

Case Report

Thromboembolic complications at the onset of nephrotic syndrome

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ABSTRACT

Nephrotic syndrome is associated with hypercoagulable states and a subsequent high risk of venous and rarely arterial thromboembolism. Although venous thromboembolism has been a recognised risk, prevalence of pulmonary embolism in patients with nephrotic syndrome is based on data from different case series. Here we report a 5 year old child with nephrotic syndrome who developed life threatening cerebral dural venous sinus thrombosis and pulmonary embolism within a month of disease onset.

Keywords

Children, Embolism, Nephrotic, Paediatric, Thrombosis.

INTRODUCTION

Nephrotic syndrome (NS) is associated with a hypercoagulable state due to increase in the plasma levels of fibrinogen and coagulation factors, urinary loss of antithrombin III, changes in the fibrinolytic system and increased platelet activation and aggregation [1]. Thrombosis can be venous or arterial,

although arterial events are less commonly associated with NS. Pulmonary embolism (PE) has been reported in 15% of cases with the advent of more sensitive methods [1]. Cerebral venous sinus thrombosis is a rare life threatening complication of nephrotic syndrome, with only few cases described in the literature [2]. We report a case of nephrotic syndrome complicated by cerebral venous sinus thrombosis and bilateral pulmonary artery embolism within a month of disease onset.

CASE REPORT

A 5 year male child who was recently diagnosed as a case of nephrotic syndrome with no similar illness in the past, presented with 2 days history of difficulty in breathing and decreased urine output. He was diagnosed outside about 28 days back by an adult nephrologist. Review of documents suggested nephrotic range proteinuria, hypoalbuminemia and hypercholesterolemia. He was started on oral Prednisolone at 60 mg/m²/day and achieved remission within 15 days of steroid initiation. On the 20th day he developed headache following which steroid dose was reduced to 40 mg/m²/day keeping a possibility

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of steroid-induced hypertension. Five days later he developed fever with breathing difficulty following which prednisolone was stopped. He was referred to our centre for persistent respiratory symptoms, headache and reappearance of oedema. On admission, he was irritable and dyspneic and had generalized oedema, ascites and cold extremities. He had a pulse rate of 112/min (low volume), blood pressure of 140/100 mm of Hg, respiratory rate of 42/min and SPO₂ of 95% on room air. Other systemic examinations were unremarkable. Routine haematological evaluations were normal. Urinalysis revealed 3+ protein, 2-4 RBC/hpf, and 5-8 pus cells/hpf. Serum albumin was 1.6 mg/dl (Normal reference range 3.5-5.5 gm/dl) while serum cholesterol was found to be 733 mg/dl (Normal reference range <200 mg/dl). Urine culture showed no growth at 72 hours of incubation. Serum electrolytes,

renal and liver function tests were normal. He was started on 60 mg/m²/day Prednisolone and Enalapril. In the meantime, his dyspnea worsened and he was unable to maintain SPO₂ >90% even at very high free flow oxygen. Chest X-ray was unremarkable and electrocardiogram (ECG) showed sinus tachycardia. 2-D Color Doppler echocardiography revealed mild tricuspid regurgitation, mild pulmonary artery hypertension and right ventricular systolic pressure of 50 mm Hg. His D-dimer value was 5308.63 ng/ml (Normal reference range <500 ng/ml) and INR was 0.9 (Normal reference range <1.3). Computed tomography (CT) pulmonary angiography revealed pulmonary thromboembolism in bilateral pulmonary arteries (Figure 1). Retrospectively we tried to correlate the headache episode in the past to possible cerebral venous sinus thrombosis (CVST).

