Case reports

A commentary on the following three case reports appears on pp 1164-5.

Partial resolution of acute interstitial pneumonia in native lung after single lung transplantation

Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College of Science, Technology and Medicine, London SW3 6LY, UK
D S Robinson

Department of Respiratory Medicine
D M Geddes

Department of Imaging
D M Hansell

Royal Brompton Hospital NHS Trust, London SW3 6NP, UK

Department of Respiratory Medicine, Queen Mary's Hospital, Sidcup NHS Trust, Kent, UK
C D Shee

Department of Histopathology
C Corbishley

Department of Transplantation
A Murday
B P Madden

St George's Hospital NHS Trust, London SW17 0RE, UK

Correspondence to:
Dr D S Robinson.

Received 3 May 1995
Returned to authors
26 July 1995
Revised version received
27 September 1995
Accepted for publication
3 October 1995

D S Robinson, D M Geddes,
D M Hansell, C D Shee, C Corbishley,
A Murday, B P Madden

Abstract

The case of a 49 year old man presenting with rapidly progressive interstitial lung disease is described. Radiological findings and the lung biopsy specimen were compatible with an acute interstitial pneumonia, as was the relentless clinical course culminating in hypoxic respiratory failure. After right single lung transplantation there was considerable improvement in lung function and radiographic clearing of disease in the native left lung.

(Thorax 1996;51:1158-1159)

Keywords: acute interstitial pneumonia, transplantation.

The label of Hamman-Rich syndrome has been applied to several interstitial lung diseases including idiopathic pulmonary fibrosis.¹ However, recent reviews have clarified that the acute syndrome as originally described² is distinct from idiopathic pulmonary fibrosis and represents an organising form of diffuse alveolar damage termed acute interstitial pneumonia.^{3,4} We present a case of acute interstitial pneumonia which failed to respond to high dose oral corticosteroids or cyclophosphamide, but showed unequivocal improvement in the remaining native lung following single lung transplantation for fulminant respiratory failure.

Case report

In January 1994 a 49 year old builder had a febrile illness with breathlessness on one flight of stairs and a cough productive of clear sputum. His sweats and joint symptoms settled but he was left with skin lesions and breathlessness. Examination in February 1994 revealed inspiratory crackles at both lung bases, and there was basal shadowing on a chest radiograph. He was treated with 50 mg of oral prednisolone daily which continued for two months. Despite this treatment, his symptoms progressed to breathlessness on dressing by mid March 1994. He had never smoked, had not been exposed to asbestos, and had no pets. Lung function values from March 1994 are shown in table 1 and the chest radiograph in fig 1. Laboratory investigations revealed normal blood count without eosinophilia, normal biochemistry including protein electrophoresis and creatinine clearance, normal immunoglobulin levels and subclasses, erythrocyte sedimentation rate of 17 mm/hour and C-reactive protein levels of 6 mg/l (normal range 0-10 mg/l). Serological tests for aspergillus, legionella, mycoplasma,

Figure 1 (A) Chest radiograph showing extensive peripheral and lower zone ground glass and confluent nodular shadowing with considerable loss of volume in the lower lobes. (B) Following right lung transplantation the native left lung appears normal; the right middle lobe is collapsed.

Table 1 Lung function before and after lung transplantation was performed on 1 July 1994

	Predicted	15 March 1994	3 August 1994	19 October 1994
FEV ₁ (ml)	3030	2020	2140	3050
FVC (ml)	3900	2110	2380	3610
TLC (ml)	5750	3180	4010	5060
RV (ml)	1850	1060	1610	1140
TLCO (mmol/min/kPa)	8.65	3.50	4.56	5.69
VA (ml)	5650	2440	4400	5100
Kco (mmol/min/kPa/l)	1.53	1.43	1.03	1.11

FEV₁=forced expiratory volume in one second; FVC=forced vital capacity; TLC=total lung capacity; RV=residual volume; TLCO=carbon monoxide transfer factor; VA=alveolar volume; Kco=carbon monoxide transfer coefficient.

influenza A and B, coxiella, chlamydiae, Epstein-Barr virus and cytomegalovirus were negative, as was the autoimmune profile (rheumatoid factor, antinuclear factor, dsDNA antibodies, immune complexes, pANCA and cANCA). The results of electrocardiography and echocardiography were normal. Arterial blood gas tensions were P_{aO_2} 7.69 kPa and P_{aCO_2} 4.65 kPa breathing air.

Because he had shown symptomatic progression on high dose steroids these were reduced to allow an open lung biopsy specimen to be taken which showed moderate interstitial inflammation, together with loose myxoid interstitial fibrosis with little well polymerised collagen. The alveolar walls were thickened and there was intra-alveolar organisation.

