

Case Report

Neonatal Cerebral Infarction Diagnosed by Diffusion-Weighted MRI Pseudonormalization Occurs Early

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Background—Seizures in the neonatal period may be the single symptom of acute ischemic cerebral infarction. It may be difficult to establish the diagnosis in the acute phase by the use of ultrasound, CT, and conventional MRI because of the high water content of the immature brain. Diffusion-weighted (DW) MRI is a very sensitive and fast imaging modality to visualize acute ischemic stroke in infants even before conventional MR images become abnormal. Signal abnormality in DW MRI, however, seems to follow a different time course than in older patients.

Case Description—DW MRI became falsely negative 1 week after stroke (pseudonormalization) in 2 newborn patients during persistence of signal abnormalities on turbo spin-echo images, whereas the so-called pseudonormalization in adults normally occurs within 10 to 14 days.

Conclusions—T2-weighted sequences should supplement DW images to reliably detect subacute ischemic infarctions in the neonatal period. (*Stroke*. 2002;33:1142-1145.)

Key Words: cerebral infarction ■ infants ■ magnetic resonance imaging, diffusion-weighted

Vascular diseases of the neonatal period include hemorrhage, venous thrombosis, and arterial infarctions.¹ In contrast to stroke in adults and older children, neonatal stroke often presents clinically with seizures but not with focal neurological deficiencies.² Diagnosis in the acute state may be difficult to establish because ultrasound, CT, and conventional MRI have a limited ability to visualize infarcted brain parenchyma. Diffusion-weighted (DW) MRI has had a great impact on the diagnosis of acute infarctions in adults³ because it can reliably detect intracellular edema,⁴ the hallmark of cerebral ischemic damage. However, little is known about the imaging characteristics of acute infarctions of neonates with the use of DW MRI⁵ and of the time course of these changes.

We report acute phase imaging signs in 2 patients with a neonatal infarction, both with very fast restitution of diffusion abnormalities within 1 week. This is the first report on the time courses of diffusion abnormality in newborns.

Case Reports

MRI Examination Protocol

All examinations were performed on a 1.5-T MRI system (SIEMENS Magnetom Vision) with echo-planar imaging capability with the use of a standard protocol. The examinations were performed during natural sleep or under mild oral sedation with chloral hydrate.

In both patients, multislice, DW, single-shot, echo-planar, spin-echo images (repetition time [TR]=0.8 ms; echo time

[TE]=123 ms; acquisition time=4 seconds; slice thickness=4 mm; $b=1100 \text{ s/mm}^2$) were acquired. A mean image of 4 measurements of this anisotropic sequence was used for its demonstrated high sensitivity.⁶ Additionally, a multislice, single-shot, DW sequence was acquired with b values of 0, 500, and 1000 s/mm^2 . Diffusion sensitivity in this sequence was measured in 3 orthogonal planes, and an apparent diffusion coefficient map was calculated.

The imaging protocol for both patients further contained T2-weighted images of the whole brain (TR=5400 ms; TE=119 ms; slice thickness=3 mm) as well as T1-weighted images (TR=500 ms; TE=12 ms; slice thickness=3 mm). Gadolinium-DTPA was given in 1 patient (patient 2).

Clinical History

Patient 1

This female child was delivered with normal body weight after 40 weeks of gestation. The physical examination after birth did not reveal any abnormality. Gestation and delivery had been uneventful. There were no risk factors. After 24 hours, the child spontaneously developed clonic seizures of the right side of the body involving both arm and leg.

Transfontanel ultrasound and lumbar puncture were normal, ruling out intracranial hemorrhage or meningitis. The first MRI was performed 36 hours later to rule out cerebral hypoxia or infarction (Figure 1). While T2- (Figure 1A and 1B) and T1-weighted (Figure 1C) sequences did not show an

