

Serial Magnetic Resonance Imaging Changes in Hypoglycemic Encephalopathy

Chuo-Yu Lee, Kuang-Chung Liou, Lu-An Chen

Abstract-

Purpose: Reports of serial magnetic resonance imaging (MRI) in hypoglycemic encephalopathy were limited because MRI is not routinely performed in these patients. Here we present one patient with a history of hypoglycemic encephalopathy and discuss sequential neuroimaging findings.

Case Report: A 53-year-old male mistakenly took oral hypoglycemic agents developed hypoglycemic encephalopathy. Immediate brain diffusion-weighted image (DWI) demonstrated extensive symmetrical hyperintensive lesions over bilateral subcortical white matter. 14 days later, new hyperintensive lesions involving bilateral cerebral cortex were found on DWI, while previous subcortical white matter lesions disappeared. On day 86, diffusion-weighted images abnormalities vanished and diffuse brain atrophy was noted.

Conclusion: Although subcortical white matter involvement in hypoglycemic encephalopathy was occasionally reported in the literature, few report revealed similar serial MRI changes as our case. Although its mechanism is still unknown, it is important to follow sequential images in hypoglycemic encephalopathy. The brain tissue which was normal in early DWI may not necessarily guarantee undamaged.

Key Words: hypoglycemic encephalopathy, magnetic resonance imaging

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INTRODUCTION

Hypoglycemia may cause diverse neurologic manifestations, ranging from focal neurologic deficits to irreversible coma. Magnetic resonance imaging (MRI) is not routinely performed because these symptoms usually resolve shortly after glucose supplementation. Thus,

it is difficult to determine how often neuroimaging abnormalities might be observed in these patients. Most investigators have described a predilection for hypoglycemic damage in the cerebral cortex. We present a case of hypoglycemic encephalopathy with uncommon findings of MRI, and sequential neuroradiological changes.

From the Department of Neurology, Mackay Memorial Hospital, Taiwan.

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Correspondence to: Lu-An Chen, MD. Department of Neurology, Mackay Memorial Hospital, Taiwan. No. 92, Sec. 2, Zhongshan N. Rd., Zhongshan Dist., Taipei 10449, Taiwan.
E-mail: julius897@gmail.com

CASE REPORT

A 53-year-old male patient presented to our emergency department with altered consciousness. He mistakenly took oral hypoglycemic agents from his friend (Glibenclamide 5mg and Metformin 500mg) before he went to bed without any food intake at night. He was found unresponsive in the next morning. On arrival at emergency department, he was comatose with preserved brainstem reflexes. Blood glucose level was 39 mg/dL (2.16mmol/L). His consciousness didn't recover after dextrose and thiamine supplement. Blood chemical examinations including electrolyte, blood count and arterial blood gas were normal. MRI of brain performed immediately showed symmetrical hyperintensity lesions on diffusion-weighted images (DWI) (Fig. 1A) with decreased apparent diffusion coefficient (ADC) (Fig. 1B) over bilateral fronto-parieto-occipital deep and subcortical white matter. No other possible cause of acute leukoencephalopathy such as hypoxia, carbon monoxide or methanol poisoning was identified. Cerebrospinal fluid analysis and toxicology screen were normal.

Hypoglycemic encephalopathy appeared to be the most likely cause. During hospitalization, no further episode of hypoglycemia or hypoxia was identified. However, MRI of brain performed 14 days later showed new hyperintensity DWI lesions involving bilateral fronto-temporo-parietal cortex (Fig. 2A,B,C), while disappearance of previous subcortical white matter lesions were found (Fig. 2A). T2-weighted image (T2WI) and fluid

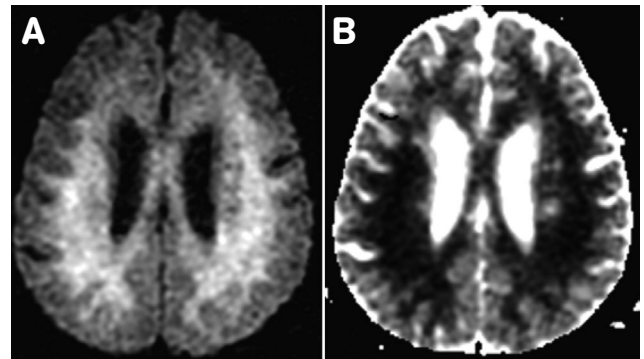


Figure 1. On day 1, DWI (TR/TE=10000/90, b value 1000 seconds/mm²) showed symmetrical hyperintensity over bilateral fronto-parieto-occipital deep and subcortical white matter (A). ADC showed decreased in these lesions (B).

