ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR 2019; 5(1): 77-80
www.allresearchjournal.com
Received: 09-11-2018
Accepted: 13-12-2018

Dr. Prerna Bhat
Dr. D.Y. Patil Medical College and Hospital, Pimpri Pune, Maharashtra, India

Dr. Sharad Agarkhedkar
Dr. D.Y. Patil Medical College and Hospital, Pimpri Pune, Maharashtra, India

Correspondence
Dr. Prerna Bhat
Dr. D.Y. Patil Medical College and Hospital, Pimpri Pune, Maharashtra, India

Cerebral sinovenous thrombosis in a child with steroid dependant nephrotic syndrome

Dr. Prerna Bhat and Dr. Sharad Agarkhedkar

Abstract
Nephrotic syndrome (NS) is a renal disorder characterized by heavy proteinuria, hypoalbuminemia, edema, and hypercholesterolemia. The reported annual incidence of nephrotic syndrome is between two and seven per 100 000 children aged 1 to 18 years.
Children with NS are at risk for venous and arterial thrombosis, uncommon but serious complications of the nephrotic syndrome. Multiple factors contribute to the hypercoagulable state in nephrotic children. The reported incidence of thromboembolic complications in nephrotic children is relatively high, ranging from 1.8% to 5.3%.
We a report a previously healthy boy who was diagnosed idiopathic nephrotic syndrome at six years of age who developed sudden onset of convergent strabismus of his right eye without deterioration of his sensorium. A Magnetic Resonance (MR) scan of the brain with venography was performed, and which revealed:- Posterior segment of superior sagittal sinus right transverse and sigmoid sinuses, right internal jugular vein shows loss of flow void on all pulse sequences along with absence of flow signal suggestive of dural venous sinus thrombosis.
Conclusion: Children with nephrotic syndrome are at risk of thromboembolic complications including CSVT. The present case report highlights the importance of having a high index of suspicion for cerebral sinovenous thrombosis in cases of nephrotic syndrome with any neurological symptoms. If available, MRI coupled with MRV is the imaging modality of choice. Early recognition, immediate anticoagulation therapy, and control of nephrotic syndrome are essential measures to ensure a good prognosis.

Keywords: nephrotic syndrome, cerebral sinovenus thrombosis

Introduction

- Nephrotic syndrome (NS) is a renal disorder characterized by heavy proteinuria, hypoalbuminemia, edema, and hypercholesterolemia. The reported annual incidence of nephrotic syndrome is between two and seven per 100 000 children aged 1 to 18 years.
- Children with NS are at risk for venous and arterial thrombosis, uncommon but serious complications of the nephrotic syndrome. Multiple factors contribute to the hypercoagulable state in nephrotic children. The reported incidence of thromboembolic complications in nephrotic children is relatively high, ranging from 1.8% to 5.3%.
- Cerebral sinovenous thrombosis (CSVT) is very rare and serious, with only few isolated reports in the literature. It may have a nonspecific and variable presentation, and the diagnosis can be difficult without appropriate imaging. CSVT may carry increased morbidity, and its treatment consists mainly of anticoagulant therapy.

This report describes a eight-year-old boy with steroid-dependant nephrotic syndrome resulting from a minimal-change nephrotic syndrome, which developed into multiple cerebral sinovenous thrombosis.

Case Report

- A previously healthy boy developed idiopathic nephrotic syndrome at six years of age. He was initially treated with steroids, with complete remission occurring on day ten of treatment with 2 mg per kg per day.
- Two months later, while the patient was on 1.5 mg/kg prednisone every other day, he developed a first relapse.

- Subsequently he was diagnosed as a case of steroid-dependent nephrotic syndrome.
- Following treatment of relapse, prednisolone was gradually tapered to maintain the patient in remission on alternate day dose of 0.5 mg/kg and later levamisole was added.

1 year later (during this episode) he was brought to the emergency room with the complaints of persistent headache since 10 days with facial puffiness progressing to generalised edema.
The headache was acute onset, generalized, continuous and more in the frontal region, for which he had received symptomatic treatment.

Physical examination

- Generalized edema with increased body weight of 12 kg over basal conditions
- He had severe edema on the face, lower extremities, and abdomen with ascites and bilateral scrotal edema.
- Blood pressure of 120/90 mm Hg.
- The rest of his examination was normal.

Laboratory findings

- Urinary protein excretion >120 mg/kg/day,
- Total serum protein 3.5 g/L,
- Serum albumin 2.0 g/L,
- Hypercholesterolemia
- Urine protein: creatinine ratio 3.2
- Electrolyte and Renal function: Normal.
- Normal blood count (Hemoglobin 12.9 g/dL, white blood cell count 11500 cells/μL, platelet count 420000/cumm).
- Serum complements C3 and C4: Normal.
- A coagulation profile showed prothrombin time 15 seconds (reference range: 12 to 14.5), INR of 1.15, PTTK of 34 seconds.

