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CASE REPORT

Cerebellar hemorrhage in full-term neonate: a case report and literature review

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Summary

Introduction/Objective: Cerebellar hemorrhage is a common condition in neonates born before the 32nd week of gestation, and it rarely occurs in full-term neonates. The most important risk factors for cerebellar hemorrhage in full-term neonates include traumatic delivery, instrumentation-assisted vaginal delivery, emergency cesarean section, perinatal asphyxia as well as perinatal infection.

Patient Review: We present a case of cerebellar hemorrhage and cerebral edema in a neonate with culture-negative early-onset sepsis. A full-term male neonate born from uncontrolled pregnancy developed respiratory distress, as well as clinical and laboratory signs of sepsis. The neonate's condition was complicated by respiratory failure, neurological deterioration and neonatal seizures. Chest radiography showed right-sided pneumonia and the head ultrasound showed cerebral edema and hemorrhage in right cerebellar hemisphere. Blood culture, tracheal aspirate and cerebrospinal fluid culture were sterile. The studies showed low incidence of blood culture confirmed early-onset sepsis due to high use of antibiotics in neonatal units. However, the course of the disease and resulting complications suggest that group B β-hemolytic Streptococcus may be a possible cause, as it is the most common pathogen responsible for early-onset sepsis in full-term neonates. Given the relationship between poor neurodevelopmental outcome in children and neonatal cerebellar hemorrhage, long-term follow-up by a pediatric neurologist is required.

Conclusion: Despite the incidence of cerebellar hemorrhage in full-term neonates is low, due to the poor neurodevelopmental outcome, head ultrasound through the "mastoid window" is advised in all critically ill neonates to detect cerebellar hemorrhage.

Keywords: cerebellar hemorrhage, brain edema, brain injury, newborn, sepsis

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INTRODUCTION

Cerebellar hemorrhage (CH) is the most common acquired lesion in the posterior cranial fossa (PCF) in the neonatal period, especially in preterm neonates born before the 32nd week of gestation. In full-term neonates, CH is a rare condition that affects critically ill neonates (1,2). The incidence of CH is inversely proportional to gestational age (GA) and birth weight (BW). The increase in the incidence of CH that has been reported in recent years due to advances in neuroradiological diagnostic techniques (3). In late preterm and full-term neonates, risk factors for CH include primiparity, traumatic delivery, assisted vaginal delivery using forceps and vacuum, occipital osteodiastasis, perinatal asphyxia, delivery completed by emergency cesarean section and the need for resuscitation in the delivery room, as well as perinatal infection. Also, coagulation disorders, such as fetal and neonatal alloimmune thrombocytopenia and vitamin K deficiency, and rare organic acidopathies can be the cause of CH (1). We present a full-term neonate with culture-negative sepsis complicated with pneumonia, cerebral edema (CE) and CH.

CASE PRESENTATION

A 40-week gestation, 2800 g male neonate was born via spontaneous vaginal delivery to a 30-year-old mother, this being her fourth uncontrolled pregnancy. The Apgar scores were 9 at one minute and 10 at five minutes after birth. The initial physical examination was normal in the delivery room. The neonate received 1 mg vitamin K and then was given to the mother for routine care in the Maternity Ward. At the end of the first day of life (DOL), the neonate developed signs of respiratory distress. His blood gas analyses showed respiratory acidosis, but complete blood count (CBC) showed thrombocytopenia and elevated concentration of C-reactive protein (CRP). Oxygen therapy was applied. After blood culture was taken, empirical antibiotic therapy (ampicillin and amikacin) with intravenous fluid infusion was started. In the further course, the neonate vomited fresh blood, so 1 mg of vitamin K was repeated and fresh frozen plasma was administered. The next day, meropenem was added to the therapy. On the third DOL there was a sudden clinical deterioration and the neonate was resuscitated, intubated, and placed on mechanical ventilation (MV).

