Acute massive pulmonary haemorrhage, pulmonary embolism and deep vein thrombosis in a patient with systemic lupus erythematosus and varicella


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Introduction

Acute massive pulmonary haemorrhage (AMPH) is a rare but highly fatal complication in systemic lupus erythematosus (SLE) (1,2). Its pathogenic mechanisms can be multifactorial, including the deposition of immune complexes, microangiitis, pulmonary infection and coagulopathy (3-5). Deep vein thrombosis with pulmonary embolism as a complication of SLE is also rare (6). The causes for this complication include lupus anticoagulant, thrombophlebitis and nephrotic syndrome (6-8). Varicella is usually self-limited and confined to the skin in a normal individual. An SLE patient developing systemic varicella and complications of deep vein thrombosis, pulmonary embolism and AMPH is described here. The role of systemic varicella in these complications is discussed.

Case Report

Our patient, a 19-year-old girl, was diagnosed in 1987 to have SLE because of polyarthritis, malar rash and positive tests for antinuclear and anti-dsDNA antibodies. In July 1989, nephrotic syndrome developed. Renal biopsy disclosed a picture of diffuse proliferative glomerulonephritis, but evidence suggestive of Goodpasture's syndrome was lacking. She was treated with prednisolone (0.551 mg kg⁻¹ day⁻¹) and cyclophosphamide (1-2 mg kg⁻¹ day⁻¹) with much improvement.

One month after the renal biopsy, she was admitted because of severe back pain for 1 day and the appearance of bean-sized vesicles on the face and back for 4 days. On admission, mild leg oedema and ascites were found. The superficial veins on abdomen and chest were not engorged. Evidence of vasculitis or thrombophlebitis was not found. There was no history of protracted bed rest or usage of oral contraceptives. Complete blood counts showed a haemoglobin level of 6.0 mmol l⁻¹, white blood cell count of 15 x 10⁹ l⁻¹ and normal platelet count. Proteinuria (++) was noted. Serum level of albumin was 27 g l⁻¹; of creatinine 150 µmol l⁻¹ (normal <106 µmol l⁻¹) and of total cholesterol 12.56 mmol l⁻¹. Serum concentrations of anti-dsDNA, C3 and C4 were all within normal limits. Serum lupus anticoagulant, anti-glomerular basement antibody and anti-cardiolipin antibody were absent. The chest X-ray was normal except for mild cardiomegaly. Computerized tomogram of the abdomen disclosed low-density substances in the inferior vena cava and bilateral renal veins, indicating the presence of thrombi in these vessels, which appeared normal in the sonographic examination performed 1 month before. All these findings and the whole clinical course indicated thrombosis formation a few days prior to this admission. She was then treated with prednisolone (40 mg day⁻¹), acyclovir and low-dose heparin therapy (3000 IU, b.i.d. subcutaneously). Prothrombin time and activated partial thromboplastin time (aPTT) were kept at 1-1.5 times normal values. No bleeding was noted until the fourth hospital day when the patient developed haemoptysis and dyspnoea. The dyspnoea worsened and massive haemoptysis occurred 5 h after onset of haemoptysis. Complete blood count and chest radiography were rechecked 1 h before massive haemoptysis occurred. The haemoglobin level was 2.6 mmol l⁻¹ lower than 1 day before. Alveolar infiltrations were found over the middle and lower lung fields on both sides. The arterial blood gas
disclosed acute respiratory failure with metabolic acidosis (pH: 6.8, \( PCO_2: \) 8.9 kPa, \( PO_2: \) 9.8 kPa, \( CO_2 \) content: 9.7 mmol l\(^{-1}\), oxygen saturation: 72%) (on 100% oxygen, but without ventilator). The patient expired 20 min after AMPH occurred.

On autopsy, big thrombi were found in the inferior vena cava and bilateral renal veins. Microscopically, pulmonary oedema, haemorrhage and emboli in the small and middle-sized pulmonary arteries were diffusely seen in both lungs, but there was no alveolitis or interstitial pneumonitis (Plate 1). Systemic varicella involving kidney, lung, liver, pancreas, adrenal gland, oesophagus, vagina, ovary and skin was disclosed on the immunoperoxidase staining with anti-herpes simplex monoclonal antibody. Thrombi in the renal vessels with intranuclear inclusion bodies were also found (Plate 2).

**Discussion**

We report an SLE patient with systemic varicella who subsequently developed acute deep vein thrombosis, pulmonary embolism and AMPH. The clinico-pathological findings of pulmonary haemorrhage in this patient fulfilled the characteristic manifestations of AMPH, as reported by other authors (1,2). Pulmonary embolism can decrease pulmonary vascular beds and induce pulmonary arterial constriction. If severe enough, pulmonary arterial pressure may subsequently become raised (8). In our patient, emboli were diffusely found in both lungs; pulmonary arterial pressure was therefore speculated to be high, although there was no time for haemodynamic measurement. Haemoptysis is common in patients with varicella pneumonia but massive pulmonary haemorrhage seems to be very rare (9,10). In our patient, SLE-associated alveolitis or interstitial pneumonitis was not found on autopsy, lupus anticoagulant was absent, and prothrombin time and aPTT were kept in the safe range when AMPH developed. All these findings indicated that AMPH in our patient was the outcome of interaction between varicella pneumonia, pulmonary embolism and the anticoagulant therapy. Both anticoagulant and increased pulmonary arterial pressure may have
transformed the pre-existing pulmonary haemorrhage, caused by varicella pneumonia, into the more severe one.

The temporal relationship between formation of deep vein thrombosis and appearance of varicella and the finding of thrombi in the renal vessels with intranuclear inclusion body, indicated that varicella was involved in the formation of deep vein thrombosis in our patient. Systemic varicella can be complicated by deep vein thrombosis and/or pulmonary embolism, although it rarely occurs (11,12). Endothelial cells infected by varicella may proliferate and become swollen, subsequently serving as initiating sites of platelet aggregation and red thrombus formation. There is still no other report concerning varicella in the development of deep vein thrombosis or AMPH in SLE.

Systemic lupus erythematosus patients may have a higher risk of developing systemic varicella, especially after having been treated with immunosuppressed drugs. Once it occurs, treatment must be given aggressively and as early as possible so that deep vein thrombosis and pulmonary haemorrhage may thus be prevented. In the presence of varicella pneumonia and pulmonary embolism, anticoagulant should be cautiously administered to avoid the occurrence of AMPH.

Acknowledgement

This work is supported, in part, by grants CI 84-13 from Ching-Ling Aging Foundation and NSC 85-2331-B-075-050 from the National Science Council.

References