

# Can Doppler sonography be used to diagnose neonatal cerebral infarction caused by portal vein thrombosis

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## ABSTRACT

تعتبر الجلطة الدماغية لدى الأطفال حديثي الولادة شديدة الخطورة ومسببة للإعاقة، إلا أنها تعتبر نادرة خصوصاً إذا كان السبب مصاحب لتخثر في الوريد البابي. نستعرض في هذا التقرير حالتين لطفلين حديثي الولادة أصيبا بجلطة دماغية. كما سنناقش التقنية الفريدة للجلطة الدماغية. ونقترح مع غياب أعراض الجلطة في الوريد البابي، عمل أشعة دوبلر الصوتية للأطفال حديثي الولادة الذين أصيبوا بجلطة دماغية وذلك لتأكيد التشخيص.

Neonatal cerebral infarction is a serious and disabling condition. It is extremely rare if it occurs in association with portal vein thrombosis. We are reporting 2 cases of neonatal cerebral infarction with this etiology. The unique mechanism of cerebral infarction will be discussed. We propose that in the absence of any identifiable cause for the cerebral infarction, portal vein thrombosis should be considered and a Doppler sonography for the portal system is worth carrying out to confirm the diagnosis.

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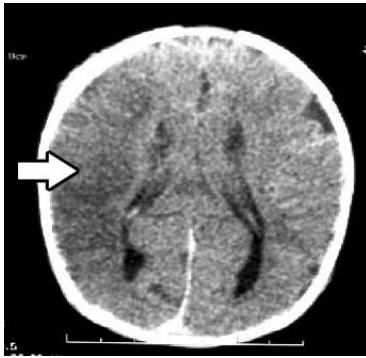
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Neonatal thromboembolic events are being increasingly recognized, and they may lead to serious long-term complications. The usual presentation is seizures during the first few days of life, but most of the affected newborns can be asymptomatic. The pathogenic mechanisms of neonatal cerebral infarction are complex. The diagnosis of portal vein thrombosis

(PVT) during the neonatal period is frequently an incidental ultrasonography finding. This tool is not often reliable to confirm the diagnosis.<sup>1</sup> A Doppler sonography might be more accurate, especially if no clear etiology is found. Our 2 cases are an example of neonates with stroke without clear etiology, and in which Doppler sonography helped us to identify the underlying etiology of PVT.

**Case Report. Patient 1.** The first case is a full term female infant, the product of vacuum extraction due to prolonged second stage of labor, and poor maternal effort. She had Apgar scores of 9 and 9 at one and 5 minutes, with a birth weight of 3500 gm. The mother is 29-year-old Saudi lady, primigravida with a history of prolonged rupture of membranes. She had no history of fever, and she received 2 doses of intravenous antibiotics. The umbilical cord blood gases were normal. At the age of 11 hours, she developed repeated episodes of left sided focal seizures lasting up to 2 minutes, which were controlled with Phenobarbital. A CT of the brain was carried out at the age of 15 hours, and revealed subtle hypo density with effacement of the sulci over the right frontotemporoparietal lobe, and mild subdural bleeding seen over the straight sinus (Figure 1). An MRI brain (T1, Figure 2) revealed decreased signal intensity over the right frontotemporal and parietal areas, as well as increased signal intensity over the right thalamus and basal ganglia. A DWI (Figure 3) showed increased signal intensity over the same areas, consistent with acute infarction. An MRI angiography revealed filling defects noted in the distal branches of the right middle cerebral artery suggesting small emboli (Figure 4). An EEG showed spikes and sharp waves over the right hemisphere. An echocardiogram showed patent foramen ovale. Liver Doppler revealed decreased peak flow velocity (Figure 5), and thrombus in the left portal vein. Other work up, including sepsis and metabolic screen, lactate, pyruvate, liver function test, coagulation profile (prothrombin time), activated partial thromboplastin time, thrombin time, fibrinogen, von Willebrand factor antigen, factor VIIIc, protein C, protein S, antithrombin III, factor V Leiden, and antiphospholipid antibodies were unremarkable. She



**Figure 1** - Subtle hypo density with effacement of the sulci over the right frontotemporoparietal lobe (arrow).



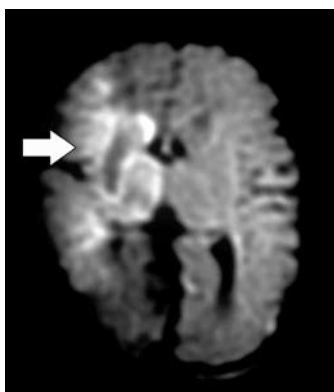
**Figure 4** - An MRA shows filling defects noted in the distal branches of right middle cerebral artery suggesting small emboli (arrow).



