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Utility of Diffusion-Weighted Magnetic Resonance Imaging for Predicting a Prognosis in Hypoglycemic Encephalopathy: Two Case Reports

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Cases:
Case 1: A 71-year-old male with a long history of chronic alcoholism was transferred to our emergency department because of a disturbance of consciousness. On arrival, his Glasgow Coma Scale (GCS) was E1V1M2 (4/15) and blood glucose level was 30 mg/dL.
Case 2: A 66-year-old female with dermatomyositis and a long history of steroid-induced diabetes mellitus, who was treated with a sulfonylurea, was transferred to our department because of an altered mental state. Her GCS was E3V2M4 (9/15) and blood glucose level was 32 mg/dL. We observed abnormalities on diffusion-weighted magnetic resonance images (DWI-MRI) in both cases.
Outcomes: Although intravenous thiamine and glucose was immediately administered because of suspected hypoglycemic encephalopathy, case 1 died after 3 days, and case 2 remained in a persistent vegetative state more than 90 days after onset.
Conclusion: Unlike conventional MRI, DWI-MRI abnormalities can be used as predictors of poor prognosis in patients with severe hypoglycemia.

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Keywords: Hypoglycemic encephalopathy; diffusion-weighted magnetic resonance imaging; diabetes mellitus.

1. INTRODUCTION

Severe hypoglycemia is the most common acute adverse effect of glucose-lowering therapy among patients with diabetes mellitus and is associated with poor outcomes, including death. The increased intensity of diabetes mellitus management over the past decade has resulted in lower incidence rates of hyperglycemia, but it has increased the incidence rates of hypoglycemic emergencies [1]. Hypoglycemia may cause diverse neurologic complications, ranging from focal reversible neurologic deficits to irreversible neurologic manifestations like coma. Magnetic resonance imaging (MRI) is not routinely performed on patients with hypoglycemia because their symptoms generally resolve shortly after glucose supplementation. Most investigators have described a predisposition for hypoglycemic damage in the cerebral cortex on using MRI [2,3]. It is important to predict prognoses of patients with hypoglycemic encephalopathy as soon as possible, because it may affect patients' neurological functions later in life [4]. Diffusion-weighted (DWI)-MRI provides a more sensitive way than conventional MRI to characterize tissues as it based on the rate of water diffusion (actual water movement) in tissues, as opposed to relying on the concentration of water in a given tissue. Here, we present MRI findings from two cases of hypoglycemic encephalopathy, and the usefulness of DWI-MRI for predicting prognosis.

2. CASE REPORT

2.1 Case 1

A 71-year-old male with a long history of chronic alcoholism was transferred to the emergency department of our hospital because of disturbance of consciousness which had started at least 4 h earlier. He may have been unable to go to the hospital because he lived alone and had a gait disturbance caused by alcoholic neuropathy. On arrival, his Glasgow Coma Scale (GCS) was E1V1M2 (4/15), and his pupillary light reflexes were dull positive. His vital signs were as follows: blood pressure, 71/57 mmHg; pulse, 45 b.p.m.; and body temperature, 37.2ºC. Deep tendon reflexes in the upper and lower extremities were normal with preserved brainstem reflexes. His blood glucose level was 30 mg/dL; therefore, intravenous glucose (40 ml of a 50% solution) and intravenous thiamine was immediately administered because of suspected hypoglycemic coma and suspected Wernicke's encephalopathy, respectively. Approximately 30 min later, his blood glucose level recovered to 165 mg/dL, although his consciousness level did not change. Cranial computed tomography (CT) scanning performed immediately did not reveal any abnormalities. Subsequently, DWI-MRI showed symmetrical hyper-intense signals in the posterior cerebral cortex (Fig. 1A), the caudate and lenticular nuclei excluding the thalamus (Fig. 1B), and the hippocampus (Fig. 1C). The apparent diffusion coefficient (ADC) did not show any signal abnormalities in the above mentioned areas (Fig. 1D). However, brain MRI showed hyper-intense lesions in the mamilary bodies and periaqueductal gray matter were not visible in T2-weighted image, which was consistent with the diagnosis of Wernicke's encephalopathy (Fig. 1E). After admission, intravenous infusion of glucose was continued to maintain glycemic control. However, his coma state did not improve, and the patient died 3 days after admission because of cerebral edema related to hypoglycemic encephalopathy.