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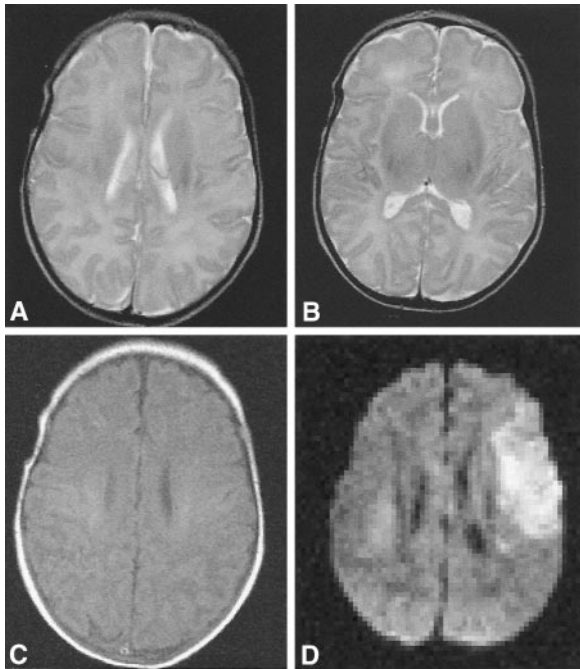


Figure 1. Patient 1 at 36 hours after onset of symptoms. A, B, T2-weighted turbo spin-echo images. The infarction is indicated by a slight obscuration of the gray matter in the left hemisphere compared with the right side. C, T1-weighted spin-echo image. There is hyperintensity of the appropriately myelinated pyramidal tracts on both sides. There is no sign of a cerebral infarction. D, DW MRI clearly shows a large infarction in the territory of the left middle cerebral artery.

infarction beyond doubt, DW MRI revealed an abnormality in the territory of the left middle cerebral artery (Figure 1D). MR angiography, in which a time-of-flight technique was used, was normal.

A follow-up scan was performed after 1 week (Figure 2) because the conventional sequences had failed to demonstrate the infarction. This time the infarcted brain area was clearly visible on spin-echo images (Figure 2A through 2C). The DW sequence now showed a decreased signal in the infarcted area (Figure 2D). T1- and T2-weighted images revealed a subtle hemorrhagic transformation of cortical infarcted brain areas.

Patient 2

The first child of nonconsanguineous parents was born at term with normal birth weight after an uneventful pregnancy. The girl developed clonic seizures of the right side of the body on her second day of life. Otherwise, the physical examination was normal.

Transfontanel ultrasound and cerebrospinal fluid studies did not reveal any abnormality. MRI was performed because of clinically suspected arterial infarction 48 hours after the onset of symptoms (Figure 3). Spin-echo sequences were mostly degraded by patient motion. A large posterior cerebral artery infarction could be seen on the right. DW images showed this infarction but additionally detected small infarctions in the territory of the left middle cerebral artery. These had not been noticed on the spin-echo images.

A follow-up study was performed after 1 week (Figure 4). This time the examination was supplemented by administra-

tion of contrast agent. While the infarctions were still well visible in the T2 sequences, detectability was low in T1 images. T1- and T2-weighted images were suspicious for a subtle hemorrhagic transformation of cortical infarcted brain areas. There now was a subtle diffusion abnormality in the left hemisphere lesions, but the large infarction on the right was invisible on the DW images.

Discussion

The incidence of neonatal ischemic stroke has been estimated to be in the range of 1 in 4000 deliveries.⁷ The causes of neonatal stroke often remain obscure,^{2,8} although many reasons for neonatal infarctions have been reported.^{2,9} Ischemic stroke in neonates often presents clinically with seizures but not with focal neurological deficits such as hemiparesis. This was the case in both patients described in this report. Transfontanel ultrasound, performed to rule out an intracerebral lesion as cause of the seizures, did not show any abnormality, thereby excluding intracerebral hemorrhage.

The detection of cerebral infarctions in neonates by cross-sectional imaging methods is impeded by the low myelination of the cerebral white matter. Edema caused by ischemic damage is hardly separable from the normal high water content of the neonatal brain.¹ The most important diagnostic sign in CT and conventional MRI is the obscuration of the gray/white matter distinction in the basal ganglia or the cerebral cortex.¹ However, this may escape detection if the infarctions are small or the image quality is marred by movement artifacts.

