Diagnostic evaluation of a symptomatic cerebrovascular accident in a neonate with focal convulsions

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Focal neonatal convulsions are usually related to perinatal asphyxia with hypoxic ischemic encephalopathy or cerebrovascular accidents which include hemorrhagic lesions (including hemorrhagic periventricular leukomalacia), arterial ischemic stroke or sinus venous thrombosis.

With an estimated incidence of 1 in 4'000 deliveries, ischemic infarction is a rare cause of neurological symptoms in the neonatal period (1). Occlusion of a major cerebral artery can be due to an embolic or thrombotic event. Clinically, patients typically present with focal seizures and no altered consciousness between the episodes. Standard techniques such as cerebral ultrasound, electroencephalograms (EEGs) and magnetic resonance imaging (MRI) aid in early diagnosis (2). Additional information from cerebral blood flow velocity measurements using transcranial Doppler examinations might be useful for early differentiation between perinatal arterial stroke and other types of cerebral vascular lesions. Thus, diagnostic MRI may not be required as an emergency examination.

This male patient was born by Cesarean section because of failure of labor progression at 37 weeks and 3 days of gestation with a birth weight of 3050 g. Neonatal adaption was normal with Apgar scores of 9, 10, and 10 at 1, 5, and 10 minutes, respectively. Family history revealed no convulsive, hematologic or neurologic disorders.

On day 3 of life, there were three episodes of convulsions, which were initially focal with cloni of the right arm and eye deviation to the upper right, then generalized secondarily with symmetric cloni and nystagmus. Each episode lasted for 2-3 minutes, and was accompanied by tachycardia and falling oxygen saturations. Adequate behavior was observed between the episodes. Serum concentrations of glucose and electrolytes were normal. After the third episode, phenobarbital treatment was started with a loading dose of 10 mg/kg followed by a maintenance dose of 5 mg/kg/d. No more clinical episodes of convulsion were recorded thereafter.

Initial laboratory analyses of blood and cerebrospinal fluid showed normal values for electrolytes, ammonium, pyruvate, coagulation factors as well as infectious parameters. Common metabolic disorders were excluded with normal newborn screening results (Guthrie test).

Within 30 min after admission to NICU, cerebral artery flow velocity (CAFV) measured with transcranial Doppler ultrasound of the left middle cerebral artery (MCA) was diminished compared to the right MCA. Peak systolic blood flow velocities were more than 25% higher (45 cm/s vs. 35 cm/s), and the end-diastolic blood flow velocities were more than 60% (20 cm/s vs. 12 cm/s) higher in the right MCA when compared to the left MCA. There were also marked differences in the resistance index values between the right and left MCA (0.55 vs. 0.66) (Fig. 1). In addition, thalamic hyperechogenic signals were detected on the initial cerebral ultrasound.

Magnetic resonance imaging (MRI) 2 days after the convulsions showed extensive acute ischemic lesions in the left temporal lobe, as well as involvement of the left thalamus, the posterior part of the left internal capsula, and the left peduncle of the splenium of the corpus callosum. No thrombus could be detected on MR angiography (Fig. 2-4).

