Cerebral Venous Sinus Thrombosis in a 7-month old child: A Rare Case Report

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ABSTRACT

Neonatal cerebral sinovenous thrombosis (CSVT) compromises nearly 50% of all pediatric-related CSVT. Although guidelines support anticoagulation in pediatric CSVT, the role of anticoagulation in infant's CSVT remains controversial. This case report presents a case of 7-month old infant with CSVT necessitating anticoagulant therapy and describes the course of CSVT diagnosis.

Keywords: Anticoagulants; Conservative Treatment; Infant; Protein C Deficiency; Sinovenous Thrombosis

INTRODUCTION

Cerebral venous thrombosis (CVS) primarily originates from blocking of a venous sinus and/or cortical vein and is initiated by a partial thrombus or an extrinsic compression which consequently grows to complete occlusion. In some cases, the thrombus might extend to veins draining into the sinus and cause cortical venous infarction with petechia or overt hemorrhage and regional ischemia at the grey-white matter junction or white matter [1].

Thrombosis of the cerebral venous sinuses (or CVST) is a somewhat rare condition in pediatrics; the incidence of pediatric CSVT is estimated between 0.34 and 0.67/100 000 children with neonatal CSVT constituting approximately 30–50% [2, 3]. Most cases present with acute neurological symptoms comprising lethargy, headache, vomiting or seizures while in some cases there might even be focal neurological signs/or symptoms [4]. CVST has been linked with a high morbidity and requires extensive care and examination since it is among the top ten causes of death in the pediatric population [1, 5, 6].

Here we report a case of a 7-month old infant diagnosed with CSVT and the need of initiating anticoagulant therapy.

CASE REPORT

A seven-month old male infant, with a previously well-being health condition, referred to the Emergency Department of Taleghani Hospital (Gorgan, Northern Iran) with a history of loss of consciousness and 4 times focal seizures thereafter a week prior to his reference; no history of recent (brain) trauma was declared by his parents.

He was the fifth child of non-consanguineous Turkmen parents from Northern Iran, born at term weighing 3kg via natural vaginal delivery with normal APGAR scores. The pregnancy and delivery was uneventful and the family history was unremarkable for any neurologic and hematologic conditions. He had shown normal developmental features until this presentation. Standard National Vaccination Protocol was completely done.

On arrival he was found to have pulse of 133bpm, respiratory rate of 29 cycles/min and temperature of 37.5°C. On neurological examination his cranial nerves and deep tendon reflexes were intact but he had muscle weakness in all four limbs with hypotonicity. Rest of the systemic examination was unremarkable. His baseline lab workup was normal and ruled out any metabolic cause of seizures (Table 1).

His seizures were initially being managed with phenobarbital and diazepam but he developed a high grade fever with hypotension and status epilepticus. He was immediately intubated and kept on supportive ventilation for 72 hours. Further investigations detected no infectious sources or organisms in blood and cerebrospinal fluid (CSF) cultures, rapid antigen tests or PCR. The EEG recorded a non-specific abnormality with diffuse excess theta.

Patient then had a Computed Topography (CT) of his brain which showed some focal frontal intracerebral bleed with surrounding edema. The Magnetic Resonance Imaging (MRI) reported signal change in superior venous sagittal sinus with ischemia of the underlying cortex. His cerebral arteriogram proved a probable cortical vein thrombosis. Additionally, a venogram showed a filling defect in the sagittal sinus indicative of a possible thrombus. His Doppler scan of the leg vessels, skeletal survey and renal ultrasound were unremarkable. None of the imaging displayed sign of a causal vascular malformation. Prothrombotic workup was also reported as normal (Table 2).

We managed the child conservatively with empirical antibiotics; he received vancomycin and meropenem during his 9 days of admission. His anticoagulation therapy including heparin and warfarin was started and levetiracetam was started for his seizures as well. He was vitally and clinically stable hence was discharged on Tab warfarin, folic acid and ferrous sulfate. On routine follow-ups for a whole year, the patient remained vitally and clinically stable.