The patient was labelled as relapse and treated with prednisone @ 2mg per kg every day.
On day two of his hospitalization he developed sudden onset of convergent strabismus of his right eye without deterioration of his sensorium. The patient had no fever, and blood pressure was high: 120/90 mm Hg (>95th centile), his visual acuity in both eyes was normal, both pupils reacted well to light, and the anterior segment was normal. However there was convergent strabismus of the right eye with paralysis of lateral movements of the right eye, and there was papilledema.
A Magnetic Resonance (MR) scan of the brain with venography was performed, and which revealed: - Posterior segment of superior sagittal sinus right transverse and sigmoid sinuses, right internal jugular vein shows loss of flow void on all pulse sequences along with absence of flow signal suggestive of dural venous sinus thrombosis. (Figure1, 2, 3, 4).

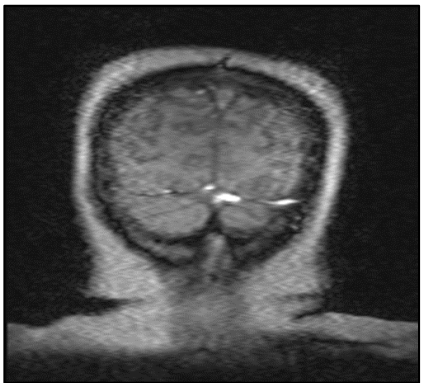

Fig 1

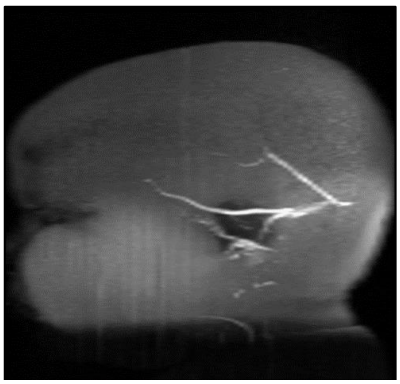

Fig 2

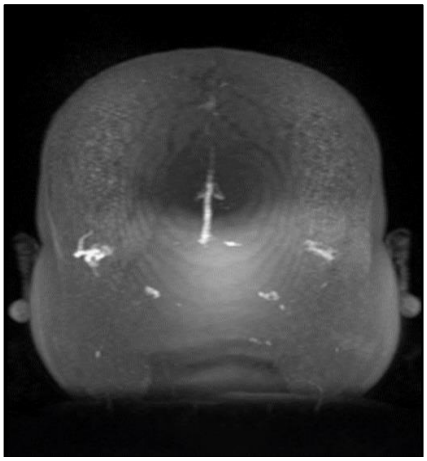

Fig 3

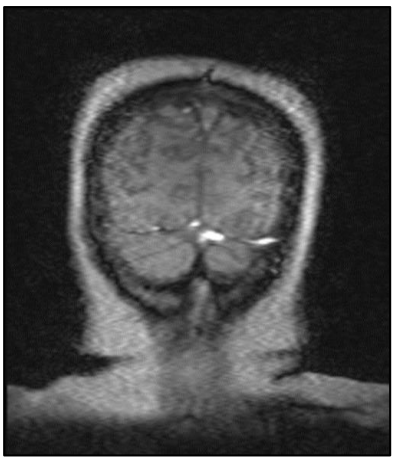

Fig 4

Fig 1, 2, 3, 4: Posterior segment of superior sagittal sinus right transverse and sigmoid sinuses, right internal jugular vein shows loss of flow void on all pulse sequences along with absence of flow signal suggestive of dural venous sinus thrombosis

Treatment of cerebral venous thrombosis was started immediately with unfractionated heparin for 10 days that was later changed to subcutaneous low-molecular-weight heparin (LMWH) for two months.

The nephrotic state was treated with prednisone (2mgper kg/day), and remission of the nephrotic syndrome occurred two weeks after the institution of prednisone.

The child made a complete neurologic recovery (conjugate Eye movements appeared to be normal) within one month of treatment.

After two months of LMWH, treatment was switched over to vitamin K antagonists, and he is being monitored with regular international normalized ratio (INR).

Follow up after 2 months

The child remains steroid dependent on low-dose prednisone alternate days with levamisole, without recurrence of thrombosis and without relapses since then.

A repeat MRI Venography was done which showed recanalization of the bilateral transverse and sigmoid sinuses with partial recanalization of the posterior half of superior sagittal sinus and residual thrombosis in the anterior half.