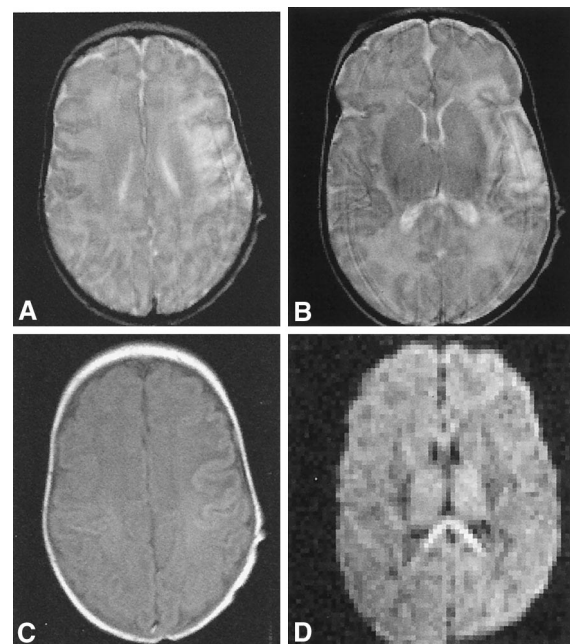


Figure 2. Patient 1, 7 days later. A, B, T2-weighted turbo spin-echo images. The middle cerebral artery infarction is now clearly visible in the white matter. The cortex is hypointense, probably because of hemorrhagic transformation. C, T1-weighted spin-echo image shows a cortical hyperintensity due to a slight hemorrhagic transformation. D, In the DW MR image, the infarcted parenchyma is slightly hypointense compared with the unaffected right side. This indicates an increased diffusion rate, unusual for this early time point in adults.

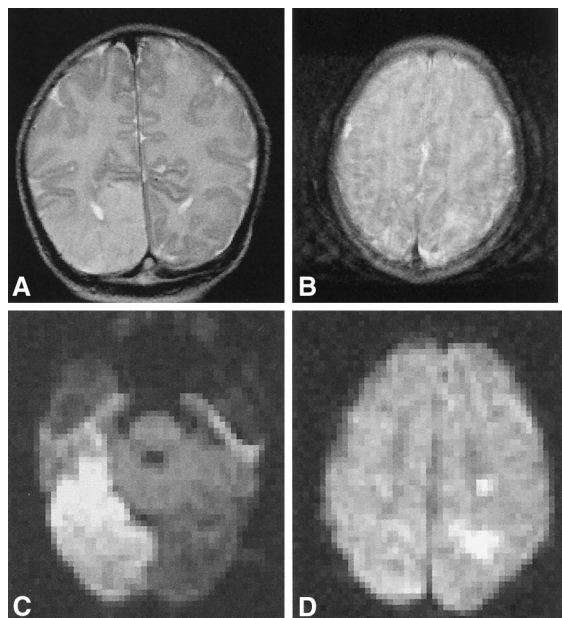


Figure 3. Patient 2 at 48 hours after onset of symptoms. A, B, T2-weighted turbo spin-echo images in the coronal (A) and axial (B) plain. The infarction in the right posterior cerebral artery territory is clearly visible. Additional lesions are found in the left precentral and postcentral gyrus, slightly blurred by motion artifacts (B). C, D, The DW images show a striking abnormality in the right posterior cerebral artery territory (C). Furthermore, there are 2 left hemisphere lesions (D). The small white matter infarction in the centrum semiovale was not visible on the spin-echo images.

In contrast to conventional sequences, echo-planar images can be acquired within a few seconds. Therefore, patient motion does not create problems in these examinations. After the first report of the application of DW MRI in neonates,⁵ few cases have been published.¹ Even a large recent study on neonatal intracranial ischemia did not address this topic.¹⁰ DW sequences have been shown to display intracellular edema with a high sensitivity, the initial finding in ischemic stroke.

In both cases presented here, DW MRI was highly abnormal in the territory of cerebral arteries. Patient 1 had a hyperintense signal abnormality in the left middle cerebral artery territory. Patient 2 had a large hyperintense lesion in the territory of the posterior cerebral artery on the right and several smaller lesions in the territory of the middle cerebral artery on the left.

Subsequent spin-echo images were less impressive in the acute phase. In the first patient, the infarction was nearly invisible. In the second case, a large posterior cerebral artery infarction was visible on T2- and T1-weighted images, mainly by obscuration of the gray/white matter border. However, the contralateral small infarctions in the middle cerebral artery territory would have escaped detection. Demonstration of bilateral infarcts is highly suggestive of systemic embolic disease and virtually excludes local vessel occlusion as cause of stroke.

