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Ischemic stroke as a rare cause of seizures in a newborn – case report

Karolina Widłak[1,a], Agnieszka Wójtowicz[1], Robert Ściślak[1], Justyna Drankowska[1], Michał Kos[1], Aleksandra Szuster[1], Agata Tarkowska[2], Elżbieta Szponar[2], Wanda Furmaga-Jabłońska[2]

[1]Students' Scientific Group at the Department of Neonate and Infant Pathology
[2]Department of Neonate and Infant Pathology, Medical University of Lublin
[a]E-mail address: karo.widlak@gmail.com

Abstract

Background: Identifying etiology of seizures is the primary clinical objective in the management of neonatal seizures (NS). About 85 % of NS cases occurr as a consequence of a specific, identifiable etiology. Causes of symptomatic NS can be broadly categorized as: hypoxic-ischemic encephalopathy, electrolyte or metabolic disturbances, CNS or systemic infections, developmental defects and acquired structural brain lesions, including hemorrhagic or ischemic stroke. Ischemic stroke is characterized as a sudden focal or generalized brain function disruption, whose symptoms tend to last longer than 24 hours (or cause death) and have no other reason but a vascular one. The reported annual incidence is estimated at one per 4000 live births for neonates.

The aim of this case report is to present diagnostic difficulties in case of ischemic stroke in apparently healthy neonate.

This case concerns a patient – a full-term male newborn, who was in a good condition in the first 3 days after birth. At the beginning of the 4th day of life 3 episodes of right-sided clonic seizures with right-sided nystagmus occurred and which was the reason for admitting the

patient to the Department of Neonate and Infant Pathology. Shortly after arrival the seizures appeared again. Laboratory tests showed slightly lowered glucose level and elevated serum concentration of lactic acid. The ultrasound examination of the head revealed a small right-sided subependymal cyst. The patient's condition was deteriorating, with recurring righ-sided clonic and tonic seizures accompanied by apnea and desaturation that required resuscitation efforts. Because of worsening state of the patient, CT scan was performed. The CT examination revealed a hypodensic area in the left parietal region and cerebral edema, which indicated a possible ischemic stroke.

Conclusions: The absence of visible pathologies in the ultrasound examination of the head does not necessarily indicate a lack of CSN abnormalities. More precise imaging tests are needed to identify the cause of NS.

Key words Ischemic stroke

Introduction

The rapid depolarization in neonatal's brain cell leads to excessive synchronous electrical activity, which manifests as neonatal seizures (NS) [1]. The incidence of NS is difficult to estimate – most of the studies used electrodiagnostic techniques for NS diagnosis, but in some of them the diagnosis was based on clinical observation of abnormal movements which amounts to approximately 0.95-5.0 per 1000 live births [2 – 7]. A low birth weight and preterm labor were identified as the strongest risk factors for NS [1, 8], others are listed in Table 1.

Table 1. Risk factors for neonatal seizures [5, 7, 9].

Infant	• Lower gestational age in preterm infants • Low birth weight • Post term >42 weeks • Male sex
Intrapartum	• Evidence of fetal distress • Placental abruption, cord prolapse, prolonged second stage • Maternal pyrexia, chorioamnionitis
Maternal	• Advancing maternal age >40 years • Nulliparity • Pre-existing/gestational diabetes mellitus

The occurrence of seizures in a neonate may be the first and only sign of central nervous system disorders, therefore, one should strive to explain their etiology and initiate proper therapy [1]. About 85 % of them appear as a consequence of specific, identifiable reason (Table 2).

