Case Report

Near normalization of spirometry in a subject with severe emphysema complicated by amiodarone lung

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Introduction

Emphysema and interstitial lung disease produce opposing effects on lung volumes and spirometry (1). This makes lung function difficult to interpret vis-à-vis the severity of either condition. While this conundrum is familiar to respiratory clinicians, there is little literature on the subject. We report a patient with severe stable emphysema (forced expiratory volume in 1 sec, FEV₁ 40–50% predicted) whose spirometry approached normal when his condition was complicated by amiodarone pulmonary toxicity.

Case Report

A retired male farmer born in 1920 has had diagnosed emphysema for many years. He stopped smoking (40 pack-years) in 1976 at the time of an inferior wall myocardial infarction. Exertional dyspnoea progressed until he presented in 1991 with marked reduction in exercise tolerance (75–100 m or one flight of stairs), little cough or sputum, severe fixed airflow obstruction (FEV₁ 1.01 l, 45% of predicted), resting oxygen saturation 88% and a chest radiograph showing hyperinflation, vascular deficiency with numerous bullae and cardiomegaly. He had no clinical findings of cardiac failure. He was reluctant to consider prednisone; a trial of beclomethasone dipropionate 500 µg b.d. resulted in a slight non-significant and unsustained improvement in FEV₁ (1.19 l) and oxygen saturation (90%). FEV₁ declined slowly over 4 years (Table 1) with slowly decreasing exercise tolerance. In 1994, home oxygen was started following an infective exacerbation leading to hospitalization.

In October 1995, life-threatening ventricular tachycardia with hypotension developed. After stabilization with medical treatment, amiodarone was prescribed 200 mg 5 days a week. Cardiac catheterization revealed a left ventricular aneurysm, 80% stenosis of the LAD artery and complete stenosis of the right coronary artery. Furosemide and potassium were added in 1995 and lisinopril in 1996. Over 27 months, exercise tolerance was stable (50–75 m), SaO₂ was stable (92–3% on 2 l O₂ min⁻¹), and FEV₁ was slightly improved (Table 1). In January 1998, a non-life-threatening wide complex tachycardia (heart rate 140) resolved promptly with intravenous lidocaine. Amiodarone was increased to 200 mg daily (a 40% increase in total dose).

Progressive worsening of exertional dyspnoea led to hospitalization in April 1998, at which time oxygen saturation on supplemental oxygen had fallen to 88% (arterial blood gas). Lung function showed an approximately 30% increase in FEV₁ and a significant decrease in carbon monoxide diffusing capacity. Chest radiograph showed patchy, mixed interstitial and airspace disease most marked bilaterally in the mid- to upper lung zones. There was also parenchymal scarring, architectural distortion and a moderate decrease in lung volume. These findings were gradually progressive since the introduction of amiodarone therapy in October 1995, but were acutely worse since the most recent radiograph of January 1998 prior to increase in the amiodarone dose. Left ventricular failure was excluded clinically with no clinical response to diuretic therapy.

Amiodarone toxicity was suspected. The patient and his family were reluctant to discontinue amiodarone and also reluctant to consider either prednisone therapy or an implantable defibrillator. One month later, he was extremely breathless, exercise tolerance was limited to 10 steps, the FEV₁ had further increased and the diffusing capacity had further decreased (Table 1). Chest radiograph now showed the above-mentioned changes plus ground-glass opacification in the left lower lobe suggesting an acute alveolitis.
TABLE 1. Lung function

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</thead>
<tbody>
<tr>
<td>FEV₁ (l)</td>
<td>1.02–1.19</td>
<td>0.83–0.98</td>
<td>0.78–1.15</td>
<td>1.16</td>
<td>1.47</td>
<td>1.70</td>
<td>1.99</td>
<td>1.68</td>
</tr>
<tr>
<td>(% pred)</td>
<td>(51)</td>
<td>(65)</td>
<td>(76)</td>
<td>(88)</td>
<td>(75)</td>
<td>(48)</td>
<td>(30)</td>
<td></td>
</tr>
<tr>
<td>FEF₂₅–₇₅% (l s⁻¹)</td>
<td>0.33–0.37</td>
<td>0.17–0.26</td>
<td>0.21–0.36</td>
<td>0.35</td>
<td>0.57</td>
<td>0.94</td>
<td>1.01</td>
<td>0.62</td>
</tr>
<tr>
<td>(% pred)</td>
<td>(17)</td>
<td>(27)</td>
<td>(45)</td>
<td>(48)</td>
<td>(30)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVC (l)</td>
<td>2.40–2.90</td>
<td>2.49–2.93</td>
<td>2.36–3.32</td>
<td>2.88</td>
<td>2.79</td>
<td>2.57</td>
<td>3.19</td>
<td>3.15</td>
</tr>
<tr>
<td>(% pred)</td>
<td>(83)</td>
<td>(81)</td>
<td>(75)</td>
<td>(92)</td>
<td>(92)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>TLC (l)</td>
<td>n.d.</td>
<td>5.7</td>
<td>4.8</td>
<td>n.d.</td>
<td>5.1</td>
<td>3.7</td>
<td>5.1</td>
<td>5.5</td>
</tr>
<tr>
<td>(% pred)</td>
<td>(97)</td>
<td>(73)</td>
<td>(97)</td>
<td>(107)</td>
<td></td>
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<tr>
<td>DLCO (ml min⁻¹ mm Hg⁻¹)</td>
<td>n.d.</td>
<td>5.9–6.5</td>
<td>6.0–7.0</td>
<td>n.d.</td>
<td>4.4</td>
<td>3.4</td>
<td>6.3</td>
<td>5.2</td>
</tr>
<tr>
<td>Amiodarone (mg) week⁻¹</td>
<td>0</td>
<td>0</td>
<td>1000</td>
<td>1400</td>
<td>1400</td>
<td>0</td>
<td>0</td>
<td>Start Nov. 1995 Stop</td>
</tr>
<tr>
<td>Prednisone (mg) day⁻¹</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>30</td>
<td>5</td>
<td>Start</td>
</tr>
</tbody>
</table>

n.d. not determined.