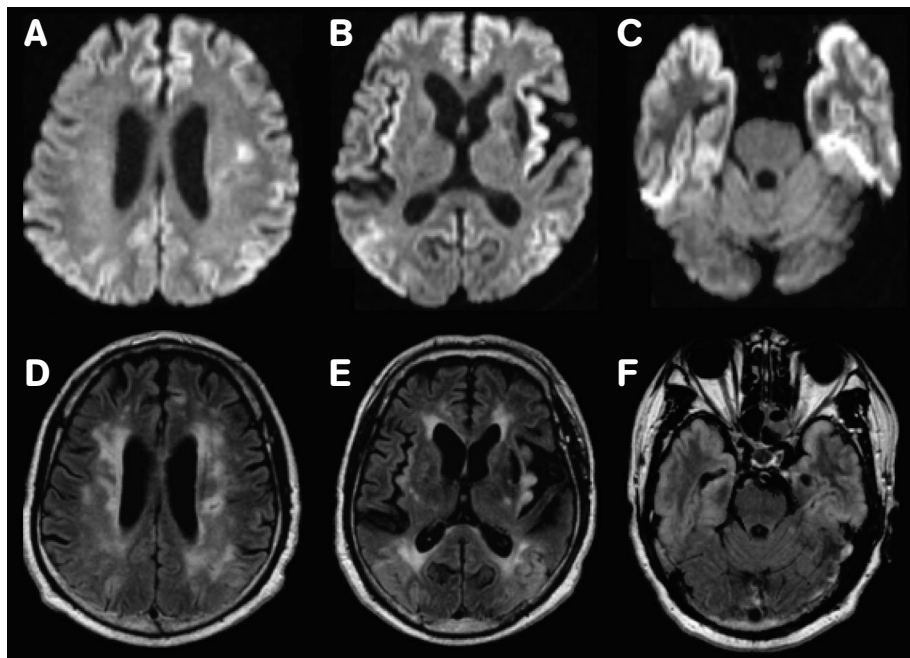


Figure 2. 14 days later, new DWI (TR/TE=3600/84, b value 1000 seconds/mm²) hyperintensity over bilateral fronto-temporo-parietal cortex came out (A,B,C), while previous DWI subcortical white matter lesions disappeared (A). T2 FLAIR (TR/TE=9000/110) revealed hyperintensity lesions involving bilateral periventricular white matter and bilateral temporal cortex (D,E,F).

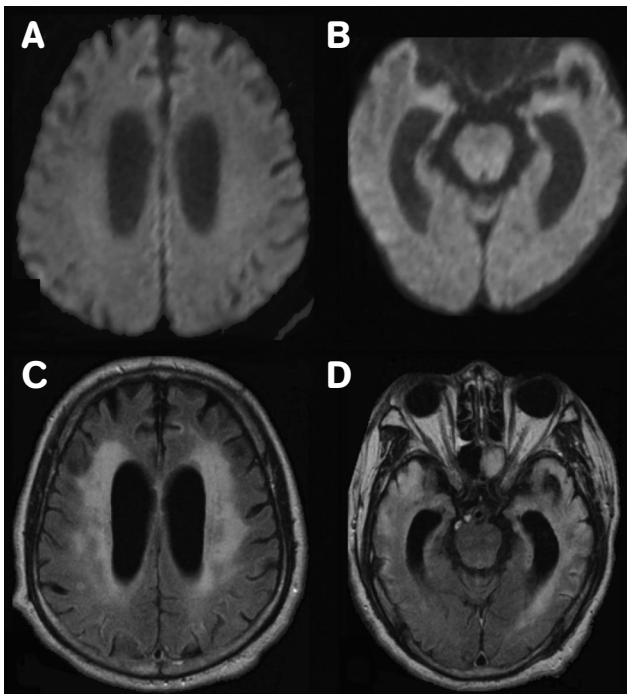


Figure 3. On day 86, DWI (TR/TE=3600/84, b value 1000 seconds/mm²) abnormalities all vanished (A,B). T2 FLAIR (TR/TE=9000/110) showed brain atrophy and persisted hyperintensity over bilateral periventricular white matter (C) and bilateral temporal cortex (D).

attenuated inversion recovery (FLAIR) revealed hyperintensity lesions involving bilateral periventricular white matter and bilateral temporal cortex (Fig. 2D,E,F). On day 86, DWI abnormalities vanished and diffuse brain atrophy was noted (Fig. 3A,B). T2WI and FLAIR showed persisted hyperintensity over bilateral periventricular white matter and bilateral temporal cortex (Fig. 3C,D). The patient remained in a persistent vegetative state with quadriplegia at the time of discharge.

