Case report

Acute systemic lupus erythematosus with fatal pneumonitis and disseminated intravascular coagulation

MIRIAM CHELLINGSWORTH AND DAVID G I SCOTT

From the Department of Rheumatology, Queen Elizabeth Hospital, Edgbaston, Birmingham B15 2TJ

SUMMARY We report the case of a 40-year-old female with acute onset of systemic lupus erythematosus, followed rapidly by the development of fatal pneumonitis and disseminated intravascular coagulation. The likely relationship between these events and the therapeutic options are discussed.

Key words: fibrosing alveolitis, pneumonitis, systemic lupus erythematosus, overlap syndromes, disseminated intravascular coagulation.

Acute pneumonitis is a rare complication of systemic lupus erythematosus (SLE). It may be a presenting feature of the disease and carries a poor prognosis.¹ Minor coagulation abnormalities are common in SLE, but severe disseminated intravascular coagulation (DIC) has rarely been reported.

We report a patient who died of acute lupus pneumonitis complicated by DIC. The likely relationship between these two events and the therapeutic options for such a problem are discussed.

Case history

A 40-year-old Indian woman presented in 1982 with a six-week history of symmetrical polyarthritis involving proximal interphalangeal joints, wrists, elbows, knees, and toes. She had a 3-year history of Raynaud's phenomenon but no history of alopecia, sun sensitivity, oral ulceration, serositis, renal, or central nervous system disease. Treatment included a variety of non-steroidal anti-inflammatory drugs.

Investigations showed haemoglobin 11.6 g/dl, leucocytes $4.9 \times 10^9/l$ (lymphocytes $0.54 \times 10^9/l$), ESR 34 mm/h; Rose-Waaler negative, antinuclear factor positive (titre 1/1600—speckled) precipitating antibody to nRNP positive; C3 1.24 g/l (normal); C4 0.11 g/l (low). Renal function tests and x-rays (including chest x-ray) were normal.

Five weeks later she was admitted as an emergency with a five-day history of increasing dyspnoea and a dry cough, unresponsive to amoxycillin. There was no history of recent foreign travel, exposure to dust, birds, or paraquat. On examination she was dyspnoeic at rest, cyanosed, pyrexial (38.2°C), and had a tachycardia (110/min). Widespread inspiratory crackles were noted in both lung fields, especially in the middle and lower zones. Chest x-ray showed bilateral mid zone alveolar mottling. Arterial blood gases while breathing air: Po_2 5.05 kPa, Pco_2 3.11 kPa. She was treated with oxygen and erythromycin with little initial improvement. Further investigations included fiberoptic bronchoscopy, which was normal, but alveolar washings and transbronchial lung biopsy showed changes consistent with desquamative interstitial pneumonitis (increased neutrophils in alveolar lavage and increased desquamation of macrophages into the alveolar spaces). There was no evidence of infection or of

Accepted for publication 10 July 1984.

Correspondence to Dr D G I Scott, Department of Rheumatology, Queen Elizabeth Hospital, Edgbaston, Birmingham B15 2TJ.

Table 1 Serial data showing the development of DIC. Coagulation tests

Day after admission	Prothrombin ratio (n=1·0)	Partial thromboplastin time (n=41 s)	Thrombin time (n=16 s)	Fibrinogen (n=1·5–4·0 g/l)	Fibrin degradation products (n<10 mg/l)	Platelets (n=150–400×10 ⁹ /l)
5	1·1	38	ND	ND	ND	313
7	1·2	49	20	1·42	115	124
10	1·3	45	19	1·05	140	95
11	1·4	64	36	0·57	240	24

ND=test not done.

interstitial fibrosis. Treatment was begun with hydrocortisone 200 mg 4 times daily.

