Portal Vein Thrombosis: A Rare Complication of Nephrotic Syndrome

Abstract

Deep vein thrombosis, renal vein thrombosis, and cerebral venous sinus thrombosis in children are frequently described complications of nephrotic syndrome (NS). Early diagnosis and treatment with anticoagulants is the key for a good outcome. There are a few reported cases of portal vein and superior mesenteric thrombosis in adults in association with NS. Here, we describe two cases of portal vein thrombosis with variable extent of involvement of superior mesenteric vein in association with relapse of NS. A high degree of suspicion, ultrasonography of the abdomen along with Doppler study of abdominal vessels, and computed tomography angiography can only pick up such unusual sites of thrombosis and facilitate early management.

Keywords: *Anticoagulation, computed tomography angiography, Doppler study, nephrotic syndrome, portal vein thrombosis*

D. N. Gera, J. Patel, K. Patel[1], V. B. Kute

Departments of Nephrology and Clinical Transplantation and [1]Radiology, Institute of Kidney Diseases and Research Center, Dr. HL Trivedi Institute of Transplantation Sciences, Ahmedabad, Gujarat, India

Introduction

Thromboembolic complications of peripheral and deep veins are well known in nephrotic syndrome (NS) because of a hypercoagulable state. These complications though less frequent in children tend to be more severe than in adults.[1] Cerebral venous sinus thrombosis though rare is quite often reported in children with NS with complaints of headache and vomiting.[2] Similarly, pain in abdomen and vomiting in association with ascites is a very common symptom. The following two cases of portal vein thrombosis demonstrate this rare but potentially lethal complication of NS. Since the outcome may be variable, depending on the onset, extent of involvement, and timing of diagnosis and intervention, a high degree of suspicion is very important while treating such patients. Easy availability of imaging techniques such as Doppler study, computed tomography (CT) angiography, and increasing awareness of the condition should make it a more frequently diagnosed entity, with scope of its reversal with early treatment.

Case Reports

Case 1

A 12-year-old boy, weighing 24 kg, was suffering from steroid-dependent NS for 8 years. He presented with generalized anasarca at 4 years of age. At that time, his 24 h urinary protein excretion was 3.5 g/day, serum creatinine was 0.6 mg/dl, serum albumin was 1.3 g/dl, and serum cholesterol was 650 mg/dl. He was treated with prednisolone, 20 mg/day initially for 4 weeks, and then was tapered to 10 mg/day over 2 months. However, the child had >3–4 relapses per year associated with respiratory infection. He could never be weaned off steroids. Renal biopsy was performed at 10 years of age in August 2013, which showed idiopathic mesangioproliferative glomerulonephritis with negative immunofluorescent staining. Tacrolimus 0.5 mg twice a day was added after renal biopsy along with prednisolone 10 mg/day. Tacrolimus trough blood level was maintained at 3 ng/ml during the course of treatment. He went into remission after 3 weeks of therapy. In July 2014, he had a proteinuria of 300 mg/24 h, serum creatinine of 0.6 mg/dl, and serum cholesterol of 360 mg/dl on routine follow-up.

In September 2014, he was admitted with a relapse with oliguria, facial puffiness, abdominal distension, and pain. Abdominal pain was dull aching and continuous in character. There was no complaint of constipation or vomiting. He was being treated with prednisolone 10 mg, tacrolimus 0.5 mg twice a day, atorvastatin 10 mg, and calcium and Vitamin D supplements.

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Address for correspondence:
Prof. Dinesh Gera, Department of Nephrology and Clinical Transplantation, Institute of Kidney Diseases and Research Centre, Dr. HL Trivedi Institute of Transplantation Sciences, Civil Hospital Campus, Ahmedabad - 380 016, Gujarat, India.
E-mail: dineshgera@ymail.com

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On clinical examination, his vitals were normal, he was afebrile, pulse was 82/min and regular, and blood pressure (BP) was 110/72 mmHg. There was periorbital edema and ascites. There was no tenderness or rigidity of abdominal wall and bowel sounds were normal.

