 Venous Sinus Thrombosis in A Preterm Male Neonate with Elevated Anti-Phospholipid Antibodies: A Case Report

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Abstract

Background: Cerebral venous sinus thrombosis (sinovenous) (CSVT) is a rare and yet an important cause of morbidity and mortality in neonates. The Canadian registry quotes an incidence of 41 per 100,000 newborns per year. Cerebral sinovenous thrombosis is rarely reported in preterm infants. Although it is a potentially devastating condition with poor neuro developmental outcome, the risk factors are still poorly understood and the awareness to diagnose this condition is lacking. Males are at higher risk for both arterial ischemic stroke and for the sinovenous thrombosis.

Case Report: We report a preterm, male neonate with right transverse venous sinus thrombosis, who had perinatal risk factors and elevated antiphospholipid antibodies on follow up. No other known risk factors for thrombosis were identified. High levels of anti phospholipid antibodies in this infant, could have possibly lead to venous sinus thrombosis in neonatal period.

Keywords: Venous Sinus Thrombosis; Antiphospholipid Antibodies; Neonate

Abbreviations: CVST: Cerebral Venous Sinus Thrombosis; APLA: Anti Phospholipid Antibody

Introduction

Cerebral Venous Sinus Thrombosis (sinovenous) (CVST) is a rare yet an important cause of morbidity and mortality in children [1] primarily affecting neonates [1-6]. The risk factors for arterial ischemic stroke and cerebral sinovenous thrombosis in neonates are poorly understood. Males are at higher risk, although the reason for sex predilection is unknown.

The Canadian Pediatric Ischemic Stroke Registry, the largest registry for stroke and neonatal CVST, quotes an incidence of 0.6 per 100,000 population per year [7] and 41 per 100,000 newborns per year, accounting for half of all pediatric cases.

Case Report

A 33 weeks male neonate, weighing 2700 grams was admitted to the neonatal unit at few hours of life. The neonate was born to a 30 years old primigravida by vaginal delivery. There was no history of consanguinity. Antenatal risk factors were pre-eclampsia, glucose intolerance and urinary tract infection. The neonate had delayed cry and required resuscitation for half of all pediatric cases.

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were bilateral adrenal hemorrhages, which resolved in follow up. As the neonate showed improvement in the neurological status from 10th day onwards, oral spoon feeds as well as breast feeding was initiated and the neonate was subsequently discharged on 24th day (Figure 2).

In view of CVST, procoagulant work up was done at three months of age, which showed absence of factor V Leiden mutation, normal protein C levels and low protein S levels (Subsequently normalized at 6 months). Interestingly anti β2 glycoprotein-1 IgG antibody levels were elevated (at 3 months-32.5 G units/ mL). However anti β2 glycoprotein-1 IgM antibodies, Lupus anticoagulant and IgG and IgM isotypes of Anticardiolipin were negative. To fulfill the criteria for APLA syndrome, repeat APLA levels done at 6months of age showed persistent positivity (anti β2 glycoprotein 1 IgG antibody levels-18.5 G units/ml). Normal levels of antibodies in neonates are not available, however the prescribed cutoff is <5 units/ml. Both values in the index case were well over these levels. Antibodies retested at 6months interval showed high levels. Anti double stranded DNA was positive with titers of 73 (>40 significant) at one year of life, but became negative at 2 years of age. Both parents prothrombotic work up showed normal protein C & S levels. Since APLA syndrome in neonates is associated with maternal SLE, the mother was evaluated for SLE. She had 4 +ANA (coarse speckled pattern), positive double stranded DNA, while remaining asymptomatic. Immuno dot test to detect the nature of antibodies showed weakly positive Sm antibody. However her APLA work up was negative.

Follow-up

Developmental assessment at the age of 33 months ( by Denver developmental screening test) showed normal gross motor, language, socio-personal milestones with delay in fine motor quadrant. Initial eye examination at six months showed bilateral convergent non paralytic squint and subsequently at 33months, the power in the right eye was- 2.0, and in the left eye was- 2.75 with spectacles, for which unilateral occlusion was advised. Evaluation for hearing revealed normal Brainstem Auditory Evoked Responses at three and six months of corrected age. In view of APLA positivity, infant was started on aspirin (75 mg), which was continued till two and half years of age.

Discussion

The neonates are at highest risk for thrombosis when compared to any other age group, due to their physiological prothrombotic status. Various physiological as well as pathological factors in pre natal, natal or postnatal period can predispose to neonatal CVST. The most frequently involved sinuses in neonate are the superior saggital sinus and lateral sinuses [8]. The deep sinovenous system is less frequently involved. Cortical venous thrombosis is even rare.

Index neonate had multiple known predisposing perinatal risk factors such as preeclampsia, glucose intolerance and urinary tract infection in mother [1]. There was perinatal asphyxia and significant hyperbilirubinemia with dehydration and hypernatremia (highest serum sodium level of 156 m eq/ l). Also the neonate had sepsis with meningitis and disseminated intravascular coagulation [1,8] which were reported risk factors [9]. Apart from these, persistently elevated antiphospholipid antibodies could possibly have lead to thrombotic event in neonatal period.

Canadian stroke registry [1] reported the role of these perinatal and prothrombotic risk factors in a cohort of 160 children, including neonates. Acute systemic illneses were present in 84 percent of neonates. Perinatal complications (51%) were most frequently present, followed by dehydration (30%). A strong association has been quoted between preeclampsia [1,3,10], prothrombotic disorders and neonatal venous thrombosis [11-13], along with dehydration, sepsis and meningitis. Tests for prothrombotic disorders performed in 123 patients, showed 32 % abnormal results. Presence of anticardiolipin antibody being the most frequent abnormality(IgG titers: 15- 60 IgG phospholipid units /ml). Index case manifested lethargy, poor feeding, hypotonia and depressed

A preterm male neonate presents with right transverse venous sinus thrombosis in the setting of early & persistent anti-beta 2 GP1 antibodies, a rare thrombotic disorder associated with both maternal and neonatal risk factors.

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Authors Contribution

S C: Recruited patient, collected the data, and drafted the manuscript; K M: Edited the manuscript; J A: Necessary hematological Workup, edited the manuscript; S S: Follow up of the neonate, edited the manuscript; P K: Edited the manuscript; J N: Drafted and edited the manuscript.

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