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CASE REPORT

Cerebral Venous Thrombosis in a Term Child: A Case Report

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Abstract

Thrombosis of cerebral venous sinuses is a rare condition but can be associated with serious clinical consequences. Pathogenesis of thrombosis of cerebral venous sinus is still not clear. As there is diverse etiology but presentation is subtle, it often leads to delay in the diagnosis. We are reporting the case of a term male neonate born by LSCS (indication obstructed labour with meconium stained amniotic fluid) with diagnosis of severe birth asphyxia, Hypoxic Ischemic Encephalopathy- stage II, probable sepsis, shock and Germinal Matrix Haemorrhage. The magnetic resonance imaging (MRI) of brain and magnetic resonance (MR) venogram done at 2 weeks of age showed superior saggital sinus thrombosis. Baby received anticoagulation therapy and extensive workup was done. Early neuroimaging in all the babies who has neonatal seizures will improve the identification and will warrant early treatment.

Keywords: Cerebral venous thrombosis, Neonatal thrombosis, Prothrombosis

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Introduction

Thrombosis of cerebral venous sinuses is a rare but potentially a life threatening condition in neonates with a prevalence of 1.4-12 per 100,000 live births [1]. Its etiology is diverse with dehydration being the most common cause. The other associated conditions are sepsis, hypercoagulable conditions like polycythemia, deficiency of Protein C and/or Protein S, deficiency of antithrombin III, factor V leiden and mutation of G20210A prothrombin gene [2-4]. Additionally the risk factors during pregnancy like chorioamnionitis, preeclampsia, eclampsia and gestational diabetes mellitus (GDM) may also be associated and leading to thrombosis in neonate [5].

Being described first as rare and fatal condition in 19th century [6], its most common manifestations are seizures and altered sensorium [7].

Case Report

A term male neonate was born to 31 years old G3P2L2 mother from non consanguineous marriage, at 38 weeks 6 days of gestation by LSCS (indication obstructed labour) weighing 3185 gms. Mother experienced antenatal complications of obstructed labour, MSAF grade 3 and mild anemia. Baby suffered from severe birth asphyxia, seizures within 24 hours of birth with hypoxic ischemic encephalopathy stage II (HIE–II). Later he developed shock. The neurosonogram done on day three of life showed germinal matrix hemorrhage (GMH) grade 1 on left side and grade II on right side. Baby required ventilator support for 7 days followed by continuous positive aiway pressure (CPAP) support for 4 days and oxygen for 2 days. Central line was removed after 7 days. The family history revealed history of hemiparaesis and developmental delay in elder sibling.

Investigations

Laboratory findings indicated hyponatremia (S.Na levels-127 mEq/L), hypocalcemia (S.Ca levels-6.3 mg/dL), anemia, elevated CRP (61.43mg/dL), yeast like cells in urine and metabolic acidosis. Blood culture and urine culture were sterile. Mother's high vaginal swab showed growth of staphylococcus aureus. Neurosonogram (NSG) showed germinal matrix haemorrhage (GMH) grade 1 on left side and grade II on right side. The electroencephalography (EEG) was normal. The magnetic resonance imaging (MRI) of brain done at period of 2 weeks of life showed superior saggital sinus thrombosis. Coagulation profile (PT, APTT, INR) was normal. The magnetic resonance venogram confirmed MRI the findings (Figure 1-3). Further workup revealed normal Homocysteine levels (17.4 umol/L), normal Protein C activity of 94.4% (chromogenic) and free Protein S levels of 92% (immunoturbidometry). The next-generation sequencing (NGS) testing showed heterozygous missense variant of uncertain significance on EXON 2 , PROS1 deletion , AD- Protein S , AR- protein S deficiency.

Treatment

Baby was started on IV anticoagulation with low molecular weight heparin (LMW) {Inj Enoxaparin (dose

1.5mg/kg sc q12H)} and after 5 days was switched to oral anticoagulant Warfarin (loading dose of 0.2mg/kg, then 0.32mg/kg OD orally) with monitoring of international normalized ratio(INR) between 2-3.There was no repeat seizure once baby was started on anticonvulsant monotherapy. The infant was discharged on 28th day of life, in a stable condition on exclusive breast feeding and on anticonvulsant (phenobarbitone at maintenance dose of 5 mg/kg/day) and Warfarin at doses titrated as per INR values. Later baby was shifted to Rivaroxaban (oral anticoagulant, factor Xa inhibitor) and warfarin was stopped. At age of three month, rivaroxaban was discontinued and phenobarbitone was gradually tapered and stopped as neonate was neurologically stable and there were no repeat seizures. At three months age, baby is developmentally normal and repeat neurosonogram (cranial+doppler) illustrated partial recanalization of superior saggital sinus. In the follow-up period, at six months of age there was mild interval decrease in superior saggital sinus thrombosis with partial recanalization on neurosonogram. Repeat MRI brain will be done at 1 year of age. The neurodevelopment assessment of the baby till 9 months of age, appears to be normal.