The neonate was admitted to the Neonatal Intensive Care Unit (NICU) of the Institute of Neonatology on the third DOL in extremely severe condition, orotracheally intubated, in sopor, with generalized hypotonia, scarce spontaneous mobility and clinical signs of seizure with jerking movements of the limbs. The anterior fontanelle was not bulging. The seizure stopped after the neonate received loading dose of phenobarbital. After admission in our NICU, MV and antibiotic therapy were continued, as well as the maintenance dosage of phenobarbital. Additionally, due to hemodynamic instability, inotropic support by dopamine was started. Blood gas analysis showed a mild metabolic acidosis, and the CBC showed the leukocyte level of 31.500/mm^3 (neutrophils 65%, lymphocytes 19%, monocytes 3%), platelets of 44.000/mm^3, CRP of 59.5 mg/L. Chest radiography showed right-sided pneumonia. A head ultrasound (HUS) was performed, revealing signs of CE, including effacement of the cerebral sulci, compressed slit-like ventricles, and narrowing of the interhemispheric fissure **(Figure 1)**. Additionally, the scan showed hemorrhage in the right cerebellar hemisphere and increased echogenicity of the brain parenchyma.

Abdominal ultrasound and echocardiography showed normal findings. The next day the CBC showed a further increase in CRP of 98.2 mg/L, which was also the maximum value of CRP during hospitalization. In serum biochemistry analysis, the concentration of urea, creatinine, total protein, albumin and electrolyte, as well as activity of aspartate aminotransferase, alanine aminotransferase and

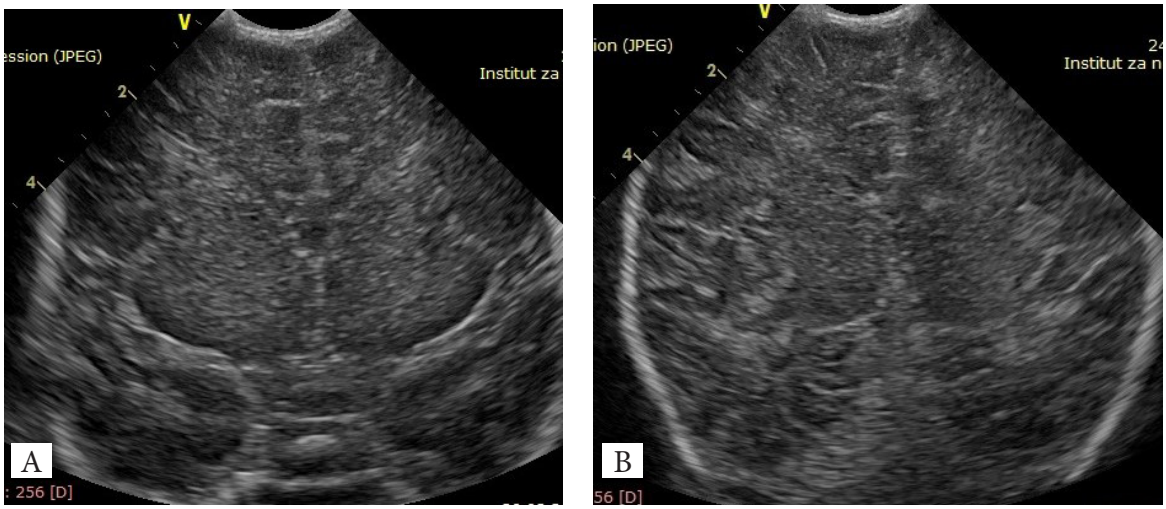

Figure 1. Head ultrasound showed effacement of the cerebral sulci, compressed slit-like ventricles, and narrowing of the interhemispheric fissure (A and B: coronal images)

γ-glutamyl transferase were within normal ranges. During the video electroencephalography (EEG), irregularity of the basic activity with epileptic discharges was recorded, so phenobarbital was continued. After extubation on the fourth day after admission, oxygen therapy was continued for 10 days. Cytological and biochemical analysis of cerebrospinal fluid (CBF) was normal. Blood culture, tracheal aspirate and CBF culture were sterile. During control HUS registered a gradual reduction of CE and CH. On control video EEG, the finding was normal for GA without epileptic discharges, the neonate had no seizures, so he was discharged home without phenobarbital.

