Diffusion-Weighted and Gradient Echo Magnetic Resonance Findings of Hemichorea-Hemiballismus Associated With Diabetic Hyperglycemia

A Hyperviscosity Syndrome?

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Background: The magnetic resonance (MR) imaging findings of hemichorea-hemiballismus (HCHB) associated with hyperglycemia are characterized by hyperintensities in the striatum on T1-weighted MR images and computed tomographic scans, with a mechanism of petechial hemorrhage considered to be responsible. Diffusion-weighted MR imaging (DWI) has been reported to detect early ischemic damage (cytotoxic edema) as bright areas of high signal intensity and vasogenic edema as areas of heterogeneous signal intensity. We report various DWI findings in 2 patients with hyperglycemic HCHB.

Objectives: To describe the DWI and gradient echo findings and characterize the types of edema in HCHB associated with hyperglycemia.

Setting: A tertiary referral center neurology department.

Design and Methods: Two patients with HCHB associated with hyperglycemia underwent DWI, gradient echo imaging, and conventional MR imaging with gadolinium enhancement. The patients had an elevated serum glucose level on admission and a long history of uncontrolled diabetes, and the symptoms were controlled by dopamine receptor blocking agents. Initial DWIs were obtained 5 to 20 days after symptom onset. Apparent diffusion coefficient (ADC) values were measured in the abnormal lesions with visual inspection of DWI and T2-weighted echo planar images.

Results: T1- and T2-weighted MR images and brain computed tomographic scans showed high signal intensities in the right head of the caudate nucleus and the putamen. Gradient echo images were normal. The DWIs showed bright high signal intensity in the corresponding lesions (patient 1), and the ADC values were decreased. The decrease in ADC and the high signal intensity on DWI persisted despite the disappearance of HCHB, even after 70 days.

Conclusions: Gradient echo MR imaging findings were normal in HCHB with hyperglycemia, whereas DWI and the ADC map showed restricted diffusion, which suggests that hyperviscosity, not petechial hemorrhage, with cytotoxic edema can cause the observed MR abnormalities.

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rates of the surrounding lesions were 519\(\times 10^{-6}\) mm\(^2\)/s, while those of the contralateral side were normal (419\(\times 10^{-6}\) mm\(^2\)/s).

**Patient 2**

A 69-year-old woman was admitted for sudden onset of hemichorea associated with hyperglycemia. The DWI findings showed restricted diffusion in the striatum and not intrinsically lower in specific areas. Regions of interest were carefully drawn in the abnormal areas on calculated average ADC maps, as well as in normal-appearing areas. The region of interest (25 mm\(^2\)) was selected with the help of T2-weighted echo planar images of the same acquisition as the diffusion images (ie, images generated from the diffusion sequence with diffusion sensitivity \(b=0\)) to avoid errors in selection of region of interest due to spatial distortion problems causing discrepancies between diffusion images and conventional MR images.

The brain MR images of patient 2, performed on the 21st day after onset of symptoms, showed high signal intensities in the right striatum on T1-weighted MR images (Figure 2A). The T2-weighted MR images showed low to mild high signal intensities in the corresponding lesions (not shown). The DWI and GE presented normal findings (Figures 2B-C), and the ADC map showed decreased ADC values in the corresponding lesions (650\(\times 10^{-6}\) to 695\(\times 10^{-6}\) mm\(^2\)/s) compared with the contralateral side (854\(\times 10^{-6}\) to 912\(\times 10^{-6}\) mm\(^2\)/s).

**COMMENT**

Our 2 patients had hemichorea associated with hyperglycemia. The DWI findings showed restricted diffusion in both patients and bright high signal intensity on the striatum and not intrinsically lower in specific areas. Regions of interest were carefully drawn in the abnormal areas on calculated average ADC maps, as well as in normal-appearing areas. The region of interest (25 mm\(^2\)) was selected with the help of T2-weighted echo planar images of the same acquisition as the diffusion images (ie, images generated from the diffusion sequence with diffusion sensitivity \(b=0\)) to avoid errors in selection of region of interest due to spatial distortion problems causing discrepancies between diffusion images and conventional MR images.
DWI in patient 1. There was no evidence of petechial hemorrhage on GE images. The DWI and ADC map of patient 1 displayed low ADC values in surrounding areas as well as T1 hyperintensity lesions. The ADC values were as low as in acute arterial ischemia, being the lowest ($419 \times 10^{-6}$ to $432 \times 10^{-6}$ mm$^2$/s) in the focal high-signal-intensity lesion on T1- and T2-weighted MR images and DWI. The surrounding areas showed T1–high density, T2-isodense, and DWI-isodense lesions with low ADC values ($519 \times 10^{-6}$ to $597 \times 10^{-6}$ mm$^2$/s). The brain MR image of patient 2 displayed high signal intensities on T1-weighted images with normal DWI and GE findings. The ADC values of the corresponding area were slightly decreased. The time from onset to MR imaging was variable, ranging from 4 to 21 days, which implied that different MR imaging stages could occur.

