Respiratory Medicine (1995) **89,** 387–389

Platypnoea-orthodeoxia in cryptogenic fibrosing alveolitis

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Introduction

Platypnoea and orthodeoxia are terms used to describe the rare phenomena of dyspnoea and hypoxaemia accentuated by the upright posture and relieved by recumbency (1–3). We report these features in a patient with cryptogenic fibrosing alveolitis and review the differential diagnosis.

Case Report

A 64-year-old woman presented with a 5-month history of progressive dyspnoea. In the month before admission to hospital, she had experienced platypnoea, such that she was having difficulty sitting upright to eat. She had had diabetes for 3 yr for which she was taking chlorpropamide. She had smoked 5 cigarettes daily until 20 yr previously. She had no digital clubbing but auscultation of her chest revealed bilateral basal crackles. Chest radiograph showed interstitial reticulo-nodular shadowing, particularly affecting the lower lung fields (Fig. 1). Pulmonary function tests showed a vital capacity of 0·65 l and a FEV_1, of 0·6 l. In the supine position, PaO_2 was 5·3 kPa, $PaCO_2$ 4·2 kPa and O_2 saturation 81% while breathing room air; after breathing 100% oxygen PaO_2 was 45·9 kPa and $PaCO_2$ was 4·2 kPa giving an estimated shunt of 16%. She was unable to maintain the upright posture long enough for the shunt measurement to be repeated in that position. On changing from the supine to the upright posture, her O_2 saturation fell from 93% to 86% (breathing 35% oxygen), respiratory rate rose from 26 to 46 breaths min^{-1}, pulse rate from 110 to 127 beats min^{-1} and blood pressure remained constant at 140/70 mmHg. Perfusion lung scans were performed after injection of technetium-99m labelled macro-aggregated albumin with the patient in the supine and upright positions. As expected, there was greater perfusion of the lung bases in the upright position but there was no early systemic accumulation of the isotope suggesting that there was no anatomical right-to-left venoarterial communication. Echocardiography and electrocardiogram were normal. Transbronchial biopsies from the right lower lobe showed advanced fibrosis consistent with a diagnosis of cryptogenic fibrosing alveolitis. She was treated with prednisolone 60 mg daily but continued to deteriorate and died 1 month later.

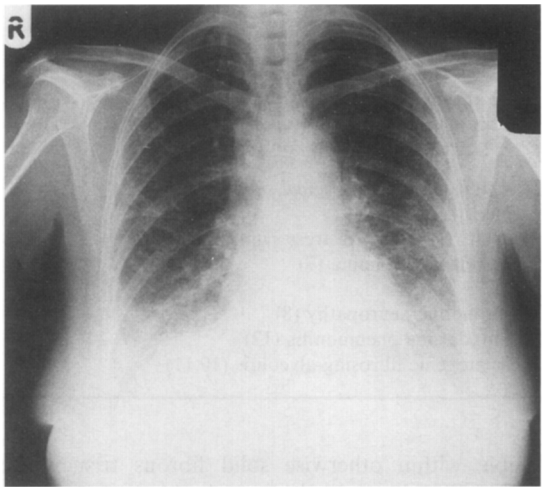

Fig. 1 Chest radiograph showing basal interstitial shadowing.

Autopsy examination confirmed severe diffuse pulmonary fibrosis which involved virtually the whole of both lower lobes and the lower half of both upper lobes.

Histologically, there was interstitial fibrosis of the pattern seen in 'usual interstitial pneumonitis'. (Fig. 2). However, both lungs predominantly showed intra-alveolar fibrosis consisting of granulation tissue wholly or partially filling alveoli, with capillaries

Received 14 February 1994 and accepted in revised form 10 November 1994.

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0954-6111/95/050387+03 $08.00/0

Table 1 The differential diagnosis of platypnoea–orthodeoxia

Diagnosis	Postulated Mechanism
Intraplumonary, intracardiac or pulmonary physiological shunts	Gravitational effect of upright posture on blood flow and thoracic mechanics
Intrapulmonary anatomical shunts	
Pulmonary arteriovenous malformation (1)	Increased flow through basal shunts
Hepatic cirrhosis (2)	Increased shunting through basal pulmonary spider naevi
Intracardiac shunts (3,4)	
Lung disease with patent foramen ovale	Mechanical distortion of fossa ovalis
– pneumonectomy	with 'streaming' of blood
– lobectomy	
— pulmonary embolism	Pressure gradient across shunt due to fall in systemic blood pressure or increased pulmonary vascular resistance
Atrial septal defect	Increased gradient across shunt in upright position
Tetralogy of Fallot	
Intrapulmonary physiological shunt	
Emphysema (5)	Increased dead space ventilation
Adult respiratory distress syndrome (6)	Increased dead space ventilation
Bronchial carcinoma (7)	Intermittent postural compression of bronchial artery by tumour
Autonomic neuropathy (8)	Loss of orthostatic cardiovascular reflexes
Amiodarone pneumonitis (12)	Increase shunting through basal
Cryptogenic fibrosing alveolitis (10,11)	fibrosis in upright position

visible within otherwise solid fibrous tissue. The pulmonary arteries were normal without features of pulmonary hypertension and there was no evidence of an anatomical intrapulmonary or intracardiac venoarterial communication.