DISCUSSION

Glucose is the brain's main energy substrate, and profound hypoglycemia could cause neuronal death. Brain MRI reports on hypoglycemic encephalopathy typically describe lesions involving cerebral cortex, basal ganglia, and hippocampus, while cerebellum, brainstem, and thalamus are spared⁽¹⁾. One major difference between hypoglycemic and hypoxic encephalopa-

thy was identified: MRI showed symmetrical thalamic lesions in hypoxic encephalopathy but not in hypoglycemic encephalopathy⁽¹⁾. DWI can be an earlier and more sensitive tool than conventional MRI sequences for detecting abnormalities in hypoglycemic encephalopathy⁽²⁾. Recently, extensive white matter lesions in hypoglycemic coma were occasionally reported⁽³⁻⁴⁾. A retrospective study of 17 patients revealed that selective white matter involvement is more frequently seen in hypoglycemic injury than previously thought. Early DWI abnormalities could be found over either white or gray matter, or both⁽⁵⁾. Besides, there are other acquired metabolic or toxic disorders which may cause similar widespread symmetric injury over deep gray matter or cerebral cortex. The differential diagnosis may include hepatic encephalopathy, osmotic myelinolysis, carbon monoxide poisoning, methanol toxicity, Ethylene Glycol toxicity, Metronidazole toxicity, Cyclosporine toxicity, and Cocaine encephalopathy⁽⁶⁾. In our case, no toxin exposure or metabolic disorders was identified.

The pathophysiology of hypoglycemic encephalopathy remains unclear. Glucose deprivation leads to energy failure and tissue alkalosis. Then neuroactive amino acid (aspartate) is released into extracellular space, leading to selective neuronal necrosis, especially in the cerebral cortex, basal ganglia, and hippocampus⁽⁷⁾. Cortical laminar necrosis may be the most likely mechanism for the hyperintensity revealed by DWI during subacute period⁽⁸⁾. Besides, increased extracellular glutamate causes calcium and sodium entering into cells, inducing apoptosis. On the other hand, glutamate induces edema of glial cells and myelin sheaths, called excitotoxic edema, which might protect axons from irreversible damage. According to this mechanism, DWI abnormalities may normalize with time after correction of hypoglycemia⁽⁹⁾. In addition, investigators have shown that the receptors related to excitotoxic mechanisms are widely distributed in the brain; both gray and white matter⁽¹⁰⁾. This may explain the widely distribution of early DWI abnormalities as mentioned before.

Although the clinical outcome is correlated with the severity and duration of hypoglycemia, the duration is often uncertain in most cases. The distribution of DWI

lesions may be useful for predicting prognosis. Previous studies suggested that involvement of basal ganglia correlates with poor outcome (eg, persistent vegetative state or severe motor impairment)⁽²⁾. However, other investigators concluded that poor outcome correlates with diffuse and extensive DWI abnormalities, with no specific association whether cerebral cortex, basal ganglia, and/or white matter were affected⁽⁵⁾.

Reports of serial MRI in hypoglycemic encephalopathy were limited. In our case, serial images revealed temporal evolution of DWI abnormalities. Along with the vanishing DWI hyperintensity over white matter, new DWI hyperintensive lesions came out over bilateral fronto-temporo-parietal cortex. No further episode of hypoxia, hypoglycemia, or hypotension occurred between this period. Therefore, we believe that both bilateral cortex and white matter were injured in the same time of hypoglycemic insult. To the best of our knowledge, there was only one case report written in Japanese also demonstrated similar DWI serial changes⁽¹¹⁾. But the explanations of these unusual findings remain unknown. As mentioned before, receptors related to excitotoxic mechanism are widely distributed, including gray and white matters⁽¹⁰⁾. We proposed that brain tissue have different vulnerability to hypoglycemia, therefore, gray matter showed delayed presentation of DWI abnormalities. These hypotheses may partially explain such a sequential change in our case. Finally, we conclude that it is important to follow sequential images in hypoglycemic encephalopathy, especially those whose initial DWI lesions are only limited to white matter. The brain tissue which appeared normal in early DWI may not necessarily guarantee undamaged.

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