The critical pathophysiology of HCHB associated with hyperglycemia is unknown. Hyperglycemia can disrupt the blood-brain barrier and produce a global decrease in regional cerebral blood flow, intracellular acidosis, accumulation of extracellular glutamate, brain edema formation, and decreased activity of γ-aminobutyric acid–enkephalin inhibitory neurons. The decreased γ-aminobutyric acid activity due to its metabolism as an alternate energy substrate during hyperglycemic crisis has been proposed. The fact that the chorea may persist well beyond the episode of hyperglycemia argues against this mechanism. In addition, the MR imaging abnormalities, including high signal intensities on computed tomography and T1-weighted MR imaging, cannot be explained. The nature of the characteristic MR signal changes associated with HCHB has been the subject of considerable controversy. Petechial hemorrhage, myelinolysis, and calcifications have been suggested as possible mechanisms. Petechial hemorrhage with blood-brain barrier breakdown in the striatum has been suggested as the most plausible mechanism.

However, the GE findings presented here suggest that petechial hemorrhage cannot be responsible for the lesions. Recently, a salient autopsy report of HCHB was published. The main findings included multiple infarcts associated with reactive astrocytic and interneuronal response, not with petechial hemorrhage and calcification. Shan et al hypothesized that the possible cause of...
the MR imaging abnormalities might be the mild ischemia with gemistocyte accumulation, and they described one patient whose biopsy specimen showed gliotic brain tissue with abundant gemistocytes. Gemistocytes are swollen reactive astrocytes, containing a rich protein content, that usually appear during acute injury but later gradually shrink. Shortening of T1 relaxation time can result from the protein hydration layer inside the cytoplasm of swollen gemistocytes, as in a reported case of gemistocytic astrocytoma. The T1 relaxation time depends on the protein content, the rate of protein hydration, and the intracellular and extracellular water compartments. The core lesion on DWI might result from transient, mild ischemia due to high viscosity and decreased perfusion. The MR image of patient 2 showed the subacute findings of HCHB. The DWI and T2-weighted MR image began to be normalized, but the abnormalities on T1-weighted MR images remained. The ADC values of patient 2 were slightly lower despite the normal DWI, and T2-weighted MR images showed low to normal signal intensities in the corresponding lesions. In DWI, high-amplitude bipolar gradients sensitize a T2-weighted MR image to the brownian motion of water molecules. Despite the small magnitude of motion during diffusion gradient, it results in intravoxel dephasing and signal loss. Signal intensity on DWI is thus due to 2 intrinsic competing components: degree of T2 signal intensity and degree of diffusion. Provenzale et al. have shown normal DWI findings despite significant vasogenic edema in posterior reversible encephalopathy syndrome. They term this phenomenon T2 washout, since the intravoxel dephasing related to the increased water diffusion in the vasogenic edema washes out the inherent increased T2 signal intensity in the lesions. A T2 shortening in HCHB has been well known with T1 shortening. The T2 washout effect can be applied in the normal DWI findings of patient 2, since decreased water diffusion in the hyperviscous striatum may wash out the decreased T2 signal intensity in the corresponding lesions.

The restricted diffusion of water (low ADC values) has been reported in various diseases, such as acute stroke, Wernicke encephalopathy, epidermoid mass, brain abscess, and status epilepticus. The proposed mechanisms of ADC decrease, which are still being discussed, address changes in the diffusion characteristics of the intracellular and extracellular water compartments, including restricted diffusion, water exchange across permeable boundaries, the concept of extracellular tortuosity, and the intracellular and extracellular volume fraction. In addition, while the initial triggering factors leading to restricted diffusion may vary according to the main conditions, the subsequent results may be similar, leading to cell death. In arterial ischemia, the cessation of blood flow can cause initiation of the ischemic cascade of cell death. In status epilepticus, the primary mechanisms are neuronal hyperexcitability and the excessive release of excitatory amino acids, such as glutamate. In brain abscess and high-cellularity tumor, hyperviscosity can be the probable mechanism of restricted diffusion. Shan and coworkers’ results and our DWI findings suggest that hyperviscosity can be responsible for the restricted diffusion in HCHB caused by hyperglycemia, which can cause the partial neuronal death and dysfunction on the vulnerable striatum, similar to the partial ischemic injury model, in predisposed individuals.

The MR imaging abnormalities in HCHB are often reversible, but the mechanisms of such abnormalities are unknown. We suggest that the ADC threshold values might play a role in determining the “tissue fate.” Dardzinski et al. reported the ADC changes over time after permanent occlusion of the middle cerebral artery and suggested the following ranges of ADC values: (1) less than $450 \times 10^{-6} \text{mm}^2/\text{s}$: severe ischemia and irreversible damage occur; (2) greater than $550 \times 10^{-6} \text{mm}^2/\text{s}$: infarction will not occur; (3) $450 \times 10^{-6}$ to $550 \times 10^{-6} \text{mm}^2/\text{s}$: potentially reversible. Our results (ADC values of patient 1: core, $419 \times 10^{-6}$ to $432 \times 10^{-6} \text{mm}^2/\text{s}$; surrounding areas, $519 \times 10^{-6}$ to $597 \times 10^{-6} \text{mm}^2/\text{s}$; patient 2: $650 \times 10^{-6}$ to $695 \times 10^{-6} \text{mm}^2/\text{s}$) corresponded well to the
previous reports and hence suggest that, with adequate treatment, the DWI abnormalities (cytotoxic edema) might be reversible, as with the cells in the ischemic penumbra.13

The DWI and GE MR imaging findings in HCBH associated with hyperglycemia suggest that gemistocyte accumulation, hyperviscosity, neuronal dysfunction, and possible cytotoxic edema can cause the observed MR imaging abnormalities in possible susceptible individuals. Diffusion-weighted imaging can be used in determining the tissue fate with the analysis of ADC values.

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