2.2 Case 2

A 66-year-old female with dermatomyositis and a long history of steroid-induced diabetes mellitus, who was treated with a sulfonylurea, was transferred to the emergency department of our hospital because of an altered mental state lasting more than 12 h. Her blood glucose level was well-controlled until then (HbA1c, 6.8%). On arrival, her GCS was E3V2M4 (9/15) and pupillary light reflexes were positive. Her vital signs were as follows: blood pressure, 141/80 mmHg; pulse, 90 b.p.m.; body temperature, 38.2°C. Deep tendon reflexes in the upper and lower extremities were negative with preserved brainstem reflexes. Her blood glucose level was 32 mg/dL; consequently, intravenous glucose (80 ml of a 50% solution) was immediately administered. Approximately 30 min later, her blood glucose level recovered to 112 mg/dL, although her consciousness level did not recover even after thiamine supplementation.

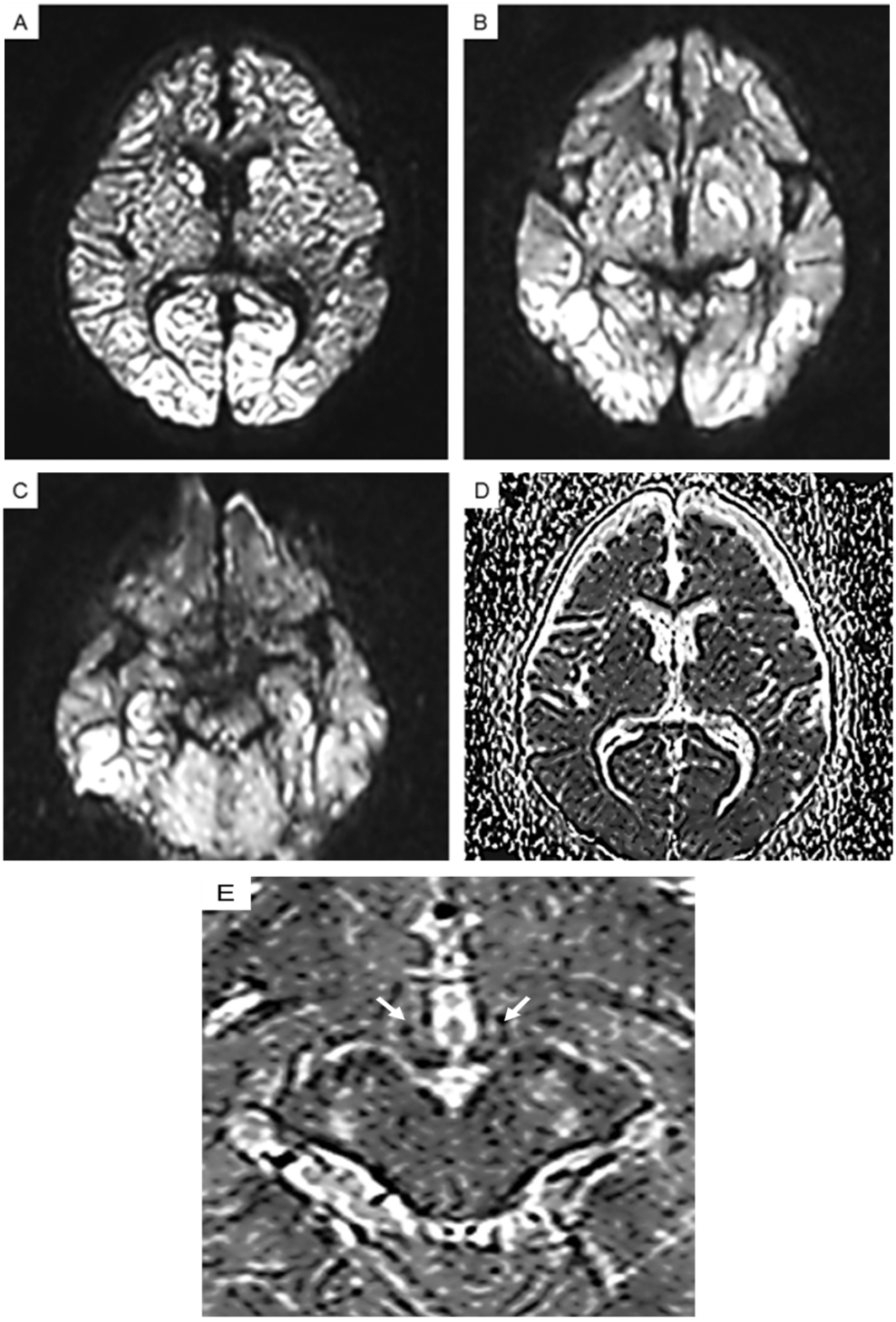

Fig. 1. On day 1, DWI-MRI showed symmetric hyper-intense signals in the posterior cerebral cortex (A), and the caudate and lenticular nuclei except for the thalamus (B), and the hippocampus (C). ADC did not show any signals abnormalities in the posterior cerebral cortex, caudate, lenticular nuclei and hippocampus (D). Bilateral hyper-intense lesions were not noted in the mamilary bodies on T2-weighted images (arrows) (E)

