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EXTENSIVE CEREBRAL SINOVENOUS THROMBOSIS AS A COMPLICATION IN NEPHROTIC SYNDROME : A CASE REPORT

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ABSTRACT Nephrotic syndrome (NS), a renal disorder, can lead to rare thromboembolic complications like cerebral sinovenous thrombosis (CSVT), even in children. Children with nephrotic syndrome (NS) are susceptible to venous and arterial thrombosis, which are serious though infrequent complications of the condition. Several factors contribute to the hypercoagulable state seen in these children. The reported frequency of thromboembolic complications in pediatric NS patients is notable. Cerebral sinovenous thrombosis (CSVT) is an exceptionally rare and serious condition, with only sporadic reports in medical literature. Its presentation can vary widely and may lack specific symptoms, making accurate diagnosis challenging without appropriate imaging. An 8-year-old with steroid-dependent nephrotic syndrome presented with headache and giddiness, signaling CSVT. Diagnosis via cranial MRI and magnetic resonance angiography confirmed CSVT, prompting anticoagulant therapy. This case emphasizes the importance of considering thromboembolic complications in nephrotic syndrome management, especially in pediatric patients. A thorough evaluation and early intervention are crucial for optimizing outcomes in such cases, ensuring prompt recognition and appropriate treatment to mitigate potential complications associated with CSVT.

KEYWORDS : Nephrotic syndrome, CSVT, Hypercoagulation

INTRODUCTION

Classical features of Nephrotic syndrome (NS) include proteinuria, low albumin, edema and raised cholesterol levels. Infection, anasarca, hypovolemic shock, anemia, and renal failure are prevalent complications of NS. Thromboembolism, particularly cerebral venous sinus thrombosis (CVST), is infrequent with few reported cases in the literature.[2]

Thromboembolism in NS include complex pathophysiology which is connected to excessive urinary excretion of antithrombin III, protein C, protein S, raised procoagulant activity and increased platelet counts. Above mentioned factors lead to generation of state of hyper-coagulability [3].

A keen clinical suspicion not only drives early imaging assessment but also kick-starts timely administration of anticoagulant therapy, pivotal factors linked to a more promising prognosis [4]. This report unveils the journey of an 8-year-old girl battling steroid-dependent nephrotic syndrome triggered by minimal change disease, ultimately confronting multiple cerebral sinovenous thromboses.

Case Report

A previously healthy female child developed nephrotic syndrome at the age of 4yrs. She was treated with prednisolone with the dose of 60mg/m2/day. She was found to be steroid responsive and achieved complete remission on day 12 of the treatment. 6 months later she developed 1st relapse and was treated adequately. But after 4 yrs she again developed edema of face and both the lower limbs. She was started with prednisolone 60mg/m2/day. On day 6 of her treatment she developed severe headache, giddiness and multiple episodes of vomiting.

She was immediately taken to the hospital , physical examination revealed no fever and no hemodynamic instability (BP 100/60mmhg). Ophthalmological examination revealed visual acuity in both the eyes was normal, both pupils reacted normal to light and anterior segment was normal. However there was no evidence of paralysis of extra ocular muscles. Rest of the physical examination showed no abnormalities.

Lab findings included urinary protein excretion >150 mg /kg/day, serum protein 5.73 g/dl, serum albumin 2.79g/dl, serum cholesterol 388mg/dl, serum electrolytes and renal functions were normal. Complete hemogram revealed hemoglobin 13.9 gm/dl, TLC 27920/cumm, PLT 432000/cumm. Serum complements C3 & C4 were normal. There was no family history suggestive of congenital or acquired thrombophilia.

Magnetic resonance imaging of brain (Figure 1) and MR Venogram (Figure 2) revealed absent flow signals in superior sagittal, right sigmoid and transverse sinuses. Hence she was diagnosed to have CSVT secondary to nephrotic syndrome. Renal USG with Doppler flow was normal.

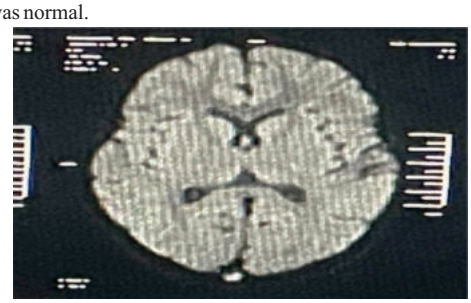

Figure 1: MRI Brain Showing High Signal Intensity In The Posterior Part Of The Sagittal Sinus.

