

Neonatal Cerebral Sinovenous Thrombosis: A Rare Case Report and Literature Review

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Abstract

Neonatal cerebral sinovenous thrombosis is a rare and potentially life-threatening disorder associated with various long-term neurological deficits. The pathogenesis of cerebral sinovenous thrombosis in neonates is still unclear. Many potential risk factors have been identified, such as gestational or delivery complications or neonatal comorbid conditions including dehydration, sepsis, or cardiac defects. A correct diagnosis is often delayed due to the subtle presentation of the disorder, leading to delayed treatment with poor outcomes. Herein, we report a preterm female neonate who was born only with the presentation of intrapartum maternal fever. Routine brain sonography showed intraventricular hemorrhage. In a further study, brain magnetic resonance imaging revealed neonatal multiple sinovenous thrombosis. To prevent potential thrombosis development and ameliorate possible thrombosis-related problems, the infant immediately received anticoagulation therapy. At the 3-month follow-up, developmental milestones were within the normal range, and the follow-up brain MRI scans also showed normal results. In conclusion, early recognition and proper treatment may yield a better prognosis for neonatal cerebral sinovenous thrombosis, especially when patients exhibit any possible risk factors, which should alert healthcare professionals.

Keywords: Perinatal stroke, Maternal fever, Perinatal infection, Cerebral Sinovenous Thrombosis, Coagulopathy

Introduction

Cerebral sinovenous thrombosis during the neonatal period is a relatively rare disorder, and its clinic presentations are often obscure, making early and correct diagnosis difficult. The estimated incidence of the disorder is 0.67 per 100,000 children, with approximately half of the cases occurring in the neonatal period [1]. Etiologies of cerebral sinovenous thrombosis are diverse. Some risk factors include dehydration, sepsis, or cardiac disorders [2, 3]. Some authors have also identified hypercoagulation risk factors such as polycythemia, protein C deficiency, protein S deficiency, antithrombin III deficiency, factor V Leiden, G20210A prothrombin gene mutation, and antiphospholipid antibody [4-7]. Moreover, obstetric risk factors including chorioamnionitis, preeclampsia, and gestational diabetes mellitus all may link to neonatal cerebral sinovenous thrombosis [8]. Herein, we report a case of a preterm neonate with a history of intrapartum maternal fever and who presented neonatal fever and lethargy after birth and who was diagnosed with multiple neonatal cerebral sinovenous thrombosis and intraparenchymal hemorrhage. This case might be due to intrapartum fever, which causes an unstable

neonatal hemodynamic status, leading to sinovenous thrombosis formation. Written informed consent was obtained from the parents to publish the case report, including the use of images and other relevant information.

Case Study

A preterm female neonate was delivered by normal spontaneous vaginal delivery at the gestational age of 34 and 5/7 weeks to a 28-year-old gravida 1, para 0, mother, who had an uncomplicated pregnancy. At birth, the neonate's weight was 2870 g (90th percentile), length was 47.5 cm (70%), and head circumference was 34.5 cm (75%). No family history of coagulopathy was detected. Throughout the labor course, no fetal distress was recorded, rupture of the membranes occurred within 18 h before her birth, and her doctor prescribed ampicillin (150 mg/kg/day) and gentamicin (5 mg/kg/day) due to intrapartum fever.

The amniotic fluid was clear, and no meconium or microorganisms (Gram staining) were detected after her delivery. The neonate's initial Apgar score was 8 at 1 min and 9 at 5 min. Subsequently, the infant showed lethargy, decreased activity, and fever. A full sepsis work-up, including blood and urine, were within the normal

range. However, the cerebrospinal fluid (CSF) was bloody and was xanthochromic after centrifuging. The differential cell count of CSF showed a red blood cell count of 2.1×10^5 cells/ μL and a white blood cell count of 9.0×10^3 cells/ μL (30% segmented neutrophils and 70% monocytes). CSF total protein and glucose were 1358 mg/dL and 36 mg/dL, respectively, but the CSF culture grew no bacteria. Serum biochemistry data were within the normal range, including liver function, blood urea nitrogen, creatinine, glucose, free calcium, and electrolytes. Hematological tests revealed a hemoglobin level of 14.7 g/dL and a platelet count of 22,900/ μL .

Her brain sonography showed grade II, bilateral intraventricular hemorrhages (Figure 1). Other imaging study results such as those of echocardiography, abdominal ultrasound, Doppler ultrasound of the renal vessels, and chest radiography were normal.

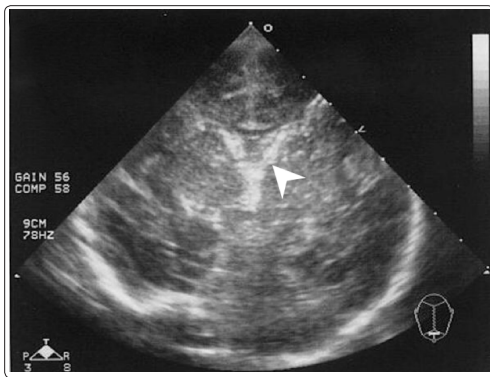


Figure 1: Cranial ultrasonography in the coronal sagittal plane shows increased echogenicity in the bilateral and third ventricles, revealing echogenic hemorrhage (arrowhead)

Magnetic resonance imaging (MRI) of the brain revealed multiple cerebral sinovenous thrombosis in the bilateral transverse sinuses and the straight sinus, with confluence of the sinuses. Additionally, intraparenchymal hemorrhages in the right posterior periventricular white matter and the left cerebellum were identified (Figure 2). Disseminated intravascular coagulation panel showed a D-dimer level of 955 ng/mL (normal range <500 ng/mL), fibrin degradation products of 10–40 $\mu\text{g}/\text{dL}$ (normal range <10 $\mu\text{g}/\text{dL}$), and fibrinogen of 555 mg/dL (normal range = 125–300 mg/dL). The coagulation testing results, including activated partial thromboplastin time, prothrombin time, levels of coagulation inhibitors (antithrombin III, protein S, and protein C), and antiphospholipid antibodies, were within normal limits. Screening for hyperhomocysteinemia was negative. Anticoagulation therapy (low molecular weight heparin) was prescribed immediately.