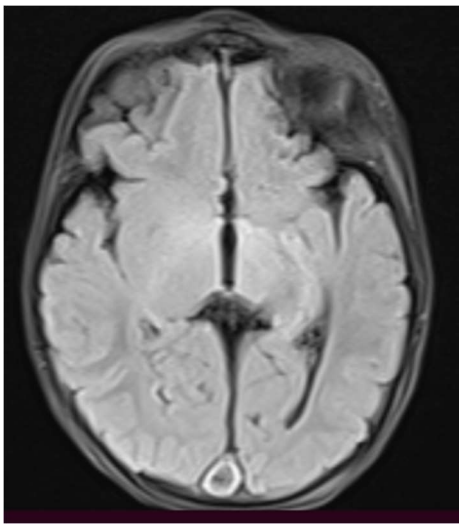

Figure 1. MRI Brain (Axial view): Prominent Superior Saggital Sinus

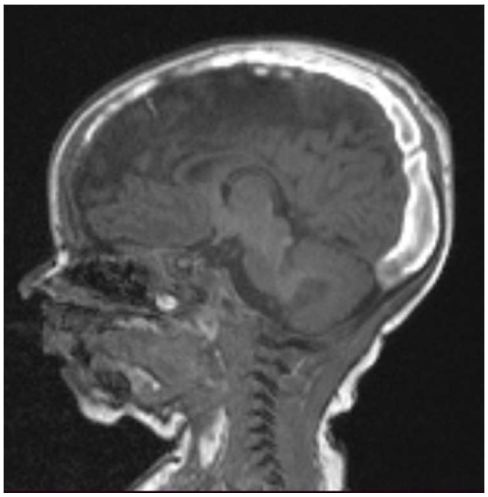

Figure 2. MRI Brain (Coronal section): Prominent Superior Saggital Sinus

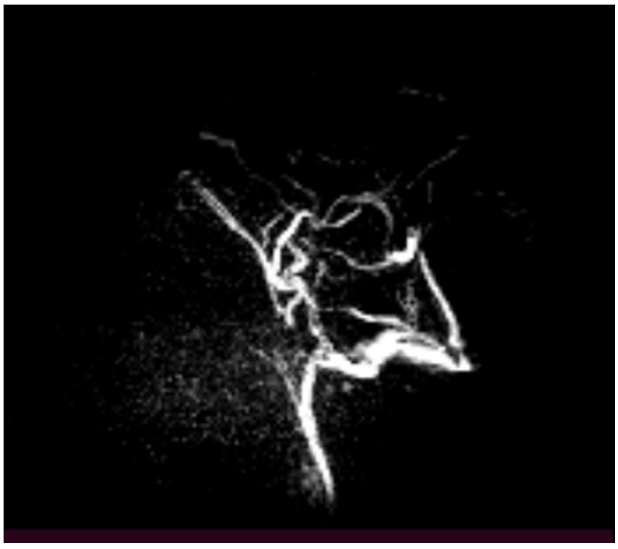

Figure 3. MR Venogram- No flow signal was identified in superior saggital sinus representing underlying thrombosis

Discussion

Neonatal venous sinus thrombosis is a rare condition with prevalence of 1.4-12 per 100,000 live births [1]. It is mainly caused by combination of various factors triggering prothrombosis like presence of birth asphyxia, dehydration, dysfunction of the liver, inflammation, presence of risk factors in mother, central venous long lines, septicemia and premature [2-4]. Furthermore at birth, the neonatal hemostatic system has reduced levels of multiple procoagulant proteins like coagulation factors (II,VII,IX,X) that are dependent on vitamin K, protein C, protein S, anti-thrombin and heparin cofactor II. They might be augmenting the risk of developing thrombosis over the older children as well [8].

Manifestations of neonatal sinus thrombosis vary with age and the most common presentation being seizures in neonates. The clinical symptoms and signs in neonates are often subtle and nonspecific

with increased risk of deranged neurological sequelae. The other primary features of presentation include lethargy, excessive irritability, decreased feeding, apnea, variation in muscle tone and neonatal seizures [9].

Cranial Doppler ultrsonography provides an initial assessment for suspected diagnosis but MRI brain reveals intraparenchymal haemorrhage and different phases of sinovenous thrombosis [10,11]. In our case report neurosonogram showed GMH only and could not pick up thrombosis but MRI brain revealed superior saggital sinus thrombosis.

Mine Ozdil reported a case of term neonate in early period of life with diagnosis of thrombosis of cerebral venous sinus and chronic hemorrhagic ischemia. There was history that this neonate was born to a mother who had been infected with COVID 19 infection in her last trimester. COVID-19 infection is speculated as pathogenic causes that exaggerated the hypercoagulability state leading to neonatal thrombosis [12]. The baby, on extensive workup, was found to have heterozygous MTHFR A1298C mutation but is not linked to elevated homocysteine levels and hypercoagulability. This mutation is common in Turkish population but it is found to be significant if it is associated with MTHFR C677T mutation also [13].

Another case report on cerebral venous sinus thrombosis by Jani S et al, was of a seven-day-old female term neonate who was reported to the emergency department with decreased responsiveness, poor feeding and neonatal seizures. There was history of inadequate breast feeding and significant weight loss (20%).She had hypernatremic dehydration and on magnetic resonance imaging of the brain there was a stable IVH within all the ventricles of brain. On arterial and venous angiography, there was no flow in the intracranial arteries and no flow in dural venous sinuses respectively, suggestive of cerebral venous sinus thrombosis [14]. Similar presentation was also reported by Maghsoudi et al. on neonatal sinus thrombosis with underlying history of hypernatremic dehydration [9].

As neonatal thrombosis of sinuses has diverse etiology and the clinical features are highly variable so the diagnosis is grueling and needs a high degree of suspicion. The analysis of multiple predisposing risk factors in mother during antenatal period, fetal and neonatal period and pro-thrombotic factors contributing to thrombosis is done by case to case basis but the mainstay of the treatment for neonatal thrombosis includes stabilization of vitals, controlling seizures, treating the root cause that may have predisposed the neonate to risk of thrombosis along with anticoagulation therapy [1].

Conclusion

The inherited or acquired thrombophilia in neonates can significantly elevate the coagulation potential, particularly when merged with other risk factors. The clinicians should be prudent in monitoring of sick neonates for thrombotic complications. Early neuroimaging is strongly recommended along with intensive care management for the favourable outcomes.

Statements and Declarations

Conflicts of interest

The authors declares that they do not have conflict of interest.

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