

# Diffuse alveolar haemorrhage associated with progressive systemic sclerosis

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## Abstract

**A 41 year old man with an eight year history of progressive systemic sclerosis developed severe diffuse alveolar haemorrhage and died. The importance of diffuse alveolar haemorrhage as a rare but potentially serious complication of connective tissue disease should not be overlooked.**

Diffuse alveolar haemorrhage is defined as bleeding from the microvasculature into alveolar spaces of the lung.<sup>1</sup> It is a rare complication of collagen vascular diseases, usually systemic lupus erythematosus and systemic necrotising vasculitis.<sup>1-4</sup> We describe a case in a patient with systemic sclerosis.

## Case report

A 41 year old man, a former iron ore miner, was admitted to hospital in August 1987 with a four day history of influenza like symptoms. Progressive systemic sclerosis had been diagnosed in 1979, and since then his only medication has been prednisone 5 mg daily and penicillamine 500 mg daily. A chest radiograph showed a left lower lobe infiltrate. The white cell count was  $12.3 \times 10^9/l$  (neutrophils 84%); blood urea was 7.3 mmol/l and serum lactate dehydrogenase activity was raised at 234 IU/l.

The patient was treated for a lower respiratory tract infection. He appeared to improve initially but then developed small haemoptyses, which became larger over the next few days in association with breathlessness, cyanosis, and respiratory acidosis. His pulse rate was 110/min (regular) and blood pressure 140/80 mm Hg. Multiple ecchymoses developed on the face and trunk. A further chest radiograph showed extensive infiltrates in both lungs (fig 1). The white cell count was  $13.6 \times 10^9/l$  (neutrophils 93%), haemoglobin 12.9 g/dl, and platelet count  $399 \times 10^9/l$ ; the prothrombin time and activated partial thromboplastin time were normal.

Ten days after admission he developed a right pleural effusion. As the radiographic appearance suggested pulmonary embolism the patient was given 16 400 IU heparin over 11 hours. A sudden drop in the haemoglobin concentration, however, accompanied by severe respiratory distress necessitated transfusion and intubation, with aspiration of large

amounts of fresh blood and old blood clots. A left sided tension pneumothorax developed, from which 650 ml of fresh blood was drained. The blood urea increased to 27.5 mmol/l and creatinine rose to 173 mol/l with the development of haematuria and proteinuria. Antiglomerular basement membrane antibody studies gave negative results.

The patient's condition continued to deteriorate with profound acidosis (pH 7.24). He died 13 days after admission.

**Pathology** At necropsy widespread ecchymoses were present on the head, trunk, and extremities. The pleural cavities together contained 1500 ml fresh blood. The right lung weighed 1450 g and the left 1880 g. There was extensive extrapleural and parenchymal haemorrhage with pleural and parenchymal fibrosis and bilateral honeycomb changes in both lower lobes. A localised area of early pneumonia was present in the right middle lobe.

Microscopic examination showed diffuse alveolar haemorrhage and extensive capillaritis in the form of neutrophil infiltration within alveolar septa (fig 2). Occasional septa showed nuclear dust with foci of fibrinoid necrosis. Methods using immunofluorescence, peroxidase labelled antibodies to immunoglobulins, and electron microscopy failed to detect immune complexes within the alveolar septa. Other findings included interstitial fibrosis and multiple extensively calcified hyalinised silicotic nodules containing silica, haematite, and ferruginous bodies. Gram staining and culture gave negative results.

Typical changes of scleroderma were present in the skin, oesophagus, and colon. The skin contained a mild non-specific perivascular lymphocytic infiltrate with extravasation of red blood cells and ectatic blood vessels, consistent with scleroderma. No neutrophilic vasculitis was seen in the skin or any other organ with the exception of the

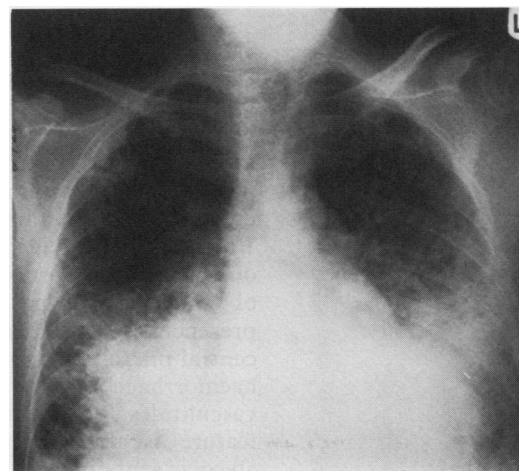


Figure 1 Chest radiograph showing infiltrates in the middle and lower lobes of the right lung with superimposed acute airspace disease in the mid zone; infiltrates are also present in the middle third of the left lung, and both lower lobes show bilateral honeycomb changes.

