr P Lee, Department of Respiratory Medicine, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433.

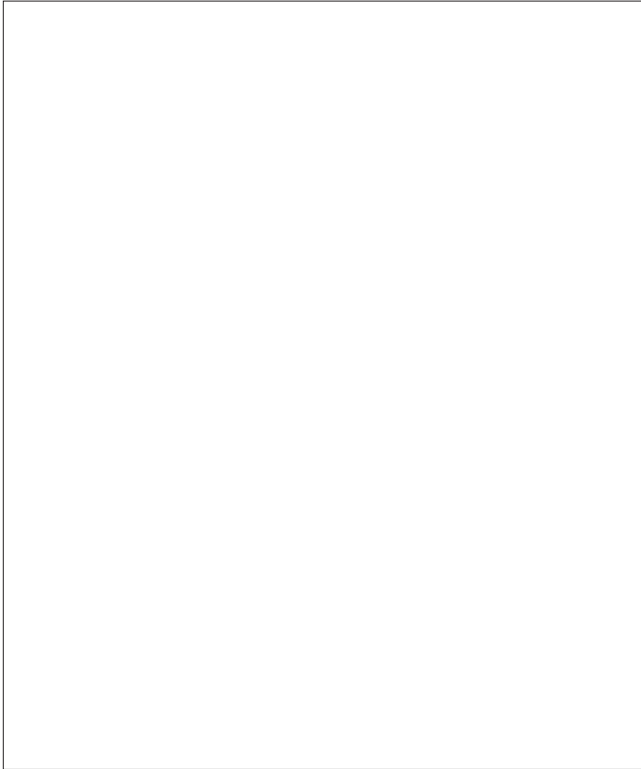


Fig. 1. Normal chest X-ray upon hospital admission.

incremental doses of diethylcarbamazine, prednisolone (PO) 30 mg om, inhaled steroid and nebulised salbutamol.

He improved for 4 days but deteriorated subsequently with severe bronchospasm requiring high dose steroid therapy. His condition did not improve and a repeat chest X-ray on day 5 of hospitalisation (Fig. 2) showed bilateral lower zone infiltrates. Repeat arterial blood gas showed hypoxia and hypercapnoea and he was mechanically ventilated. The white cell count increased to $21,200/\text{mm}^3$ with ANC $19,000/\text{mm}^3$ and eosinophil count $0/\text{mm}^3$. Intravenous imipenem was started empirically and bronchoscopy was performed 24 hours after intubation.

Bronchoscopy revealed multiple white plaques adherent to the bronchial mucosa and occluding the right upper lobe bronchus, bronchus intermedius and left upper lobe bronchus. Underlying mucosal erythema and bleeding were noted when the plaques were biopsied endoscopically. Histology of the bronchial biopsies showed fungal hyphae with acute angle branching (Fig. 3). Smears from the bronchial aspirate showed fungal hyphae as well as many eosinophils, neutrophils and macrophages. Acid-fast bacilli, *Pneumocystis carinii* and malignant cells were not seen. Bronchial aspirate culture revealed *Acinetobacter baumannii* sensitive to imipenem and ampicillin/sulbactam as well as two fungal sub-species, *Aspergillus fumigatus* and *Aspergillus flavus*.

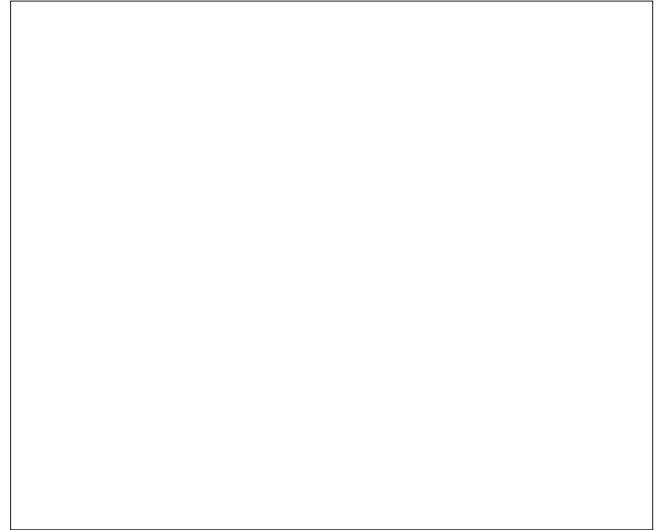


Fig. 2. Chest X-ray showing alveolar infiltrates involving the lower and mid-zones of both lung fields on day 5 of hospitalisation.

