Case report

Pulmonary haemorrhage, pulmonary infarction, and the lupus anticoagulant

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SUMMARY A patient with systemic lupus erythematosus developed pulmonary haemorrhage and pulmonary infarction as rare initial manifestations of her disease. The latter was associated with the presence of the circulating lupus anticoagulant. She recovered with pulse doses of methylprednisolone and plasmapheresis. Anticoagulants were not administered.

Key words: systemic lupus erythematosus.

Diffuse pulmonary haemorrhage is a serious complication of systemic lupus erythematosus (SLE) with a high mortality. The underlying histopathological changes have been reported to consist of a microangiitis in addition to alveolar haemorrhage.¹ Diagnosis has depended on recognising the clinical picture of haemoptysis, dyspnoea, and anaemia in association with alveolar infiltrates shown by chest x ray.² The finding of haemosiderin laden sputum macrophages is additional confirmation of alveolar haemorrhage. Treatment of this life threatening complication has comprised high dose steroids, including pulse methylprednisolone, cytotoxic chemotherapy, and plasmapheresis in combination with ventilatory and haemodynamic support.^{3,4}

The presence of the lupus anticoagulant in patients with SLE has been associated with an increased risk of thromboembolic phenomena, such as deep vein thrombosis and pulmonary embolism, etc. Numerous reports have confirmed the clinical importance of this autoantibody.

We report a patient with SLE who presented with pulmonary haemorrhage and pulmonary infarction as an initial manifestation of her illness. In addition, there was evidence of the presence of a circulating anticoagulant.

Case report

The patient, a 13 year old Malay schoolgirl, was admitted with a one month history of fever and vasculitic spots appearing at intervals over the limbs. One week before admission she developed arthritis of the left knee, after which the right knee and both elbows were affected. A few days before entry she became progressively more breathless.

The findings on admission were that of an ill, febrile individual with a vasculitic rash over the left elbow and a healed vasculitic infarct over the left shin. The blood pressure was 110/80 mmHg and there was a tachycardia of 136/min. A pleural rub was heard over the left lung. The abdomen was distended, but no tenderness or mass was present. There was arthritis of the left knee with limitation of extension. There was exquisite tenderness of the quadriceps and calf muscles.

The haemoglobin was 126 g/l, the total white cell count $3.2 \times 10^9/l$ platelet count $150 \times 10^9/l$, and erythrocyte sedimentation rate 87 mm in the first hour. The initial chest x ray showed a faint interstitial infiltrate, which progressed within the next three days to an alveolar infiltrate opacifying three quarters of both lungs (Fig. 1). At this point (fifth hospital day) the haemoglobin had also fallen to 64 g/l. The blood gas on room air showed an arterial oxygen pressure (Pao₂) of 9.96 kPa and an arterial carbon dioxide pressure (Paco₂) of 4.34 kPa. The oxygen saturation was 94.1%. The direct

Fig. 1a

Fig. 1b

Fig. 1 (a and b) Initial chest radiographs showing progressive alveolar, interstitial infiltrates of pulmonary haemorrhage.

Coombs' test was negative and the prothrombin time (PT) and partial thromboplastin time (PTT) were normal. The patient became hypotensive and required colloid and inotropic (dopamine) support. The abdominal x rays showed generalised ileus not accounted for by the serum urea and electrolytes, which were essentially normal except for prerenal increase of the urea to 32.84 mmol/l. The electrocardiogram showed sinus tachycardia. The serum creatine kinase and aldolase were markedly raised being 3310 U/l (normal range (NR) 38–164) and 54.6 U/l (NR 3–12) respectively. The antinuclear antibody test, double stranded DNA antibody test, the Venereal Disease Research Laboratory test, and LE cells were all negative. The serum complement was less than 10 units (NR 20–40) and the rheumatoid factor was positive (1/120). Anti-Sm antibodies were positive. She was diagnosed as having SLE with pulmonary haemorrhage, and treatment was started with intravenous hydrocortisone at doses of 800 mg/day. On the fourth hospital day she was put on mechanical ventilatory support because of worsening hypoxaemia and exhaustion. She was treated with pulse methylprednisolone 1 g daily for the next three days. Despite this, new vasculitic lesions appeared over the ankle, as well as subconjunctival haemorrhages. Plasmapheresis was carried out on the 6th, 10th, and 12th hospital days with 1.5 to 2 litre exchanges. Before plasma exchange the PT was 12 seconds (control 12.5 seconds) and PTT 48 seconds (control 26 seconds). The prolonged PTT was not corrected with the addition of normal plasma, showing evidence of the presence of a circulating inhibitor. Fibrin split products and fibrinogen levels were not assayed. On the sixth hospital day a wedge shaped opacity was noted over the right mid-zone on the chest film (Fig. 2). After

plasmapheresis she improved and was taken off ventilatory support on the 13th hospital day. Her chest radiographs also stabilised. Haemosiderin laden macrophages were seen on sputum examination.

