

Case Report

Asymptomatic Intracardiac Thrombus in A Child with Nephrotic Syndrome

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Nephrotic patients are at risk of developing venous and arterial thromboses. Various organ manifestations have been reported. Intracardiac thrombi associated with multiorgan thrombosis have been reported in autopsy in the earlier literature, but there is only one case report in living patients with nephrotic syndrome. Here we report a 9-year-old boy with steroid-resistant nephrotic syndrome who developed an asymptomatic but potentially hazardous large intracardiac thrombus.

Archives of Iranian Medicine, Volume 9, Number 4, 2006:426 – 428.

Keywords: Hypercoagulability • intracardiac thrombus • nephrotic syndrome (NS) • thrombosis

Introduction

Hypercoagulability state leading to thromboembolic events is one of the most serious complications of nephrotic syndrome (NS). The possible mechanisms are multifactorial. Serum concentrations of plasminogen, antithrombin III, protein C, and protein S are reduced through urinary loss. Compensatory protein synthesis results in elevated levels of macroglobulins, fibrinogen, thromboplastin, and factors II, V, VII, VIII, and X.¹⁻³ Therefore, there is an imbalance between thrombotic and antithrombotic factors in NS. Other contributing factors include: volume depletion, thrombocytosis, platelet hyperactivity,² hypercholesterolemia,⁴ and infections.

Also, numerous iatrogenic factors such as immobilization, trauma, multiple vein punctures,⁵ diuretics, and treatment with steroids increase the risk of thrombosis.

Additional inherited risk factors that contribute to hypercoagulability state are homozygous gene mutations of methylenetetrahydrofolate reductase, factor V and factor II.^{6,7}

Both arterial and venous thromboses have been recognized in NS. The most common sites are deep leg veins followed by inferior vena cava.⁵ Primary arterial thrombosis is less common, but it has been reported in the pulmonary artery as a cause of sudden death,¹ in the abdominal aorta,⁸ and even coronary arteries.⁹ This article presents a child with steroid-resistant NS who developed a large asymptomatic intracardiac thrombus.

Case Report

A previously healthy boy developed NS at the 9th year of life. On admission, he had generalized edema with massive ascites, hydrocele, and right pleural effusion. His blood pressure was 105/75 mmHg and cardiac auscultation was normal. His family history was negative for coagulation disorders. Urinalysis showed protein 4⁺ and RBC = 0 – 1. Twenty four-hour urine protein was 5360 mg. Other laboratory tests showed cholesterol = 570 mg/dL, triglyceride = 520 mg/dL, albumin = 1.7 g/dL, Hb = 15.6 g/dL, platelets = 600000/mL, and creatinine = 0.5 mg/dL. C₃ and C₄ were in normal range. ANA and HBsAg were negative. Initially, he was treated with prednisolone 60 mg/m²/day and hydrochlorothiazide 2.5 mg/kg/day. Infusion of albumin 1 g/kg/dose with furosemide (1 mg/kg) was given on alternate days for ten days, because of severe edema.

In spite of significant reduction of edema, after

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Accepted for publication: 1 January 2006

4 weeks of treatment with oral prednisolone, 24-hour urine protein measured 2800 mg. So, kidney biopsy was performed and its result was compatible with focal segmental glomerulosclerosis. At this stage, we initiated methylprednisolone pulse therapy according to the protocol of Mendosa et al.¹⁰ After receiving intravenous methylprednisolone 30 mg/kg/dose every other day for 2 weeks, and then weekly for 8 weeks, proteinuria declined to 220 mg per day. So, we discharged the patient. After two weeks, he was readmitted for every other week treatment with pulse of prednisolone. On this admission, he had a good general condition without edema.

On physical examination, we discovered a grade 3/6 systolic murmur in upper left sternal border, but the patient had no signs and symptoms of cardiac failure. Echocardiography revealed a moving cylindrical mass measuring 60 × 10 mm in the right ventricle (RV), originating from the superior part of tricuspid valve and extending from the RV outlet to the pulmonary valve (Figure 1). There was a turbulent flow with 35 mmHg gradient in the RV outlet. The other cardiac chambers were intact.

Doppler ultrasound examination revealed no thrombus in the inferior vena cava. We measured protein C, protein S, and fibrinogen level, which were in normal range.

We initiated heparin and then referred the patient to cardiology unit. He underwent an open heart surgery and the intracardiac mass was extruded by surgery (Figure 2).

Two different pathologists evaluated the mass microscopically and confirmed its thrombotic nature.

Now, after 9 months of follow-up, the patient is



Figure 1. Transthoracic echocardiogram (parasternal short axis view) showing large thrombus (arrows) in the RV outlet and main PA.



Figure 2. The thrombus that was extruded by surgery.

in a good clinical condition and his NS is in remission. In control echocardiogram, there is no thrombus (Figure 3). He receives warfarin, monthly methylprednisolone pulse, and oral prednisolone (0.5 mg/kg) on alternate days.

Discussion

The incidence of thromboembolic complications in children with NS is 1.8 – 5%.¹¹ The incidence is higher in steroid-resistant compared with steroid-responsive NS.⁶ Although most thromboembolic complications have been reported in adults especially with membranous nephropathy,⁴ there is some evidence that subclinical thrombosis may be frequent in children.⁵

Hoyer et al evaluated 26 nephrotic children in remission period with pulmonary ventilation/perfusion test and found that 28% had evidence of pulmonary embolism. This finding



Figure 3. Transthoracic echocardiogram after the surgery (parasternal four-chamber view).

reveals the high frequency of asymptomatic thromboembolic events in children.¹²

Depending on the location of thrombosis, various clinical presentations have been reported such as hemiparesis, seizure and stroke due to cerebral sinovenous thrombosis,^{3, 13, 14} chylothorax due to superior vena cava thrombosis,¹⁵ Budd-Chiari syndrome due to inferior vena cava thrombosis¹⁶, and short bowel syndrome due to mesenteric thrombosis.⁶

Intracardiac thrombi in NS have rarely been described in children. Weisz et al reported the first case of an asymptomatic intracardiac thrombus in a child with steroid-responsive NS and underlying ventricular septal defect.² In their patient the thrombus, measuring 12 × 8 mm, was located and fixed at the wall of the interatrial septum. It was a calcified thrombus, without any moving parts and was managed conservatively.

In most reported cases of thromboembolic events in NS, treatment with high-dose heparin with or without thrombolytic agents, has been effective in resolution of thrombus.^{3, 4, 12, 13, 15}

Our patient had a large moving thrombus just near the pulmonary valve. It could result in a massive pulmonary embolism and even sudden death. Therefore, it needed open heart surgery in addition to anticoagulation. He had a protracted course of edema and hypoalbuminemia, and it was unclear at what stage the thrombus actually developed. Other contributing factors in this patient were immobilization (because of massive ascites and hydrocele), thrombocytosis, hyperlipidemia, and long-term treatment with steroids and diuretics.

Our presented case is an example of asymptomatic but potentially life-threatening thrombotic event that raises the question of prophylactic treatment with anticoagulants in children with steroid-resistant NS and refractory edema.

Although there are no prospective studies providing data on prophylactic treatment, some authors recommend prophylactic use of warfarin or aspirin in high-risk patients with plasma albumin less than 2 g/dL, fibrinogen level over 600 mg/dL, or an antithrombin III level below 70% of normal.¹

In conclusion, children with NS have increased risk of thrombosis and patients with severe hypoalbuminemia should be observed carefully.

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