

Short reports

Granulomatous *Pneumocystis carinii* pneumonia in a patient with the acquired immunodeficiency syndrome

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Abstract

A patient with an unusual granulomatous response to infection with *Pneumocystis carinii* is described. The diagnosis was made by open lung biopsy after two negative bronchoalveolar lavages.

Pneumocystis carinii pneumonia is the most common opportunist lung infection in patients who have AIDS. Radiographically it most commonly presents as perihilar "ground glass" or reticulonodular opacities that may progress to more diffuse lung disease,¹ though there are several reports of atypical appearances, including a normal chest radiograph, lobar or segmental changes, cavitation, pleural effusions and hilar or mediastinal lymphadenopathy. We describe a case in which nodular shadowing seen on a chest radiograph and thoracic computed tomogram was found to be due to focal granulomatous *Pneumocystis carinii* infection. The patient was receiving treatment with nebulised pentamidine and zidovudine, treatments that may have modified the intrapulmonary response to pneumocystis infection.

Case report

A 45 year old white homosexual man presented with a 10 day history of increasing exertional dyspnoea, an unproductive cough, and fever with night sweats. Four months previously he had presented with pneumocystis pneumonia, diagnosed by bronchoscopy and bronchoalveolar lavage. At that time cutaneous lesions of Kaposi's sarcoma had been noted on the trunk, face, and palate; a test for antibodies to HIV-1 gave a positive result. He had been treated with daily nebulised pentamidine at a dose of 8 mg/kg a day via a Respigard II nebuliser for 21 days. With this regimen he had made a rapid clinical recovery and the chest radiograph and arterial blood gas tensions had returned to normal. After this episode he was started on zidovudine 250 mg four times daily and began

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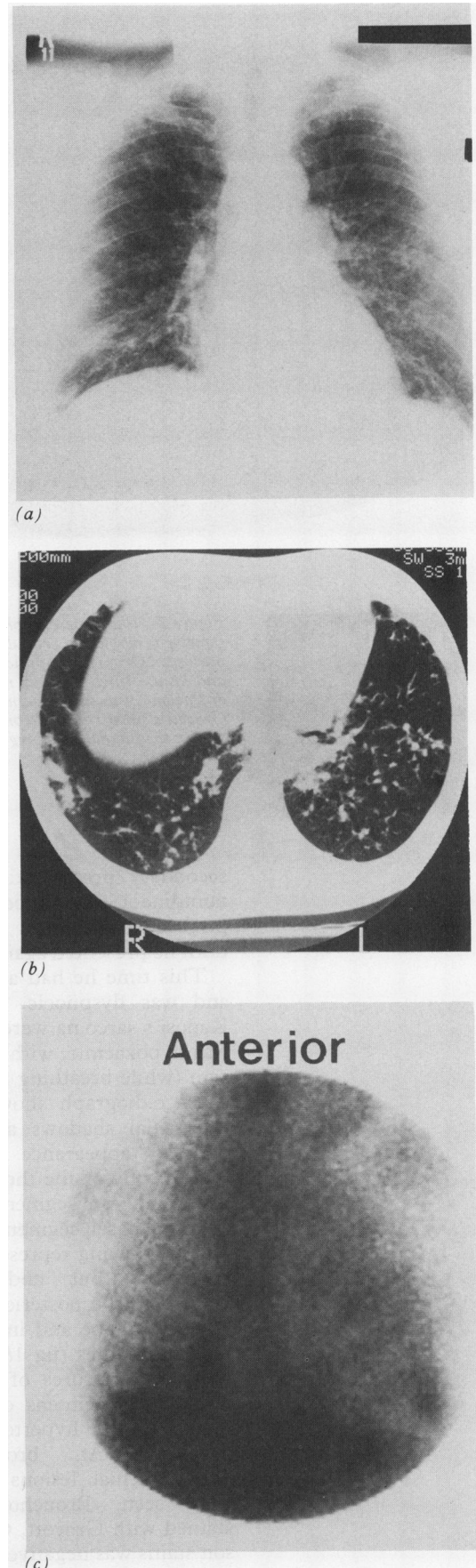


Figure 1 (a) Chest radiograph showing bilateral interstitial shadowing; some areas have a nodular appearance. (b) Computed tomogram of a section through the lower lobes, showing bilateral nodular opacities and subpleural consolidation in the right lung. (c) Gallium-67 citrate scan showing patchy focal uptake of tracer; increased uptake is seen in the lingula, the periphery of the left lower lobe, and the right lower lobe.

