Venous Thromboembolism and Infection in a child with Nephrotic Syndrome: Dangerous interplay of Old enemies

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ABSTRACT

Venous thrombosis a known complication of Nephrotic syndrome. High IgE levels are commonly seen in children with Nephrotic syndrome. High IgE levels at onset of Nephrotic syndrome with sepsis are risk factors for venous thromboembolism. We present through this a severe case of venous hromboembolism and sepsis in a child with Nephrotic syndrome.

Key words: High IgE levels, Sepsis in Nephrotic syndrome, Venous thromboembolism

Children with nephrotic syndrome are prone to venous thrombosis; especially, cerebral sinus venous thrombosis and renal vein thrombosis and very rarely portal or splenic vein thrombosis [1]. These children are also extremely prone to serious systemic infections, the etiology of which is multifactorial [2]. Children with nephrotic syndrome have been described to have high serum IgE levels [3]. An association has been shown between high serum IgE levels and venous thrombosis [4]; though, not so far reported in a child with nephrotic syndrome. We describe a rare case of a boy with high serum IgE levels at onset of nephrotic syndrome at 13 years of age who presented to the hospital emergency with pain abdomen. It was found to be due to portal and splenic vein thrombosis with sepsis and disseminated intravascular coagulation (DIC), precipitated most likely by a minor skin infection while in remission of the nephrotic state. We took written informed consent from his parents for publishing this case.

Our patient, a 13-year-old boy, presented to the pediatric nephrology outpatient department of our hospital with periorbital swelling, mild pedal edema, and ascites of 2 weeks duration. There was no history of oliguria or hematuria. On examination, the patient was normotensive for age but had anasarca. The rest of the physical examination was normal. The child's investigations (Table 1) revealed a urine protein of 3+ by dipstick with no red blood cells or white blood cells on routine microscopy, urine protein to creatinine ratio of 3.8 g/mg, and 2.8 g of urine protein in 24 h. The serum IgE levels were 5813 IU/ml.

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He was started on prednisolone at 2 mg/kg/day. His proteinuria and edema resolved in 2 weeks. He was shifted to alternate day steroids at 1.5 mg/kg/alt day after 6 weeks. Five days later, the child reported with a furuncle over his nose for which he was given topical mupirocin and oral amoxycillin. Next day the child complained of pain in his chest and abdomen and brought to the hospital emergency. On examination, the child was sick looking with tachycardia and tachypnea, feeble peripheral pulses, capillary filling time between 2 and 3 s, and BP of 98/64 mHg. His abdomen was distended with diffuse tenderness but no organomegaly or free fluid.

Investigations (Table 1) showed neutrophilic leukocytosis, mild thrombocytopenia, deranged prothrombin time, international normalized ratio, transaminitis, and elevated lactate dehydrogenase. X-ray abdomen showed multiple air fluid levels (Fig. 1a) and multiple subcapsular hypoenhancing areas were seen in the spleen on the portovenous phases likely due to splenic and portal vein infarcts on computed tomography abdomen (Fig. 1b). In view of the deranged coagulation profile, fresh frozen plasma was transfused and the child started on intravenous (IV) meropenem and clindamycin along with IV hydrocortisone in stress dose. The patient, however, continued to deteriorate and was placed on mechanical ventilation and noradrenaline infusion. Despite all these measures, he suffered cardiac arrest after 2 h and could not be revived despite cardiopulmonary resuscitation as per the standard protocol.

Our patient had first episode of nephrotic syndrome at the age of 13 years, and therefore, we investigated him for a secondary cause though we did not find any underlying cause. His serum IgE levels were elevated. The child responded to the

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Table 1: Summary of investigations at onset and when child presented in emergency

Investigation	Onset of nephrotic syndrome	Next admission
Hemoglobin (g/dl)/total WBC count (cells/mm^3)/ platelet (lakh)	10.5/9000/4.44	10.1/26,500/1.21
Cholesterol (mg/dl)	290	220
Albumin (mg/dl)	2.2	3.9
Urea/creatinine (mg/dl)	25/0.6	17/0.7
ANA (by Elisa)/DsDNA	0.03 (<0.9 negative)	Not repeated
Complement 3	132 (90–180 mg/dl)	Not repeated
c-ANCA and p-ANCA	Normal	Not repeated
SGOT/SGPT (U/L)	35/38	237/111
LDH (U/L)	Not done	1134
IgE levels (IU/ml)	5813	Not repeated
Blood culture	-	No growth
D-Dimers	-	1590 µg/l
LDH	-	1134 IU/l
PT	-	31.6 (control 12–14)
APTT		50.2 (control 28.8)
INR		3.19 (<1.4 normal)

PT: Prothrombin time, INR: International normalized ratio, LDH: Lactate dehydrogenase

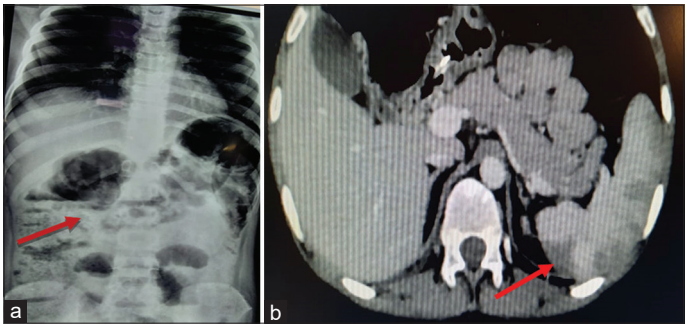

Figure 1: (a) Multiple air fluid levels in the abdomen and (b) splenic infarct

corticosteroids and his nephrotic state went into remission. He was brought in critically ill state with sepsis and DIC with portal and splenic vein thrombosis to which the child succumbed despite aggressive supportive therapy. Venous thrombosis is a serious complication in children with nephrotic syndrome and typically reported early in course of the disease [1]. This is chiefly due to a prothrombotic state created because of high plasma concentrations of procoagulant proteins and urinary losses of antithrombin in these children [1,5]. The clinical outcome is also influenced by risk factors such as use of central venous catheters, diuretics, and intravascular volume depletion [1] and underlying genetic risk factors for thrombosis [5].

Our patient developed a furuncle after which he apparently had portal and splenic venous thrombosis, sepsis, and DIC while he was in remission. Risk for venous thromboembolism (VTE) in nephrotic syndrome has been shown to correlate with severity of proteinuria [1]; however, the timeline for the reversal of all the pathophysiological changes responsible for the increased tendency for VTE is not really known. It is more in the presence of precipitating factors such as bacteremia following infections and elevated IgE levels which have been shown to be associated with VTE [6,4].

Elevated IgE levels in patients with asthma have been shown to be a significant risk factor for pulmonary VTE as well as deep vein thrombosis [4]; although, we could not find any published literature on children with nephrotic syndrome with high IgE levels with venous thrombosis. This may be partly because serum IgE levels are not routinely done in these children. Furthermore, portal and splenic venous thrombosis has been rarely described in children with nephrotic syndrome with cerebral venous thrombosis more commonly reported [7].

CONCLUSION

Children with nephrotic syndrome are at high risk for infections which can precipitate VTE, to which these children are inherently susceptible and their interplay in presence of associated factors like raised IgE levels can be potentially fatal, and therefore, we need to carefully evaluate and monitor these children.

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