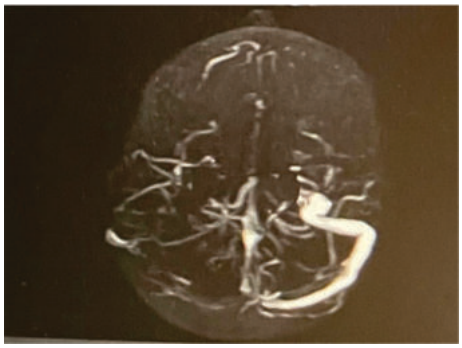

Figure 2: MR Angiogram Showing Thrombosis Involving Superior Sagittal, Right Sigmoid And Transverse Sinuses.

A coagulation profile showed prothrombin time to be 13.5sec, high fibrinogen levels 4.88g/L (Reference range (Rr) 2 -4 g/L), platelet counts 432000/cumm, D - Dimer 2630ng/ml. A thrombophilia screen was done which showed a reduced Antithrombin III 66% (Rr 80 – 120%), low protein C 60% (Rr 70 -120%) and normal protein S 90%(Rr 65 – 140%). Antiphospholipid and Anticardiolipin antibodies were normal. After diagnosing CSVT we started LMWH according to anti XA antibody levels (therapeutic range 0.5 – 1 unit/ml).

After 7 days of LMWH treatment we performed MRI brain and MR angiogram , that revealed same findings as earlier but were in a resolution phase. The nephrotic state was treated with prednisolone, remission was achieved 2 weeks after the institution of prednisolone. Complete neurological recovery was achieved within 1 month of the treatment. At the end of 1 month of anticoagulant therapy a cranial MR angiogram was performed, that revealed complete resolution of thrombosis of cerebral venous sinuses. Child was on oral vit k antagonist (Acenocoumarol) and was monitored with regular INR. Oral prednisolone was stopped since she achieved complete remission but was on oral anticoagulant therapy, hence adviced frequent followup.

DISCUSSION

This report illuminates a fascinating case of pediatric nephrotic syndrome complicated by cerebral sinus venous thrombosis, emphasizing the need for astute diagnostics. Thromboembolic events are notably more frequent in relapsing cases of NS[2].

CVST could be initiated by acquired thrombophilia due to significant urinary excretion of antithrombin (AT). Remarkably, the molecular weight of AT is lower than that of albumin, meaning reductions in plasma levels owing to proteinuria usually correspond with hypoalbuminemia.

The clinical manifestations of CVST vary depending on age. In a current case, the child presented with headache, giddiness and signs indicative of raised intracranial tension. Timely analytical examination and early imaging are crucial for accurate diagnosis, as effective treatment and antithrombotic therapy initiation are pivotal for favourable outcomes.

Brain computed tomography (CT) serves as a primary tool, spotlighting the cord sign as indicative of cortical vein thrombosis. Despite its utility, CT has limitations, with false-negative rates reaching 40%, especially in advanced stages. Magnetic resonance imaging (MRI) offers detailed lesion characterization. While lumbar puncture isn't standard, understanding that the superior sagittal sinus is primarily involved, followed by the straight sinus and transverse sinuses [5,6].

The hypercoagulation observed in NS stems from a dysregulation between the clot activator and inhibitor systems [3,7]. While nephrotic syndrome predisposes individuals to thrombosis, some authors propose that inherited thrombophilia may further heighten the risk of thrombosis in affected children [8]. In a case reported by Balci et al, 5 yr old child presented with same complaints and found to have FV Leiden, G1691A mutation, which was heterozygous in nature, congenital thrombophilia G20210A of FII mutation 14 [9].

In addition to corticosteroids for NS remission induction, standard therapy includes antithrombotic agents [10]. Upon confirmation of thromboembolic complications, immediate initiation of antithrombotic therapy is advised. This usually involves an initial course of low molecular weight heparin for 5-7 days, followed by oral anticoagulants administration for another 3-6 months (target INR 2-3). Treatment should continue until remission or as long as nephrotic range proteinuria and/or hypoalbuminemia < 2g/dL persists.

CONCLUSION

Children with nephrotic syndrome are susceptible to thromboembolic complications like CSVT. This case report emphasizes the need for a high level of suspicion for CSVT in nephrotic syndrome cases with neurological symptoms. MRI with MRV is the preferred imaging. Early recognition, immediate anticoagulation therapy, and nephrotic syndrome control are crucial for a positive outcome.

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