

Localized Reversible Reduction of Apparent Diffusion Coefficient in Transient Hypoglycemia-Induced Hemiparesis

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Background and Purpose—The pathophysiology of hypoglycemia shares a common mechanism with cerebral ischemia, but so far, little is known regarding MRI of humans with hypoglycemia.

Methods—We report a patient with left hemiparesis and dysarthria associated with a blood glucose level of 1.7 mmol/L. The patient recovered completely after glucose infusion.

Results—The initial diffusion-weighted imaging (DWI) showed increased signal intensities and a reduction of apparent diffusion coefficient (ADC) values localized in the corpus callosum (splenium) and asymmetrically in the corona radiata. After 48 hours, follow-up revealed complete recovery of DWI and ADC signal abnormalities.

Conclusion—To our knowledge, this is the first presentation of a case with transient hypoglycemia-induced focal neurological deficits revealing completely reversible MRI changes in terms of disturbed DWI and ADC with a peculiar as yet undescribed topography. (*Stroke*. 2005;36:e20-e22.)

Key Words: apparent diffusion coefficient ■ diffusion-weighted imaging ■ hypoglycemia
■ magnetic resonance imaging

Severe hypoglycemia can cause a variety of different neurological symptoms, ranging from focal deficits to severe coma and death.^{1,2} Especially in the setting of acute onset, it can be difficult to differentiate hypoglycemia-related symptoms from stroke.³

MRI techniques, particularly diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping, are the most useful tools in diagnosing early ischemic injury.⁴ The detailed mechanism for the alterations of DWI and ADC values in the event of acute ischemic brain injury is not precisely understood. However, ischemia results in metabolic energy failure with a disruption of water and electrolyte homeostasis consecutively leading to impairment of cell membrane potential. The ionic imbalance provokes an osmotically driven flow of water into the cells and a consecutive reduction of the extracellular space (ECS). It has been speculated that the reduction of the ECS and the diminished diffusibility of water intracellularly contribute to the changes of ADC in ischemia. Complete or partial recovery of ADC reductions could be demonstrated in transient ischemia, suggesting that early ADC decreases do not necessarily represent irreversible tissue damage.^{4,5} ADC reductions are not unique to ischemia and occur in different pathological conditions, such as seizures, spreading depression, excitotoxic cerebral injuries, as well as hypoglycemia.^{4,5} However, the pathophysiology of these conditions and therefore most likely the reasons for ADC changes are heterogeneous.

In animal *in vivo* studies, the visualization of hypoglycemia-induced changes of signal intensities for DWI and ADC imaging is documented in detail and could be reversed by glucose intake.⁵ We report a case with transient hypoglycemia-related neurological deficits combined with reversible DWI and ADC changes in the corona radiata asymmetrically and in the splenium of the corpus callosum.

Materials and Methods

Case Report

A 77-year-old male patient with a 15-year history of type 2 diabetes who was receiving a total of 4 mg Glimepiride daily developed a progressive reduction of mental status and dysarthria 1 day prior to admission. He had no history of vascular disease but a renal insufficiency with serum creatinine of 488 $\mu\text{mol/L}$ (5.51 mg/dL) and proteinuria (4964 mg/L). Initial neurological examination revealed a somnolent patient with left hemiparesis (Medical Research Council grade 3), including facial paresis and dysarthria.

MRI examination was performed immediately, and the following laboratory findings could be documented: plasma glucose level of 1.71 mmol/L, serum chloride of 116 mmol/L, serum potassium of 7.09 mmol/L, and serum calcium of 2.03 mmol/L. The patient showed a marked recovery within 2 hours after glucose substitution and was back to normal 12 hours later.

Neuroimaging

MRI was performed on a 1.5T magnetic resonance (MR) scanner (Sonata; Siemens) with standard sequences (diffusion-weighted sequence, fluid-attenuated inversion recovery [FLAIR] sequence, MR

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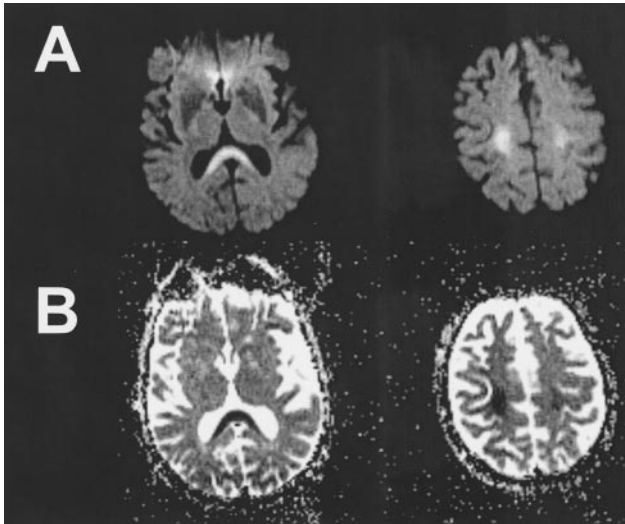


Figure 1. A, Initial DWI (repetition time/echo time/ α 4100/96/90; $\beta=1000$ s/mm²; field of view 230 mm; matrix: 128×128) with increased signal intensities in bilateral corona radiata and splenium. B, Initial ADC maps with signal reduction also in bilateral corona radiata and splenium corresponding to DWI images.

perfusion and MR angiography of intracerebral and extracerebral arteries, T1-weighted spin-echo, and T2*-weighted sequence). ADC maps were automatically calculated from DWI.