Urine analysis showed + 4 proteinuria with normal sediment, 24 h urinary protein was 5.5 g, hemoglobin (Hb) was 12.8 g/dl, total white blood cell (WBC) count was 8300/cmm, platelet count was 3.3 lakh/cmm, serum creatinine was 0.93 mg/dl, serum albumin was 1.8 g/dl, serum cholesterol was 350 mg/dl, serum bilirubin was 0.4 mg/dl, and serum glutamic pyruvic transaminase (SGPT) was 26 IU with normal electrolytes. Ultrasonography of the abdomen revealed normal-sized kidneys without dilatation of pelvicalyceal system and presence of moderate ascites. Liver and gall bladder were normal. Portal vein was 11 mm at porta filled with echogenic material extending to splenoportal confluence, suggesting portal vein thrombosis. Doppler images showed echogenic filling of portal vein extending into the superior mesenteric vein (SMV) with absent color flow within it and a few periportal collaterals adjacent to it [Figure 1]. CT angiography of the portal vein confirmed the same by absent filling of portal vein and SMV by contrast and delineating echogenic thrombus within it. Diagnostic ascitic taping revealed transudative fluid with 0.8 g protein/L, 8–10 lymphocyte/cmm, and culture was negative. His coagulation profile showed prothrombin time (PT) of 11 s (control – 11 s) with international normalized ratio (INR) of 1.1 and activated partial thromboplastin time (APTT) of 26 s (control – 32 s). Protein C and Protein S levels were normal.

Expert opinion of a gastroenterologist and a vascular surgeon was sought and both of them advised conservative management. The child was kept nil by mouth with continuous Ryle's tube aspiration for 4 days. He was treated with dalteparin, a low-molecular-weight heparin 2500 unit subcutaneously 12 hourly (75–100 unit/kg each dose) for 5 days. Warfarin was added on the 4th day at a dose of 1 mg twice a day to keep INR between 2 and 2.5. His nephrotic state was treated with human albumin 20% 100 ml for 5 days along with increasing dose of prednisolone to 30 mg/day and tacrolimus 0.5 mg twice a day. Parenteral ceftriaxone 500 mg twice a day was given for 5 days. The child responded to conservative treatment and there was remission of proteinuria after 10 days. Ascites as well as abdominal pain resolved, and the patient was discharged after 10 days. The patient was continued on warfarin 1 mg twice a day for 6 months with weekly monitoring of PT with INR along with treatment of NS.

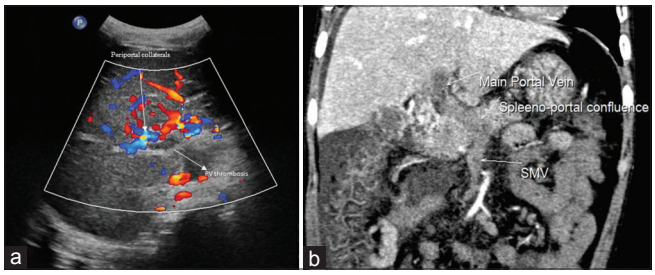

Figure 1: (a) Doppler image showing portal vein thrombosis with periportal collaterals and (b) computed tomography angiography showing noncontrast filling of main portal vein extending up to the splenoportal confluence and into the superior mesenteric vein

On follow-up after 3 months, Doppler and CT angiography study of portal vein showed well-canalized portal vein with periportal collaterals [Figure 2a].

During a further 18-month follow-up, the child developed distended vertical superficial veins on abdomen and chest with frequent pleural effusion on the right side requiring intercostal drainage and pleurodesis [Figure 2b]. Pleural fluid protein level was 1.5 g/dl and cells were 3–4 lymphocytes/cmm. His esophago-gastroscopy was normal. At present, with 3 years of follow-up in September 2017, his NS is under remission with normal renal function and without any evidence of portal hypertension. At present, the child is taking 10 mg prednisolone, tacrolimus 0.5 mg twice a day, and Vitamin D and calcium supplements. The last tacrolimus level was 2.8 ng/dl. Tacrolimus levels were maintained between 2.8 and 3.5 ng/ml during treatment.

