ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 10 | October - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A RARE OCCURRENCE OF EXTENSIVE THROMBOSIS IN A CASE OF NEPHROTIC SYNDROME

Paediatrics

Dr. Asma Azad* MD, DNB, Pediatrics, LTMMC, Mumbai *Corresponding Author
Dr. Purvi Kamath MD, DNB, Pediatrics, LTMMC, Mumbai
Dr. Devina Dutta MD, Pediatrics, LTMMC, Mumbai

ABSTRACT

Nephrotic Syndrome (NS) is the most frequent glomerular disease in childhood, affecting 2-7/ 100,000 children (1). Infection, anasarca, hypovolemic shock, anaemia and renal failure are common complications. Thrombosis is a rare but life-threatening event, commonly involving the pulmonary artery, renal vein, inferior vena cava, femoral vessels and cerebral venous sinuses. Here we report a case of Steroid Dependent Nephrotic Syndrome (SDNS) complicated by extensive venous thromboembolism (VTE) involving the Cerebral Venous Sinus and Inferior Vena Cava extending into left renal vein and iliac veins. The state of hypercoagulability associated with NS is the major risk factor for thromboembolic complications apart from treatment related factors and inherent or acquired thrombophilia. Early identification of pathology and prompt intervention aids in better prognosis.

KEYWORDS

Nephrotic Syndrome, Venous Thromboembolism, Pediatric Nephrology

INTRODUCTION

Nephrotic syndrome (NS) is the most common glomerular disease in children affecting 2-7 per 100,000 children [1]. Thromboembolism associated with NS is a rare life-threatening complication, reportedly affecting 1.8-4.4% children [2], but can increase upto 25% in high risk groups. Venous thromboembolisms (VTE) predominates over arterial ones. The pathophysiology of NS-related VTE is likely multifactorial in nature, and can be attributed to patient's underlying thrombophilic tendency, treatment-related hazards, and the most important, disease-related hypercoagulopathy [3]. Early diagnosis and recognition of risk factors causing VTE, followed by prompt intervention aids in better prognosis.

Case Report

A 3 years old boy, resident of Mumbai, 1st born to non-consanguineous parents with an unremarkable family history was diagnosed to have Nephrotic Syndrome 7 months back. He relapsed for the 2nd time during tapering dose of steroids, suggesting traits of steroid dependency. His presenting complaints were abdominal pain, vomiting, headache and periorbital puffiness for 5 days, with no history of extrarenal fluid loss. On presentation child was in hypertensive emergency, had altered sensorium and an episode of convulsion on the 3rd day of admission. A contrast enhanced Computed Tomography (CECT) of Brain showed extensive cerebral venous sinus thrombosis (CVST). A complete Doppler study of the body followed by CT Abdominal Angiography unveiled the vast extent of thrombosis- involving the Right Internal Jugular Vein, the Hepatic, Supra Renal and Renal segments of Inferior Vena Cava extending into the Left Renal Vein upto the Right Atrium and bilateral External Iliac and Common Femoral Veins. Patient was started on Low Molecular Weight Heparin (LMWH) which was titrated in dosage. Invasive interventions- (IVC filter and Thrombectomy) were deferred because of the extensive involvement of thrombus and high risk. A strict fluid balance was maintained for the edema and simultaneous prevention of intravascular volume contraction.

INVESTIGATIONS	VALUE	NORMAL RANGE
Spot Urine Albumin	4+	Nil
Serum Albumin	1.8 g/dl	3.4 to 5.4 g/dl
Urine Protein/Creatinine Ratio	54.9	< 0.2
Renal Function Test (BUN/Creatinine)	22 mg/dl / 0.8 mg/dl	6 to 18 mg/dl / 0.3 to 0.7 mg/dl
Haemoglobin/Haematocrit	14 g/dl / 43%	11 to 13.7 g/dl/ 35 to 40%

A secondary Nephrotic work up was negative. Complete bleeding profile and Prothrombotic workup during the acute stage showed reduced levels of Protein C & S and elevated d-Dimer levels of >3000ng/ml. A diagnostic Thrombophilia profile sent 4 months later had normal Protein S levels of 111%, ruling out hereditary thrombophilia. Follow up scans 4 months later revealed complete recanalization of the IJV and IVC. However, there was persistent Left Renal Vein thrombosis and consequently contracted left kidney, which was confirmed non-functional on DTPA Renogram.