O_2 saturation was measured by oximetry in the supine and upright positions in a further 10 patients with advanced cryptogenic fibrosing alveolitis who were being considered for lung transplantation. None of these patients showed evidence of platypnoea–orthodeoxia.

Discussion

Platynoea–orthodeoxia has been described most frequently in situations where shunting of blood occurs from right to left through an intracardiac shunt, an anatomical intrapulmonary shunt or a physiological shunt in diseased lungs. It seems that a specific combination of anatomical circumstances is necessary for the flow of blood through the shunt to increase in the upright position due to gravitational effects (Table 1).

Several different mechanisms of gravitationally dependent intrapulmonary physiological shunting have been described. Altman and Robin (5) described platypnoea–orthodeoxia in a patient with emphysema and suggested that the upright posture resulted in a fall in pulmonary artery pressure to the upper parts of the lung such that the increased alveolar pressure caused compression of small pulmonary capillaries, resulting in ventilated but under-perfused areas in the upper zones of the lung (5). A similar mechanism was postulated to explain orthodeoxia in a patient recovering from adult respiratory distress syndrome with basal post-pneumonic pneumatoceles (6). Gacad *et al.* reported platypnoea–orthodeoxia in a patient with carcinoma obstructing the left main bronchus (7). Here it was suggested that the tumour compressed the pulmonary artery in the supine position but that this compression was relieved in the upright position resulting in shunting of blood through a perfused but non-ventilated lung. Loss of cardiovascular reflex responses was thought to account for orthostatic ventilation–perfusion mismatch in a patient with autonomic neuropathy (8).

There have been only rare reports of platypnoea–orthodeoxia in patients with cryptogenic fibrosing alveolitis (9,10). Our patient showed a rapid dramatic fall in oxygen saturation without a fall in blood pressure on assuming the upright position. The pulmonary fibrosis was predominantly basal and

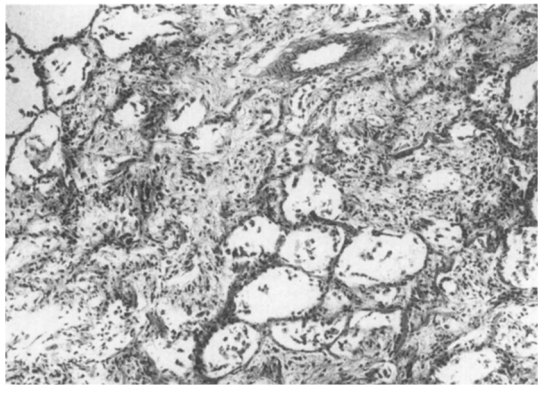

Fig. 2 Lung histology showing interstitial and intra-alveolar fibrosis.

perfusion scans in the supine and upright positions showed the expected gravitationally increased blood flow to the bases in the upright posture but without any evidence of a true anatomical right to left shunt. An orthostatic increase in physiological shunting through the basal pulmonary fibrosis is the likely explanation for the findings in this patient. It was noteworthy that intra-alveolar fibrosis, although a well recognized pattern of tissue involvement in cryptogenic fibrosing alveolitis (11), was much more prominent than usual and was found in sections from both lungs. It may be that persistence of capillaries within these areas contributed to the non-aerated vascular bed within the lungs and played a part in causing orthodeoxia.

This conclusion is similar to that reached by Tenholder *et al.* (9) in two patients with cryptogenic fibrosing alveolitis and platypnoea–orthodeoxia. The exact mechanism of the physiological shunt is unclear but it is suggested that in severe fibrosis, the air spaces may be so far separated from the pulmonary vasculature as to seriously impair diffusion of oxygen. The gravitational effect of the upright posture presumably aggravates the problem by increasing blood flow through this physiological shunt. However, it is likely that other factors are involved since other patients with apparently similar basal fibrosis do not manifest this phenomenon. It is noteworthy that despite chronic hypoxaemia our patient did not have clinical or pathological evidence of pulmonary hypertension. Similarly, pulmonary artery pressure was normal in the two patients reported by Tenholder *et al.* (9). The development of pulmonary hypertension in response to hypoxaemia is an adaptive mechanism which reduces the extent of ventilation–perfusion mismatching and which would be expected to increase perfusion to the upper zones in the upright posture. Failure of the vasoconstrictor response to hypoxaemia may therefore be an important factor contributing to the occurrence of platypnoea–orthodeoxia in some patients with cryptogenic fibrosing alveolitis.

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