Amiodarone was discontinued, prednisone 30 mg per day started, and exercise tolerance returned to baseline in a few days. When reviewed 18 days later, his spirometry had nearly normalized (FEV₁ 88% predicted), diffusing capacity had returned to baseline and the computerized axial tomographic scan showed extensive centrilobular emphysema and marked bullous disease, findings consistent with emphysema. In addition, there was moderate parenchymal scarring and architectural distortion throughout both lungs, as well as left basilar ground-glass pacification and some interlobular septal thickening (Fig. 1). Although non-specific, these findings can be seen with amiodarone-induced pulmonary toxicity. Incidentally, no evidence of amiodarone deposition within the liver was noted.

Recurrent life-threatening ventricular tachycardia led to prescription of sotalol and mexilitine. When seen in follow-up 2 months later, prednisone had been tapered to 5 mg per day, exercise tolerance remained stable and the FEV₁ had begun to decline. Post-bronchodilator spirometry, nitrogen wash-out TLC, single breath DLoCO, and doses of amiodarone and prednisone are shown in Table 1. Selected maximal expiratory flow volume curves are shown in Fig. 2.

**Discussion**

This patient has a presumptive diagnosis of amiodarone toxicity complicating his severe chronic emphysema. The interstitial process was associated with marked increase in exercise limitation, a further reduction in his diffusing capacity and an almost doubling of his FEV₁ from severely reduced to within the normal range. This is an unusual situation and, to our knowledge, has not been prospectively reported.

It is appreciated that emphysema and interstitial lung disease have opposite physiological effects on lung volumes and flow rates (1). Airflow obstruction in chronic airflow limitation is due to diffuse narrowing of small airways or emphysematous loss of elastic recoil, or more often to a combination of both. Hyperinflation (increases in TLC, FRC and RV) develops secondary to airflow obstruction and may be particularly marked when emphysema/loss or recoil is prominent. By contrast, interstitial lung disease leads to increased elastic recoil with an increased FEV₁ to FVC ratio and small lung volumes. The diffusing capacity is typically reduced in both conditions; in emphysema because of reduced total surface area of alveolar capillary membrane and in interstitial disease because of increased thickness of the membrane. It seems likely that our patient suffered mainly from loss of elastic recoil (emphysema) which reversed, approaching normal, with the superimposition of amiodarone toxicity. This was associated with a severe reduction of the already low DLoCO and marked exacerbation of breathlessness. Lung compliance (pressure-volume) curves would have been of interest in further elucidating the physiology. It is likely that the wash-out technique underestimated lung volumes compared to whole body plethysmography however, it is the policy in our laboratory to standardize techniques within a patient so as to make serial studies more comparable.

The role of prednisone in the FEV₁ improvement is uncertain. The FEV₁ had improved to 76% predicted in (May 1998) prior to instituting prednisone and discontinuing amiodarone (Table 1). There was a further improvement 18 days later (to 88% predicted). This additional improvement may have been in whole or in part a corticosteroid response, probably within the airways as we would expect corticosteroid improvement of the interstitial...
Fig. 1 Computerized axial tomographic thin slice (1 mm) cut through upper lungs showing the marked bullous emphysema and 'ground glass' interstitial changes (see text).

Fig. 2. Selected maximum expiratory flow-volume curves with flow (l sec⁻¹) on the vertical axis and volume (l) on the horizontal axis.

disease should reduce elastic recoil and therefore reduce FEV₁. Two recent studies stress the difficulties in evaluation of subjects with cryptogenic fibrosing alveolitis when there is concomitant chronic airflow limitation/emphysema (2,3). When emphysema and cryptogenic fibrosing alveolitis are present together, lung volumes tend to be preserved (2,3) and flow rates (FEV₁:FVC ratio) were less likely to be
elevated as expected in pulmonary fibrosis (2,3). The value of high resolution computerized tomography in assessing for the presence of magnitude of interstitial disease has been noted (3). In our patient, the advanced emphysema made it difficult to appreciate significant interstitial disease on the chest radiograph, even though it was suspected. The high resolution computerized tomographic scan proved very helpful in documenting the ground-glass interstitial pattern. The computerized tomographic scan was performed 18 days after amiodarone was stopped and prednisone commenced, at a time when the patient was clinically much improved, and we suspect therefore that the changes observed may already have been improving.

In summary, we present the case of a man with severe emphysematous chronic airflow limitation complicated by at least moderately severe interstitial lung disease, probably amiodarone toxicity, whose FEV₁ and FEV₁/FVC ratio improved to the normal range from a severely obstructed pattern.

Acknowledgements

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References