Child was being followed up as high dose Steroid Dependent Nephrotic Syndrome on subcutaneous LMWH, alternative immunosuppression with Mycophenolate mofetil and tapering steroids, and was in remission with serum creatinine of 0.4 mg/dl and eGFR of 95ml/min/1.73m^2. However, during a subsequent relapse few months later, he succumbed to the complications of Nephrotic Syndrome.

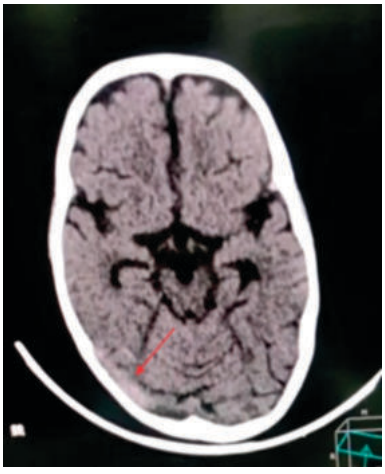

Fig. 1 CECT Brain Showing Right Transverse Sinus Thrombosis.

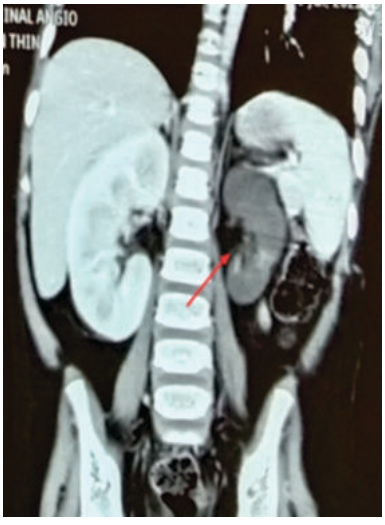

Fig. 2 CT Abdominal Angiography Showing Contracted Left Kidney.

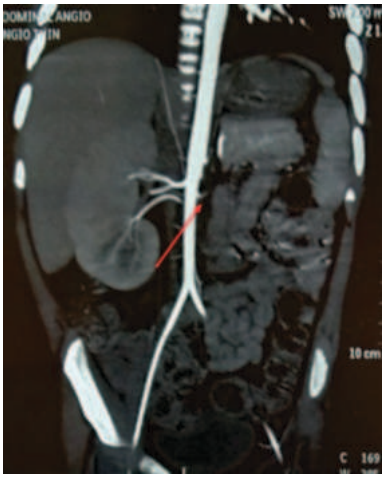

Fig. 3 Non-visualization of Left Renal Vein on CT Abdominal Angiography.

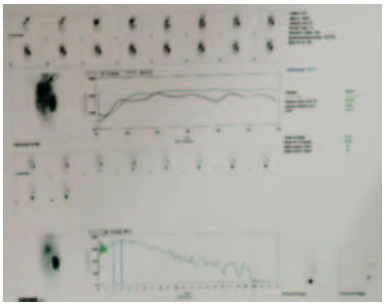

Fig. 4 DTPA Renogram Showing Non-visualized, Non-functional Left Kidney.

DISCUSSION

Nephrotic Syndrome (NS) is a complex of symptoms arising due to filtration of proteins across the glomerular basement membrane. The dramatic and variable shifts in plasma concentration of proteins and enzymes involved in the coagulation and fibrinolytic system, results in an increase in plasma levels of fibrinogen and coagulation factors and urinary loss of antithrombin III, with some studies demonstrating increased adherence and aggregation properties of red cells and platelets as well [5-7]. All these factors potentiate procoagulation and antifibrinolytic system activity making NS a hypercoagulable state.