DISCUSSION

The incidence of pediatric CSVT is approximately between 0.34 and 0.67/100 000 children, with neonatal CSVT constituting about 30–50% of all reported cases [2, 3]. Studies report that infant's CSVT usually presents with seizures [2, 3, 7-11] with a gender predisposition towards male infants suffering CSVT. The pathophysiology of pediatric CSVT consists of varied risk factors which includes maternal hypercoagulable pregnancy state, obstetric instrumentation, and lower than normal adult values of antithrombin 3, protein-C and protein-S. Moreover, many infants diagnosed with CSVT have a systemic comorbid inflammatory condition (sepsis, dehydration, and hypoxic–ischemic injury) precipitated by hypovolemia, malignancy, autoimmune disease, sickle cell status and congenital cyanotic heart disease [2-4, 12].

The prothrombotic work-up of pediatric CSVT is inadequate in most studies; yet, literature reports that 15–50% of infants have prothrombotic abnormalities at the time of diagnosis, unlike our case. The persistence of these prothrombotic abnormalities is nearly 20%, suggesting that the factors resulting in thrombosis in the infant are chiefly linked to the perinatal period and will likely not recur [13]. The thrombus reappearance risk in young children with congenital thrombophilia is still not well defined. Conversely, in a strong meta-analysis of children with deep venous thrombosis, recurrence in patients less than 2 years old was rare [14]. Similarly, the reappearance risk for all neonatal thrombosis detected is very low at 3% [5, 14].

CVST can be reported in routine CT scan with contrast enhancement or MRI could illustrate a dense-triangle sign [4]. Though in such an approach, about 40% of cases might be missed out [4-8, 14, 16]. CT venography or Magnetic Resonance Venography (MRV) is the investigation of choice which we used as well [5]. Parenchymal MR and MRV are important in the demonstration of both the infarct and the clot within the vessels. Perfusion and diffusion MRI can help diagnose edema/cerebral congestion secondary to obstruction but will not be able to distinguish from arterial infarct or venous infarct [5, 16].

Consequently a low threshold for CT or MR venography is needed in children with acute neurological signs and symptoms [4]. Precise imaging is wanted to exclude anatomical anomalies as well. Variants of venous anatomy are not uncommon, and a hypoplastic or diminished transverse sinus, besides noticeable arachnoid granulations may bear a resemblance

Table 1: Routine laboratory workup

WBC: 12.4* 10^3/UL	Neutrophils: 70%
	Lymphocytes: 28%
	Monocytes: 1%
	Eosiniphils: 1%
RBC: 3.10* 10^6/ UL	Ca: 9.9 mg/dL
HB: 7.7	Mg: 1.8 mEq/
PLT: 306* 10^3	Blood sugar: 80 mg/dl
ESR: 56 mm/h	BUN: 8 mg/dl
Na: 141 mEq/L	Cr: 0.5 mg/dL
K: 5 mEq/L	HCO3:20

Table 2: Prothombotic workup to investigate cause of CVST in our patient

Protein –C: 40.8 % (70-140)	Anti-Thrombin III: 131% (80-120)	Ammoniac: 87 µmol/L (95-180)
Protein-S: 70.8 % (55-160)	Homocysteine: 12.3 umol/L (<15 year :< 10, adults: 5-15, >60 year: 5-20)	Lactate: 12meq/L (4.5-20)
Factor V Leiden: 3.3 Ratio (Normal >2)	PT: 21 , INR: 1.2	APTT: 39 sec

to a CVST [5].

Treatment of this pathology is similar to that in adults: physiological homeostasis should be maintained to avoid herniation. The use of anticoagulation is controversial in pediatrics [4, 5]. Initial concerns about intracranial hemorrhage from thrombolytic therapy have not been sustained by single case reports or any series, although there are worries within pediatrics related to the safety of the monitoring systems [5, 10, 17, 18]. So far, relatively few infants with CVST have been treated with anticoagulants and this would therefore be suggested in those with clinical deterioration, or with radiological evidence of clot spread as in our current case with repeated seizures and developing high fever and status epilepticus [5]. Work with fairly small series of children has proposed that there is a better outcome in patients treated with anticoagulation therapy allowing patients with repeated thrombosis to get benefits from anticoagulation therapy [15, 19]. In detail, treatment with low molecular weight heparin (LMWH) in newborn infants with a thalamic hemorrhage due to CVST appears to be safe. It is proposed that since treatment of CVST in adults with anticoagulation agents is not postponed needlessly, a similar strategy should be applied to children and so facilitate natural recanalization and avoid thrombosis [5].

CONCLUSION

A case of thrombosis in a sagittal venous sinus, initiated by probable protein C deficiency, revealed a somewhat good outcome with anticoagulation but there is a need for large trials to define exactly the benefit of anticoagulation therapy in children.

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