DISCUSSION

This neonate admitted to the NICU due to early-onset sepsis (EOS) and neurological deterioration. Cerebral edema and CH associated with pneumonia and culture-negative sepsis were diagnosed in the neonate. In perinatal history, there were no common known risk factors for CH in full-term neonates such as perinatal asphyxia and hypoxic-ischemic encephalopathy (HIE), delivery by emergency cesarean section, resuscitation at birth, traumatic delivery and instrumentation-assisted vaginal delivery. The incidence of CH in full-term neonates is difficult to estimate because they undergo neuroimaging much less frequently compared to preterm neonates. In addition, small hemorrhagic lesions in the cerebellum are asymptomatic, so it is likely that these lesions often go undiagnosed (3-5).

Perinatal infection is also identified as a risk factor for cerebellar injury in the neonatal period (3,4). The retrospective study conducted in the NICU in Kuwait showed that the risk of CH in preterm neonates increased after infection with *Klebsiella pneumoniae* and *Enterococcus faecalis* (6). Similar studies in full-term neonates are rare, due to small sample sizes and predominantly single cases of CH. The cross-sectional study conducted in Canada identified 35% of mothers positive for group B β-hemolytic Streptococcus (GBS) at the time of delivery, whose neonates had cerebellar injury. However, there were no neonates with CH and non-hemorrhagic cerebellar lesions of positive blood culture for GBS (4). In our case, we had a sterile blood culture, tracheal aspirate and CBF culture, but the neonate had clinical and laboratory signs of sepsis. We had no data on maternal infections during pregnancy because it was uncontrolled. Also, due to high use of antibiotics in the NICU, the incidence of culture-positive EOS is low, about 0.4–0.8/1000 full-term neonates in high-income countries (7). In late preterm and full-term neonates, GBS and *Escherichia coli* are the leading causes of EOS and meningitis and are usually due to vertical transmission from a colonized mother (8). Complications of GBS meningitis, including arterial or venous cerebral infarction are described within the cerebellar hemisphere (9,10). Experimental studies have shown that GBS leads to changes in blood flow and perfusion within the brain parenchyma, as well as disrupting the integrity of the blood-brain barrier and overall impairing cerebral autoregulation. Additionally, GBS can cause damage to the endothelial cells of the brain's blood vessels (11-14). As a result of bacterial endotoxin activity, cytokines are released, triggering a systemic inflammatory response. During sepsis and septic shock, blood pressure instability, combined with impaired coagulation and/or thrombocytopenia, increases the risk of intracranial hemorrhage, including CH (6).

Besides sepsis and meningitis, several other complications of GBS infection in the neonatal period have been described, such as pneumonia and CE (15,16). These complications are also described in our case. However, despite sterile blood culture, tracheal aspirate and CBF culture, the clinical picture points to a high probability of GBS as the cause of sepsis and its complications. Other risk factors for CH in our case were MV, use of inotropic drug, and severe thrombocytopenia.

Full-term neonates with CH may present with irritability, apnea and seizures. These can also be signs of neonatal sepsis, so the clinical picture is non-specific, especially in minor CH. However, if these non-specific signs are associated with bulging fontanelle, separated sutures on the skull, bradycardia, horizontal deviation of the bulbs, facial paresis, intermittent tonic extension of limbs and opisthotonos, it is necessary to think about possibility of the brainstem compression. To confirm CH, it is necessary to perform HUS through the mastoid fontanelle **(Figure 2)**. This is especially true for critically ill neonates who have unexplained neurological signs, as well as signs of brainstem compression, and/or increased intracranial pressure (1,3). Although brain magnetic resonance imaging (MRI) is more sensitive neuroimaging modality, especially for the detection of pathological processes in the PCF, it is not the first method of choice in critically ill neonates (3,10). Our choice was HUS, because the neonate was not trans-