Discussion

- Cerebral sinovenous thrombosis in children is a serious but uncommon diagnosis that can be associated with several underlying systemic conditions. The current incidence of CSVT in children based on the Canadian registry is 0.67/100.000. Thromboembolic events are known to complicate nephrotic syndrome. The incidence of thromboembolic complications in nephrotic children is close to 2% with a higher incidence in steroid-resistant NS (3.8%) than steroid-responsive NS (1.5%).
- Involvement of cerebral vessels has been rarely reported in nephrotic children. Sinovenous thrombosis is probably less recognized or remains underreported in children with nephrotic syndrome.
- Clinical presentation of CSVT in children is extremely variable and nonspecific. The diagnosis of CSVT should be considered in any patient with nephrotic syndrome who develops neurologic symptoms: these symptoms include focal or generalized seizures; signs of raised intracranial pressure including headache, vomiting, lethargy, irritability; a decreased level of consciousness, focal neurological deficits such hemiparesis, cranial nerve palsies, and papilledema.
- In the presence of the appropriate clinical history, brain CT is usually the first investigation performed. However, conventional CT can miss the presence of CSVT in up to 40% of children and underestimate both the extent of the thrombus and the presence of venous infarcts. Brain magnetic resonance imaging (MRI) and MR venography are considered to be a superior modality for diagnosis and follow-up of CSVT. MRI depicts direct signs of thrombosis of one or more venous sinuses, thrombosis of cortical veins, and focal parenchymal lesion. The most frequently involved sinuses were the superior sagittal sinus followed by the straight sinus and the transverse sinuses. Deep venous system involvement was rarely reported.
- The relation of NS with hypercoagulability and thromboembolic complications is well known. Hyper coagulation in NS is the consequence of an imbalance between the clotting activator system and the inhibitor system. These include increased procoagulatory activity (fibrinogen, factors V and VIII), urinary loss of anticoagulants (ant thrombin III, protein C, and protein S), altered fibrinolysis system, thrombocytosis, and enhanced platelet activation and agreeability.
- Other factors that increase thrombotic risk in nephrotic children include hyperlipidemia, haemo concentration, hypoalbuminemia (less than 2.5 g/dL) high rate of protein excretion (more than 10 g/day), low anti thrombin III levels, diuretic use, corticosteroid treatment, and indwelling catheters.
- The risk of thrombosis is higher at the onset of the disease or during a relapse when AT III levels and albumin levels were decreased. Hypo albuminaemia not only reflects intravascular volume depletion, causing increased blood viscosity, but may also be directly related to platelet hyperaggregability and alteration in the fibrinolysis system.
- Acute anticoagulant of choice is heparin. Authors prefer to use unfractionated heparin (UHF) acutely, as the effects of heparin can be reversed if intracranial haemorrhage occurs. Treatment with UHF for 5 to 7 days is often followed by chronic anticoagulation with LMWH or vitamin K antagonists for 3 to 6 months.

Conclusion

Children with nephrotic syndrome are at risk of thromboembolic complications including CSVT. The present case report highlights the importance of having a high index of suspicion for cerebral sinovenous thrombosis in cases of nephrotic syndrome with any neurological symptoms. If available, MRI coupled with MRV is the imaging modality of choice. Early recognition, immediate anticoagulation therapy, and control of nephrotic syndrome are essential measures to ensure a good prognosis.

References

1. Eddy A, Symons JM. Nephrotic syndrome in childhood, Lancet. 2003; 362(9384):629-639.
2. Abella EM. Haemostatic problems associated with renal disease. International Journal of Pediatric Hematology/ Oncology. 1994; 1:43-51.
3. Gangakhedkar Wong W, Pitcher LA. Cerebral thrombosis in childhood nephrosis, Journal of Paediatrics and Child Health. 2005; 41(4):221-224.
4. Shoroff M, de Veber G. Sinovenous thrombosis in children, Neuroimaging Clinics of North America. 2003; 13(1):115-138.
5. Lilova MI, Velkovski IG, Topalov IB. Thromboembolic complications in children with nephrotic syndrome in Bulgaria (1974-1996)," Pediatric Nephrology. 2000; 15(1-2):74-78.
6. Divekar US, Ali MD, Ronghe AR, Single Dalvi RB. Superior Sagittal sinus thrombosis in a child with rephrotic syndrome, Pediatric Nephrology. 1996; 10:206-207.
7. Fluss J, Geary D, de Veber G, Cerebral sinovenous thrombosis and idiopathic nephrotic syndrome in childhood: report of four new cases and review of the literature. European Journal of Pediatrics. 2006; 165(10):709-716.
8. Singhal R, Brimble KS. Thromboembolic complications in the nephrotic syndrome: pathophysiology and clinical management, Thrombosis Research. 2006; 118(3):397-407.

9. Schlegel N. Thromboembolic risks and complications in nephrotic children, Seminars in Thrombosis and Hemostasis. 1997; 23(3):271-280.
10. Rabelink JT, Zwaginga JJ, Koomans HA, Sixma JJ. Thrombosis and hemostasis in renal disease," Kidney International. 1994; 46(2):287-296.
11. Monagle P, Chan A, Massicotte P, Chalmers SE, Michelson AD. Antithrombotic therapy in children: the seventh ACCP conference on antithrombotic and thrombolytic therapy, Chest. 2004; 126(3):645S-687S.
12. Dlamini N, Billinghurst L, Kirkham F. Cerebral venous sinus (Sinovenous) thrombosis in children, Neurosurgery Clinics of North America. 2010; 21(3):511-527.