CASE REPORT

Pneumocystis carinii pneumonia with pleurisy, platypnoea and orthodeoxia

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We present a patient who collapsed with chest pain and dyspnoea on a transatlantic flight. She was found to have *Pneumocystis carinii* pneumonia (PCP) and human immunodeficiency virus infection. Platypnoea and orthodeoxia, which have not been previously reported in association with PCP, were major features of her illness. The PCP predominantly affected her lung bases and it is likely that gravity increased intrapulmonary blood flow through poorly ventilated lung bases with failure of pulmonary vasoconstriction to increase upper zone perfusion, exacerbating desaturation on sitting up. The partial DNA sequence of the infecting *P. carinii* was identical to previously described isolates.

CASE HISTORY

A 45 year old white housewife collapsed on a transatlantic flight with sudden onset retrosternal pleuritic chest pain, severe dyspnoea, and a cough which was unproductive apart from one haemoptysis. She had never smoked and had spent the preceding 6 months visiting relatives in northeastern USA where, over the previous 4 months, she had developed wheeze, mild dyspnoea, and worsening intermittent pleuritic retrosternal chest pain aggravated by sitting forward.

On arrival in hospital she was apyrexial but in respiratory distress when sitting up, partially relieved by lying flat. She was normotensive but tachycardic. Her jugular venous pressure was not visible, the heart sounds were normal with bibasal lung crepitations. A chest radiograph showed poor expansion but no focal abnormality. An electrocardiogram demonstrated sinus rhythm with a normal axis but the S₁Q₃T₃ pattern. Arterial blood gas measurements when supine on 24% oxygen by face mask yielded pH 7.45, Pco₂ 4.2 kPa, Po₂ 6.2 kPa, with an oxygen saturation of 85%.

A clinical diagnosis of pulmonary embolism was made and she was treated with intravenous heparin and oxygen. A supine radionuclide scan did not show any perfusion defects. However, 12 hours after admission she underwent supine pulmonary angiography because of worsening hypoxaemia which showed no evidence for acute pulmonary thromboembolic disease. There were, however, widespread minor fine filling defects with occasional distal occlusions in the right lower zone and similar changes in the left upper zone suggestive of old pulmonary emboli. The transthoracic echocardiogram was normal. Computed tomographic scanning showed a very coarse ground glass appearance at the lung bases with linear elements extending to the pleura.

The diagnosis was therefore revised to viral or atypical pneumonia, including *Pneumocystis carinii* pneumonia, or a rapidly progressive alveolitis. On further questioning she had

no history of blood transfusions or intravenous drug use but one of her sexual partners had been bisexual. Examination revealed no stigmata of human immunodeficiency virus (HIV) infection. She was treated with high dose intravenous co-trimoxazole, prednisolone 60 mg once a day, and low molecular weight heparin.

An HIV ELISA was positive with a total lymphocyte count of $0.67 \times 10^9/l$ (CD4 cells $0.16 \times 10^9/l$). Investigations gave no evidence for bacterial or viral co-infection. As she was too unwell to withstand a bronchoscopy but no aetiological diagnosis had been made, sputum was induced uneventfully using hypertonic saline on days 7 and 15. The samples were negative for acid-fast bacilli and inadequate for silver staining. Polymerase chain reaction (PCR) for *Pneumocystis carinii* using the oligonucleotide primers pAZ102-H and pAZ102-E designed to a portion of the gene encoding the mitochondrial large subunit ribosomal RNA (rRNA)¹ was strongly positive for both samples.

Sitting up was associated with great respiratory distress (platypnoea) and was consistently coupled with a fall in her oxygen saturation (orthodeoxia). On day 11 she deteriorated with fever and hypoxia and died on day 31 despite treatment with clindamycin, methylprednisolone, atovaquone and empirical ganciclovir, *Mycobacterium tuberculosis* therapy, foscarnet, itraconazole, and ventilation.

At necropsy large numbers of *P. carinii* cysts were identified throughout the alveoli of both lungs by methanamine silver staining. There was mild chronic inflammation of the pleura but no organisms were identified in the pleura or other organs. No evidence for pulmonary emboli, ARDS, or deep venous thrombosis was found. The DNA extracted from the induced sputum sample was amplified using primers designed to the internal transcribed spacer regions of the *P. carinii* nuclear rRNA operon.² The DNA sequence was identical to one of the previously described sequences (B₁d).

DISCUSSION

The PCR technique allowed the diagnosis of *P. carinii* pneumonia in a situation difficult for conventional methods. The *P. carinii* DNA detected might have been derived from the oropharynx rather than from the lungs, and throat samples instead of induced sputum might have sufficed.³ Dyspnoea and oxygen desaturation exacerbated by sitting upright—platypnoea and orthodeoxia, respectively—were the patient's most striking clinical features. They have not been previously reported in association with PCP. Investigations gave no evidence that previously reported causes of this syndrome—particularly intracardiac or intrapulmonary anatomical shunts, pericardial effusions, or constriction or emphysema—were responsible.^{4–7}

The initial diagnosis of acute pulmonary emboli was suggested by the history of sudden collapse with dyspnoea, chest pain, and haemoptysis on a flight with arterial hypoxia and electrocardiographic S₁Q₃T₃ without any evidence for sepsis. The S₁Q₃T₃ pattern is a well known associate of pulmonary

*Deceased

emboli with very low sensitivity (16%) but high specificity (93%).⁸ Pulmonary angiography suggested that she had had pulmonary emboli, probably before the presenting illness. The absence of significant large emboli on pulmonary angiography some 16 hours after collapse, with continuation of her symptoms and signs for 31 days, argues against emboli being the main cause of the patient's pleurisy and platypnoea.

Platypnoea and orthodeoxia probably arose as gravity increased intrapulmonary blood flow shunting through poorly ventilated damaged lung bases, with failure of pulmonary vasoconstriction to increase upper zone perfusion exacerbating dyspnoea and desaturation while sitting up.⁴⁻⁷ Indeed, the computed tomographic scan suggested that the lung bases were predominantly affected by the PCP. The analysis of two different genetic loci suggested that the isolate of *P carinii* infecting this patient was not substantially different from previously described isolates, despite the atypical clinical presentation.

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