The EEG on day 3 of life showed no abnormalities. Further laboratory analysis did not reveal an underlying coagulation disorder (antithrombin III, factors II and V, protein C and S). Maternal anticardiolipin antibodies, lupus anticoagulants, ac-ß2-microglobulin could not be detected.
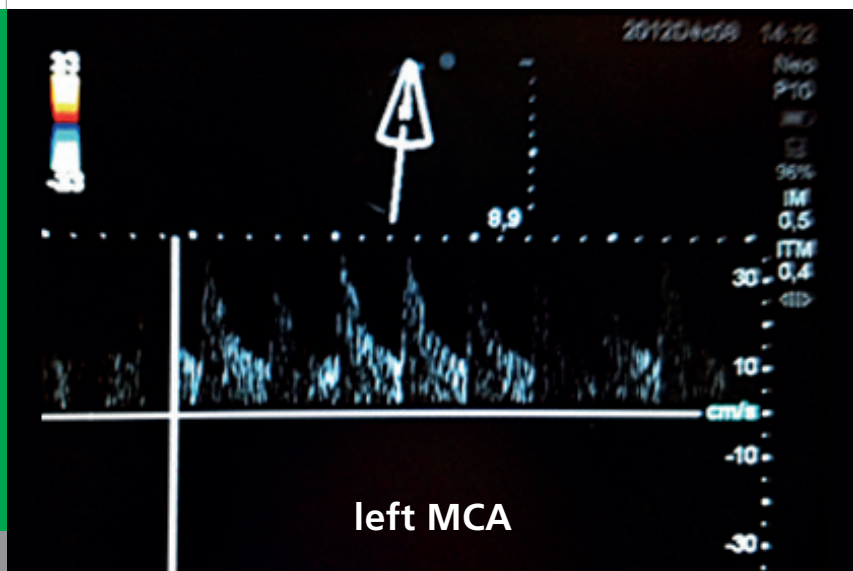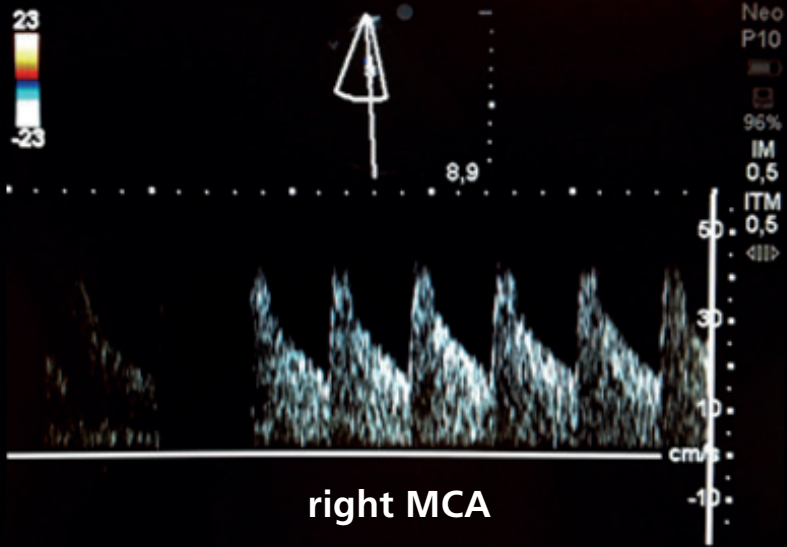
Fig. 1

Cerebral artery flow velocity (CAFV) of the middle cerebral arteries (MCA): The peak systolic blood flow velocities were at 35 cm/s and 45 cm/s, the end-diastolic blood flow velocities at 12 cm/s and 20 cm/s in the left and right MCA, respectively. The resistance indices were 0.66 (left) and 0.55 (right).
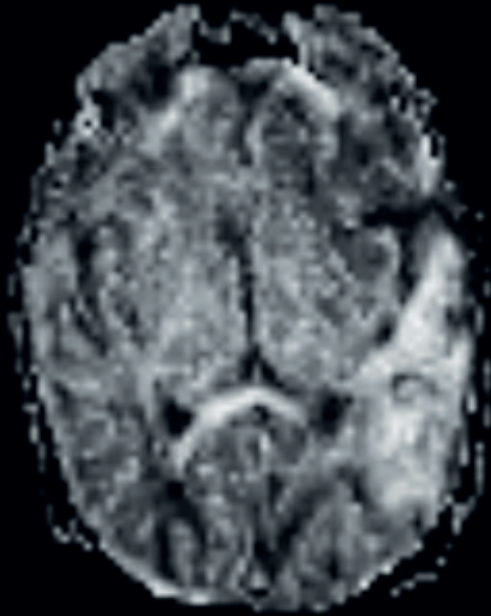
Fig. 2

PWI (perfusion weighted imaging) sequence on day 4, 48h after the convulsions, revealing diminished perfusion of the left temporal lobe.

Neonatal seizures, one of the most common clinical manifestations of central nervous system disorders in the neonatal period, with a reported incidence of 1.5–14/1000 live births, can be either symptomatic or idiopathic. Perinatal hypoxic ischemic insults (reported seizure incidence of 40%-60%) and cerebrovascular accidents (reported seizure incidence of 8%-20%), birth trauma, perinatally acquired infections and metabolic disturbances can be the cause of early symptomatic neonatal seizures. Furthermore, although rare, congenital brain anomalies, inborn errors of metabolism and genetic disorders can lead to neonatal seizures (3). Cerebrovascular accidents can be divided into either non-hemorrhagic arterial ischemic strokes, or hemorrhagic insults. The latter are often related to sinus venous thrombosis (SVT). Perinatal arterial ischemic stroke is the second most common underlying etiology of neonatal seizures in the full-term newborn. The prognosis of arterial ischemic stroke is generally better than of SVT.

