A previously well 10.5-year-old boy was found to have proteinuria and hematuria on urinalysis prior to tonsillectomy and myringotomy. He was not nephrotic and weighed 31.1 kg. Investigations performed 6 weeks later revealed microscopic hematuria, 24 h urinary protein excretion of 2.9 g, serum urea 14 mmol/l (39 mg/dl), serum creatinine 80 μmol/l (0.90 mg/dl), total serum protein 43 g/l, serum albumin 22 g/l and normal concentrations of the third and fourth components of complement (C3 and C4, respectively). Renal biopsy revealed focal segmental glomerulosclerosis. He was commenced on prednisone 60 mg/day.

Two weeks later he was admitted to The Hospital for Sick Children with massive generalized edema resulting in a weight gain of 8 kg. His blood pressure was 135/95 mmHg, respiratory rate 32/min and pulse 88 beats/min. Serum biochemical results were similar to those above. A chest X-ray demonstrated large bilateral pleural effusions and no parenchymal abnormalities. His hemoglobin concentration was 158 g/l (15.8 g/dl), and his platelet count was 176 × 10^9/l (1.76 × 10^10/mm^3). Coagulation studies revealed a normal prothrombin time (PT 9.9 s) and a normal partial thromboplastin time (PTT 29.9 s). Prednisone was continued and infusions of 25% albumin (1 g/kg body weight) with intravenous furosemide (1 mg/kg body weight) were given daily for 6 days. Intravenous hydralazine (0.5 mg/kg per dose) and oral nifedipine (5 mg short-acting preparation) were used intermittently to control his hypertension over the first days of hospitalization.

During the 1st week of hospitalization he responded to this treatment with a diuresis and his weight decreased by 1 kg/day. Four days following admission, he had an episode of shortness of breath, mild chest pain and abdominal pain. These symptoms completely resolved within 1 h and no abnormal physical signs were found on examination. A chest X-ray demonstrated smaller bilateral pleural effusions and an electrocardiogram was normal.

In the 2nd week of hospitalization he developed glycosuria and he had mildly elevated blood glucose concentrations: fasting blood glucose 6.9 mmol/l (123 mg/dl) and 2 h postprandial blood glucose 12 mmol/l (216 mg/dl). He was treated with a diabetic diet. He continued to have heavy proteinuria and 14 days following admission he received one dose of 75 mg cyclophosphamide.

He developed mild right-sided pleuritic chest pain on the 15th day of hospitalization and produced blood tinged sputum. Examination revealed a temperature of 36.4 °C, pulse rate 80/min, respiratory rate of 20/min and a blood pressure of 120/80 mmHg. Chest X-ray revealed clear lung fields and a small left pleural effusion. Arterial PO_2 was 88 mmHg, PCO_2 38 mmHg, pH 7.48 and bicarbonate 27 mmol/l in room air. His serum albumin concentration was 18 g/l. Radionuclide ventilation and perfusion scans (Fig. 1) revealed both decreased ventilation and absent perfusion to the right lung. The coagulation studies performed were normal (PT was 9.7 s, PTT 29.1 s, fibrinogen 3.46 g/l, and fibrin split products 40–80 mg/l). He was given a loading dose of 150 units/kg intravenous heparin and then an infusion of heparin at 25 units/kg per hour was started and adjusted so that the PTT was 1.5–2 times the normal value.

The following day (day 16) he was asymptomatic with a respiratory rate of 16–20 breaths/min, a pulse rate of 60 beats/min and a normal blood pressure. Angiography of the inferior vena cava was normal. Pulmonary angiography revealed an extensive lesion in the lumen of the right pulmonary artery occluding 95% of the lumen with only a minimal amount of contrast demonstrated distal to the lesion (Fig. 1). A pulmonary artery catheter was placed next to the lesion. Heparin was discontinued and an infusion of streptokinase (100 units/kg per hour) was administered through the pulmonary artery catheter for the next 72 h. Serial angiograms were used to monitor therapy. Twenty four hours later (day 17) the lesion was reduced to 50% of the original size, 48 h later
Fig. 1. $^{99m}$Tc-chelated diethylene triamine penta-acetic acid lung perfusion scans on the day of pulmonary thrombosis (day 15, A) showing complete absence of right lung blood flow, and after 4 days of intra-arterial streptokinase treatment (B) when significant blood flow to the right lung was restored. A pulmonary arteriogram performed on day 16 (C) showed the convex edge of the thrombus in the right main pulmonary artery almost completely obstructing flow to the right lung (arrow), and after 4 days of treatment an arteriogram (D) showed residual thrombi blocking peripheral pulmonary artery branches (arrows).

there was a small portion of thrombus at the trifurcation of the inferior branch of the right pulmonary artery, and 72 h later a few small fragments were seen in the distal pulmonary vascular bed. The streptokinase infusion was discontinued, the pulmonary artery catheter was removed, and heparin was recommended for 2 days while the patient began treatment with warfarin (maintenance dose 4 mg/day).

The patient continued to have heavy proteinuria with serum albumin concentrations of less than 25 g/l, although his edema resolved. The dose of prednisone was slowly tapered after 6 weeks and cyclophosphamide 75 mg/day was recommenced and given for 9 weeks. Four months later he had normal pulmonary function tests and warfarin was discontinued. He developed progressive renal impairment and 12 months after the pulmonary thrombosis he underwent a successful cadaveric renal transplantation and was well at follow-up at 22 months post transplant.

Discussion

Major venous and arterial thrombosis and thromboembolism are well documented in children with the nephrotic syndrome [1–6]. These events have been reported as fatal in the 11 patients of these six reports. In contrast, this case of complete right pulmonary artery occlusion produced minor symptoms and was successfully treated with thrombolytic therapy. The relative lack of symptoms in this case is an important but under-recognized feature of pulmonary thromboembolism in the nephrotic syndrome in children. The patient’s symptoms of pleuritic pain and hemoptysis demanded investigation. His vital signs were normal and the recorded lack of dyspnea is supported by the arterial blood gas results showing no reduction in $PCO_2$, as would be expected with hyperventilation, and only a mild reduction in the $PO_2$. Thus, the clinical state suggested a minor lesion. The finding of completely absent perfusion of the right lung on the day of symptoms and 95% occlusion of the right main pulmonary artery the day following the onset of symptoms seemed out of keeping with these clinical findings.

There is evidence that pulmonary thromboembolism complicating childhood nephrosis may often be silent. The incidence of symptomatic thrombotic events was found to be 1.8% by Egli et al. [7] in a survey of 3377 nephrotic children in European dialysis units. Similarly, Mehls et al. [8] found an incidence of symptomatic thrombotic events in 4.1% in the longitudinal study of 200 children over 10 years. However, Hoyer et al. [9] investigated 26 asymptomatic children using combined scintigraphic pulmonary ventilation and perfusion scans and found that 7 children had a pattern consistent with pulmonary embolism, 10 had abnormal findings and only 9 had normal findings. Hence, the comparison of the study of Hoyer et al. with those of Egli et al. and Mehls et al. suggests that many children with thromboembolic complications of the nephrotic syndrome are not diagnosed. The incidence of symptomatic thrombotic events has been found to be greater in nephrotic adult patients than in nephrotic children [10]. The cause of this age-dependent change in symptoms is unclear.

The hypercoagulable state that exists in the nephrotic syndrome has been extensively investigated and involves abnormalities in the concentrations and activities of many of the coagulation pathway factors, their cofactors, and clotting inhibitors, and also abnormalities in fibrin forma-