

Research Article

An Unusual Presentation in Neonatal Cerebral Sinovenous Thrombosis: A Case Report and Literature Review

Yan-Jun Wu¹ and Ann-Ching Wang^{1-3*}

¹Department of Pediatrics, Taoyuan Armed Forces General Hospital, Taiwan

²Department of Life Sciences, National Central University, Taiwan

³National Defense Medical Center, Taiwan

Abstract

Neonatal cerebral sinovenous thrombosis is a rare and potentially life threatening disease, leading to long term neurological deficits. The pathogenesis of cerebral sinovenous thrombosis in neonates is still unclear. Many potential risk factors have been drawn such as gestational or delivery complications, or co-morbid conditions including dehydration, sepsis or cardiac defects. Nevertheless, the clinical presentation of this disorder in newborns is too subtle or not significant, leading to delayed diagnosis. Here, we report a preterm female neonate who was delivered with a suspected perinatal infection due to maternal fever. The infant underwent brain sonography for a routine evaluation, while her echogram showed an intraventricular hemorrhage and subsequent a seizure attacked. Unpredictably, brain MRI revealed neonatal multiple sinovenous thromboses. The infant then immediately received anticoagulation therapy. Upon follow-up 3 months later, the developmental milestones were in the normal range; repeated brain MRI showed normal results. In conclusion, neonatal cerebral sinovenous thrombosis should be diagnosed early, especially when patients exhibit the above threatening risks. It is highly important that early intensive therapy could be linked to a better prognosis.

Keywords: Maternal fever; Perinatal infection; Neonatal cerebral sinovenous thrombosis

Introduction

Cerebral sinovenous thrombosis during the neonatal period is a relatively rare disorder and its clinic presentation remains obscure and difficult to diagnosis. The incidence is estimated at 0.67 per 100,000 children, with approximately half occurring among neonates [1]. The etiology of cerebral sinovenous thrombosis of the brain is diverse. Some factors commonly associated with conditions such as dehydration, sepsis or cardiac disorders [2,3]. Recently, some authors identified some hypercoagulation risk factors such as polycythemia [4], protein C deficiency [5], protein S deficiency, antithrombin III deficiency, factor V Leiden, G20210A prothrombin-gene mutation [6], or antiphospholipid antibody [7]. Moreover, obstetric risk factors including clinical chorioamnionitis, preeclampsia [8], and gestational diabetes mellitus [1] are suggested to be linked to neonatal cerebral sinovenous thrombosis.

Previous studies [9,10] showed that intrapartum maternal fever, even in the absence of infection, was associated with development of hypotension and metabolic acidosis in fetus, which could contribute

to fetal hypoxia and that presented with sinovenous thrombosis.

We report the case of a preterm neonate who presented with neonatal fever and seizure, was diagnosed with multiple neonatal cerebral sinovenous thromboses and intraparenchymal hemorrhage, which could have been due to maternal fever underlying perinatal infection.

Case Presentation

A female preterm newborn 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, and mother who had an uncomplicated pregnancy. At birth, her weight was 2,870 g (90th percentile), her length was 47.5 cm (70%), and her head circumference was 34.5 cm (75%). No family history of coagulopathy existed among her relatives.

Throughout the labor course, no fetal distress was recorded, but rupture of the membranes occurred about 18 hours before delivery. Simultaneously, her mother was prescribed with antibiotics of ampicillin (150 mg/kg/day) and gentamicin (5 mg/kg/day) for intrapartum fever.

After birth, no meconium staining or microorganisms (Gram stain) were detected in the amniotic fluid. The neonate's initial Apgar score was 8 at 1 min and 9 at 5 min. Subsequently, we observed that the infant had lethargy, decreased activity, and fever. Therefore, she underwent a full sepsis screening of blood, urine, and Cerebrospinal Fluid (CSF). Unpredictably, the spinal tap disclosed bloody CSF, and was xanthochromia after centrifuging. The differential cell count of the CSF showed a red blood cell count of 2.1×10^5 cells/ μ L, a white blood cell count of 9.0×10^3 cells/ μ L (30% segmented neutrophils and 70% monocytes). CSF total protein and glucose were 1,358 mg/

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***Corresponding author:** Ann-Ching Wang, Department of Pediatrics, Taoyuan Armed Forces General Hospital, No.168, Zhongxing Road, Longtan Dist, Taoyuan 325, Taiwan, Tel: 886-03-4802663; Fax: 886-03-4802663; E-mail: wanganching@gmail.com

dL and 36 mg/dL respectively. No microorganisms were observed on the Gram stain or isolated from any of the cultures. The serum biochemistry data was normal, including liver function, blood urea nitrogen, creatinine, glucose, free calcium, and electrolytes. Hematological tests revealed hemoglobin of 14.7 g/dL, and a platelet count of 22,900/ μ L.