Twenty-four hours after admission she was still severely hypoxic and dyspnoeic and was therefore electively intubated and ventilated. To obtain a satisfactory arterial oxygen pressure she required an inspired oxygen concentration of 70% and positive end-expiratory pressure (PEEP) of 8 cm of water. The steroid dosage was changed to 40 mg prednisolone twice daily with bolus doses of 1 g methylprednisolone on days 3, 4, and 7 after admission. Despite this her lung function did not alter significantly. During this period coagulation tests were performed serially and the results are shown in Table 1. On day 7 a diagnosis of DIC was made and fresh frozen plasma infusions were given on days 8 and 9. At no stage was there any clinical evidence of haemorrhage. Frequent examinations of tracheal aspirate, urine, faeces, and blood failed to show any evidence of infection.

During this time her lung disease assessed clinically and by serial blood gas estimations and x-rays remained static. Cyclophosphamide was given as a single dose of 500 mg and was associated with some improvement in lung function such that PEEP was discontinued. However, by day 11 her PaO_2 fell and there was further deterioration in coagulation. Despite further treatment with fresh frozen plasma her condition deteriorated and on day 12 she was noted to have fixed dilated pupils. An electroencephalogram showed no activity, and tests of brain stem function were negative. These were repeated after 24 hours and ventilation was discontinued.

POST-MORTEM FINDINGS

At necropsy there was evidence of a haemorrhagic tendency with petechiae on pleural surfaces and subendocardially, and blood stained pleural and pericardial effusions. Thromboses were widespread, visible to the naked eye in the superior vena cava and pelvic veins, and on microscopy in small vessels in the myocardium, lungs, kidney, spleen, brain, and bone marrow. Several organs contained

infarcts, including the myocardium, kidney, and spleen. The brain was diffusely swollen and almost entirely necrotic. There was no evidence of glomerulonephritis, but immunofluorescence of a frozen section showed glomerular deposition of IgG, A, M, and C3.

The lungs were consolidated and showed a mixture of fairly acute changes, with vascular thromboses and intra-alveolar haemorrhage and rather older changes. There was fibrous thickening of alveolar walls and polypoid intra-alveolar projections with hyperplastic granular pneumocytes and few giant cells. There were no granulomas, rheumatoid nodules, or significant inflammatory infiltrate, and there was no evidence of arteritis. Immunofluorescence of a frozen section showed periarterial deposition of immunoglobulin and complement.

These necropsy findings are consistent with the diagnoses of systemic lupus erythematosus, fibrosing alveolitis (of fairly recent onset), and widespread disseminated intravascular coagulation.

Discussion

A diagnosis of SLE was made before our patient's terminal illness on the basis of non-deforming polyarthritis, Raynaud's phenomenon, strongly positive antinuclear factor, lymphopenia, and hypocomplementaemia. Although DNA antibodies were negative and precipitating antibodies to nRNP were positive, our patient had no features of other connective tissue disease (scleroderma, polymyositis) to suggest an overlap syndrome, and none of the typical finger changes seen in mixed connective tissue disease (MCTD).² Antibodies to nRNP are no longer considered diagnostic of MCTD, and as found in many connective tissue diseases, the commonest being SLE.³

Acute interstitial pneumonitis was diagnosed in our patient by bronchoalveolar lavage and transbronchial biopsy. Infection and other causes of pneumonitis were excluded by the history, histology, persistently negative sputum cultures, cyto-

ogy, and failure to respond to cessation of all anti-inflammatory drugs or addition of corticosteroids. Acute interstitial pneumonitis is a rare complication of SLE, the largest series reporting 12 patients, six of whom died.³ Pneumonitis occurs more frequently in MCTD, but is usually responsive to corticosteroids. More severe cases, unresponsive to steroids, sometimes have pulmonary vasculitis, which was not present in our case.⁴

Disseminated intravascular coagulation was diagnosed in our patient on the basis of thrombocytopenia, prolonged prothrombin time, partial thromboplastin time and thrombin time, low fibrinogen, and the presence of fibrin degradation products. In addition our patient had widespread thrombosis at necropsy. Severe DIC is rare in SLE^{5,6} and has not been reported in MCTD. There has been recent interest in the role of the lupus anticoagulant in thrombosis in SLE.⁷ We did not specifically look for this in our patient's short illness, and it is possible that it played a part in the widespread thrombosis found post mortem. It is interesting that the renal histology and immunofluorescence were similar to those in the series of SLE patients with lupus anticoagulant described by Kant *et al.*⁸

DIC may be a primary cause of lung disease manifest as the adult respiratory distress syndrome.⁹ In our patient coagulation tests were normal at the onset of her illness, suggesting that DIC was a secondary event. DIC may also cause deterioration of lung function in severely ill patients by means of thrombosis in small pulmonary vessels, and it is likely that this was a major factor in our patient.

