

Case report

Pulmonary hypertension, systemic lupus erythematosus, and the contraceptive pill: another report

MARIAN H MILLER

From Prince Henry's Hospital, Melbourne, Australia

SUMMARY I report the case of a woman with systemic lupus erythematosus who had pulmonary hypertension unassociated with chronic interstitial lung disease or pulmonary emboli. She had started taking the contraceptive pill seven months previously.

Key words: oestrogen therapy, vasculitis, Raynaud's phenomenon.

Pulmonary hypertension unassociated with chronic interstitial lung disease or pulmonary emboli is an uncommon but serious complication of systemic lupus erythematosus (SLE).¹ The presence of lupus inhibitor or raised titres of anticardiolipin antibody, or both, has been recorded in some such cases.^{1,2} Recently the acute and rapidly progressive onset of symptomatic pulmonary hypertension in a woman with SLE eight months after commencement of the oral contraceptive pill was reported.³ Lupus inhibitor and anticardiolipin antibodies were not found. I report the development of pulmonary hypertension seven months after commencement of the contraceptive pill in a 17 year old woman with SLE in the absence of interstitial lung disease, pulmonary emboli, lupus inhibitor, or anticardiolipin antibodies. The pulmonary hypertension contributed to her death 18 months after diagnosis of SLE and six months after diagnosis of pulmonary hypertension.

Case report

A diagnosis of SLE was made in a 16 year old white woman in July 1984, the clinical features being fevers, anaemia, malaise, weight loss, Raynaud's phenomenon, digital vasculitis, mucous membrane ulcers, pleuritic chest pain, photosensitive skin rash, and myositis. Cardiovascular examination was normal. On admission to hospital haemoglobin (Hb)

was 10.6 g/dl (106 g/l), leucocytes $4.5 \times 10^9/l$, platelets $291 \times 10^9/l$, erythrocyte sedimentation rate (Westergren) 98 mm/1st h, antinuclear antibody titre 1/2560 with speckled pattern, antibody to double stranded deoxyribonucleic acid (Farr assay) 66% (normal <20%), C3 0.11 g/l (normal 0.80–1.50), C4 0.05 g/l (normal 0.12–0.36), anti-ribonucleoprotein (anti-RNP) antibodies positive, and rheumatoid factor positive. Creatine phosphokinase (CPK) was 12 300 IU (normal 0–215) and electromyographic findings were consistent with myositis. CPKMB was normal. The following investigations were normal or negative: LE cell preparation, urinary sediment, 24 hour urinary protein, creatinine clearance, partial thromboplastin time kaolin, chest x ray, and electrocardiogram. Pulse intravenous methylprednisolone therapy was started (500 mg daily for three consecutive days), followed by oral prednisolone 20 mg daily and hydroxychloroquine 200 mg daily. She was discharged after 10 days, clinically much improved. All laboratory abnormalities improved markedly with the exception of the CPK, which fell very slowly. Severe weight gain and Cushingoid appearance developed. In late August 1984 new vasculitic lesions appeared on the fingers, at which time the CPK was still markedly raised at 5600 IU. The prednisolone dosage was increased to 40 mg daily. The vasculitis resolved and the CPK level fell further. Tapering of the prednisolone dosage was commenced in mid-September, and a month later she was clinically well with a steadily falling CPK level and receiving

Accepted for publication 2 July 1986.

Correspondence to Dr Marian H Miller, Suite 4, 36 Clarendon Street, East Melbourne 3002, Australia.

prednisolone 20 mg daily. Slow reduction in the prednisolone dose was continued, interrupted by mild flares in which synovitis, pleuritic chest pain, and severe Raynaud's phenomenon predominated. By February 1985 the disease was clinically and serologically quiescent at a dose of prednisolone 10 mg daily. The patient stated that she had started to take an oral contraceptive pill (ethinylloestradiol 30 µg, levonorgestrel 150 µg) in December 1984 and expressed a determination to remain on it. She sought no further medical attention until July 1985 when she was admitted to hospital with synovitis, skin rash, nasal ulcers, digital vasculitis, pleuritic chest pain, and myositis (CPK 6080 IU with normal CPKMB) associated with a recurrence of the serological abnormalities. The prednisolone dosage was increased from 5 mg to 20 mg daily. In addition to the typical SLE manifestations, the patient complained of the recent onset of exertional dyspnoea and was found to have a right ventricular heave, pulmonary artery impulse, and loud pulmonary second sound, none of which had been present at the previous admission. Chest x ray showed prominence of the pulmonary artery trunk. Electrocardiogram and echocardiogram confirmed right ventricular hypertrophy. A ventilation/perfusion lung scan showed no evidence of pulmonary emboli. Pulmonary function tests showed normal spirometry and diffusing capacity. Right heart catheterisation confirmed raised right pulmonary artery pressures of 59/22 mmHg before exercise and 72/33 mmHg after exercise. Normal pulmonary artery wedge pressure and oxygen saturation excluded a significant left to right shunt. Lupus anticoagulant and anticardiolipin antibodies were not found.