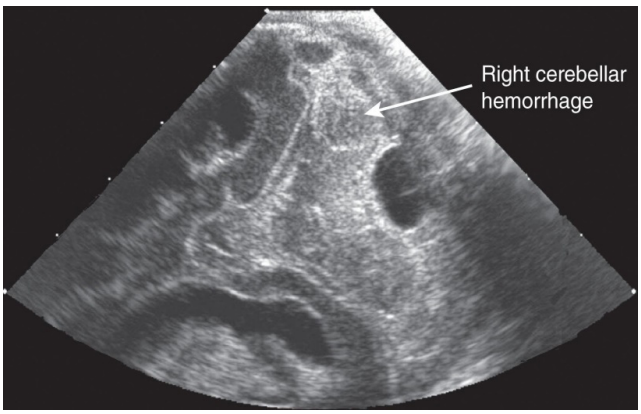

Figure 2. A head ultrasound of the posterior cranial fossa, obtained through the mastoid fontanelle, revealed a right cerebellar hemorrhage (from Limperopoulos C, Benson CB, Bassan H, et al. Cerebellar hemorrhage in the preterm infant: ultrasonographic findings and risk factors. *Pediatrics*. 2005; 116:717–724)

portable, and serial HUS examinations showed a gradual reduction of CH and CE with an improvement in the clinical findings of the neonate.

A limited number of studies have investigated the relationship between CH and neurodevelopmental outcome in full-term neonates. Infants and children with larger CH in neonatal period that led to cerebellar hemispheric and/or vermian atrophy had an increased risk for gross motor, cognitive, behavioral, and expressive language deficits (1,4). Therefore, in our case with CH and neonatal seizures at the time of discharge from the Institute, a brain MRI was advised, as well as a follow-up by a pediatric neurologist.

CONCLUSION

In conclusion, routine head ultrasound (HUS) examination through the anterior fontanelle, typically performed in preterm neonates, should also be conducted in full-term neonates, particularly those born from high-risk pregnancies. Although the incidence of CH in full-term neonates is low, due to the poor neurodevelopmental outcome, a HUS through the mastoid fontanelle is advised in all critically ill neonates to detect CH. It is necessary to carry out adequate prevention of intracranial hemorrhage, HIE and perinatal infection. Furthermore, additional studies are needed to explore cerebellar hemorrhage (CH) in full-term neonates and to investigate the relationship between perinatal infections and CH.

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CEREBELARNO KRVARENJE KOD TERMINSKOG NOVOROĐENČETA: PRIKAZ SLUČAJA I PREGLED LITERATURE

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Sažetak

Uvod: Cerebelarna hemoragija je često stanje kod novorođenčadi rođene pre 32. nedelje gestacije i viđa se retko kod terminske novorođenčadi. Najvažniji faktori rizika za cerebelarnu hemoragiju kod terminske novorođenčadi su traumatski porođaj, instrumentalno završen vaginalni porođaj, hitan carski rez, perinatalna asfiksija, kao i perinatalna infekcija.

Opis pacijenta: Predstavljamo slučaj cerebelarne hemoragije i edema mozga kod novorođenčeta sa sepsom sa ranim početkom i sterilnom hemokulturom. Terminsko novorođenče, rođeno iz nekontrolisane trudnoće, razvilo je respiratorni distres, kao i kliničke i laboratorijske znake sepse. Stanje novorođenčeta se komplikovalo respiratornom insuficijencijom, pogoršanjem neurološkog statusa i neonatalnim konvulzijama. Radiografija grudnog koša pokazala je desnostranu pneumoniju, a ultrazvuk glave edem mozga i hemoragiju u desnoj cerebelarnoj hemisferi. Hemokultura, trahealni aspirat i cerebrospinalna tečnost su bili sterilni. Studije su pokazale nisku incidencu hemokulturom potvrđenu sepsu sa ranim početkom usled visoke upotrebe antibiotika u neonatalnim jedinicima. Međutim, tok bolesti i nastale komplikacije sugerišu kao mogući uzročnik β-hemolytic Streptococcus grupe B, kao najčešći uzročnik sepse sa ranim početkom kod terminske novorođenčadi. S obzirom na povezanost lošeg neurorazvojnog ishoda kod dece i neonatalne cerebelarne hemoragije, potrebno je dugoročno praćenje od strane dečjeg neurologa.

Zaključak: Uprkos tome što je incidenca cerebelarne hemoragije kod terminske novorođenčadi niska, usled lošeg neurorazvojnog ishoda, ultrazvuk glave kroz "mastoidni prozor" je preporučen kod sve kritično bolesne novorođenčadi u cilju detekcije cerebelarne hemoragije.

Ključne reči: cerebelarna hemoragija, edem mozga, oštećenje mozga, novorođenče, sepsa

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