Effective therapy of acute pneumonitis in connective tissue diseases is not established. In a series of patients with interstitial pneumonitis survival depended on the initial degree of dyspnoea, age, cellular histology, and early response to steroid.¹⁰ The presence of a connective tissue disease did not affect the outcome. There are also occasional reports of benefit from azathioprine, cyclophosphamide, and penicillamine.^{11,12} Our clinical impression was that cyclophosphamide was beneficial for a short time and in similar cases a trial of cyclophos-

phamide in higher doses and earlier in the illness may be indicated.

This patient represents the most severe end of the connective tissue disease spectrum. It is important to realise that despite the absence of renal disease and the presence of nRNP (previously associated with a good prognosis) severe and fatal problems such as acute lupus pneumonitis and DIC can occur.

We are grateful to Professors O Wade and P A Bacon for their permission to report this case, to Dr A J Howie for the report on the necropsy, and to Professor K W Walton for the report on the immunofluorescence.

References

- Matthay R, Schwarz M, Petty T, *et al.* Pulmonary manifestations of SLE. Review of 12 cases of acute lupus pneumonitis. *Medicine (Baltimore)* 1974; **54**: 397-409.
- Sharp G, Irvin W S, Tan E, Gould R, Holman H. Mixed connective tissue disease—an apparently distinct rheumatic disease syndrome associated with a specific antibody to ENA. *Am J Med* 1972; **52**: 148-9.
- Field-Munves E, Schur P M. Antibodies to SM and RNP—prognosticators of disease involvement. *Arthritis Rheum* 1983; **26**: 848-53.
- Weiner-Kronish J P, Solinger A M, Warrock M L, Churg A, Ordonez N, Golden J A. Severe pulmonary involvement in mixed connective tissue disease. *Am Rev Resp Dis* 1981; **124**: 499-503.
- Beall C L, Pierce L E. Intravascular coagulation in acute lupus erythematosus. *JAMA* 1975; **234**: 518-9.
- McKay D G. Diseases of hypersensitivity—disseminated intravascular coagulation. *Arch Intern Med* 1965; **116**: 83-94.
- Boey M L, Colaco C B, Gharaii A E, Elkou K O, Loizous S, Hughes G R V. Thrombosis in systemic lupus erythematosus, striking association with the presence of circulating lupus anticoagulant. *Br Med J* 1980; **287**: 1021-3.
- Kant K S, Polla R V E, Weiss M A, Guieck H I, Miller H A, Hess E V. Glomerular thrombosis in SLE: prevalence and significance. *Medicine (Baltimore)* 1980; **60**: 71-86.
- Bone R, Francis P B, Pierce A. Intravascular coagulation associated with adult respiratory distress syndrome. *Am J Med* 1976; **61**: 585-9.
- Turner-Warwick M, Burrows B, Johnson A. Cryptogenic fibrosing alveolitis: response to corticosteroid therapy and its effect on survival. *Thorax* 1980; **35**: 593-9.
- Weese W C, Levine B W, Kazemi M. Interstitial lung disease resistant to corticosteroid therapy. Report of 3 cases treated with azathioprine or cyclophosphamide. *Chest* 1975; **67**: 57-60.
- Winterbauer R H, Hammar S P, Hallman K O, *et al.* Diffuse interstitial pneumonitis. Clinicopathological correlations in 20 patients treated with prednisolone/azathioprine. *Am J Med* 1978; **65**: 661-72.