Case report

Lupus cor pulmonale with electron microscope and immunofluorescent antibody studies

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Yeo, P. P. B., and Sinniah, R. (1975). *Annals of the Rheumatic Diseases*, 34, 457–460. Lupus cor pulmonale with electron microscope and immunofluorescent antibody studies. A case of systemic lupus erythematosus with an unusual complication of pulmonary hypertension leading to cor pulmonale is reported. Lung biopsy showed an interstitial pneumonitis with pulmonary vascular narrowing causing pulmonary hypertension. These changes appeared to be immunologically mediated by the utilization of IgG and C3. Microtubular virus-like particles were present in the endothelial cell cytoplasm of both lung and kidney.

Pleuropulmonary involvement in systemic lupus erythematosus (SLE) is well known (Dubois, 1974). Arteritis of the smaller pulmonary vessels leading to pulmonary hypertension is a recognized, albeit rare,

complication of SLE (Wood, 1952). A case is recorded here of a patient with SLE who developed severe pulmonary hypertension in less than 3 years during the course of her disease, culminating in cor pulmonale.

FIG. 1 Normal chest x-ray, taken on August 30, 1971, showed no cardiac enlargement or lung pathology

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FIG. 2 Chest x-ray taken on June 4, 1974 showed cardiac enlargement with dilated pulmonary arterial trunk and nodular shadowing in the lung fields, especially at the bases

Clinical history

A 23-year-old Chinese housewife presented in June 1974 with a 7-month history of malaise and fatigue, followed by palpitations with exertional dyspnoea a month before admission. There was associated progressive bilateral ankle swelling and abdominal distension. In August 1971, the patient was hospitalized at another hospital with the nephrotic syndrome. Tests for rheumatoid and anti-nuclear factors were positive but LE cells were repeatedly negative. The patient was treated with steroids and diuretics but failed to attend for follow-up in December 1971. In the cardiovascular system there was then no detectable abnormality and chest x-ray (Fig. 1) was

normal. Clinical examination on her present admission showed ankle and sacral oedema; blood pressure 110/80 mmHg; regular pulse rate 130/min; jugular venous pressure 2 cm with prominent a waves. Left parasternal heave with atrial gallop and accentuated pulmonary second sound; a soft systolic murmur in the pulmonary area, together with an early diastolic murmur. Lungs were clinically clear. The liver was palpable 1 cm below the costal margin.

Investigations

Haemoglobin was 11.1 g/dl; mean corpuscular haemoglobin count 33 g/dl (33%); red blood cells normocytic,

FIG. 3 Lung biopsy (electron microscope). There are clumps of microtubular, filamentous, virus-like structures in the endothelial cell cytoplasm of the pulmonary vessels (arrows). $\times 37000$

normochromic; total white blood count $270000 \times 10^9/l$ ($2700/mm^3$) (polymorphs 83%, lymphocytes 15%, monocytes 2%); platelets $195 \times 10^9/l$ ($195000/mm^3$); ESR 130 mm/h; blood urea 2.82 mmol/l (17 mg/100 ml); serum creatinine 44.2 $\mu\text{mol/l}$ (0.5 mg/100 ml); creatinine clearance 53.3 ml/min; proteinuria 324 mg/24 h. Serum proteins: albumin 35 g/l (3.5 g/100 ml), globulin 68 g/l (6.8 g/100 ml)— α_1 7 g/l, α_2 8 g/l, β 9 g/l, and γ 44 g/l; IgG 48 g/l (4800 mg/100 ml), IgA 3.28 g/l (328 mg/100 ml), IgM 2.1 g/l (210 mg/100 ml); total serum complement 12 CH₅₀/ml (normal 27–50), C3 0.18 g/l (18 mg/100 ml) (normal 0.68–1.58); serum cholesterol 1.2 g/l (120 mg/100 ml); RA factor, ANF, and LE cells were positive $\times 3$.

A chest x-ray (Fig. 2) showed reticular nodular shadows in both lower and midzones bilaterally, consistent with interstitial fibrosis. There was cardiac enlargement with a large main pulmonary artery trunk. ECG showed sinus tachycardia and right ventricular hypertrophy with strain pattern. Respiratory function tests were those of restrictive lung disease with impaired diffusing capacity. Lung biopsy showed the features of interstitial pneumonitis with narrowing of alveolar septal vessels. There was muscular medial hypertrophy and concentric connective tissue proliferation of the larger vessels. On electron microscope examination clumps of microtubular virus-like particles were seen, mainly in a subnuclear position (Fig. 3) in the endothelial cell cytoplasm of blood vessels. IgG and C3 were deposited in the vascular endothelium and walls of alveolar septae (Fig. 4). Renal biopsy showed similar microtubular, virus-like particles in the endothelial cell cytoplasm.

Treatment and progress

The patient's lupus cor pulmonale improved with digitalization, diuretics, and steroids. Radiologically there was significant reduction in cardiac size (15

cm–13.3 cm over 6 months). Basal lung shadows were less prominent. The patient is now on maintenance therapy.

Discussion

There are few reports of pulmonary hypertension in SLE giving rise to cor pulmonale (Aitchison and Williams, 1956; Larson 1961). The patient described here developed severe pulmonary hypertension during the 3-year interim period from when she first had the nephrotic syndrome until her present admission with cardiac failure. The pulmonary pathology of interstitial pneumonitis and vasculopathy causing cor pulmonale were apparently mediated through the utilization of IgG and C3. It may be that circulating antigen–antibody complexes formed during the course of SLE were deposited in the lungs. Microtubular virus-like particles have been described in lupus nephritis (Györkey, Sinkovics, Min, and Györkey, 1972), but there is no report in the literature of the presence of these structures in the lungs of patients with SLE. The nature of these structures has not been resolved, though suggestions have been put forward that they may be of viral origin (Györkey and others, 1972) while Schaff, Barry, and Grimley (1973) could find no evidence for a relationship to similarly sized cores of a known paramyxovirus.

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FIG. 4 Lung biopsy (immuno-fluorescent antibody study). There is heavy deposition (grade +3) of IgG in the pulmonary vascular endothelium and alveolar septae. The nuclei of endothelial and alveolar septal cells also show fluorescence against anti-Hu-IgG. 125 ASA 30 s, $\times 130$

References

- AITCHISON, J. D., AND WILLIAMS, A. W. (1956) *Ann. rheum. Dis.*, **15**, 26 (Pulmonary changes in SLE)
- DUBOIS, E. L. (1974) 'The clinical picture of systemic lupus erythematosus, in 'Lupus Erythematosus', 2nd ed. pp. 275, 404. University of Southern California Press, California
- GYÖRKEY, F., SINKOVICS, J. G., MIN, K. W., AND GYÖRKEY, P. (1972) *Amer. J. Med.*, **53**, 148 (A morphologic study on the occurrence and distribution of structures resembling viral nucleocapsids in collagen diseases)
- LARSON, D. L. (1961) 'Special laboratory features: lupus erythematosus cell factor', in 'SLE', 1st ed. p. 140. Churchill, London
- SCHAFF, Z., BARRY, D. W., AND GRIMLEY, P. M. (1973) *Lab. Invest.*, **29**, 577 (Cytochemistry of tubuloreticular structures in lymphocytes from patients with systemic lupus erythematosus and in cultured human lymphoid cells: comparison to a paramyxovirus)
- WOOD, P. (1952) *Brit. med. Bull.*, **8**, 348 (Pulmonary hypertension)