Because of maternal fever, lethargy after birth, and bloody CSF, we performed brain sonography, which showed grade II, bilateral intraventricular hemorrhages (Figure 1). Other imaging studies including echocardiography, abdominal ultrasound, doppler ultrasound of the renal vessels, and chest radiography, which showed no significant findings.

Four days after birth, the infant began having seizures, with repetitive focal jerk of the left forearm and shoulder. The seizures lasted an average of 10 sec to 30 sec. A neurological examination revealed no significance. An Electroencephalogram (EEG) was performed, which showed a high voltage burst and a synchronized discharge, especially in the frontal area. The infant was then treated with phenobarbital (5 mg/kg/day).

Magnetic Resonance Imaging (MRI) of brain unpredictably revealed multiple cerebral sinovenous thromboses in bilateral transverse sinuses and the straight sinus, with confluence of the sinuses, and intraparenchymal hemorrhages in the right posterior periventricular white matter and left cerebellum (Figure 2). Based on these findings, we examined her coagulation status. The Disseminated Intravascular Coagulation (DIC) panel including a D-dimer level of 955 ng/mL (normal range <500 ng/mL), fibrin degradation products (FDP) of 10 μ g/dL to 40 μ g/dL (normal range <10 μ g/dL), and fibrinogen was 555 mg/dL (normal range, 125 mg/dL to 300 mg/dL). In addition, the results of coagulation testing for the diagnosis of hypercoagulable states, including activated partial thromboplastin time, prothrombin time, levels of coagulation inhibitors (antithrombin III, protein S, and protein C), and lupus

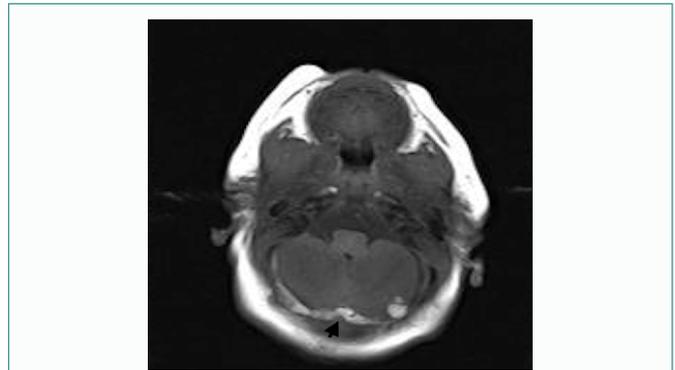


Figure 2A: Axial T1-weighted Magnetic Resonance Imaging (MRI) reveals bilateral high signal thrombi within the transverse sinuses, with confluence of the sinuses (arrow), and a high signal hematoma within the left cerebellum.

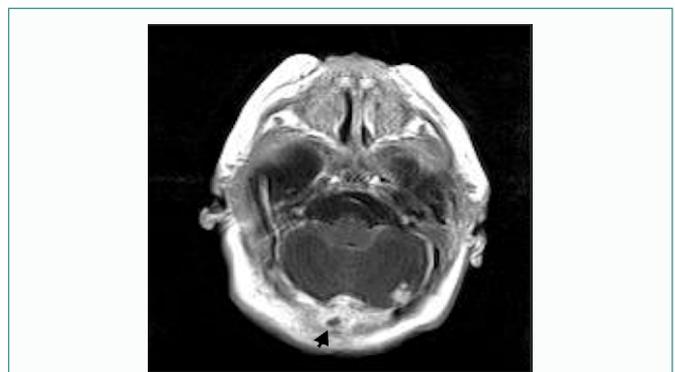


Figure 2B: Gadolinium-enhanced axial T1-weighted MRI shows a high-signal subdural hematoma and enhancement of the leptomeninges with a subarachnoid hemorrhage along the sulci of the right temporo-occipital region, with a thrombus within the straight sinus, shown as an empty delta sign (arrow).

anticoagulant, with detection of antiphospholipid antibodies, were within normal limits. Screening for hyperhomocysteinemia was negative. Subsequently, we prescribed heparin for anticoagulation and monitored the activated partial thromboplastin time to keep it within the therapeutic range throughout the course of heparin treatment.

