CASE REPORT

Nephrotic Syndrome: A Rare Cause of Acute Coronary Syndrome in a Child

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ABSTRACT

Patients with nephrotic syndrome are at risk of developing thrombosis in both veins and arteries. Various manifestations in different organs have been reported. Thrombi in heart seen, associated with multiorgan thrombosis have been reported on autopsy earlier, but only once in a living patient with nephrotic syndrome. Here, we report a 13 years old boy with steroid-resistant nephrotic syndrome, who developed an asymptomatic but potentially hazardous large intracardiac thrombus. The child developed nephrotic syndrome at the age of 9 years and had multiple recurrences. At the age of 13 years, he developed myocardial infarction (MI) due to embolism from a large intracardiac thrombus. Later on, he was treated with heparin and warfarin anticoagulation.

Key words: *Hypercoagulability. Intracardiac thrombus. Nephrotic syndrome (NS). Acute coronary syndrome. Child.*

INTRODUCTION

Increased risk of atherosclerosis and coronary heart disease (CHD) is seen in patients with nephrotic syndrome.[1] The likely cause for such a destructive atherosclerotic coronary artery narrowing is dyslipidemia and infection due to immunosuppressive and dyslipidemic drugs like steroids. Nephrotic syndrome patients frequently have hyperlipidemia and hypercoagulability and the incidence of myocardial infarction (MI) is eight times higher than normal in patients with nephrotic syndrome.[2] After infection and renal failure, nephrotic syndrome with coronary heart disease has become the third common cause of death.[2] A variety of causes such as agenesis or anomalous origin of the left coronary artery, absence of the left coronary artery, vasculitis (e.g., Kawasaki's disease), embolism, hyperlipidemia, hypercoagulability state and myocarditis have been reported as a cause of myocardial infarction in children.[3]

Although rare, children with long-lasting nephrotic syndrome may be at increased risk for ischaemic cardiovascular events, due to hyperlipidemia as well as a hypercoagulability state.[4] The possible mechanisms for hypercoagulability state leading to thromboembolic events in patients with nephrotic syndrome (NS) are multifactorial. Serum concentrations of Plasminogen, Protein C, Antithrombin III, 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. Additional causative factors include: volume depletion, thrombocytosis, platelet hyperactivity, hypercholesterolemia and infections.[6,7] In addition, many causative factors such as trauma, immobilization, diuretics, multiple vein puncture, and treatment with steroids increase the risk of thrombosis. Other inherited risk factors that add to hypercoagulability state are homozygous gene mutations of methylenetetrahydrofolate reductase, factor V and factor II.[7,8] The most common sites of thrombosis are the deep leg veins followed by inferior vena cava.[6] Primary arterial thrombosis is less common, but it has been reported in the pulmonary artery as a cause of sudden death, in the abdominal aorta,[9] and even coronary arteries.[10]

This report describes a child with NS who developed a large asymptomatic intracardiac thrombus.

CASE REPORT

A previously healthy young male of age 9 years developed nephrotic syndrome in year 2004. He was brought to Sindh Institute of Urology and Transplantation where he was diagnosed and being treated with steroid to which he responded. He had segmental glomerulosclerosis on histopathology. Later on he developed multiple recurrences for which he was put on short courses of steroids followed by maintenance dose. He presented to emergency department on November 2008 at the age of 13 years with one week old history of sudden onset of severe retrosternal chest heaviness. The pain radiated to the left shoulder and arm and was associated with diaphoresis. The pain persisted for few hours and he was diagnosed as acid peptic disease at some hospital. Later on due to incomplete response

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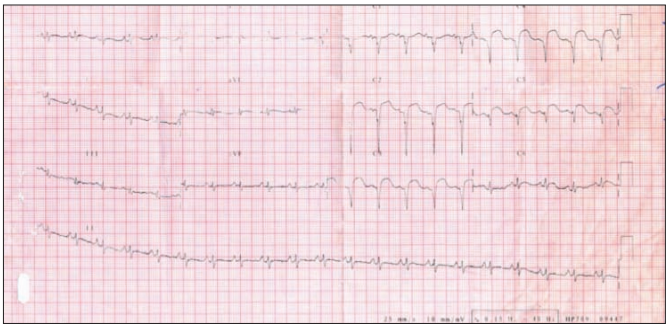

Figure 1: Showing ST-elevation from lead VI-V6, I and a VL.