**Figure 2** - An MRI brain (T1) revealed decreased signal intensity over the right frontotemporal and parietal areas and increased signal intensity over the right thalamus and basal ganglia. Thick arrow - right frontotemporal and parietal areas, and thin arrow - right thalamus and basal ganglia.



**Figure 5** - Liver Doppler revealed decreased peak flow velocity and thrombus in the left portal vein (arrow).



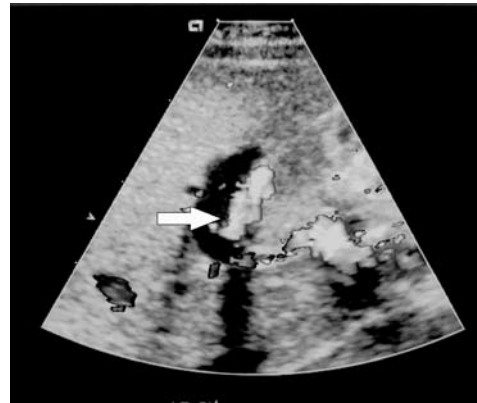
**Figure 3** - The DWI shows increased signal intensity over the right frontotemporal region (arrow).

received IV heparin then shifted to low molecular weight heparin. Repeated liver Doppler sonography at the age of one month revealed resolution of the thrombus, and the heparin was discontinued. She had mild left sided hemiparesis.

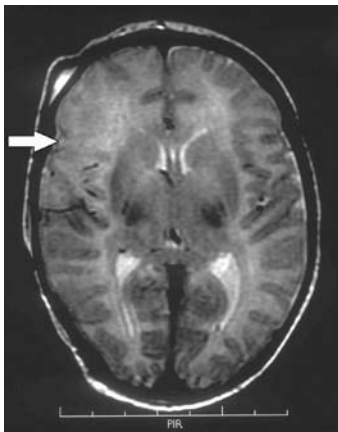
**Patient 2.** The second case was a full term male neonate, born to a 33-year-old multigravida mother (G8, P7), her antenatal course was uncomplicated. A vacuum extraction was performed following prolonged second stage of labor after epidural anesthesia. Apgar scores were 7 at one minute and 9 at 5 minutes. Birth weight was 3560 gm, and the umbilical cord blood gases were normal. Physical examination revealed a large cephalhematoma over the right parietal bone, he was grunting but no desaturation. Lung examination showed decreased air entry over the right side. The rest of the physical examination was normal. A chest x-ray revealed right side non-tension pneumothorax. At 43 hours of age, a left focal seizure occurred and it was controlled by Phenobarbital. A CT of the brain showed a low-dense area in the right frontoparietal region (Figure 6). An MRI (T2) and DWI revealed increased signal intensity over the left posterior frontal lobe (Figures 7 & 8). An MRI angiography revealed no abnormality. An EEG showed spikes and sharp waves over the right



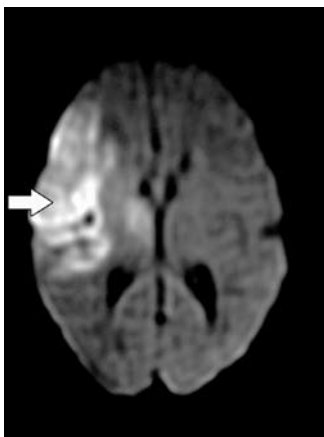
**Figure 6** - A CT of the brain showed a low-density area in the right frontoparietal region (arrow).



**Figure 9** - Liver Doppler sonography revealed decreased peak flow velocity in the left portal vein and presence of thrombus (arrow).



**Figure 7** - The MRI (T2) revealed increase signal intensity over the left posterior frontal lobe (arrow).

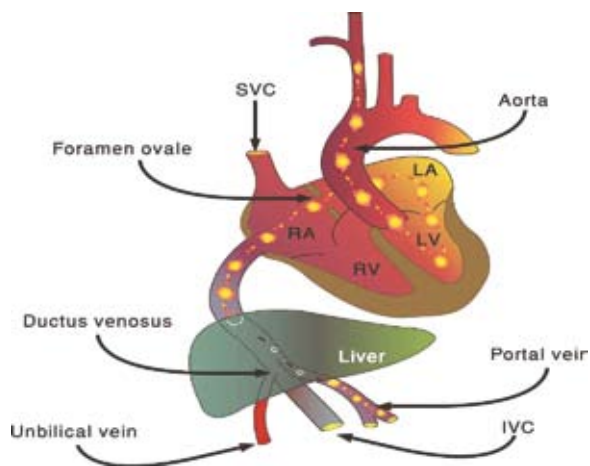


**Figure 8** - The diffusion-weighted MRI shows increased signal intensity over the left posterior frontal lobe (arrow).

frontal head region. Echocardiography showed a patent foramen ovale. Liver Doppler sonography revealed decreased peak flow velocity in the left portal vein, and the presence of thrombus (Figure 9). Similar workup was carried out as in patient one, which was unremarkable. He received heparin intravenously for one week, and was then shifted to low molecular weight heparin. Repeated liver Doppler sonography at the age of 5 months showed resolution of the thrombus. His neurological examination was normal, and heparin was discontinued.