Case 2

A 13-year-old boy weighing 25 kg was suffering from frequently relapsing NS for 6 years. He had undergone renal biopsy 4 years back, which showed focal segmental glomerulosclerosis with diffuse IgM deposits on immunofluorescence. At the time of renal biopsy, his serum creatinine was 0.3 mg/dl, serum albumin was 1.8 g/dl, serum cholesterol was 450 mg/dl, and 24 h urine protein was 2.5 g/day. After renal biopsy, he was treated with 15 mg prednisolone, 0.75 mg tacrolimus twice a day, tablet nifedipine retard 20 mg twice a day, tablet losartan 25 mg twice a day, and 10 mg atorvastatin at bedtime, along with calcium and Vitamin D supplements. His tacrolimus level was maintained at 3 ng/ml during treatment. He achieved remission after 4 weeks of therapy. Finally, before the occurrence of the present complication, he came for follow-up in April 2016. At that time, he was asymptomatic and his Hb was 9.9 g/dl, serum creatinine was 0.27 mg/dl, serum albumin was 2.8 g/dl, serum cholesterol was 320 mg/dl, and urinary protein was 600 mg/24 h.

In July 2016, he was admitted with the complaints of oliguria, facial puffiness, vomiting, and abdominal pain, which were severe and continuous for last 3 days. The child was restless and tossing in the bed. He was constipated for 24 h. His urine output was 250 ml/day. On examination, the child looked toxic and pale. Periorbital edema was present. His pulse rate was 86/min regular and BP was 116/70 mmHg. His abdomen was mildly distended and ascites was present. There was no tenderness or rigidity, but bowel sounds were absent.

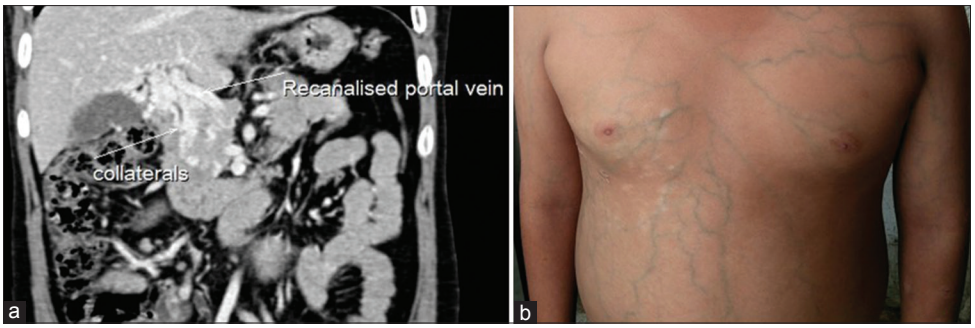

Figure 2: (a) Follow-up computed tomography angiography after 3 months of event showing contrast-filled recanalized portal vein with multiple contrast-filled collaterals and (b) clinical photograph 1 year later showing engorged vertical vein on the abdomen and chest

On investigation, urine examination showed +3 proteinuria with 10–12 red blood cells (RBCs) and occasional WBC/high-power field, 24 h urinary protein was 3.5 g, Hb was 5.3 g/dl, total WBC count was 16,600/cmm, platelet count was 1.2 lakh/cmm, serum creatinine was 2.7 mg/dl, serum albumin was 1.7 g/dl, serum bilirubin was 1.4 mg/dl, SGPT was 125 units, serum sodium was 135 mEq/l, serum potassium was 5.1 mEq/l, serum calcium was 8.6 mg/dl, PT was 22 s (11 s) with INR 1.98, and APTT was 61 s (control – 32 s). Venous blood gas analysis showed pH 7.34, HCO3 16.3, Na 136, K 5.2, and Ca 0.63 mEq/l. Ultrasonography [Figure 3a] of the abdomen revealed normal-sized kidneys without dilatation of pelvicalyceal system, with presence of moderate ascites. Liver and gall bladder were normal, and the portal vein was 8 mm at porta filled with echogenic material extending to splenoportal confluence, suggesting portal vein thrombosis. Doppler [Figure 3b] images showed echogenic filling of portal vein extending to splenoportal confluence and SMV with absent color flow within it. CT angiography [Figure 3c] of the portal vein showed diameter of 11 mm at porta with nonfilling of main portal vein, splenoportal confluence, splenic vein, and SMV, suggesting thrombosis. Wall of the duodenum and small bowel loops appeared thickened and edematous. Diagnostic ascetic taping revealed hemorrhagic fluid showing 1.6 g protein/L, 30–40 RBC/cmm, 20–25 WBC/cmm, and the culture was negative.