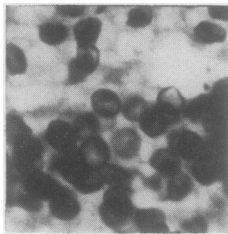
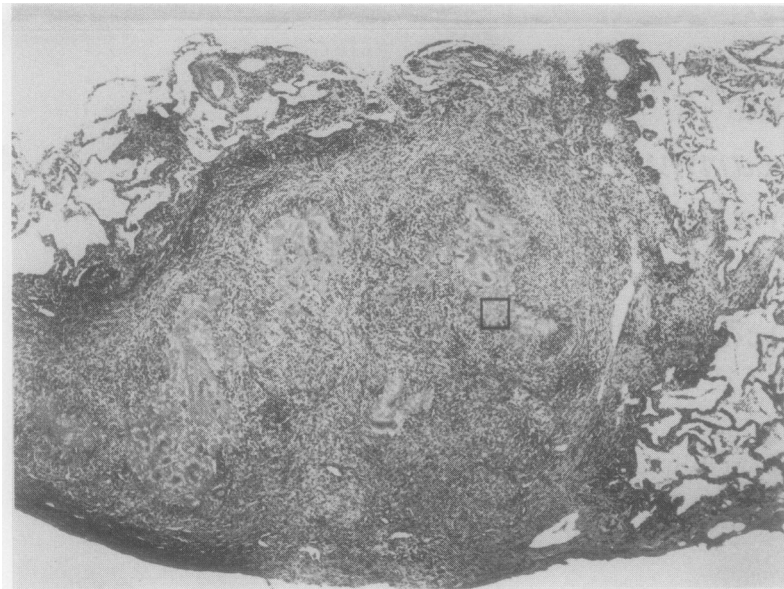


Figure 2 Photomicrograph of open lung biopsy specimen showing a subpleural granuloma with central areas of necrosis. (Original magnification $\times 20$; haematoxylin and eosin.) Inset (original magnification $\times 400$): Cysts of *Pneumocystis carinii* seen within an area of necrosis. Grocott's silver stain. No pneumocystis organisms were seen in the surrounding lung parenchyma.

secondary prophylaxis with nebulised pentamidine 150 mg once a fortnight via a Respirgard II nebuliser. He then remained well until he presented again.

This time he had a temperature of 38.9°C and was dyspnoeic. Many new lesions of Kaposi's sarcoma were noted on the skin. He was hypoxaemic, with an arterial oxygen tension (while breathing room air) of 9.1 kPa . A chest radiograph showed extensive bilateral interstitial shadows and some areas had a nodular appearance (fig 1a). Computed tomography of the thorax showed shadowing in the anterior segments of both upper lobes and the basal segments of the lower lobes. The shadowing represented non-specific consolidation, but nodular infiltration was present in the posterior basal segment of the left upper lobe and in the basal segments of the lower lobes (fig 1b). Multiple blood cultures and cultures of stool and urine were negative. Specimens of sputum induced by inhalation of hypertonic saline were also negative. At bronchoscopy multiple endobronchial lesions of Kaposi's sarcoma were seen. Bronchoalveolar lavage fluid stained with Grocott, Gram, and Zeihl-Neelson stains was negative for bacteria, mycobacteria, and *P. carinii*, and no organisms were isolated from cultures. The patient remained unwell with persistent symptoms and hypoxaemia. Repeat fiberoptic bronchoscopy 10 days later showed the same endobronchial appearances; no organisms were cultured from the lavage fluid. A gallium-67 citrate scan showed patchy focal uptake of tracer in

both lungs (fig 1c). In view of the two negative bronchoscopies and the abnormal gallium-67 citrate scan an open lung biopsy was performed. At operation the lung tissue appeared healthy, with no evidence of Kaposi's sarcoma on either the pleural or the cut surfaces of the lung, but there was a pale nodule 3 mm in diameter visible on the cut surface of one of the biopsy specimens. Microscopically the nodule and several smaller lesions were granulomas, composed of foamy histiocytes, which palisaded towards the centre around a series of irregular eosinophilic areas of apparent caseation necrosis. With Grocott's silver stain these areas were seen to contain numerous cysts of *P. carinii* (fig 2). No fungi or acid fast bacilli were seen. Outside the granulomas in the lung parenchyma there was an interstitial infiltrate of plasma cells and lymphocytes; the alveolar spaces did not contain *P. carinii* organisms. Kaposi's sarcoma was not detected in the biopsy specimens.

The patient made a rapid clinical and radiological recovery with intravenous high dose co-trimoxazole. Computed tomography at the end of three weeks of treatment showed disappearance of the discrete nodular shadows, though the areas of non-specific consolidation remained, which were attributed to Kaposi's sarcoma.