**Discussion.** Although thromboembolic disease in the neonate is uncommon, its management remains a challenge. Over 80% of thrombotic events in neonates are associated with venous or arterial catheters.<sup>1</sup> Symptomatic neonatal stroke occurs in approximately one in 4000 term neonates.<sup>1</sup> Racial and gender differences have been identified for pediatric stroke, but such information is not available for neonatal stroke,<sup>2</sup> and 12-17.5% of neonatal seizures can be attributed to stroke.<sup>1</sup> Risk factors for neonatal stroke have been assessed on limited evidence from selected case series and case reports. The mechanisms by which ischemic stroke occurs include thromboembolism from an intracranial or extracranial vessel, or the heart or placenta. Commonly the source is undetermined.<sup>2</sup> The incidence of PVT in neonates is unknown. The most common cause is instrumentation, particularly umbilical vein catheterization.<sup>3</sup> Other causes include sepsis, hyper viscous state, venous compression, metabolic disorders, and hypercoagulability.<sup>3</sup> There were no identifiable risk factors for PVT or stroke in our cases. They were born by vacuum extraction, which is not a known risk factor for cerebral infarction.<sup>4</sup> In our patients, the EEG revealed epileptiform activities. This is a non-specific finding. The EEG can be normal, or it may show focal slowing, spikes and sharp waves, or periodic lateralized epileptiform discharges in neonatal stroke.<sup>5</sup> Neuroimaging of the brain is the best tool to detect and

characterize infarcts in terms of number, size, vascular territory, and the presence or absence of hemorrhagic conversion. The CT brain was reported as normal in the first case. An MRI is more sensitive to detect small or early infarcts that are frequently missed by CT. The diffusion weighted MRI scan is the best to detect early abnormalities.<sup>6</sup> Normal long-term development can be found in one third of term infants with cerebral infarction in the neonatal period. A history of seizures and the presence of abnormal neurologic examination might be associated with long-term poor prognosis. The extent of the lesion on the MRI is a better predictor. In addition, EEG findings may be helpful in terms of long-term prognosis, for example, abnormal background activity either unilateral or bilateral might be associated with neurologic deficit. In contrast, the presence of a normal background is not related to abnormal outcome.<sup>7</sup> Parker et al<sup>8</sup> reported 2 cases of neonatal cerebral infarction. No clear etiology or risk factors were found in these cases after thorough work up of neonatal stroke, however, when 2-dimensional echocardiography was performed, it did show PVT. In this report, we used Doppler sonography for the portal system to diagnose PVT causing neonatal cerebral infarction; 2-dimensional echocardiography might miss it.<sup>9</sup> The unique characteristics of prenatal circulation provide a portal vein to the cerebral vessels of the fetus (Figure 10). In the fetus, blood flows through the ductus venosus, which carries blood from the portal and umbilical veins to the inferior vena cava and right atrium. From the right atrium, most blood flows into the right ventricle and then to the main pulmonary artery. The PVT with paradoxical emboli may help to explain the phenomenon of 'idiopathic' cerebral infarction among healthy full term neonates.<sup>8</sup>



**Figure 10** - Paradoxical thromboemboli could travel from the portal vein to the systemic circulation as shown by arrows. LA - left atrium, LV - left ventricle, RA - right atrium, RV - right ventricle, SVC - superior vena cava, IVC - inferior vena cava.

The optimal treatment of thromboembolic disorders in newborns is uncertain since current guidelines are extrapolated from studies in adults and older children, which is not optimal. Options include thrombolytic therapy, or close monitoring of the thrombus with objective tests and treating with anticoagulants if extension occurs.<sup>10</sup> The most comprehensive discussion of recommendations for antithrombotic therapy in children and neonates is reported from the 7th American College of Chest Physicians Conference on Anticoagulation and Thrombolytic Therapy.<sup>10</sup> They suggested in case of symptomatic venous thromboembolism and if clinicians elected to use anticoagulation therapy, to administer unfractionated heparin or low molecular weight heparin, and subsequently administer low molecular weight heparin for 10 days to 3 months. Since the efficacy and safety of tissue plasminogen activator thrombolysis and warfarin are not well studied in neonates,<sup>10</sup> we elected not to treat our patients with these drugs.

In conclusion, we propose that in the absence of any identifiable cause for neonatal stroke, the cerebral infarction may be considered due to PVT, and Doppler sonography for the portal system is worth carrying out.

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