

Pulmonary embolism in a child of nephrotic syndrome: A rare but serious complication

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ABSTRACT

Thromboembolic complications are well-documented but rare complications of nephrotic syndrome (NS). NS is a hypercoagulable state associated with venous and rarely, arterial thromboembolism with an estimated risk of up to 1.8–5%. We report a case of a 10-year-old boy who was a known case of NS with frequent relapses that had a massive pulmonary embolism, although clinical signs and symptoms were minimal. Raised D-dimer and computed tomography pulmonary angiography established the definitive diagnosis. The child was started on low molecular weight heparin treatment and responded well.

Key words: D-dimer, Nephrotic syndrome, Pulmonary angiography, Pulmonary embolism

Nephrotic syndrome (NS) is a primary glomerular disease. The earliest recorded description of NS was from the 15th century. The concept of “nephritis in contrast to nephrosis” was further popularized by Volhard *et al.* It was used to describe a major classification of bilateral renal disease. Now, NS is recognized as a common chronic illness in childhood. It is characterized by proteinuria defined by urine protein >3.5 g/24 h or urine protein-creatinine ratio >2 mg protein/mg creatinine, edema, hyperlipidemia (>200 mg/dl), and hypoalbuminemia. Hypoalbuminemia causes increased production of coagulation factors in the liver which leads to a hypercoagulable state and an increased risk of thrombotic events, including pulmonary embolism (PE) [1,2].

NS is a hypercoagulable state associated with venous and rarely, arterial thromboembolism with an estimated risk of up to 1.8–5% [3,4]. It involves abnormalities in fibrin formation and platelet aggregation, vascular stasis, loss of antithrombin III, Protein C and S in urine, and increased production of fibrinogen [5]. Thromboembolic events can occur in both venous and arterial territories. The more frequently involved are the cerebral venous sinuses and middle cerebral arteries, deep veins of the lower limbs, vena cava, renal and hepatic veins, pulmonary, and mesenteric artery [6]. PE may present with minimal clinical signs or may be asymptomatic for life and lead to sudden death. Here, we describe the subtle presentation of a massive PE in a boy with steroid-dependent NS.

CASE REPORT


A 10-year-old male child who was a known case of NS reported to our department with edema over bilateral eyelids and lower limbs and cough and cold for 7 days which was associated with intermittent episodes of chest pain and shortness of breath. He was diagnosed with NS at 2 years and had started with prednisolone. Since then, the patient had three episodes of relapse. The patient was on prednisolone therapy with a dosage of 40 mg/m² daily at the time of admission.

On physical examination, the patient had mild edema at the extremities and tachypnea (respiratory rate 36/min). The body temperature was 37°C, blood pressure 106/72 mm-Hg, heart rate 85–95 bpm, and oxygen saturation were 98% (at room air). Urinalysis showed 4+ of protein on the dipstick and urinary protein/creatinine ratio was 14 mg/mg. Blood investigations revealed hemoglobin of 15.6 g/dL with hematocrit 45.2%, platelet count 173000/μL, total leukocyte count 11400/mm³, low serum albumin 2 g/dl, raised total cholesterol 598 mg/dl, and raised serum triglycerides 300 mg/dl. There was difficulty in breathing. Chest X-ray was suggestive of bilateral hilar prominence which led to a differential diagnosis of PE which is a known complication of NS.

Hence, D-dimer test was done where elevated levels of 9.98 μg/mL (<0.5 μg/mL) were observed, along with a coagulation profile which was normal with prothrombin time 13.3 s, activated partial thromboplastin time 32, and international normalized ratio

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0.95. Furthermore, 2-D echocardiography and color Doppler revealed thrombus which was seen in the left pulmonary artery. There was dilated right atrium/right ventricle/microscopic polyangiitis/inferior vena cava, and normal cardiac valves with good left ventricle (LV) systolic function and left ventricular ejection fraction-60%. Electrocardiogram, renal Doppler, and deep vein thrombosis scan showed no abnormal findings.

Computed tomography (CT) pulmonary angiography (CTPA) documented thromboembolism in both right and left branches of the pulmonary artery, with suspicion of early changes of ventricular strain (Fig. 1 and 2).

After admission, the patient was given symptomatic treatment. To treat the NS relapse, the prednisolone dose was increased to 60 mg/m²/day from 40 mg/m²/day. The patient received 1 dose of 20% human albumin solution infusion. Anticoagulation with low molecular weight heparin (1 mg/kg/dose BID) was started. NS remitted after 15 days of treatment. PE showed a favorable development, with complete resolution documented by CT 4 weeks after the event. Anticoagulation with low molecular weight heparin was maintained for 6 months (1 mg/kg/dose BID).