Five months later, we repeated the brain MRI, which displayed a freely flowing cerebral sinovenous system. Clinically, the infant appeared well and seizure free after anticonvulsant and anticoagulation therapy, no other neurological problems were observed. Moreover, we examined a normal result in the assessment of her development.

Discussion and Conclusion

Sinovenous thrombosis of the brain is a serious disease and is rarely diagnosed in pediatric patients, especially in neonates. Most reported neonatal cases are in term neonates and rarely in preterm newborns [1]. Moreover, reports of our patient's presentation of severe, multiple neonatal cerebral sinovenous thromboses with intraparenchymal hemorrhage, complicated by a suspected perinatal infectious process, but without other organ involvement, is limited in the published literature [8,11,12].

The pathogenesis of intraventricular hemorrhage among neonates whose gestational is age beyond 32 weeks is unclear. However, published literature [8,13,14] shows that intraventricular hemorrhage is likely due to deep venous blood clot formation, which can lead to



Figure 1A: Cranial ultrasonography in coronal sagittal plane shows increased echogenicity in bilateral, third ventricles.



Figure 1B: Cranial parasagittal plane through the left ventricle shows an echogenic hemorrhage along the caudothalamic groove.

increased venous pressure predisposing to major bleeding along the caudothalamic groove, because the deep venous system drains the choroidal, atrial and thalamostriate veins.

Newborns also have immature physiological hemostatic systems, which are profoundly influenced by age. As an example in our case, a primary illness activated coagulation and fibrinolysis, and impaired her ability to restore normal hemostatic function. Such episodes could contribute to unbalanced hemostasis, making the deep venous system prone to bleeding and clotting [15]. The scenario of intraventricular hemorrhage in our patient may be explained by that previously reported in the literature [8,13,14]; blood clot formation in deep venous structures led to venous hypertension and venous hemorrhage upstream from the clot, leading to intraventricular hemorrhage.

Simultaneously, a suspected infectious process aggravated the intraparenchymal hemorrhage, especially the intracerebellar hemorrhage, which is also very rarely reported [16].

The role of thrombophilia in sinovenous thrombosis of the brain has been receiving increased attention among neonates and children. Prothrombotic disorders are found in 20% of neonatal cerebral sinovenous thrombosis cases [1]. Recently, an analysis of the multifactorial origin of cerebral sinovenous thrombosis in children [17] points out that most thromboses resulted from underlying prothrombotic risk factors, with concomitant underlying disease or some independent 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 [18]. As our patient showed no abnormalities when comprehensively screened for prothrombotic disorders.

Imaging techniques to diagnosis of neonatal cerebral sinovenous thrombosis have evolved significantly over the past 20 years. Cranial Doppler ultrasound provides an initial assessment of infants with suspected superior sagittal sinus thrombosis [19]. However, in our patient, multiple deep sinovenous thromboses and intraparenchymal hemorrhage were involved. Thus, the usefulness of cranial Doppler ultrasound could have been limited in our patient. Additionally, visualization of the intracerebellar hemorrhage was poor because of the highly echogenic tentorium and cerebellar vermis [20,21].

MRI delineated the extent and location of neonatal brain parenchyma change and sinovenous thrombosis. MRI can also permit interpretation of brain intraparenchymal hemorrhage and the different phases of sinovenous thrombosis [22]. If MRI was delayed by perhaps only several days, any parenchyma damage that was going to result from the thrombosis should have been already well established.

Past reports [1] of pathological studies among children have intimated that cerebral sinovenous thrombosis has diverse clinical presentations, making it difficult to find. Neonates, often lack obvious signs and symptoms because of developmental immaturity, which contributes to the elusive diagnosis. This could contribute to ongoing brain damage, and until now, little data have existed on definitive therapy and long-term outcomes of these patients.

In conclusion, we highlight that, if the neonate has any accompanying risk factors, either with or without fetal distress or clinical symptoms, physicians should be cautious of the impact of sinovenous thrombosis. Early MRI is strongly recommended if

sinovenous thrombosis is under suspicion for better depiction of its presence, size, location as compared with cranial ultrasound and early intensive treatment with favorable outcome.

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