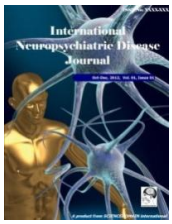

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Reversible Diffusion Restriction is Not Always Correlated with Clinical Recovery in Hypoglycemic Encephalopathy

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Authors' contributions

This work was carried out in collaboration of all authors. Authors KA and HB designed the article and wrote. All authors managed the literature search and wrote the first draft of the manuscript with assistance from author AA. All authors read and approved the final form.

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Case Study

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ABSTRACT

An 84-year-old female patient presented to our emergency department with unconsciousness. She was diabetic and the blood level of glucose was 34 mg/dL. Diffusion-weighted images (DWI) revealed symmetrical hyperintensity in perirolandic regions and posterior aspects of corona radiata. Hypoglycemic encephalopathy was diagnosed. Serum glucose level returned to normal ranges rapidly and abnormal signal on DWI resolved after glucose infusion, but the patient continued to be in coma. The clinical-MRI discrepancy in hypoglycemic encephalopathy is a really crucial issue for clinicians and has not been well-studied. We argued that the disappearance of abnormal signals on DWI does not always indicate a clinical recovery.

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Keywords: Hypoglycemia; transient / encephalopathy; coma; diffusion weighted / MRI.

1. INTRODUCTION

Hypoglycemia can result in different neurological problems when blood glucose level has dropped below 40 mg/dL. These neurological symptoms comprise focal dysfunctions, permanent changes and even death [1,2]. Mostly, the patients show a marked recovery from glucose substitution [3]. MR signal changes related to hypoglycemia are localized in the basal ganglia, the pons, the temporal and occipital cortex, and the hippocampus [4]. Injury is generally temporary and cases are back to normal after correction of hypoglycemia although sometimes not immediately in hypoglycemic encephalopathy (HE). However, severe hypoglycemia may result in irreversible diffuse brain injury and prolonged coma status. We present a woman with a permanent status of hypoglycemia-induced coma although her MRI findings showed completely reversible changes of disturbed DWI and apparent diffusion coefficient (ADC).

2. CASE PRESENTATION

An 84-year-old female patient presented to our emergency department with altered consciousness. She had a history of 20 year insulin therapies for type 2 diabetes. She had taken insulin in unknown doses at midnight. Initial neurological examination revealed a coma patient (Glasgow Coma Scale score was 6). Blood glucose level was 34 mg/dL. Despite the level of glucose returned to normal ranges rapidly after the intravenous glucose supplementation, the patient continued to be in the coma for next 20 days. Pupils were reactive and her vital signs were stable. Laboratory findings including blood counts, electrolytes and arterial blood gas measured at admission were normal. Cerebro-spinal fluid analysis was normal. Magnetic resonance imaging (MRI) was performed 1 h after glucose administration. The initial DWI showed symmetrical hyperintense signal changes in the perirolandic regions and the posterior aspects of the corona radiata with corresponding hypointense signal changes of ADC maps, representing diffusion restrictions on the cortical-pyramidal tracts (Fig. 1). The differential diagnosis included encephalitis, meningitis, osmotic myelinolysis, carbon monoxide poisoning, hypoxic encephalopathy, hepatic encephalopathy, nephritic encephalopathy, metronidazole toxicity, methanol toxicity, ethylene glycol toxicity and cocaine encephalopathy. None of them was detected in our patient. Blood glucose was within the normal range during hospitalization. Electroencephalography (EEG) records lasting at least 12 hours were performed on 21 channel EEG instruments. Four EEG records were taken on different days revealed slow and low amplitude activity, non convulsive status finding was not found. A second MRI of the brain performed 7 days later hospitalization showed resolution of restricted diffusion (Fig. 2). The rest MRI sequences including flair scans were all normal. Despite the resolution of diffusion restrictions on following up imagings, the patient continued to be in a coma for next 20 days and she was discharged from hospital. She died at the end of the third month.

3. DISCUSSION

Glucose is the main energy source of the brain and severe hypoglycemia may cause various neurological symptoms and signs, including memory loss, transient motor deficits, persistent vegetative state and death in 2%-4% of cases [1,2,5]. There are various explanations for HE. Blood glucose deprivation leads to neurochemical changes of incomplete energy failure, cellular calcium influx, intracellular alkalosis, aspartate release into the extracellular space and neuronal death [4,5]. Brain stem, cerebellum and hypothalamus are usually spared attributable to the greater activity of glucose transport mechanisms [6,7]. Another explanation of this condition is that glucose deprivation prevents the reuptake of glutamate into the cell and extracellular excess glutamate causes excitotoxicity. The excessive glutamate leads to glial cells swelling, but myelin sheaths prevent axons from irreversible damage. As a result, injury is generally temporary and cases can be back to normal after correction of hypoglycemia [8,9]. In young populations, vascular reserve is usually intact, but it is hard to say the vascular reserve is normal in elderly people. In clinical aspect, the predictors of poor outcomes in HE are prolonged hypoglycemia, normal or higher body temperature, and a low lactic acid level during hypoglycemia [10]. Although quick and prompt treatment of our patient prevented permanent changes took place on MRI including DWI, her coma was not resolved. We can explain this situation by unknown the duration of the hypoglycemia that is one of the bad prognostic factors of HE [10-12]. She was an elderly person