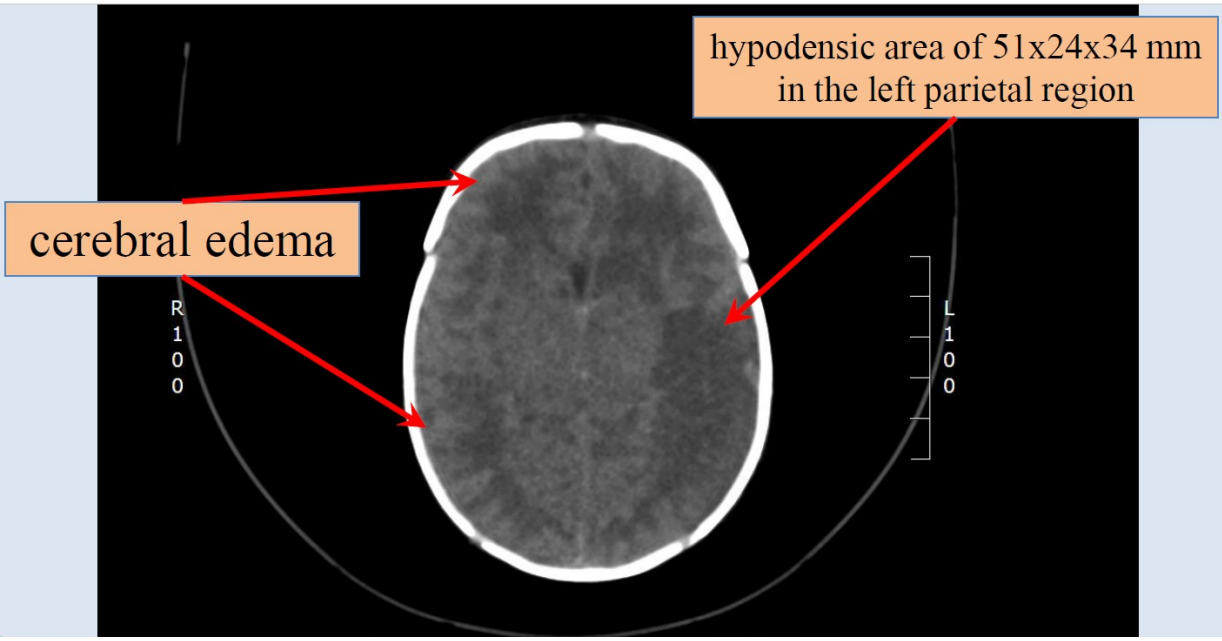
Table 2. Etiologies of neonatal seizures [1, 10 – 14].

Etiology		Frequency
1)	Hypoxia-ischemia (acute neonatal encephalopathy)	50-60%
2)	Intracranial hemorrhage	7-18%
3)	Central nervous system infection	5-20%
4)	Metabolic and electrolyte disturbance (hypoglycemia, hypocalcemia, hypomagnesemia)	3-5%
5)	Ischemic stroke	1-12%
6)	Maternal drug withdrawal	4%
7)	Inborn error of metabolism	1-4%
8)	Neonatal-onset epilepsy	1%

Case report

A full-term male newborn with birth weight of 3150 g and Apgar score of 10 points, was delivered by a planned C-section due to incorrect engagement of the fetal head in pelvis. The newborn was in a good condition for the first 3 days after birth. At the beginning of the fourth day of life the newborn was transmitted from Neonate Department (which is the part of Obstetrics Clinic) to the Department of Neonate and Infant Pathology, because of 3 episodes of right-sided clonic seizures with right-sided nystagmus lasting up to 7 minutes, which occurred at the beginning of the same day. At the time of admission the patient was stable without deviations in physical examination. Shortly after admission the seizures appeared again (initially short-term and self-limiting). Between the episodes of seizures, no abnormalities were observed in the physical examination. Laboratory tests showed slightly lowered glucose level (45 mg/dl) and elevated serum concentration of lactic acid (54 mg/dl). The repeated ultrasound examination of the head revealed a small right-sided subependymal cyst (with diameter of about 3 mm) and no other pathologies. The patient's condition was deteriorating – the right-sided clonic and tonic seizures with apnea and desaturation (which required resuscitation) were reappearing every few minutes on the first day of the hospitalization. Administration of phenobarbital did not bring any effects, therefore computer tomography (CT) scan of the head was performed despite normal head ultrasound evaluation results. The examination revealed a hypodensic area of 51x24x34 mm in the left parietal region with cerebral edema (Picture 1).

Picture 1. The CT examination scan.



Based on the CT result, ischemic stroke was suspected. The patient underwent neurological consultation and anti-edema treatment (20% mannitol, furosemide) and intravenous depakine infusion were administered. The child's condition was slowly stabilizing – the episodes of NS resolved, irregular, shallow breaths and variable muscle tone were still observed. The boy was referred for further diagnosis and treatment to refrrence medical center, where the diagnosis of stroke was confirmed. Currently, the boy is 3.5 and develops properly.