A follow-up MRI after 1 week demonstrated infarctions on the T2-weighted sequences. No diffusion abnormality could

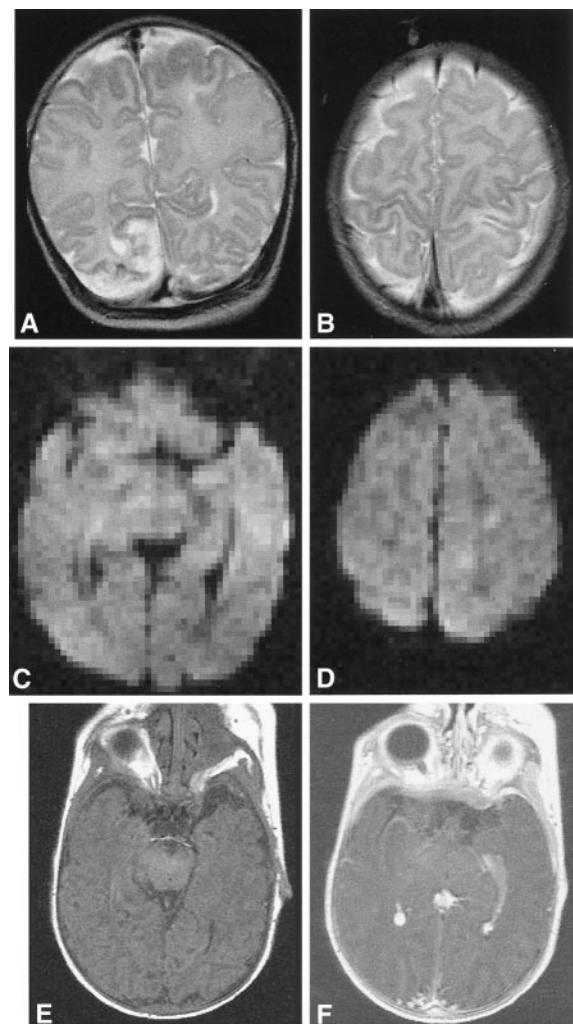


Figure 4. Patient 2, 7 days later. A, B, T2-weighted turbo spin-echo images in the coronal (A) and axial (B) plain. The infarction in the right posterior cerebral artery territory seems to be smaller than in Figure 3A. The hypointensity of the cortex suggests hemorrhagic transformation. The lesion in the left precentral and postcentral gyrus is also visible in this sequence (B). C, D, In the DW images the signal characteristics of the right posterior cerebral artery infarction have normalized (C). The left hemisphere lesions display a slight hyperintensity compared with the white matter (D). E, F, T1-weighted images before (E) and after (F) contrast administration. No abnormality is detectable.

be detected in the infarcted brain areas in patient 2, whereas in patient 1 there was already an increased rate of diffusion.

The time course of diffusion abnormality has been reported in adults only.¹¹⁻¹³ A signal abnormality occurs within minutes after ischemia because of a net shift of water from the fast diffusion compartment of the extracellular space to the slow diffusion compartment of the intracellular space. This results in a net slowing of the water diffusion.¹⁴ In the chronic state of the infarction, there is a tendency toward an increased diffusion rate. Because the cell walls break down in an infarcted area, the restriction of diffusion by the cellular walls diminishes. During this process, the rate of diffusion passes a stage of a so-called pseudonormalization, in which the diffusion characteristics of the damaged tissue are equal to

healthy brain tissue. This diffusion behavior normally occurs after approximately 2 weeks in mature myelinated brain.

The time course of the diffusion abnormality in both cases presented here showed a faster pseudonormalization than in adults. Diffusion characteristics in the newborn brain are different from those in adults. This may be due to the neonatal distribution and regulation of cerebral blood flow, incomplete myelination, immature blood-brain barrier, and brain metabolism.

It has been shown that apparent diffusion coefficient values within the brain increase with age because the number of slow-diffusion compartments increases during myelination.¹⁵ Thus, it may be speculated that the early pseudonormalization of the diffusion behavior may be due to a reduced amount of cell membranes within the unmyelinated newborn brain.

In conclusion, DW MRI is a fast and sensitive method for the detection of acute ischemic stroke in neonates within the first days after the event. DW MRI detects ischemic infarction in the immature brain of newborns before spin-echo images are diagnostic. However, after 7 days, DW MRI seems to become falsely negative in neonates and should therefore always be supplemented by conventional spin-echo images.

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