Emphysema and Bronchiectasis Secondary to Alpha-1 Antitrypsin Deficiency

Ahmed Fahim1, Rachel Wilmot2 and Simon Paul Hart1

Abstract
A 47-year-old Caucasian male presented to the chest clinic with a 4-week history of exertional dyspnea. A chest radiograph showed mild hyperinflation without any focal pathology and spirometry showed a mild obstructive defect. In view of symptoms being disproportionate to spirometric and radiologic abnormalities, a thoracic CT scan was obtained. It revealed that there was evidence of bronchiectasis and mild emphysema in basal distribution. Subsequently, he was confirmed to have severe α1-Antitrypsin deficiency. This case illustrates the importance of considering α1-Antitrypsin deficiency in patients with combination of emphysema and bronchiectasis in a basal distribution. Although basal emphysema is well-recognized pulmonary manifestation of α1-Antitrypsin deficiency, it is extremely unusual to have bronchiectasis with very mild degree of emphysema.

Key words: Alpha-1 Antitrypsin deficiency, Bronchiectasis, Emphysema.

Introduction
Alpha-1 Antitrypsin deficiency is a multisystem genetic disorder that predisposes to emphysema and liver disease. It is inherited in an autosomal co-dominant pattern and has a frequency of 1 in 1500 – 3500 in Europe.1 The pulmonary parenchymal damage is the result of proteolytic enzyme release by migrating neutrophils. The diagnosis is frequently delayed in smoking individuals with symptoms being attributed to smoking related emphysema. The most common respiratory manifestation of this disorder is emphysema in a basal distribution. Moreover, bronchiectasis may be evident in association with emphysematous destruction.2

This case illustrates the importance of considering the diagnosis of α1-Antitrypsin deficiency in a non-smoker with a combination of bronchiectasis and emphysema in a basal distribution.

Case Report
A 47-year-old man presented with recent onset of exertional dyspnea with limitation of exercise tolerance to 300 yards. He denied any cough, chest pain or syncope. He was previously fit and well and had completed a half-marathon 2 years previously. There was no history of childhood respiratory infections, previous pneumonia or tuberculosis. He had never smoked. There was no significant family history and he was not taking any regular medications. His physical examination was unremarkable. Pulmonary function tests showed mild airflow obstruction with forced expiratory volume in 1 second (FEV1) of 75% predicted with slightly increased TLC (total lung capacity) and RV (residual volume). The gas transfer evaluation was within normal limits. Moreover, there was no significant reversibility following nebulized bronchodilator. A chest radiograph showed mild hyperinflation but no focal pathology. A CT scan of thorax (Figure 1) showed bilateral basal bronchiectasis (arrows) and associated emphysematous changes affecting the lung bases. In view of basal distribution of emphysema, the possibility of α1-Antitrypsin (AAT) deficiency was considered. The serum level of α1-Antitrypsin was 0.2 g/L (reference range 1.1 – 2.1 g/L) consistent with severe α1-Antitrypsin (AAT) deficiency. Further analysis of phenotyping using

Figure 1: CT thorax showing bronchiectasis affecting the lung bases (arrows) with associated mild emphysematous changes.

1 Department of Cardiovascular and Respiratory Studies, Castle Hill Hospital, Cottingham, UK.
2 Department of Biochemistry, Hull Royal Infirmary, UK.

Correspondence: Dr Ahmed Fahim, Division of Cardiovascular and Respiratory Studies, Castle Hill Hospital, Castle Road, Cottingham, HU16 1JQ, United Kingdom. E-mail: ahmedfahim@doctors.org.uk

Received August 02, 2010; accepted June 11, 2012.
isoelectric focusing identified it as PiZZ phenotype. Coincidentally and of note, there was evidence of an absent $\alpha$ peak on serum protein electrophoresis (Figure 2). As the patient had fairly preserved lung function with a normal gas transfer, he was not considered suitable for augmentation therapy and had no specific treatment for AAT deficiency. However, he was treated for concomitant bronchiectasis with inhaled bronchodilators and clinical monitoring in respiratory outpatient every 6 months.

**DISCUSSION**

$\alpha_1$-Antitrypsin is a serine protease inhibitor (serpin), inhibiting a variety of proteases including elastase. There have been at least 100 alleles of $\alpha_1$-Antitrypsin identified. $\alpha_1$-Antitrypsin deficiency was first recognised in 1963 in Sweden when it was incidentally discovered by the observation of absence of A1 band on protein electrophoresis of a patient. Since then, it is well recognised that AAT deficiency is associated with chronic obstructive pulmonary disease, in particular emphysema, but airway involvement in AAT deficient patients has not been described to a great extent. In a study of 202 patients, Cuvelier and colleagues concluded that bronchiectasis is likely to be secondary to emphysema rather than implication of AAT genes. This case is unusual as the degree of emphysema does not explain the bronchiectatic changes and we believe that AAT deficiency is the most likely explanation for this patient’s bronchiectasis rather than emphysema per se. Furthermore, the presence of bronchiectasis in AAT deficiency is likely to be under-recognized as suggested by a recent study of 74 patients with AAT deficiency, which showed a high prevalence of radiologically detectable bronchiectasis in 95% of cases, although clinically significant bronchiectasis was observed in only 27% of patients.

This case illustrates the important association of emphysema and bronchiectasis in a patient with $\alpha_1$-Antitrypsin (AAT) deficiency. AAT deficiency should be suspected in a breathless patient with basal distribution of emphysema or bronchiectasis specially if there is no significant smoking history. Furthermore, this case also emphasizes the value of thoracic CT scan, if there is discrepancy in the intensity of symptoms and degree of spirometric abnormality. Observational studies have suggested that mortality may be reduced in patients with augmentation therapy; and it restores the deficiency to normal with amelioration of disease progression. However, the augmentation therapy is not a uniformly recommended treatment in view of lack of robust randomised trial evidence and cost implications.

**Acknowledgement:** We are grateful to Mr. R. Hoole (Immunology Department, Hull Royal Infirmary) for providing Figure 2.

**REFERENCES**