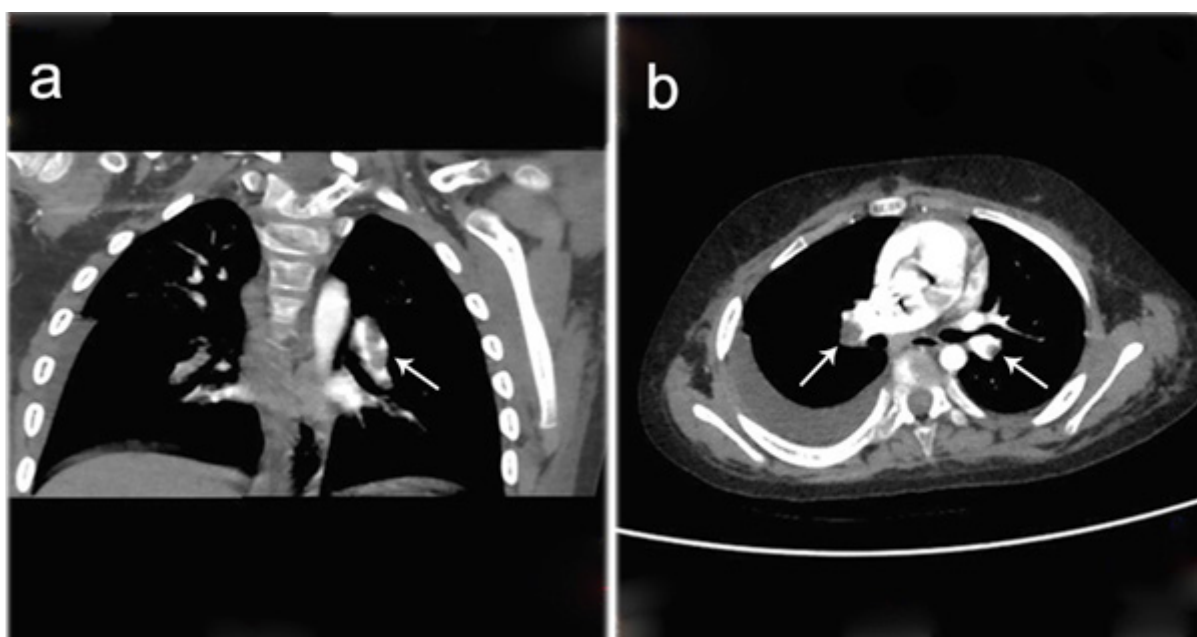


Figure 1- Computed tomography (CT) pulmonary angiogram, coronal (a) and axial (b) images showing non-enhancing partial filling defects (arrows) in bilateral pulmonary arteries near bifurcation extending into descending trunk suggestive of pulmonary thromboembolism.

Magnetic resonance venography (MRV) was carried out for persistent headache and it was suggestive of cerebral venous sinus thrombosis (Figure 2).

Color Doppler ultrasound of renal vessels didn't show any evidence of renal vein thrombosis. Unfractionated heparin infusion was continued for 48 hours and was followed by low molecular weight (LMW) heparin for 7 days. Marked oedema and ascites

were managed with 20% albumin and frusemide infusions. Antihypertensives (amlodipin, labetalol and clonidine) were added one by one after reaching highest permissible dose for each. Antithrombotic prophylaxis was continued with oral warfarin with target INR between 2 and 3. Steroids were continued at 60 mg/m²/day for 28 days but 4+ proteinuria persisted and the diagnosis was modified to steroid-resistant

nephrotic syndrome (SRNS). Renal biopsy was planned but withheld in view of oral anticoagulation and significant hypertension. Oral tacrolimus was started and steroid was modified to 40 mg/m² alternate day. Antihypertensives were gradually tapered once BP was less than 95th centile. He was discharged on tacrolimus and alternate day prednisolone along with

oral warfarin and enalapril. At 2 weeks follow up he was in partial remission (Urine protein 2+) with blood pressure <95th centile and INR of 2.8. Parents were counselled for renal biopsy once antithrombotic prophylaxis is over. Warfarin was suggested to continue for 6 months with a regular follow up plan to monitor proteinuria, INR and serum tacrolimus level.