Discussion

This patient was thought to have pulmonary Kaposi's sarcoma on the basis of the extensive cutaneous and endobronchial lesions, together with the negative findings from laboratory analysis of bronchoalveolar lavage fluid obtained on two occasions. Intrapulmonary Kaposi's sarcoma may mimic pneumocystis pneumonia and patients may present with pulmonary infiltrates, hypoxaemia, and fever.² Gallium-67 scanning, performed because of persistent symptoms, showed patchy focal uptake. This led us to perform an open lung biopsy as lesions of Kaposi's sarcoma are not known to take up gallium-67 citrate.³ The evidence of intrapulmonary uptake argued against the diagnosis of Kaposi's sarcoma as the sole intrapulmonary pathological process and suggested either a concomitant infection or another cause of inflammation.³

The histological appearances of the open lung biopsy specimen are intriguing. Pneumocystis infection is normally characterised by an intra-alveolar foamy exudate, within which lie the pneumocystis organisms, and an associated mild interstitial pneumonitis. A granulomatous response to pneumocystis infection has been described in the lungs^{4,5} and at extrapulmonary sites⁶ of patients with AIDS. LeGovan described a case of disseminated granulomatous pneumocystis infection before the AIDS epidemic⁷ and Cruickshank reported a case of pulmonary granulomatous pneumocystosis that followed renal transplantation.⁸ Of the three HIV positive patients with pulmonary granulomatous pneumocystis infection, all were taking zidovudine and two were also

receiving nebulised pentamidine prophylaxis;^{4,5} all five HIV positive patients with disseminated extrapulmonary granulomatous pneumocystis infection were receiving both zidovudine and nebulised pentamidine. Possible mechanisms to explain the granulomatous response include an improvement in host defences due to treatment with zidovudine⁵ and a local toxic reaction to nebulised pentamidine; pentamidine isethionate dissolved in water for nebulisation is both acidic and hypo-osmolar.⁹ The pallisade of histiocytes presumably walls off the pneumocystis organisms, rendering them inaccessible during bronchoalveolar lavage and preventing nebulised pentamidine from having a therapeutic effect.

In conclusion, this case shows that a positive gallium-67 citrate scan in a patient with pulmonary Kaposi's sarcoma should prompt a search for an alternative infective or inflammatory pathological process and that pneumocystis infection may be associated with a granulomatous response, which may

possibly be induced by zidovudine or nebulised pentamidine.

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Bronchoalveolar lavage via a modified stomach tube in intubated patients with the acquired immunodeficiency syndrome and diffuse pneumonia

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Abstract

A simple non-bronchoscopic bronchoalveolar lavage method was used in 30 patients with the acquired immunodeficiency syndrome undergoing assisted ventilation for respiratory failure. A modified Argyle Levin stomach tube was passed via the endotracheal tube and lavage performed. The lavage was well tolerated and performed quickly and easily, required little training, and had a high degree of sensitivity (73%—a diagnosis in 22 of the 30 cases).

Pneumonia is a common complication in the acquired immunodeficiency syndrome (AIDS),¹⁻³ and is associated with a high morbidity and mortality. Early diagnosis and

aggressive treatment improve the outcome. *Pneumocystis carinii* is the most common pathogen diagnosed, but the differential diagnosis of diffuse pneumonia in the patient with AIDS is extensive and often more than one pathogen is present. Clinical features and chest radiographs are rarely diagnostic. Invasive procedures are being replaced by the less invasive diagnostic technique of fiberoptic bronchoscopy and bronchoalveolar lavage.³⁻⁸

The increasing incidence of AIDS calls for less expensive and less time consuming methods to obtain a diagnosis. We evaluated a non-bronchoscopic bronchoalveolar lavage technique in intubated patients with AIDS. Our aim was to find a simple, safe, and sensitive technique to diagnose pneumocystis pneumonia and other causes of diffuse pneumonia in these patients.

Methods

We studied 30 patients with diagnosed or suspected AIDS who developed diffuse pulmonary infiltrates and respiratory failure requiring assisted ventilation. None of the patients required positive end expiratory pressure. The study was approved by the hospital ethics committee and written consent was obtained from the patients.

Tracheal specimens were obtained by standard endotracheal suction.⁹ About 30 minutes before the procedure the inspired oxygen concentration (FIO₂) was increased to 1.0; other ventilator settings were unchanged. Arterial blood gases were measured. A 16 FR (5 mm external diameter), 48 cm Argyle Levin type stomach tube (Sherwood Medical, St Louis, Maryland) was cut proximal to the side ports to leave only a central opening at the distal tip. The tube was inserted into the endotracheal tube via a Portex (Sims Company, Wilming-

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