The patient was treated with continuous Ryle's tube aspiration, blood transfusion, intravenous (IV) fluids, 20% human albumin, IV imipenem-cilastatin 500 mg 12 hourly, and IV metrogyl 200 mg 8 hourly. His immunosuppressants were stopped. Expert gastroenterologist's and vascular surgeon's opinion was sought. Fibrinogen, fibrin degradation product (FDP) and D-dimer were tested. D-dimer was 1200 mg/ml (Ref: 200–400 mg/ml), fibrinogen was 110 mg/dl (Ref: 150–400 mg/dl), and FDP was 46 mg/l (N: <10 mg/l). CT angiography showed a big segment of bowel loop on the verge of necrosis, but due to impending disseminated intravascular coagulation (DIC), the child could not be taken up for surgery. After few hours, the child started to

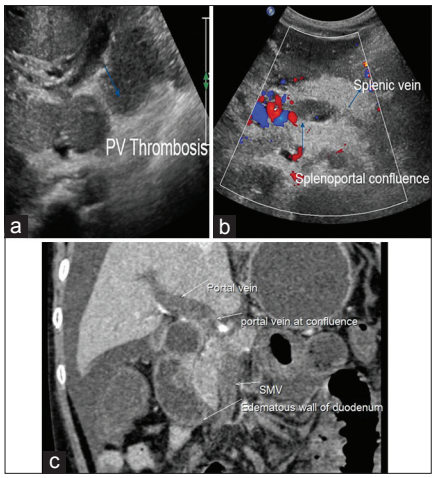

Figure 3: (a) Gray scale image of Case 2 showing portal vein thrombosis, (b) Doppler showing thrombosis of splenic vein and splenoportal confluence, and (c) computed tomography angiography showing noncontrast filling of portal vein, splenoportal confluence, and superior mesenteric vein with edematous wall of duodenum

have hematemesis. The Ryle's tube aspirate became black and smoky. The aspirated volume increased to 1.2 L. It was treated with conservative measures including fresh frozen plasma. Despite all efforts, the child became hypotensive and hypoxic, requiring ventilator support and increasing dose of inotropes. The child expired the next day morning.

Discussion

Patients with NS have hypercoagulable state arising due to alteration in blood levels of various factors involved in coagulation, fibrinolytic system, alteration in platelet function, hemoconcentration, increased blood viscosity, and possibly due to administration of steroids and diuretics.[3] Loss of antithrombin III (physiological anticoagulants) and plasminogen in urine and their low level in blood have been correlated with low serum albumin level.[4,5] Increased production of fibrinogen adds to increased viscosity and hypercoagulability.[6] These patients may suffer from various types of thromboembolic events. Thrombosis of spleno–mesenteric–portal axis is an unusual location reported in a few adult cases with NS in literature, who have

been treated with antithrombotic treatment with variable outcomes. Park *et al*.[7] and Woolf *et al*.[8] were successful in treating similar adult patients with anticoagulation therapy, whereas De Luca *et al*. reported adverse event of gastrointestinal bleeding requiring suspension of anticoagulant therapy, following which the patient died of pulmonary embolism.[9]

Here, we report two cases of portal and SMV thrombosis in pediatric age group. Both of them had different clinical conditions at the time of presentation and different clinical outcomes. The second patient, who could not be anticoagulated because of impending bowel necrosis and reports of DIC, had a poor outcome.

Conclusion

A high degree of suspicion for portal vein thrombosis in children with relapse of nephrotic syndrome, ascites, and abdominal pain may help early workup and diagnosis of such cases for early management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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