Discussion

Identifying etiology of seizures is a the primary clinical objective in management of NS, in parallel with the symptomatic treatment. Some circumstances of the appearance of convulsions may indicate their etiology. If convulsions appear shortly after birth, we can, with high probability, suspect hypoxic-ischaemic encephalopathy which usually occurs in the first day of life and which moreover is the most common cause of NS in newborns. In the case of focal or unilateral seizures appearing in the first few days after birth, as in the case of the patient described above, a diagnosis of ischemic stroke should be considered. Increased fetal movements seen on cardiotocography which are suggestive of fetal seizures may indicate congenital metobolism errors [15]. When ordering additional tests, you should also consider such important causes of NS as hypoglycaemia. electrolyte disturbances, infectious diseases (sepsis, meningitis, TORCH infections), withdrawal syndrome in a newborn of drug addict mother, venous sinus thrombosis of the brain [16, 17].

A history provided by parents can be very helpful in identifying the etiology of convulsions. It is important to ask about familial antecedents and the history of pregnancy and labor [10]. The risk factors of ischemic stroke in a newborn are listed in Table 3 (most of them would be typically identified with the help of information provided by parents). The information obtained from the parents of the described patient did not indicate a high probability of stroke as a cause of convulsions. The only risk factor listed in Table 3 that occurred in the boy was his sex.

Table 3. Risk factors for ischemic stroke in a neonate [18].

Antepartum factors	Male sex Family history of seizures Family history of neurological diseases Birthweight <third percentile Primiparity
Intrapartum factors	Maternal pyrexia PROM (premature rupture of membranes) Prolonged second stage of labor Tight nuchal cord Failed vacuum delivery

The electroencephalographic examination, routinely performed when NS are suspected, can also help in ascertaining etiology. Focal sharp persistent waves with high amplitude and complex morphology, that are present in the state of both sleep and wakefulness, suggest focal lesions. Multifocal sharp waves may indicate diffuse dysfunction [19].

Laboratory tests can show the cause of NS, which is why a number of blood, urine and cerebrospinal fluid tests should be performed (Table 4). Laboratory tests' results of the described patient showed only slightly lowered glucose level (45 mg/dl) and elevated serum concentration of lactic acid (54 mg/dl). It was still unknown what was causing the NS.

Table 4. Laboratory data to determine the etiology of NS [19].

Blood tests	Arterial blood gases and pH Sodium, glucose, calcium, magnesium, ammonia, lactate and pyruvate, serum amino acids TORCH (toxoplasmosis, other infections, rubella, cytumegalovirus and herpes simplex) titers Biotin
Urine tests	Reducting substances, sulfites, organic acids Toxicologic screen
Cerebrospinal fluid tests	Red and white blood cell counts Glucose and protein Neurotransmitter profile (in proper clinical context)

Imaging examinations should be performed as soon as possible if a stroke or more common reasons of NS such as cerebral hemorrhage or congenital malformations is suspected as causing NS. Imaging technique which is commonly used for screening neonates is head ultrasonography. It can be used in newborns, when a stroke is suspected if the computer tomography (CT) or magnetic resonance imaging (MRI) is not immediately available. The head ultrasound is an easily accessible, non-invasive and rapid examination which carries no risk of exposure to ionizing radiation [20]. Recent research shows that with the help of modern equipment, ultrasound examination can detect ischemic changes in up to 87% of newborns who have had clinical symptoms of an ischemic stroke. However, it is much less sensitive than CT or MRI [20, 21], as was shown by the case described. Currently, a head CT remains the most often used test to establish the diagnosis. CT is useful for the diagnosis of ischemic strokes, although it is insensitive in the first few hours [22-24].The disadvantages of CT are also a high dose of radiation and the need to sedate the newborn during the

examination [25]. In the described patient (as in all neonates) intravenous contrast is contraindicated during CT examination, due to physiologic renal immaturity and risk of thyroid dysfunction, which reduces the sensitivity of this study [26, 27]. Early infarction can be visualized with MRI using diffusion-weighted imaging (DWI) before the lesion can be seen with conventional MRI or CT [28-30]. The main drawbacks of MRI are the low availability of this examination and the necessity (as in the case of CT) of the pharmacological sedation of the newborn [21, 31]. The most reliable imaging examination for cerebral assessment in the case of the described patient would be MRI, but it was not made for technical reasons (no access to such examination in the afternoon and night at the hospital).

To sum up, in the case of persistent seizures in the newborn, if the cause can not be determined, it is necessary to perform an MRI or CT scan of the CNS in order to exclude e.g. ischemic stroke. The case of the patient described above proves that a head ultrasound in a newborn is not sensitive enough to detect stroke and it is necessary to perform more precise imaging tests when diagnosing NS.

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