A DWI-MRI immediately performed because of suspected hypoglycemic encephalopathy, showed symmetrical hyper-intense lesions (Fig. 2A) over bilateral fronto-parieto-occipital deep and subcortical serial white matter with decreased ADC (Fig. 2B). Intravenous infusion of glucose was subsequently continued to maintain glycemic control. A brain MRI performed 5 days later showed disappearance of serial hyper-intense DWI lesions (Fig. 2C). Fluid-attenuated inversion recovery (FLAIR) did not show any signal abnormalities in the above mentioned areas (Fig. 2D). On day 5, an electro-encephalogram showed moderate diffuse slowing (3- to 5-Hz) with an epileptiform discharge on bilateral frontal region. In addition, FLAIR-MRI did not show hyper-intense lesions even after 56 days. The patient remained in a persistent vegetative state more than 90 days after onset.

3. DISCUSSION

Hypoglycemia is characterized by a sudden decrease in serum glucose levels (≤ 50 mg/dL). There are diverse neurologic manifestations of hypoglycemia. Hypoglycemic coma is a serious but treatable condition; therefore, making a precise diagnosis as early as possible and providing appropriate treatment is the key in preventing disastrous neurological sequelae. However, if hypoglycemia is prolonged, such as in the present cases, the condition can be irreversible resulting in a persistent vegetative state or even death. Therefore, it is imperative to assess the severity of neurological dysfunction, especially in a patient with deep coma.