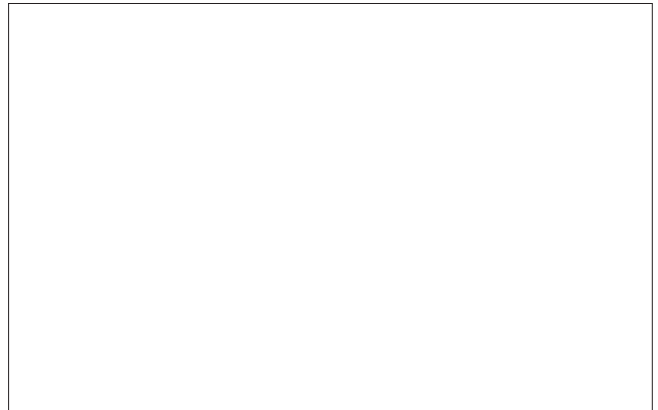


Fig. 3. Septated hyphae of *Aspergillus* spp. branching at acute angles. Original magnification $\times 400$.

Blood for bacterial and fungal cultures were negative. Human immunodeficiency virus (HIV) serology was negative and CD4/CD8 performed after institution of steroids showed a reversal of CD4/CD8 ratio of 0.8 with a decreased absolute CD4 cell count of $16.6/\text{mm}^3$.

Intravenous amphotericin was started with concurrent haemofiltration as he developed acute renal failure from septic shock. He died on the 9th day of hospitalisation from severe acidosis and ventilatory failure with an arterial blood gas on 100% oxygen of pH 6.73, pCO_2 221 mmHg and pO_2 124 mmHg. No post-mortem examination was conducted according to religious beliefs.

Discussion

Aspergillus can behave in the human respiratory tract as a saprophyte, an allergen or an infectious agent depending on the host immune status.¹⁻³ We describe a case of bronchial aspergillosis which we postulate to have arisen from

endobronchial saprophytic colonisation, due to previous tuberculous infection, and presenting with overlap features of hypersensitivity syndrome and obstructing bronchial aspergillosis (OBA).

Our patient was a life-long non-smoker with no previous history of asthma or chronic bronchitis. Therefore, the initial presentation fitted well with the diagnosis of tropical pulmonary eosinophilia viz. eosinophilia, raised Ig E (>10,000 IU/ml) and positive microfilarial serology. However, the lack of response to diethylcarbamazine instituted upon hospitalisation ruled out the diagnosis.^{5,6}

The diagnosis of allergic bronchopulmonary aspergillosis (ABPA) was entertained but serum for *Aspergillus* antibodies, skin prick test and CT scan of the thorax were not organised due to rapid decline of his clinical state. The clinical presentation and course were, however, not typical of ABPA. Firstly, it is commonly associated with asthma based on the published case series from England,^{7,8} Australia,^{9,10} India,^{11,12} and North America.^{13,14} Secondly, corticosteroid therapy should ameliorate symptoms and hasten the resolution of radiographic infiltrates.^{15,16} Our patient was stable for 4 days while on oral prednisolone but deteriorated subsequently despite intravenous steroids. Thirdly, his initial chest X-ray did not show proximal bronchiectasis or other features of ABPA.

Mucoid impaction of the bronchi noted on bronchoscopy is thought to overlap with ABPA³ but the opacities on chest X-ray usually involve the upper lobes,¹⁷ whereas our patient had opacities in the lower lobes (Fig. 2).

Denning et al⁴ reported 3 cases of HIV-positive patients with OBA, a new clinical entity characterised by mucoid impaction and predominant lower lobe involvement. It may represent a stage before recognisable invasive pulmonary aspergillosis occurs. In these patients, there was no history of asthma or chronic bronchitis and there were no pathological features of ABPA or bronchocentric granulomatosis at post-mortem. Two patients responded to itraconazole but 1 died of disseminated aspergillosis while on intravenous amphotericin. To date, there are no reports of OBA in HIV-negative patients.

In conclusion, *Aspergillus* tracheobronchitis like OBA should be considered in a patient with features of ABPA but is not improving despite high dose corticosteroid therapy. The finding of *Aspergillus* in the sputum, on many occasions, of an immunocompetent patient represents saprophytic colonisation, making the differentiation between pathogen and commensal difficult. Thus, culture and histologic examination of the bronchoscopically

identified tracheobronchial mucus plugs and necrotic material should be performed as early treatment may be life-saving.¹⁸

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