Severe pulmonary hypertension reversed by antibiotics in a patient with Whipple’s disease

H Riemer, R Hainz, Ch Stain, G Dekan, M Feldner-Busztin, P Schenk, Ch Müller, K Sertl, O C Burghuber

Abstract
The case is described of a 58 year old man with systemic Whipple’s disease with pericardial and pleural effusions and severe pulmonary hypertension. After three months of antibiotic treatment there was a complete resolution, not only of the symptoms known to be associated with Whipple’s disease (diarrhoea, arthralgia, pericardial and pleural effusions), but also of pulmonary hypertension.

Keywords: Whipple’s disease, pulmonary hypertension, pleural effusion, pericardial effusion, Tropheryma whippelii.

Whipple’s disease is characterised by weight loss, diarrhoea, arthralgia, and abdominal pain. Although the main manifestation of this disease is gastrointestinal, it is a systemic disorder and pulmonary involvement is a frequent but not well known finding. A chronic nonproductive cough, dyspnoea, and pleuritic chest pain have been reported more often than pleural effusion and nodular shadowing. Pulmonary hypertension associated with Whipple’s disease has been reported previously in only two cases. We describe a case of systemic Whipple’s disease with pericardial and pleural effusions and severe pulmonary hypertension in a 58 year old man in whom the pulmonary hypertension resolved completely after antibiotic therapy.

Case report
A 58 year old man was admitted with pericardial and pleural effusions and pulmonary hypertension of unknown origin. Three month before admission he had complained of diarrhoea and reported 6–10 bulky stools per day, a weight loss of 10 kg, progressive dyspnoea, and a dry cough. Physical examination showed a cachectic man (172 cm, 57.5 kg) with brownish hyperpigmentation. Cardiac examination revealed a very low probability of pulmonary embolism, since a small matched defect in the posterior basal area of the right lung was seen corresponding to the small amount of pleural fluid.

Tests for antinuclear antibodies and their subsets, rheumatoid factor and antineutrophil cytoplasmatic antibodies were negative as were all tests for HIV and other viral diseases.
Table 1  Pulmonary function variables (before and three months after starting antibiotic therapy)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before</th>
<th>Absolute</th>
<th>% predicted</th>
<th>After</th>
<th>Absolute</th>
<th>% predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC (l)</td>
<td>5.08</td>
<td>88%</td>
<td></td>
<td>5.60</td>
<td>91%</td>
<td></td>
</tr>
<tr>
<td>VC (l)</td>
<td>2.40</td>
<td>56%</td>
<td></td>
<td>3.37</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>FEV₁ (l)</td>
<td>1.50</td>
<td>44%</td>
<td></td>
<td>2.11</td>
<td>61%</td>
<td></td>
</tr>
<tr>
<td>FEV₁%/VC</td>
<td>78%</td>
<td></td>
<td></td>
<td>78%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TLCO</td>
<td>3.91</td>
<td>43%</td>
<td></td>
<td>5.89</td>
<td>65%</td>
<td></td>
</tr>
</tbody>
</table>

TLC = total lung capacity; VC = vital capacity; FEV₁ = forced expiratory volume in one second; FEV₁%/VC = forced expiratory volume in one second as percentage of vital capacity; TLCO = carbon monoxide transfer factor.

Table 2  Blood gas analysis (before and three months after starting antibiotic therapy)

<table>
<thead>
<tr>
<th>Blood gas</th>
<th>Rest Before</th>
<th>Rest After</th>
<th>Exercise Before</th>
<th>Exercise After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pao₂ (mmHg)</td>
<td>77</td>
<td>89</td>
<td>68</td>
<td>93</td>
</tr>
<tr>
<td>Paco₂ (mmHg)</td>
<td>37</td>
<td>32</td>
<td>28</td>
<td>37</td>
</tr>
<tr>
<td>A-aDo₂ (mmHg)</td>
<td>33</td>
<td>15</td>
<td>46</td>
<td>12</td>
</tr>
</tbody>
</table>

Pao₂ = arterial oxygen tension; Paco₂ = arterial carbon dioxide tension, A-aDo₂ = alveolar-arterial difference in Pao₂. 1 kPa = 7.5 mmHg.

After the diagnosis of Whipple's disease had been established, antibiotic therapy was started with penicillin G and gentamicin intravenously for 10 days followed by trimethoprim and sulphamethoxazole orally twice daily for one year. After beginning antibiotic treatment the diarrhoea resolved completely, the general condition of the patient improved, he started to gain weight, and the laboratory haematological values became normal. Three months after starting antibiotic therapy gastroduodenoscopic examination showed a markedly improved duodenal mucosa and increased jejunal folds. A biopsy sample of the duodenal tissue showed fewer PAS positive macrophages than at the initial examination.

A CT scan of the chest revealed complete resolution of the bilateral pleural effusions, the ground glass opacities, and the thickening of the interlobular and intralobular septa. Trans-thoracic echocardiography showed a right ventricle and atrium of normal size with no pericardial effusion. The maximum velocity of the tricuspid regurgitant jet was 2.2 m/s, indicating a pulmonary artery pressure within normal limits.

The pulmonary function data at that time showed that the total lung capacity and the carbon monoxide transfer factor per lung area were normal (table 1). Blood gas analysis revealed normoxaemia at rest and during exercise (table 2).

Discussion

Although involvement of the lung as a site of this disease was reported in Whipple's first description in 1907, it is now known that the lung and the pleura may be affected both before and after the development of diarrhoea.

The finding of severe pulmonary hypertension in Whipple's disease, however, has been reported in only two cases in the literature, in one as a result of severe aortic insufficiency and in the other by chronic progressive aortic regurgitation. Endocarditis, caused by Tropheryma whippelii, was thought to be the cause. Evidence of pericardial and endocardial involvement in Whipple's disease has been reported previously. In our patient involvement of the pericardium was evident because of the pericardial effusion.

The pulmonary function parameters demonstrated a slight restrictive ventilatory pattern and a reduced carbon monoxide transfer factor, possibly caused by the small amounts of bilateral pleural effusions and the thickening of the alveolocapillary membrane as shown by HRCT scanning. Both the small bilateral pleural effusions and the thickening of the interlobular and intralobular septa caused only mild functional impairment and cannot explain the severity of this pulmonary hypertension.

The strongest evidence for a causal relationship between Whipple's disease and pulmonary hypertension in our patient, however, was the resolution of the pulmonary hypertension after antibiotic therapy. It is therefore reasonable to assume that pulmonary vascular involvement by Tropheryma whippelii was the cause of pulmonary hypertension in this case.

7 Müller CH, Stain CH, Burghuber O. Tropheryma whippelii in peripheral blood mononuclear cells and cells of pleural effusions. Lancet 1993;341:701.
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