The SLE flare responded to prednisolone 20 mg daily, and this dosage was continued. Anticoagulation with warfarin was started, and two months later nifedipine was cautiously introduced. Maintenance dosage of nifedipine was 90 mg/day. The exertional dyspnoea, cardiovascular examination, electrocardiography, and arterial oxygen saturation remained stable during 1985. The SLE was intermittently mildly active. In January 1986, while holidaying in the country, the patient suddenly became unwell with acute abdominal pain. She was admitted to the regional hospital. There was right sided abdominal tenderness with guarding, and pain on rocking the cervix. Hb was 7.0 g/dl (70 g/l) and the prothrombin time was in the therapeutic range. Laparotomy showed bleeding from a ruptured right ovarian cyst, which was oversewn. Blood was transfused during surgery. Intraoperatively, an episode of atrioventricular dissociation with profound hypotension occurred. In the immediate postoperative period the patient was hypotensive and hypoxaemic with signs

of cerebral dysfunction. She was unfit for transfer to a large hospital. Intravenous sodium nitroprusside and controlled ventilation restored the blood pressure and arterial blood oxygen saturation to satisfactory levels. Her condition remained stable until the third postoperative day when repeated epileptic seizures occurred followed by a cardiac arrest. Permission for postmortem examination was refused.

Discussion

Pulmonary hypertension occurring as a manifestation of SLE in the absence of chronic interstitial lung disease or overt pulmonary emboli is uncommonly reported,¹ but it is important because it is a potentially lethal complication. As reported here it may lead to premature death in cases where the other SLE manifestations are benign. As the response to currently available therapy is disappointing,⁴ it is important that treatable causes such as steroid responsive pulmonary infiltrates and pulmonary emboli are sought.

The striking association of the lupus inhibitor or raised titres of anticardiolipin antibody, or both, with venous and arterial thromboses and thromboembolic pulmonary hypertension in SLE has recently been recognised.^{1,2} Lupus inhibitor and raised titres of anticardiolipin antibody have not, however, been found in SLE patients with 'solitary' primary pulmonary hypertension.⁵ There are still a small number of SLE patients with pulmonary hypertension who, like our patient, have no demonstrable predisposing factor. It is suggested that vasospasm and vasculitis may involve small pulmonary arteries, resulting in obstruction to flow,¹ an hypothesis of relevance in our case where Raynaud's phenomenon and peripheral vasculitis were prominent. Antibodies to RNP and rheumatoid factor are often present in SLE patients with pulmonary hypertension, as in this case, but no pathogenetic role has been postulated.^{5,6}

A report of a patient with SLE who developed acute and rapidly progressive pulmonary hypertension eight months after commencement of the oral contraceptive pill was published recently.³ In the present case the contraceptive pill was started seven months before the onset of symptoms and the diagnosis of pulmonary hypertension. Although the occurrence of pulmonary hypertension in otherwise healthy women on the oral contraceptive pill is recognised,^{7,8} the specific effects of oestrogens on SLE must be considered.

There is much circumstantial evidence in the literature that oestrogens encourage expression of the disease, as recently reviewed.⁹ Furthermore,

one study has suggested that almost half the patients with SLE who start to receive oestrogens experience an exacerbation of their disease within three months.¹⁰ This patient was allowed to continue the contraceptive pill as it was considered of the utmost importance that pregnancy be avoided because of the significant and established pulmonary hypertension.

The close time relationship between the commencement of the contraceptive pill and the onset of symptoms of pulmonary hypertension in these two reports has important clinical implications. As pulmonary hypertension occurs infrequently in SLE, years may elapse before prospective studies in large SLE clinics unequivocally determine whether this apparent association is real or coincidental. In the meantime it is hoped that this additional report of the development of pulmonary hypertension after the commencement of the contraceptive pill will encourage further examination of the significance of this association.

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