Her subsequent hospital course was uneventful. She had weakness of the neck muscles and proximal muscles from myositis. The ileus of the intestines resolved. Chest x rays taken serially showed gradual resolution and healing of the area of pulmonary infarction. A ventilation perfusion lung scan with technetium (Tc-99m) carried out on the 35th hospital day showed reduced ventilation in the posterior and lateral basal segment regions of the right lung and a perfusion defect corresponding to the site of abnormal ventilation. The patient was discharged five weeks after admission and treatment was continued with 45 mg of prednisolone a day. Subsequent estimation of plasma for the lupus anticoagulant (kaolin clotting time) was negative but anticardiolipin antibody (enzyme linked immunosorbent assay (ELISA)) was present.

Discussion

Pulmonary haemorrhage has been reported as an infrequent but life threatening complication of SLE. A prevalence of 1.6% was reported in one series.⁵ It has occurred as both a complication and as an initial manifestation of lupus. The histopathological changes have comprised alveolar hemorrhage in most cases, though Myers reported the presence of a microangiitis.^{1 3 5-7} Immunofluorescence studies have shown predominantly IgG deposition in the alveolar septae.^{6 8 9}

The patient that we report presented with pulmonary haemorrhage and infarction as initial mani-

festations of her disease. The other manifestations were cutaneous vasculitis, polymyositis, and gut involvement (ileus). The presence of both pulmonary haemorrhage and infarction as initial manifesta-

tions of SLE is an unusual and rare occurrence. There has only been one previous report by Carette *et al* of a patient who had a pulmonary embolism preceding the development of pulmonary haemorrhage.¹⁰ This patient, however, developed pulmonary haemorrhage while receiving heparin anticoagulation treatment and had thrombocytopenia as well. In our patient the pulmonary haemorrhage was almost certainly due to the disease process itself. Contributory factors such as thrombocytopenia, cardiac failure, and uraemia were absent. The causes of pulmonary infarction in SLE are numerous, and they include local vessel wall abnormalities, the presence of the lupus anticoagulant (LA), and pulmonary vasculitis. Complete pulmonary infarction is uncommon owing to the presence of a dual circulation to the lungs. The radiological changes described have included wedge shaped infarcts as in our patient, the melting sign, and basal atelectasis with or without pleural effusion. Ventilation perfusion lung scans are both sensitive and specific in the diagnosis of pulmonary embolism.¹¹ It was not diagnostic in our patient, however, as it was performed a month after the onset of radiological changes.

Pulmonary infarction in association with pulmonary haemorrhage and the lupus anticoagulant has not been reported before. We believe that our patient had the LA as shown by the prolonged thromboplastin time, which was not corrected by the addition of normal plasma.¹² We believe that both the lupus anticoagulant and pulmonary vasculitis might have contributed to her pulmonary infarction. The lupus anticoagulant and anticardiolipin antibody are strongly associated with venous and arterial thrombosis.¹³⁻¹⁸ This has led to the suggestion of long term anticoagulation as a method of treatment for patients with these antibodies. The optimal treatment and length of treatment of patients with the LA is by no means settled, however. Patients do improve without treatment or with treatment that did not suppress the LA.¹² Anticoagulation treatment was withheld in our patient because of the continuing pulmonary haemorrhage. The LA disappeared when she was treated with plasmapheresis for pulmonary haemorrhage. Although we do not advocate plasmapheresis as another method of treatment for the LA, we believe that this patient did benefit from plasmapheresis for her life threatening disease.

Pulmonary haemorrhage is associated with a high mortality.^{3-7, 19} Aggressive treatment with pulse doses of methylprednisolone, cytotoxic drugs, and plasmapheresis has yielded variable results.³⁻⁷ The response of our patient to treatment is compatible with that of patients with pulmonary haemorrhage, who do respond to therapy. The results of treatment

Fig. 2a

Fig. 2b

Fig. 2 (a and b) Subsequent chest radiographs showing the wedge shaped area of pulmonary infarction and its resolution.

for pulmonary haemorrhage in the absence of other contributory factors, such as cardiac failure, uraemia, and bleeding diathesis, have been variable. Some patients have responded but have had recurrences of this complication. Others have had no recurrences after the initial episode. A few have not responded even to aggressive treatment and have died.

Our patient is both interesting and unusual in that she presented with coexistent pulmonary haemorrhage and infarction in association with a circulating anticoagulant, which has not been previously described.

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