The patient came for a follow-up in May 2020. Routine investigations were within normal limits. A repeat 2D-Echo

was done which showed no signs of an embolus. The patient is currently on prednisolone therapy alone.

DISCUSSION

Patients suffering from NS are at a significantly increased risk of thrombosis, with complication rates reported as high as 40% in adults [7]. Thrombosis risk is apparently lower in nephrotic children (18–50%), but events can be much more severe [8]. However, these complications in childhood are actually under-diagnosed.

Thromboembolic events generally require three basic conditions to be fulfilled: Vascular endothelial injury, slow blood flow or stasis, and a hypercoagulable state. The pathophysiology of NS involves increased glomerular permeability to large molecules (albumin) which results in loss of albumin through the glomerulus. This leads to hypoalbuminemia which in turn causes the plasma colloid osmotic pressure to drop, producing movement of water from the blood to the tissues. This, then, decreases the circulating blood volume and leads to increased concentrations of blood coagulation factors. Concurrently, to combat the hypoalbuminemia the liver increases the production of albumin along with other substances, including coagulation factors, total cholesterol (TC), and low-density lipoprotein, and the kidney reduces the excretion of these substances (except albumin), which results in an imbalance between pro and anticoagulant factors triggering a thrombosis [9,10].

In the present case, the patient had a PE during a relapse and presented with a high urinary protein/creatinine ratio and low plasma albumin. Similar findings were reported by Safdar *et al.* [5]. Although plasma D-dimers have little evidence in children, the high levels of D-dimers are markers for thrombosis and provide an important clue to the diagnosis. In the present case, elevated levels of D-dimers were observed. Similar findings were noted by Coskun *et al.* [11]. CTPA, in the present case, established a definitive and reliable diagnosis of PE. This is in accordance with the findings by Moore *et al.* [12].

The present case was managed by the administration of low molecular weight heparin for 6 months (1 mg/kg/dose BID). In patients with a recurrent but reversible risk factor for thrombotic events, it is recommended to use prophylactic anticoagulants for at least 6 months and also during future relapses [13]. Chronic steroid therapy in patients with steroid-dependent or frequently relapsing NS is associated with numerous side effects.

CONCLUSION

PE is a known but rare complication of NS in children. A high index of suspicion is required as the clinical features may be subtle. Advanced radiological techniques help in confirming the diagnosis. Early aggressive heparin therapy followed by oral anticoagulants is necessary for a favorable outcome.

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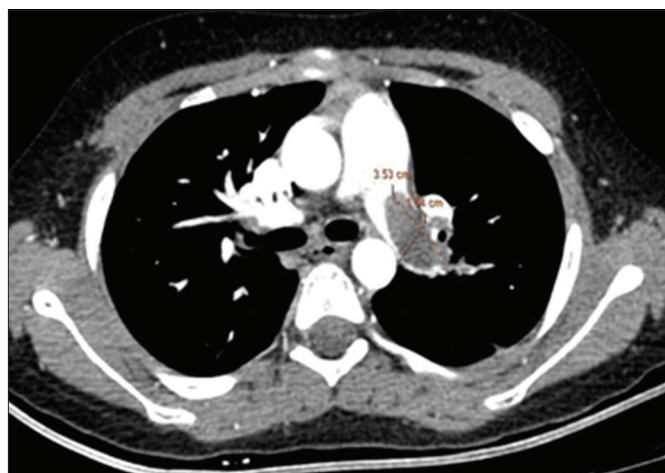


Figure 1: Computed tomography pulmonary angiography suggestive of thromboembolism in the left branch of pulmonary artery

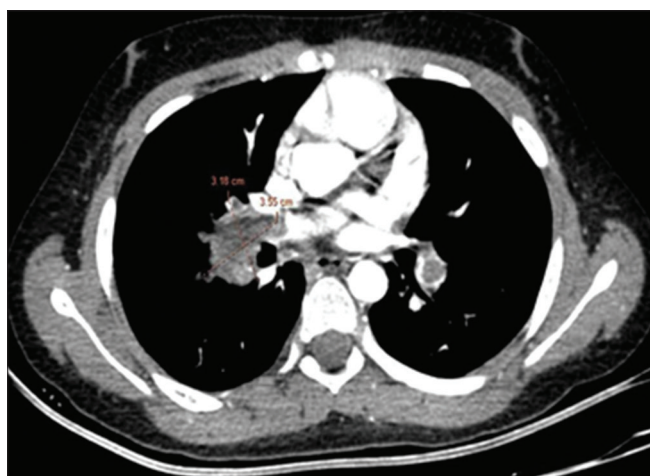


Figure 2: Computed tomography pulmonary angiography suggestive of thromboembolism in the right branch of pulmonary artery

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