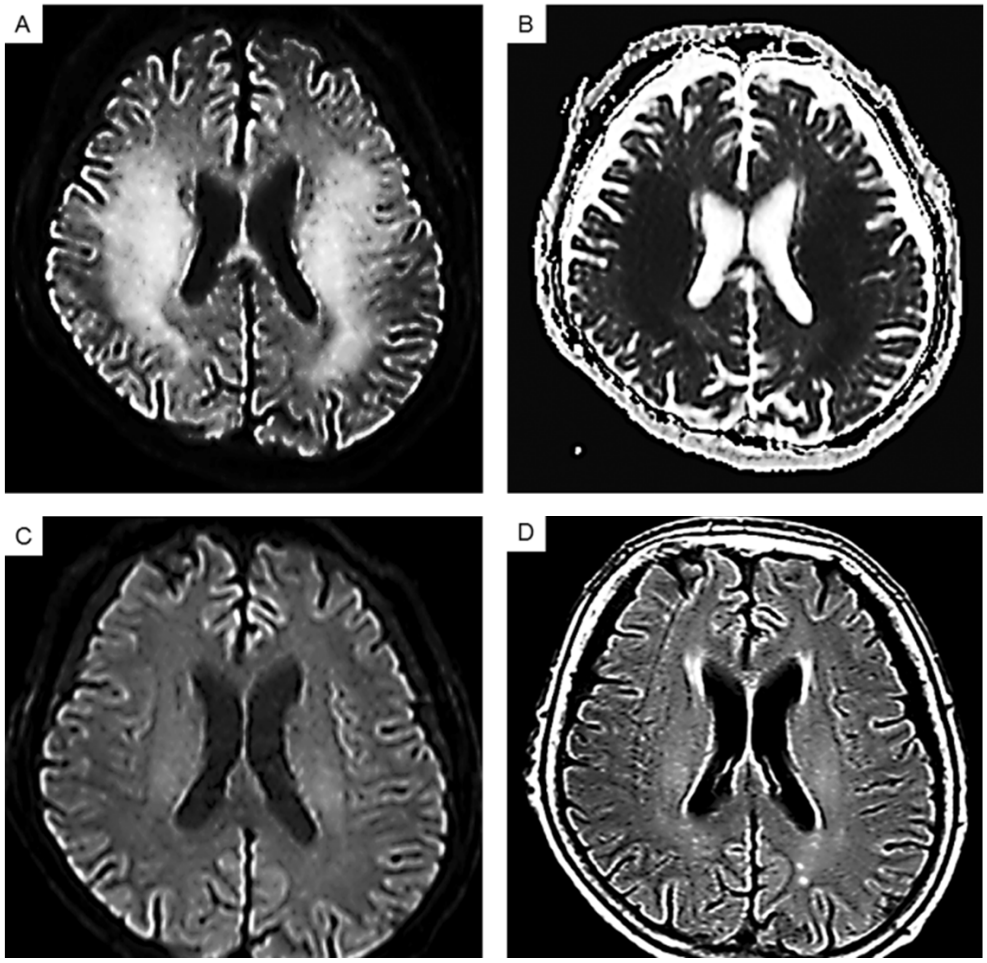

Fig. 2. On day 1, Symmetrical hyper-intensity lesions on DWI-MRI (A) over bilateral fronto-parieto-occipital deep and subcortical serial white matter were shown with decreased ADC (B). On day 5, MRI of brain showed disappearance of serial hyper-intensity DWI lesions (C), and FLAIR did not show hyper-intensity lesions in bilateral periventricular white matter (D)

Although the prognosis and neurologic sequelae of hypoglycemic encephalopathy depends on the severity and duration of hypoglycemia [4,5], the duration is uncertain in most cases. Thus, it is extremely important to diagnose the severity of hypoglycemic coma immediately. Using DWI-MRI to detect hypoglycemic-induced abnormalities in brain tissue has been previously reported [2,3] and widespread distribution of early DWI-MRI abnormalities indicates irreversible damage in hypoglycemic encephalopathy [6]. The same result was also shown by our case reports. In fact, hyper-intense lesions were observed by DWI-MRI in case 2, but no clear change was found by FLAIR-MRI in both early and late stages, unlike cerebral infarction. However, even if DWI-MRI abnormalities are reversible, severe irreversible damage resulting from hypoglycemic encephalopathy may remain according to the distribution of early DWI-MRI abnormalities.

Since glucose is the main source of energy for the brain (via ATP production), glucose deprivation during severe hypoglycemia may have led to the brain damage in these cases. A second consequence of glucose deprivation (and subsequent reduction in ATP production) is membrane ionic pump failure; the subsequent redistribution of ions causes a shift of water into the intracellular space and a drastic reduction of extracellular space volume [3]. The DWI-MRI images from our case reports support these findings. Brain MRI reports on hypoglycemic encephalopathy typically describe lesions involving the cerebral cortex, basal ganglia, and hippocampus, whereas the cerebellum, brainstem, and thalamus are excluded as in case 1 [7]. The neuroactive amino acid (aspartate) is released into the extracellular space, resulting in selective neuronal necrosis, predominantly in the cerebral cortex, caudoputamen, and hippocampus. One major difference between hypoglycemic and hypoxic encephalopathy was identified: MRI showed symmetrical thalamic lesions in hypoxic encephalopathy but not in hypoglycemic encephalopathy. Posterior reversible encephalopathy syndrome, which appears similar to hypoglycemic encephalopathy on MRI images, also showed an increased ADC signal intensity but could be differentiated from hypoglycemic encephalopathy [8]. Previously, there were a few cases reported that also demonstrated similar serial DWI changes like case 2 in the present study [9]; however, explanation of these unusual findings remains unclear.

Hyper-intense lesions were observed by DWI-MRI in case 2, but no clear change was found by FLAIR-MRI in both early and late stages, in contrast to that seen in cases of cerebral infarction. To date, there some reports that early focal DWI-MRI abnormalities are reversible with good outcome [10]. However, to the best of our knowledge, this is the first report indicating that DWI-MRI detection of widespread distribution of abnormalities in early stages is clinically useful, because that DWI-MRI change immediately disappear in late DWI-MRI like case 2. This is an extremely rare report of relationship between DWI-MRI and outcome due to hypoglycemic encephalopathy. Therefore, in cases of hypoglycemic patients who quickly do not recover, DWI-MRI should be the first choice of imaging tests to be performed as soon as possible in order to predict future neurological disease. In addition, it was more sensitive than conventional MRI for detecting abnormalities associated with hypoglycemic encephalopathy.

4. CONCLUSION

It is important to predict outcome of patients with hypoglycemic encephalopathy as soon as possible because it may affect patients' neurological functions later in life. Accordingly, early widespread DWI-MRI abnormalities can be used as predictors of poor prognosis for patients with severe hypoglycemia.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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