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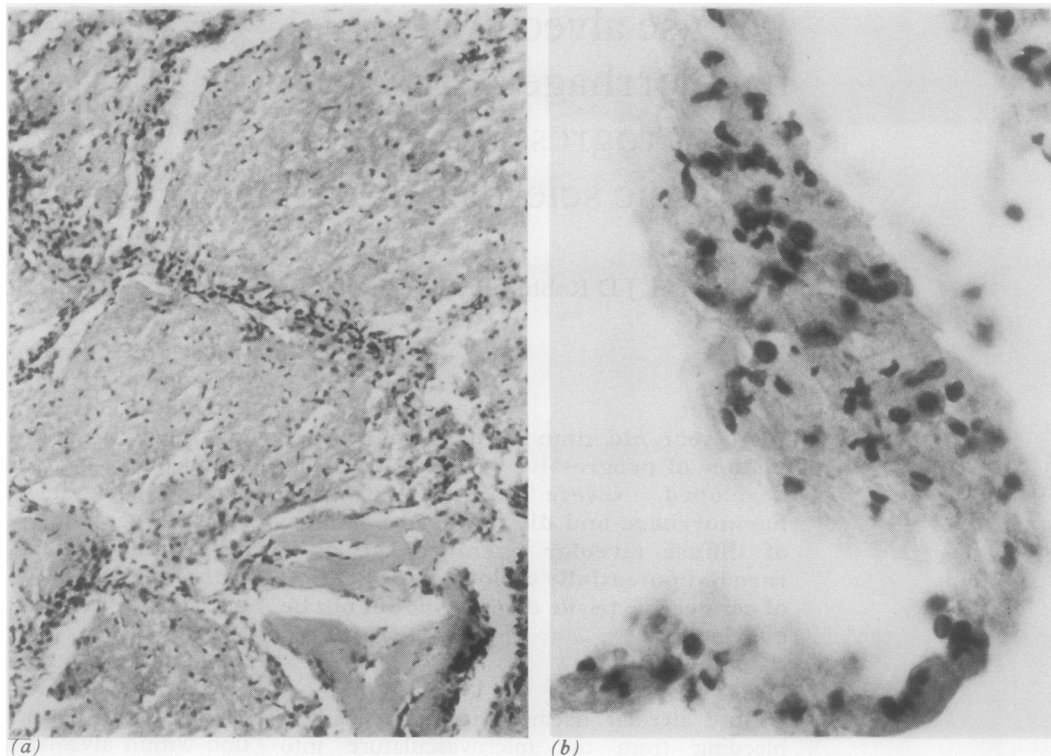
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**Figure 2** (a) Extensive alveolar haemorrhage. (b) Infiltrate of neutrophils within a thickened alveolar septum. (Haematoxylin and eosin.)



lung. The spleen showed pronounced perivascular and capsular fibrosis associated with crystals suggestive of silica and haematite.

No evidence of intravascular coagulation was found in any of the necropsy tissue sections examined.

### Discussion

Diffuse alveolar haemorrhage has seldom been described in systemic sclerosis, but a case was reported in a 48 year old man with a five year history of progressive systemic sclerosis who presented with haemoptysis.<sup>5</sup> An open lung biopsy showed diffuse haemorrhage, interstitial fibrosis, and thickening of arteries with no evidence of pneumoconiosis. This patient's haemoptysis responded to 40 mg prednisone daily and he remained well with 80 mg prednisone on alternate days.

The microscopic findings were similar in our case with the important additional features of capillaritis and foci of fibrinoid necrosis. These findings are similar to those described in a recent review of patients with pulmonary capillaritis and haemorrhage in association with systemic vasculitis.<sup>2</sup> Evidence of immune complex deposition was not found in our case. Immune complex deposition has been found in only a small proportion of the published cases of diffuse alveolar haemorrhage.<sup>2,6,7</sup> The presence of capillaritis therefore seems to be a central microscopic feature of diffuse alveolar haemorrhage arising from connective tissue vasculitides. The most suggestive microscopic feature is the presence of neutrophils in alveolar septa but not in alveolar spaces. The aetiology is unknown, though the presence of immune complexes in some published cases<sup>2,6,7</sup> suggests an abnormal immune response due to unknown stimuli. In our patient, the absence of renal glomerular disease argues against the

possibility of alveolar damage caused by penicillamine. The presenting respiratory infection may have induced an aberrant immune response. The presence of this infection was not, however, confirmed with positive cultures and the pulmonary haemorrhage could account for the vague respiratory symptoms. The absence of true vasculitis in any organ other than the lung does not support the presence of systemic vasculitis leading to haemorrhage. The diffuse alveolar haemorrhage in our patient is most likely to have arisen from his connective tissue disease, systemic sclerosis. Diffuse alveolar haemorrhage has not been described in cases of pneumoconiosis, though a more than chance association of the latter with systemic sclerosis has been documented.<sup>8</sup> It is important to recognise that diffuse alveolar haemorrhage may complicate systemic sclerosis as well as other collagen vascular diseases. The mortality is high but some cases respond to immunosuppressive treatment.<sup>1,2,5-7</sup>

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