

Pulmonary veno-occlusive disease presenting with thrombosis of pulmonary arteries

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Abstract

Pulmonary veno-occlusive disease is a rare cause of pulmonary hypertension. An unusual case presenting with thrombosis of the right pulmonary artery and serological evidence of autoimmunity is reported.

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A 35 year old mildly obese white woman without significant past medical history presented with a sudden onset of dyspnoea on exertion. Before this she had been able to walk four miles without difficulty but was now unable to walk one city block. There was no history of Raynaud's phenomenon, and the patient denied taking anorectic agents or crotaline-containing herb substances such as Bush tea. On admission to another institution physical examination was unremarkable and chest radiographs revealed only left lower lobe scarring. A ventilation-perfusion scan showed multiple large areas of ventilation and perfusion mismatch. A pulmonary angiogram showed a large thrombus in the right pulmonary artery, almost completely

occluding it. At angiographic examination the systolic pressure in the pulmonary artery was 60 mm Hg. Doppler ultrasound examination of both lower extremity venous systems was unremarkable. Anticoagulation was started but the dyspnoea on exertion persisted.

Four months later she was admitted to our institution for additional evaluation. Physical examination was again unremarkable. The ECG was normal. The erythrocyte sedimentation rate was 100 mm/hour, rheumatoid factor was positive (to 1 in 5120), lupus anticoagulant was mildly positive, antinuclear antibodies were positive (homogeneous to 1:6250, speckled to 1:1250), and complement levels were elevated. Breathing room air, the arterial blood gas results were as follows: pH 7.34, P_{CO_2} 6.3 kPa, P_{O_2} 5 kPa, and the percentage oxygen saturation was 68. The FEV₁ was 1.87 l, the FVC was 2.28 l (50% of predicted), and the diffusion capacity and total lung capacity were markedly reduced. There was only a small peripheral perfusion defect in the right upper lobe on a repeat ventilation-perfusion scan.

Cardiac catheterisation and repeat pulmonary arteriography were performed. Four days before catheterisation the oral anticoagulant had been stopped and the patient noted worsening dyspnoea on exertion.

At angiographic examination there was good filling of the right pulmonary artery but several small branches to the right upper lobe were now abruptly occluded. The pulmonary arterial pressure was 28/12 at rest and 50/14 with exercise. Pulmonary capillary wedge pressure was not determined. Mixed venous saturation decreased from 59.5% at rest to 37.5% with exercise.

To investigate for possible vasculitis a thoracoscopic wedge biopsy of the right lower and upper lobes was performed. A repeat lung scan two weeks after discharge demonstrated a new, large perfusion defect in the superior segment of the left lower lobe.

Microscopic examination of the biopsy specimen showed evidence of moderate pulmonary hypertension with medial hypertrophy and intimal fibrosis in muscular pulmonary arteries. Many of the arteries also contained organised, recanalised thrombi (fig 1). Pulmonary veins showed luminal occlusion by fibrosis and organised thrombi, and there were small venous infarcts located adjacent to interlobular septa. The latter findings were diagnostic of pulmonary veno-occlusive disease (fig 2).

Discussion

Pulmonary veno-occlusive disease is a rare cause of pulmonary hypertension, usually affecting children and young adults. Patients present with dyspnoea, orthopnoea, syncope, hypoxaemia, and right heart failure.¹ Chest radiographs demonstrate right ventricular and pulmonary arterial enlargement, and signs of pulmonary oedema.² The characteristic feature of pulmonary veno-occlusive disease is widespread occlusion of small pulmonary veins and venules by fibrosis and intimal proliferation

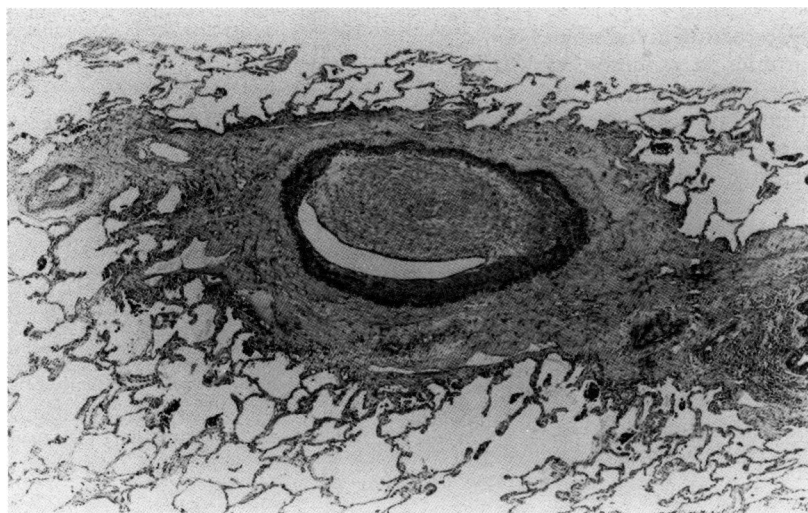


Figure 1 Photomicrograph showing a pulmonary artery whose lumen is almost completely replaced by an organising thrombus. Stain: modified Verhoeff van Gieson elastic tissue, original magnification $\times 110$ reduced to 60% in origination.