Our patient had a rather stormy course of NS with two relapses within 7 months of diagnosis. First was within 14 days of stopping steroids and second during tapering dose of steroids, which highly suggested steroid dependency. The frequent relapses, prolonged the state of hypercoagulability, making him susceptible to thromboembolic complications. Andrew et al in his study on haemostatic complications in renal disorders of the young, predicted the median time from NS diagnosis to first thromboembolic event was relatively brief- 70.5 days, suggesting that thromboembolism (TE) is more likely to occur close to the time of diagnosis than during subsequent relapses [8]. The prevalence of subclinical VTE in children with NS is more- 24-25%, compared to the prevalence of clinically significant VTE, which is 3% [9]. This could be the case with our patient who might have had subclinical VTE until it worsened and the complication surfaced with clinical symptoms.

The risk of thromboembolic complications is further increased by dehydration, infection, immobilization, arterial or venous puncture, diuretic or corticosteroid use, haemoconcentration (Hb >14g/dl), thrombocytosis (4,50,000 plt/dl), severe proteinuria, hypo-albuminemia (<2g/dl), hyperfibrinogenemia and hypo-antithrombinemia (<75%) [2]. Age ≥12 years and severity of proteinuria are the most significant independent risk factors for TE according to a multivariate analysis [10]. Although our patient was only 3 years old, he had other risk factors favouring thromboembolism like severe proteinuria, hypoalbuminemia and haemoconcentration.

Children with hereditary thrombophilias and secondary NS with acquired antiphospholipid antibodies (autoimmune glomerulopathies) have a higher risk of 17% to develop VTE vs 6% risk in primary NS [10]. It is therefore advisable to investigate into predisposition for thrombosis in patients with severe or multiple thrombosis. Our patient who had no past medical and/or family history of thromboembolic complications, had normal Protein S levels on thrombophilia profile done 4 months after recovery.

Diffuse Headache of increasing intensity with or without neurological findings or papilledema is the most common presenting symptom of CVST. History of headache and vomiting in our patient with altered sensorium and seizures on the third day of admission, steered us to perform CECT of brain which revealed extensive CVST. Raised intracranial pressure, impaired venous flow or focal brain injury from venous ischemia/ infarction are responsible for the symptoms [10].

When VTE is suspected, it is important to obtain suitable imaging studies to confirm diagnosis. Non-invasive methods without radiation exposure include Doppler compression ultrasonography and Magnetic Resonance imaging where ultrasound images are suboptimal. Following the discovery of CVST in our patient, a full body Doppler study was done which further revealed extensive thrombosis in the Inferior Vena Cava and its tributaries, including left Renal Vein and bilateral Deep Vein Thrombosis. Renal Vein thrombosis (RVT) when goes undiagnosed, leads to severe complications such as acute renal failure or retroperitoneal haemorrhage due to venous rupture. Early diagnosis with timely imaging, can prevent such complications. Unfortunately, our patient had persistent left RVT even after adequate anticoagulation therapy, which resulted in non-functional and contracted left kidney.

Anticoagulation is initiated with low molecular weight heparin (LMWH) in children because of favourable pharmacokinetics. Antithrombin supplementation may be required to maintain optimal Antithrombin (AT) levels for adequate action of heparin. Because of its longer half-life (56.8-68 hrs), plasma derived AT is preferred over recombinant AT (10.5 hrs). Entire course of anticoagulation may either be completed with LMWH or bridged to Vitamin K antagonist-Warfarin in children who do not rapidly go into remission or continue to require AT supplementation. Desired range of INR during therapy would be 2.0- 3.0 [11]. 12% of childhood VTE develop recurrent disease and require long term indefinite duration anticoagulation [12]. Our patient too had a repeat episode of VTE 6 months after remission, but unfortunately succumbed to its deadly consequences.