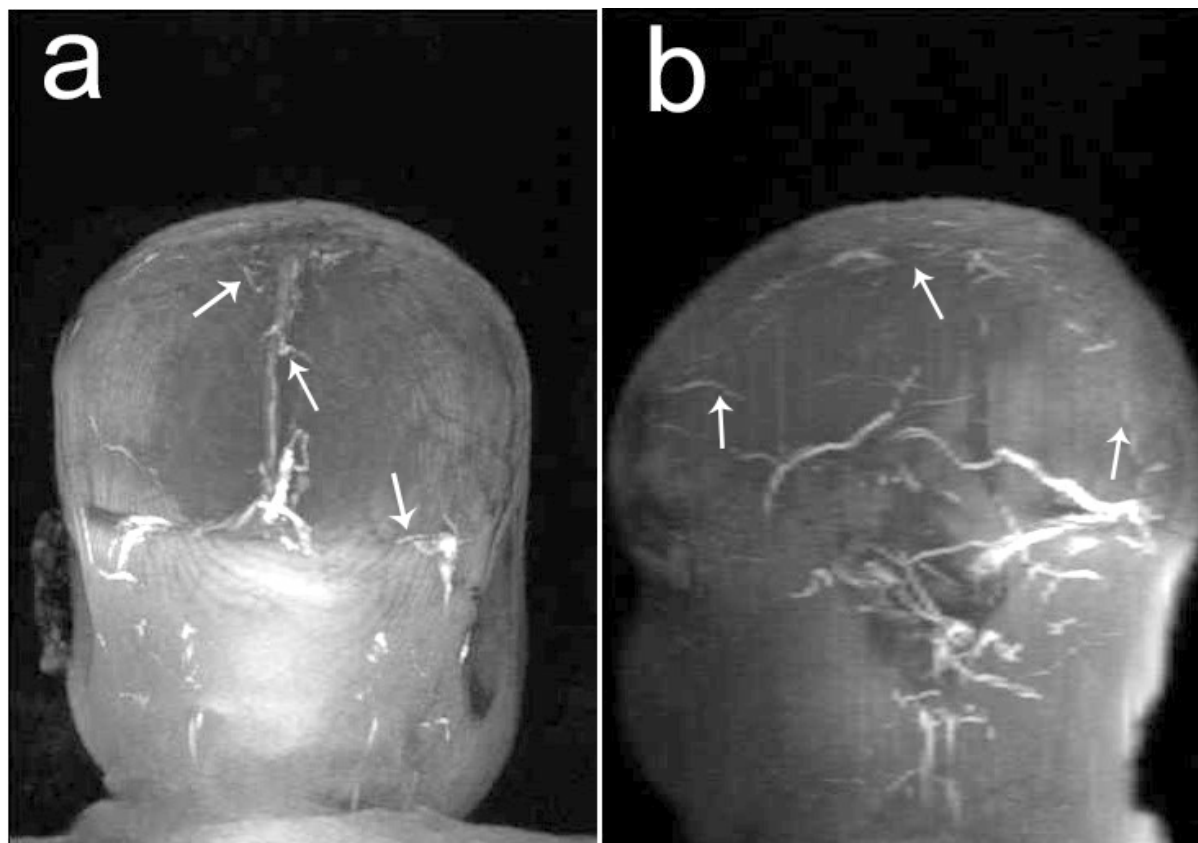


Figure 2- Magnetic resonance venography (MRV), coronal (a) and sagittal (b) images showing reduced flow related signal (arrows) with partial flow at places in superior sagittal sinus, inferior sagittal sinus, bilateral transverse sinuses, bilateral sigmoid sinuses and bilateral jugular veins suggestive of dural sinus thrombosis.

DISCUSSION

The incidence of thromboembolic complications in nephrotic children varies between 2% to 5% with a higher incidence in SRNS than steroid responsive NS [3]. Sino-venous thrombosis is probably less recognized or under-reported in children with nephrotic syndrome [4]. The median time to thromboembolic events is about 71 days after the diagnosis of nephrotic syndrome [5]. Hypercoagulability, hemoconcentration and diuretics

administration are well known risk factors. The ratio of proteinuria to serum albumin correlates better with the severity of thrombosis in NS [6]. Plasma D-dimer has almost 100% negative predictive value but is non-specific and requires further evaluation. CT pulmonary angiography has acceptable sensitivity and specificity making it a good first line investigation for PE [7]. CSVT should be considered in any child

with nephrotic syndrome who develops neurologic symptoms such as unexplained headache, focal or generalized seizures or signs of raised intracranial pressure. T2 weighted images with MRV has been found sensitive to define the extent of CVST [5]. CT venogram with comparable efficacy can be utilised in case of non-availability of MRV. Anticoagulant therapy with unfractionated heparin or LMW heparin is essential once thromboembolic events have been documented. Anticoagulant prophylaxis with oral anticoagulants for 6 months has been recommended in the absence of recurrent thrombosis with targeted INR of 2.0-3.0 [8]. Repeat MRV at 6 months to confirm recanalization of thrombosed vessels may help in deciding cessation of further anticoagulation.

The pathophysiological mechanisms of thromboembolism in patients with NS have yet to be unrevealed. The reported risks of VTE or ATE in patients with NS are based on numerous case reports and small studies with mostly short term follow-ups and therefore are of limited accuracy. Easy availability of imaging techniques like CT angiography and magnetic resonance venography (MRV) along with increasing awareness of condition should make it more frequently diagnosed, with scope of its reversal with timely treatment. This case report suggests that children with nephrotic syndrome are at risk for CVST and pulmonary embolism even at the onset of the disease and should be monitored closely for the same.

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