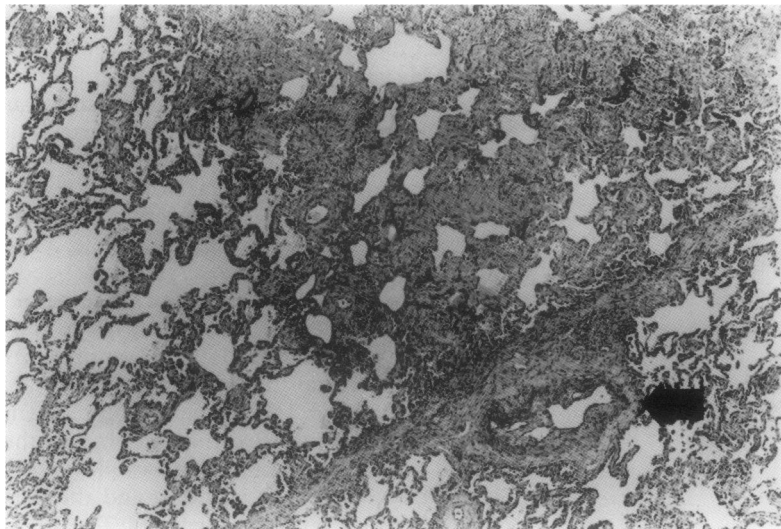


Figure 2 Low magnification photomicrograph showing infarcted lung parenchyma (top right) adjacent to interlobular septum and pulmonary vein (lower right), the lumen of which is partly occluded by intimal fibrosis suggestive of old recanalised thrombus (arrow). Stain: haematoxylin and eosin, original magnification $\times 110$ reduced to 60% in origination.

associated with histological evidence of severe pulmonary arterial hypertension.^{2,3} Intimal changes in the muscular pulmonary arteries similar to those occurring in the veins are present in about half of all cases, and are sometimes as severe as in the veins.³ Wagenvoort *et al*³ believe that the pathogenesis of the arterial lesions may be the same as for the veins and is not strictly secondary to venous obstruction. The cause of pulmonary veno-occlusive disease is unknown, with local thrombus formation as the final common feature of pathogenesis.^{3,4}

The triad of severe pulmonary arterial hypertension, radiographic evidence of pulmonary oedema, and a normal pulmonary capillary wedge pressure strongly suggests the diagnosis of pulmonary veno-occlusive disease but lung biopsy is needed for definitive diagnosis.² The average survival after diagnosis is 20 months.¹ Our patient is still alive 21 months after diagnosis. There is no known effective treatment although lung transplantation may be considered.

While in situ thrombus formation in the small muscular pulmonary arteries is common in pulmonary veno-occlusive disease,² the extent of pulmonary arterial thrombosis seen in our patient is unusual. Pulmonary arteriography in pulmonary veno-occlusive disease usually shows enlarged pulmonary arteries, slow flow, and an absence of filling defects.⁵ Lung scanning may show non-specific patchy perfusion defects.⁵ Cases with large perfusion defects on perfusion scans without any evidence of pulmonary thrombi in large pulmonary arteries on post mortem examination have also been reported.⁴ Since the pulmonary veins and arteries are connected in series, these findings are not unexpected. Nevertheless, only a few

cases of pulmonary veno-occlusive disease with proven thrombi in the major pulmonary arteries have been reported⁵; one patient developed thrombi in the main pulmonary arteries and multiple pulmonary infarcts after chemotherapy and radiation therapy for Hodgkin's disease.⁶

Another interesting aspect of our patient's disease is the serological evidence of autoimmunity. Autoimmune abnormalities have been reported in association with pulmonary veno-occlusive disease. Corrin *et al* found immune complexes in alveolar walls in a lung biopsy specimen from a patient with pulmonary veno-occlusive disease.⁷ Another case report described a positive test for antinuclear antibodies (homogeneous pattern 1:64, speckled pattern 1:4096) but negative tests for rheumatoid factor and cryoprecipitate.² This patient and at least one other⁸ also demonstrated Raynaud's phenomenon. Liang *et al* described a patient who suffered from a diffuse venulitis, involving both systemic and pulmonary veins, who intermittently had positive tests for rheumatoid factor, antinuclear antibodies, and circulating immune complexes.⁹ Sanderson *et al* reported a patient with pulmonary veno-occlusive disease who had a positive test for antinuclear antibodies in addition to polyarthritis and Raynaud's phenomenon.¹⁰ Among patients who have pulmonary veno-occlusive disease, however, such findings are unusual: there is no established connection between pulmonary veno-occlusive disease and autoimmune disease. The presence of lupus anticoagulant may cause venous or arterial thrombosis, but the test for this antibody was only mildly positive in our patient.

In conclusion, this report describes a patient with an unusual presentation of an uncommon disease: pulmonary veno-occlusive disease with episodes of thrombosis in large pulmonary arteries. The features of an autoimmune process are also unusual in this disease.

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