Pharmacologic thromboprophylaxis has been suggested for some children based upon known risk factors, however lack of robust evidence and randomized controlled trials demonstrating its safety and efficacy limits its use in both children and adults. Some of the non-pharmacologic strategies to limit VTE incidence are- regular ambulation, adequate hydration, avoidance of Central Venous Catheters and use of graduated compression stockings and/ or sequential compression devices for bedridden children.

CONCLUSION

Venous thrombosis in NS has devastating sequelae and consequences. A high index of suspicion is indispensable to identify the nonspecific signs and symptoms of VTE at presentation for early diagnosis and prompt treatment to prevent end organ damage. Non-pharmacological preventive measures are the key to reduce the incidence of subclinical TE and improve overall clinical outcome.

REFERENCES

1. Silva AI, Tavares J, Vaz AS, Brito N, Vasconcelos M, Sevivas T, Moura L, Cordinhã C. Cerebral venous sinus thrombosis in a child with idiopathic nephrotic syndrome: a case report. Brazilian Journal of Nephrology. 2018 Aug 2;40:418-22.
2. Suri D, Ahluwalia J, Saxena AK, Sodhi KS, Singh P, Mittal BR, Das R, Rawat A, Singh S. Thromboembolic complications in childhood nephrotic syndrome: a clinical profile. Clinical and experimental nephrology. 2014 Oct;18(5):803-13.
3. Kerlin BA, Haworth K, Smoyer WE. Venous thromboembolism in pediatric nephrotic syndrome. Pediatric nephrology. 2014 Jun;29(6):989-97.
4. Thanu S, Unni VN, Anil M, Rajesh R, George K. Cerebral venous thrombosis in nephrotic syndrome. Amrita J Med. 2014;10(2):1-44.
5. Gao C, Xie R, Yu C, Wang Q, Shi F, Yao C, Xie R, Zhou J, Gilbert GE, Shi J. Procoagulant activity of erythrocytes and platelets through phosphatidylserine exposure and microparticles release in patients with nephrotic syndrome. Thrombosis and haemostasis. 2012;107(04):681-9.
6. Dogra GK, Herrmann S, Irish AB, Thomas MA, Watts GF. Insulin resistance, dyslipidaemia, inflammation and endothelial function in nephrotic syndrome. Nephrology Dialysis Transplantation. 2002 Dec 1;17(12):2220-5.
7. Dogra GK, Watts GF, Herrmann S, Thomas MA, Irish AB. Statin therapy improves brachial artery endothelial function in nephrotic syndrome. Kidney international. 2002 Aug 1;62(2):550-7.
8. Andrew M, Brooker LA. Hemostatic complications in renal disorders of the young. Pediatric Nephrology. 1996 Feb;10(1):88-99.
9. Hoyer PF, Gonda S, Barthels M, Krohn HP, Brodehl J. Thromboembolic complications

in children with nephrotic syndrome: risk and incidence. Acta Pædiatrica. 1986 Sep;75(5):804-10.
10. Kerlin BA, Blatt NB, Fuh B, Zhao S, Lehman A, Blanchong C, Mahan JD, Smoyer WE. Epidemiology and risk factors for thromboembolic complications of childhood nephrotic syndrome: a Midwest Pediatric Nephrology Consortium (MWPNC) study. The Journal of pediatrics. 2009 Jul 1;155(1):105-10.
11. Kerlin BA. Current and future management of pediatric venous thromboembolism. American journal of hematology. 2012 May;87(S1):S68-74.
12. Raffini L, Huang YS, Witmer C, Feudtner C. Dramatic increase in venous thromboembolism in children's hospitals in the United States from 2001 to 2007. Pediatrics. 2009 Oct 1;124(4):1001-8.
13. Raffini L, Trimarchi T, Beliveau J, Davis D. Thromboprophylaxis in a pediatric hospital: a patient-safety and quality-improvement initiative. Pediatrics. 2011 May 1;127(5):e1326-32.