Results

The initial MRI showed circumscribed areas of reduced diffusion in the corona radiata asymmetrically and in the splenium of the corpus callosum. The DWI changes with a maximal relative 62.9% increase compared with unaffected cerebral tissue were localized in the splenium, the corona radiata of the right hemisphere, and, to a lesser extent, in the left corona radiata, but were generally not as pronounced as with acute ischemia. The reduction of ADC (maximal relative signal decline 61.3%) clearly showed a hypointense signal change (Figure 1) and revealed absolute values (unit $\times 10^{-4}$ mm²/s) of 3.07 in the splenium of the corpus callosum, 4.75 in the left, and 4.10 in the right corona radiata. All values returned to normal until follow-up.

T1-weighted images revealed no intracerebral hemorrhage, whereas FLAIR sequence and T2*-weighted images showed no significantly increased signal in the locations of reduced diffusion (Figure 2).

MR angiography documented no hemodynamically relevant stenoses or vasospasm of the extracerebral and intracerebral arteries. MR perfusion revealed no perfusion deficit. Follow-up after 48 hours showed completely normalized MR images.

Discussion

To our knowledge, this is the first case of a patient with transient hypoglycemia-induced hemiparesis and reversible ADC reduction and signal increase in DWI experiencing a complete recovery of all neurological symptoms and pathological MR alterations after glucose intake.

In many reports, different theories to explain the neurological deficits after hypoglycemia were discussed.^{1,5-7} In our case, significant cerebral vasospasm and asymmetric cerebral

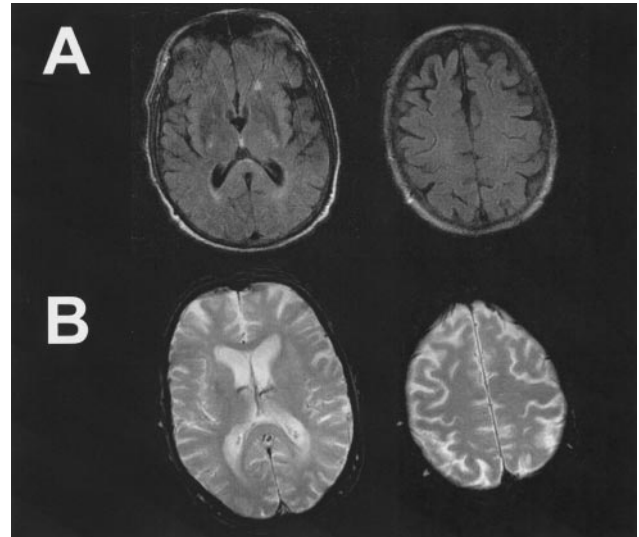


Figure 2. A, Initial FLAIR sequence (repetition time/echo time/TI/ α 9000/108/2500/150; field of view 184 mm; matrix: 448×512). B, T2*-weighted sequence showed images without visible increase of signal intensities as opposed to DWI and ADC maps (considering a different slice angulation between the imaging sessions because of patient's movement).

blood circulation could be excluded mostly by normal MR angiography and perfusion imaging.

MRI, in particular, and, in a very sensitive manner, DWI and ADC, could identify changes in brain water diffusion during hypoglycemia regarding in vivo animal models.^{4,5} In this respect, hypoglycemia shows similar MR findings as acute ischemia, but the underlying pathophysiology is distinct. Nevertheless, it is assumed widely that severe hypoglycemia causes cerebral energy failure and leads to a reduction of cell membrane ionic pump activity and a consecutive shift of cerebral water from ECS to intracellular space. Hasegawa et al⁵ suggest that this is a substantial mechanism contributing to the ADC changes in hypoglycemia. Although the exact mechanism underlying the ADC reductions is not known in detail, the results of this and several experimental studies support the assumption that ADC decline is a marker of unspecific ECS shrinkage.

The fast recovery of the clinical symptoms and the imaging abnormalities can be explained by the intravenous glucose supplementation, which was initiated immediately after the first MRI and allows exclusion of ischemic origin. Similarly, a fast normalization of signal abnormality has been reported in animal models of hypoglycemia.⁵ Most reports of MRI changes in hypoglycemic patients so far were reported on more severely affected patients who were in a vegetative state.^{2,7}

Secondly, the anatomical locations of areas with hypoglycemia-induced alteration of diffusion have not been described previously in humans. In earlier reports, MR signal changes were localized in the basal ganglia, the pons, the temporal and occipital cortex, and the hippocampus.^{1,2,6,7}

In an in vivo animal study of hypoglycemia, more detailed analysis is available that demonstrated severe and widespread ADC abnormalities only after the onset of isoelectricity of rat brains.⁵ However, earlier ADC decline, which was asymmet-

rical, was observed in isolated cortical and periventricular areas, mainly the caudoputamen, and furthermore, 10 minutes after glucose infusion, ADC normalization was complete except in the periventricular regions.⁵ The asymmetry of the transient periventricular ADC changes, as well as the reversibility of the hemiparesis after glucose infusion in our patient, corresponds well with these findings and suggests that the hypoglycemia has not been long lasting and probably was not as severe as to cause permanent cell injury.

Hasegawa et al⁵ speculate that the localized ADC changes might be caused by regional imbalances between energy supply and demand, spreading depression, or an excitotoxic mechanism. There are no data on the corpus callosum in this study.

Profound MR signal changes (in T2*-weighted imaging and DWI) in the splenium of the corpus callosum have been reported in a variety of different pathological conditions (infectious diseases, treatment with or withdrawal from anti-epileptic drugs), partially based on histopathological studies, without unraveling the reason for this localized vulnerability.

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