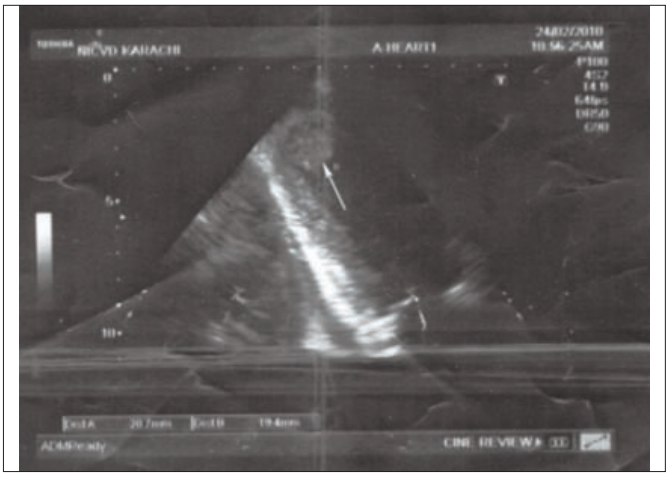

Figure 2: Echocardiography showing thrombus at LV apex (white arrow).

to treatment he was referred to National Institute of Cardiovascular Diseases where he was diagnosed as old anterior wall myocardial infarction with Q waves in anteroseptal leads (Figure 1).

At presentation, he had blood pressure of 100/70 and pulse of 101 beats per minute. He was afebrile with a respiratory rate of 14 per minute. Due to late presentation thrombolysis was not done. Cardiac auscultation was normal and chest examination was unremarkable. Troponin-I was raised to value of 12.41 ng/ml and urea and creatinine were within normal limits. Lipid profile was deranged with total cholesterol of 270 mg % and LDL of 180 mg %. Antithrombin was below 50% in this patient (the value was given as percentage of normal).

Heparin was initiated followed by Warfarin. Echocardiography revealed large akinetic area of LV apex, interventricular septum and anterior wall with a large organized apical clot (Figure 2). Left ventricular size was normal but ejection fraction was reduced to 30%. Angiography revealed normal epicardial coronary arteries. He was put on aspirin, clopidogrel, angiotensin-converting enzyme inhibitor, statin and low dose of beta blocker. The patient left Karachi for Abbottabad and was lost to follow-up.

DISCUSSION

Thromboembolic complications are seen in 1.8 - 5% of patients with nephrotic syndrome.[4] Steroid-resistant compared with steroid-responsive nephrotic patients are more prone to develop thrombosis. Although most thromboembolic complications have been reported in adults especially with membranous nephropathy, there is some evidence that subclinical thrombosis may be frequent in children.[5]

In this case premature atherosclerosis was responsible for acute myocardial infarction. Depending on the location of thrombosis, various clinical presentations have been reported such as hemiparesis, seizure and stroke due to cerebral sinovenous thrombosis, chylothorax due to superior vena cava thrombosis, Budd-Chiari syndrome due to inferior vena cava thrombosis and short bowel syndrome due to mesenteric thrombosis.[9]

Weisz *et al.* reported the first case of an asymptomatic intracardiac thrombus in a child with steroid-responsive nephrotic syndrome and underlying ventricular septal defect.[6] In this patient the thrombus was located at the LV apex. It was a calcified thrombus, without any moving parts and was managed with anticoagulation.

In most reported cases of thromboembolic events in NS, treatment with high-dose heparin with or without thrombolytic agents, has been found effective in resolution of thrombus.[6]

This patient had a large immobile thrombus. He had a protracted course of oedema and hypoalbuminemia. Other contributing factors in this patient were immobilization, thrombocytosis, hyperlipidemia, and long-term treatment with steroids and diuretics. Thrombus was asymptomatic in this case and there was no previous history of cerebrovascular events or peripheral embolism. This also raises the question of prophylactic treatment with anticoagulants in children with steroid resistant nephrotic syndrome and pedal oedema. Our patient was treated with heparin and warfarin because there was large area of apical akinesia and a large clot with potentially high risk of thrombosis. 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.[10] A clot embolism from LV apex could have caused this but it was unlikely as there was no previous history of peripheral or cerebral embolism.

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

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