He continued to deteriorate and in April 1994 he was started on cyclophosphamide 150 mg daily and prednisolone 10 mg daily. However, by June he was short of breath on minimal exertion. His P_{aO_2} was 5.6 kPa and P_{aCO_2} was 4.5 kPa on air. His lymphocyte count was $0.1 \times 10^9/l$ compatible with the immunosuppressive treatment, but there was no culture or serological evidence of infection. The chest radiograph suggested progressive disease. His condition worsened rapidly to a point where his P_{aO_2} on 93% inspired oxygen was 6.5 kPa with P_{aCO_2} 4.51 kPa, and he therefore underwent right single lung transplantation. He made good postoperative progress. His immunosuppressive regimen was cyclosporin A 200 mg twice daily, azathioprine 125 mg daily, and prednisolone 15 mg daily. He was discharged from hospital on the 29th postoperative day and continued well at home six months later.

Histological examination of the explanted right lung showed florid, diffuse interstitial and intra-alveolar fibrosis. In some areas there was evidence of hyaline membrane formation. There was marked associated type II pneumocyte hyperplasia. Intra-alveolar macrophages were prominent, but there was little inflammatory infiltrate. No evidence of infection was seen and no granulomas were present. These appearances were consistent with an acute interstitial pneumonia.

Follow up showed a marked improvement in his lung function (table 1) and this was reflected in the chest radiograph (fig 1B) and computed tomographic (CT) scan which showed considerable resolution of the abnormalities previously seen in the native left lung.

Discussion

Pathologically, acute interstitial pneumonia is characterised by extensive alveolar damage with hyaline membrane formation in most cases, relatively uniform thickening of alveolar walls with oedema, fibroblast and type II pneumocyte proliferation, but relatively little fibrosis or inflammatory infiltrate.^{3,5,6} These findings are similar to those in diffuse alveolar damage seen in adult respiratory distress syndrome.⁵ The appearances on the CT scan have been reviewed and include diffuse ground-glass attenuation and air space shadowing in a pattern

similar to that seen in the adult respiratory distress syndrome.⁴ The pathology and radiology are thus distinct from chronic idiopathic pulmonary fibrosis. Olson *et al* reviewed the features of 29 cases of acute interstitial pneumonia.⁵ The mean age at presentation was 50 years, with both sexes affected equally. All had a prodromal illness with features of viral upper respiratory tract infection (as in this case), which had been present for a mean of 18 days. All developed respiratory failure requiring mechanical ventilation. Twelve (41%) survived after a mean hospital stay of 48 days. The pathology showed diffuse oedema and interstitial fibroblast and type II pneumocyte proliferation. This is similar to changes seen during the organising phase of diffuse alveolar damage which may result from a number of causes including oxygen therapy.⁶ As in the case described here, all patients reviewed had received oxygen before a biopsy specimen was taken so that oxygen toxicity could not be entirely excluded. However, similar changes were seen in the original Hamman and Rich cases described before the advent of oxygen therapy.

The patient described here showed a rather slower progression of his disease than the cases reviewed by Olson *et al*,⁵ although the deterioration over a period of 4–6 months is similar to the cases described by Hamman and Rich.¹

We cannot distinguish between a “bridging effect” allowing spontaneous improvement of the left lung and a potential beneficial effect from the immunosuppression used following transplantation. However, before transplantation there had been no response to cyclophosphamide and prednisolone in doses sufficient to reduce the lymphocyte count to $0.1 \times 10^9/l$. There are no data on the effects of azathioprine and cyclosporin in acute interstitial pneumonia, and trials in interstitial pulmonary fibrosis do not show a conclusive benefit.^{7,8}

In conclusion, we believe that this case demonstrates the first report of improvement in acute interstitial pneumonia in a native lung following single lung transplantation. It is important that this condition is recognised since the potential recovery rate is different from that of idiopathic pulmonary fibrosis and more aggressive supportive therapy may be beneficial in acute interstitial pneumonia.

- 1 Pratt DS, Schwartz MI, May JJ, Dreisen RB. Rapidly fatal pulmonary fibrosis: the accelerated variant of interstitial pneumonitis. *Thorax* 1979;34:587–93.
- 2 Hamman L, Rich AR. Acute diffuse interstitial fibrosis of the lungs. *Bull Johns Hopkins Hosp* 1944;74:177–212.
- 3 Katzenstein A-LA, Myers JL, Mazur MT. Acute interstitial pneumonia. *Am J Surg Pathol* 1986;10:256–67.
- 4 Primack SL, Hartman TE, Ikezoe J, Akira M, Sakatani M, Muller NL. Acute interstitial pneumonia: radiographic and CT findings in nine patients. *Radiology* 1993;188:817–20.
- 5 Olson J, Colby TV, Elliott CG. Hamman-Rich syndrome revisited. *Mayo Clin Proc* 1990;65:1538–48.
- 6 Askin FB. Back to the future: the Hamman-Rich syndrome and acute interstitial pneumonia. *Mayo Clin Proc* 1990;65:1624–5.
- 7 Raghu G, Depaso WJ, Cain K, Hammar P, Wetzel CE, Dreis DF, *et al*. Azathioprine combined with prednisone in the treatment of idiopathic pulmonary fibrosis: a prospective, double-blind, randomized, placebo-controlled clinical trial. *Am Rev Respir Dis* 1991;144:291–6.
- 8 Moolman JA, Bardin PG, Rossouw DJ, Joubert JR. Cyclosporin as a treatment for interstitial lung disease of unknown aetiology. *Thorax* 1991;46:592–5.