Most cases of infants with neonatal cerebral infarction present with focal and clonic convulsions, few present with generalized and clonic, or even subtle seizures. The onset of seizure activity is between 12 and 76 hours after birth. Infants tend to be alert and responsive between episodes and are not encephalopathic. Focal convulsions are to be evaluated in their perinatal context. As a first step, in addition to standard laboratory tests to exclude possible metabolic causes, a
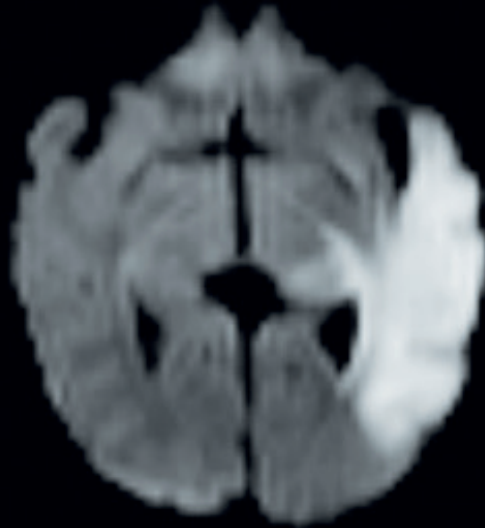
DWI (diffusion weighted imaging) sequences on day 4, 48h after the convulsions, revealing ischemic lesions of the left temporal lobe.
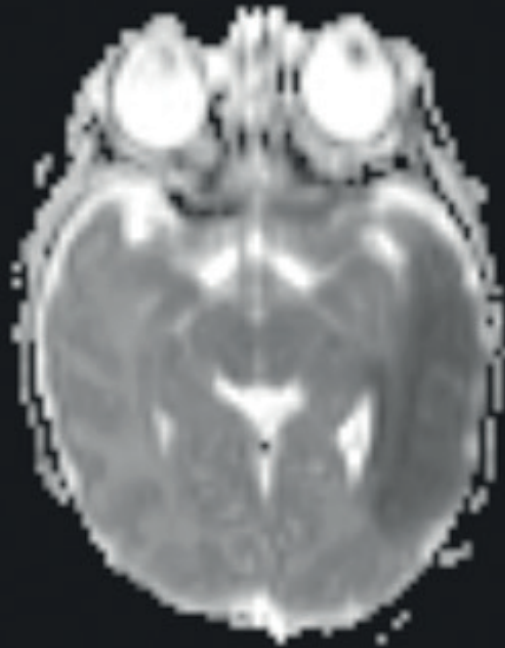
Fig. 5

ADC (apparent diffusion coefficient) sequence on day 4, 48h after the convulsions, revealing ischemic lesions of the left temporal lobe.

detailed neurological and clinical evaluation of the neonate between the episodes of convulsions is crucial. With hemorrhagic lesions (including the hemorrhagic PVL in preterm infants) patients show often an altered level of consciousness, whereas patients with an arterial ischemic stroke often display normal interictal behavior. Patients with SVT present with apneas (18%) altered consciousness (2%), agitation (6%) or sepsis-like symptoms (5%) (4).

Therapy of perinatal ischemic stroke is supportive (5). SVT in the perinatal period is often associated with hemorrhagic lesions (reported in 48-79% of the cases). Nevertheless, anticoagulation with low molecular-weight heparin has been proven to be safe (6) and several case reports have documented successful thrombolytic therapy. Therefore, early anticoagulation and/or thrombolysis may have to be considered rapidly. However, whether such treatment leads to a better short- and long-term outcomes is unclear.

Cerebral ultrasound with high frequency transducers enables examinations of high-risk neonates at the bedside. However, ischemic cerebral insults can be difficult to detect (7). Transcranial Doppler ultrasound is a flexible, accessible, routinely used tool for the assessment of several vascular pathologies (ie. vasospasm, stenosis etc.) in the adult intensive care setting. In the neonatal unit, transcranial Doppler ultrasound is

still used only rarely. Fukuda et al. (8), using this technique, described lower CAFVs in all cerebral arteries of neonates who went on to develop PVL when compared with control infants; this difference was found from day 0 onwards. In another study, Basu et al. (9) demonstrated higher CAFVs in the MCA in septic neonates with high complication and mortality rates. They consider the assessment of CAFVs early after birth as an adjunct bedside, non-invasive investigation, which may have immediate diagnostic and prognostic implications. Several case reports have described an asymmetry of CAFV and RI measurements in the MCA in neonates with cerebral infarcts (10-12). Finally, in a recent study, color Doppler ultrasound has been shown to be highly specific for ruling out SVT and therefore being useful as part of a clinical-laboratory-imaging algorithm (13).

Magnetic resonance imaging (MRI) has been established as the imaging modality of choice for the detection and evaluation of ischemic brain injury in adults, because of its high sensitivity and specificity. In the early phase of cerebral infarction of neonates, several reports have revealed the importance of diffusion-weighted imaging (DWI) MRI to detect focal ischemic brain injury in neonates (14, 15). This sequence can be used with high sensitivity during the first 2 days after a stroke. It has to be recognized that DWI alterations in do not persist for more than one week. After 5 days, diagnosis relies mainly on T2-weighted images (16).

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