

A CASE OF α_1 -ANTITRYPSIN DEFICIENCY IN AN 81-YEAR OLD LIFE TIME NON SMOKER – ARE OTHER FACTORS INVOLVED?

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INTRODUCTION

- α_1 -antitrypsin deficiency is a rare cause of emphysema.
- Most patients often present in the third or fourth decade of life leading to early death.
- We report the details of an 81-year-old man who has emphysema secondary to α_1 -antitrypsin deficiency.
- He first presented with symptoms of dyspnoea at age 74, had a radiographic diagnosis of emphysema at age 76 and is still alive at age 81.

CASE REPORT

- A 74-year-old man was first seen on March 1997 with symptoms of moderate shortness of breath on exertion.
- There was a previous history of left renal calculus, diverticular disease and pneumonia two years earlier.
- He had worked as an engineer in a timber mill and had no known exposure to environmental toxins.
- He is a life-long non-smoker and a non-drinker.
- His mother was a non-smoker who also suffered from emphysema.
- A chest radiograph in 1999 showed hyperinflated lungs (figure 1) and a subsequent thoracic CT scan (figure 2) showed emphysema that was thought to be mainly concentrated in the 'upper lobes'.
- A ventilation/perfusion scan (figures 3 a and b) showed patchy distribution of tracer with marked central airways deposition and the tracer distribution to the right lower lobe was conspicuously worse than other areas of the lungs suggesting lower lobe involvement.
- A gated cardiac blood pool scan showed normal resting left ventricular systolic function.
- Spirometry demonstrated an FEV₁ of 0.42 L (predicted 3.24) and FVC of 0.75 L (predicted 4.15).
- Detailed respiratory function testing showed a TLC of 7.79 L (predicted 6.40 \pm 0.91), an RV of 4.17 L (predicted 2.47 \pm 0.39), an FEV₁ of 0.92 L (predicted 2.46 \pm 0.50), a VC of 3.62 L (predicted 3.66 \pm 0.58), a DL_{CO} of 9.41 (predicted 23.82 \pm 4.84) and a K_{CO} of 1.88 (predicted 3.89 \pm 0.73).
- Blood gases on room air revealed a pH of 7.49, pCO₂ of 36.0 mm Hg, pO₂ of 71.0 mm Hg, HCO₃ of 27.0 mmol, base excess of 5.0 mmol and oxygen saturation of 95 percent.
- With a background family history of emphysema and being a non-smoker, α_1 -antitrypsin deficiency was suspected.
- The α_1 -antitrypsin level on two occasions was 0.4 g/L and 0.3 g/L (phenotype Pi ZZ, normal 0.8 to 2.0 g/L).
- He was later diagnosed to have diabetes mellitus and was evaluated for lung volume reduction surgery in 2000 but he was deemed unsuitable due to the lower lobe predominant disease.
- He was then referred for pulmonary rehabilitation program.
- By 2004, he remained relatively well although his exercise tolerance was limited to small distances around the house and garden.

• A repeat α_1 -antitrypsin level on March 2004 was 0.2 g/L (Pi ZZ phenotype).

• Serial spirometry from 1999 to 2003 showed FEV₁ of 0.88 L (1999), 0.78 L (2000), 0.68 L (2001), 0.70 L (2002) and 0.65 L (2003).



Figure 1 – chest X-ray showing hyperinflated lungs



Figure 2 – Thoracic CT scan showing emphysema

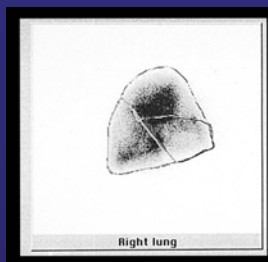


Figure 3 (a) showing perfusion scan of the right lung

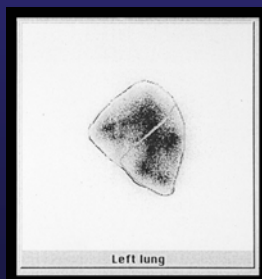


Figure 3 (b) showing perfusion scan of the left lung

DISCUSSION

• α_1 -antitrypsin deficiency is associated with clinical symptoms and diseases in several organs such as the lungs, liver, pancreas and kidneys. It is a protein that is synthesised in the liver and is secreted into the plasma. From the plasma, it diffuses into various body compartments including the lungs where it inhibits proteolytic enzymes such as trypsin, chymotrypsin and leucocyte elastase. Recent data however have shown that α_1 -antitrypsin is also locally produced on the epithelial surface of the lungs.

• Laurell and Ericksson first demonstrated in 1963 the close association between α_1 -antitrypsin deficiency and pulmonary emphysema. If not inactivated by α_1 -antitrypsin, leucocyte elastase destroys lung connective tissue particularly elastin leading to the development of emphysema. Severe α_1 -antitrypsin deficiency is characterised by a reduced serum α_1 -antitrypsin level to about 20% of the normal level.

• Several alleles associated with α_1 -antitrypsin exist including MM, ZZ, Znull, MZ, Mnull and SZ. Severely α_1 -antitrypsin deficient individuals including Pi ZZ, Pi Z null and Pi null-null are at the highest risk of developing emphysema. Pi ZZ, Pi Z null and Pi SZ are associated with very low or low serum level of α_1 -antitrypsin whereas Pi MM is associated with normal serum level of α_1 -antitrypsin. Pi MZ and Pi M null are associated with intermediate serum level of α_1 -antitrypsin.

• α_1 -antitrypsin deficiency normally leads to an earlier onset of emphysema (third or fourth decade) and can often occur in non-smokers or appears out of proportion to smoking history. The typical pattern shows lower zone predominance although the emphysema may affect all zones. However, our patient first presented in his seventh decade of life and he is a life long non-smoker.

• Our patient is not the oldest reported person ever to present or survive with Pi ZZ α_1 -antitrypsin deficiency. From large series, including α_1 -antitrypsin registries in several countries, there are a few octogenarians, although almost all of these seem to be women. In a British case series, an 82-year-old man never smoker had Pi ZZ α_1 -antitrypsin deficiency. In a New Zealand series (n=69, all Pi ZZ), there were 5 female septuagenarians, 2 female octogenarians and 1 male septuagenarian.

• Cigarette smoking is a well documented additive risk factor for emphysema development. It has been suggested that other genetic and/or environmental factors may predispose to emphysema.

• In a Swedish study of 225 non-smoking Pi ZZ individuals, it was found that lung function declined after the age of 50 years and men were at greater risk of lung function deterioration than women. Asthmatic symptoms and occupational exposure to airway irritants appear to constitute additional risk factors.

• Therefore, our patient is one of the oldest reported persons to survive with Pi ZZ α_1 -antitrypsin deficiency.