Five months later, a follow-up brain MRI scan displayed a freely flowing cerebral sinovenous system without any sequelae of sinovenous thrombosis. Clinically, the infant appeared well and seizure-free after anticonvulsant and anticoagulation therapy. No other neurological problems were observed. Moreover, on assessment, her development was normal.

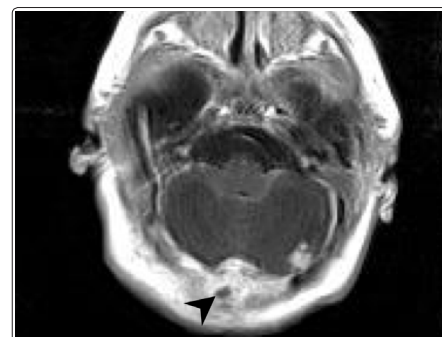
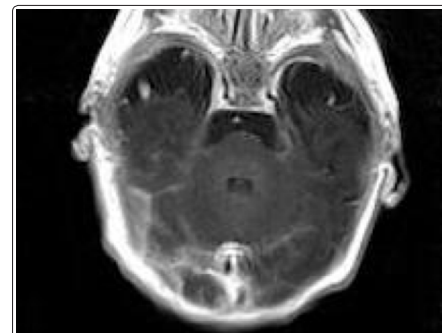
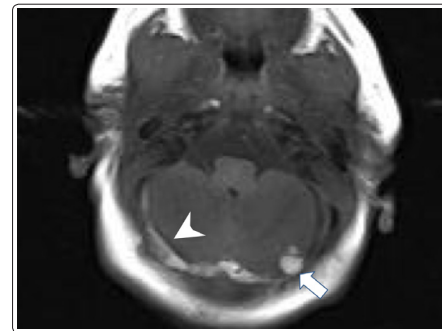


Figure 2: A) Axial T1-weighted magnetic resonance imaging (MRI) reveals a dural venous sinus thrombosis of the transverse sinus (arrowhead) and a high signal hematoma within the left cerebellum (arrow) and B) enhancement of the leptomeninges with a subarachnoid hemorrhage along the sulci of the right temporo-occipital region. C) Gadolinium-enhanced axial T1-weighted MRI shows enhancement of a hematoma within the left cerebellum and a thrombus formation within confluence of the sinuses, presenting as an empty delta sign (arrowhead)

Discussion

Sinovenous thrombosis of the brain is a serious disease, and correct diagnosis is often delayed due to its subtle presentations. [1] Most reported neonatal cases are in term neonates and rarely in preterm neonates. Cases of severe, multiple neonatal cerebral sinovenous thrombosis with intraparenchymal hemorrhage are few [11–14]. Immature physiological hemostatic systems are profoundly influenced by age. In this study, intrapartum maternal fever was associated with a number of apparently transient adverse effects in the newborn [9, 10]. Despite the lack of a definite infectious source from her mother and the patient, intrapartum maternal fever and neonatal fever were recorded, which feasibly contributed to an unstable hemodynamic status and unbalanced hemostasis, leading to the deep sinovenous system to be prone to bleeding and clotting

and intraparenchymal hemorrhage within the left cerebellum [15]. Moreover, intraventricular hemorrhage in sinovenous thrombosis has rarely been addressed. The possible explanation is that the deep venous system drains the choroidal, atrial, and thalamostriate veins; once deep venous blood clot formation is observed in the sinovenous system, this can lead to increased venous pressure and disturb the venous return and therefore predispose the patient to major bleeding along the caudothalamic groove, eventually resulting in intravenous hemorrhage, as observed in our case.

The role of thrombophilia in sinovenous thrombosis in the brain in the neonatal period and childhood has attracted huge attention. Prothrombotic disorders are found in 20% of cases of neonatal cerebral sinovenous thrombosis [1]. An analysis of the multifactorial origin of cerebral sinovenous thrombosis in children indicates that most thrombosis resulted from underlying prothrombotic risk factors, such as factor V Leiden deficiency and deficiency of proteins C and S. Genetic mutations such as those of factor V Leiden and prothrombin G20210A are common in whites but still undocumented among Taiwanese or Chinese populations [17, 18]. Cranial Doppler ultrasound might provide an initial assessment of infants suspected of having superior sagittal sinus thrombosis [19]. However, in this case, multiple deep sinovenous thrombosis and intraparenchymal hemorrhage were involved, and the locations of lesions let the cranial Doppler ultrasound having limited usefulness. Furthermore, the highly echogenic tentorium and cerebellar vermis make localization of intracerebellar hemorrhage difficult [20, 21]. By contrast, a brain MRI scan can not only delineate the extent and location of neonatal brain parenchymal changes and sinovenous thrombosis but also analyze the stages of brain intraparenchymal hemorrhage and the phases of sinovenous thrombosis [22]. In conclusion, if the neonate has any accompanying risk factors, either with or without fetal distress or clinical symptoms, physicians should be cautious of the effects of sinovenous thrombosis. Early MRI is strongly recommended if sinovenous thrombosis is suspected because this approach can better identify the presence, size, and location of lesions and provide early intensive treatment with favorable outcomes.

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