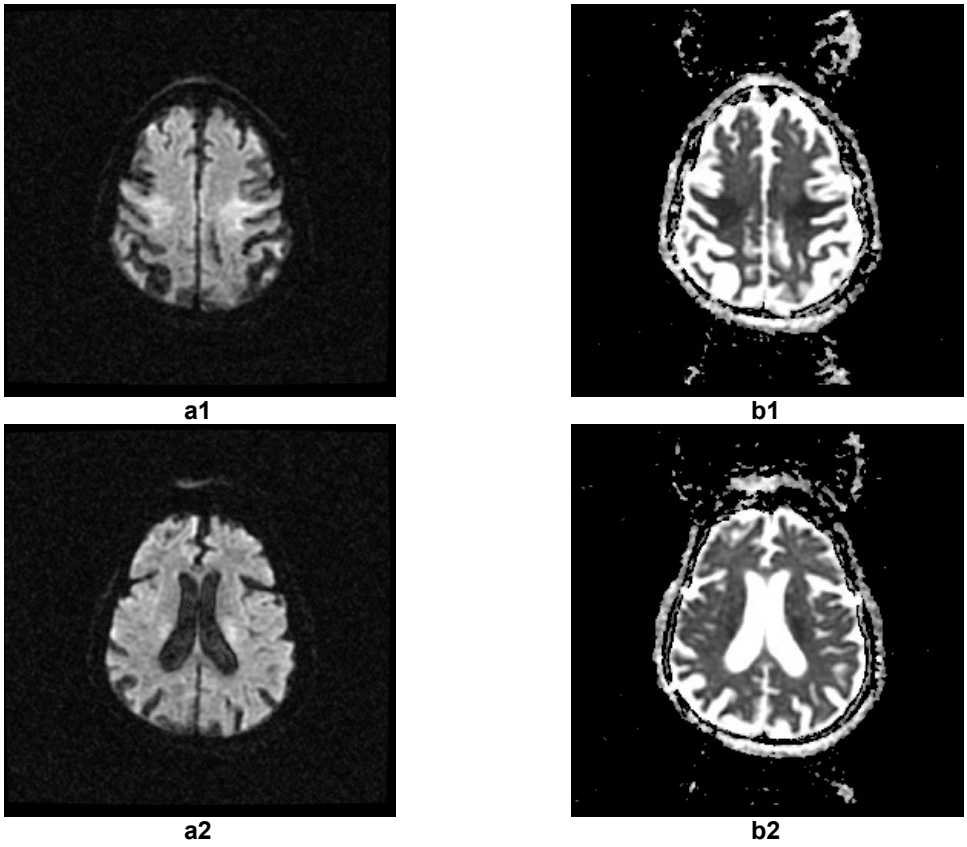

Fig. 1. Diffusion-weighted images (DWI) revealed symmetrical hyperintensity (1a1,1a2) in perirolandic region and posterior aspect of corona radiate with corresponding hypointesity (1b1, 1b2) on apparent diffusion coefficient (ADC) map, representing diffusion restriction along the cortico-pyramidal tracts

and this may be another explanation of permanent coma status of our patient. Damaged or depressed function of other extensive areas of either cerebral hemispheres or the ascending arousal system, including the paramedian region of the upper brainstem or the diencephalon on both sides of the brain may produce a coma in humans. The relay nuclei of the thalamus provide the largest ascending sources of input to the cerebral cortex. As a result, any deficit attributable to injury of a discrete cortical area can be mimicked by injury to its thalamic relay nucleus [13]. Patients with severe hypoglycemia often have focal or diffuse changes on MRI suggesting cerebral infarction (hyperintensity on DWI), but these abnormalities may reverse after treatment with glucose and thus do not imply permanent damage [14]. DWI is more sensitive than conventional MRI sequences in HE [15,16]. Neuroradiologically, the patients with hypoglycemia who were in a comatose state on arrival comprise 3 groups: 1) patients without hyperintense lesions; 2) patients with focal lesions involving highly directional large white matter tracts of the internal capsule (and sometimes involving other fibers of the cerebellar peduncle or splenium of the corpus callosum); and 3) patients with diffuse lesions involving bilateral hemispheric white matter including the internal capsule, corona radiata, and centrum semiovale (and sometimes the basal ganglia or cerebral cortices) in DWI studies [3]. Johkura et al also suggested that the absence of hyperintense lesions or the presence of only focal lesions involving the internal capsule on initial DWI predicts complete recovery from 1 day after glucose administration [3]. It is believed in that conventional MRI with DWI repeated during following up may be useful to predict outcome [17]. On the contrary, Ma et al report that there are no specific associations with the patterns of injury and clinical outcomes [12]. A new study reported by Witsch et al. [18] revealed that there was no obvious relation between lesion size or

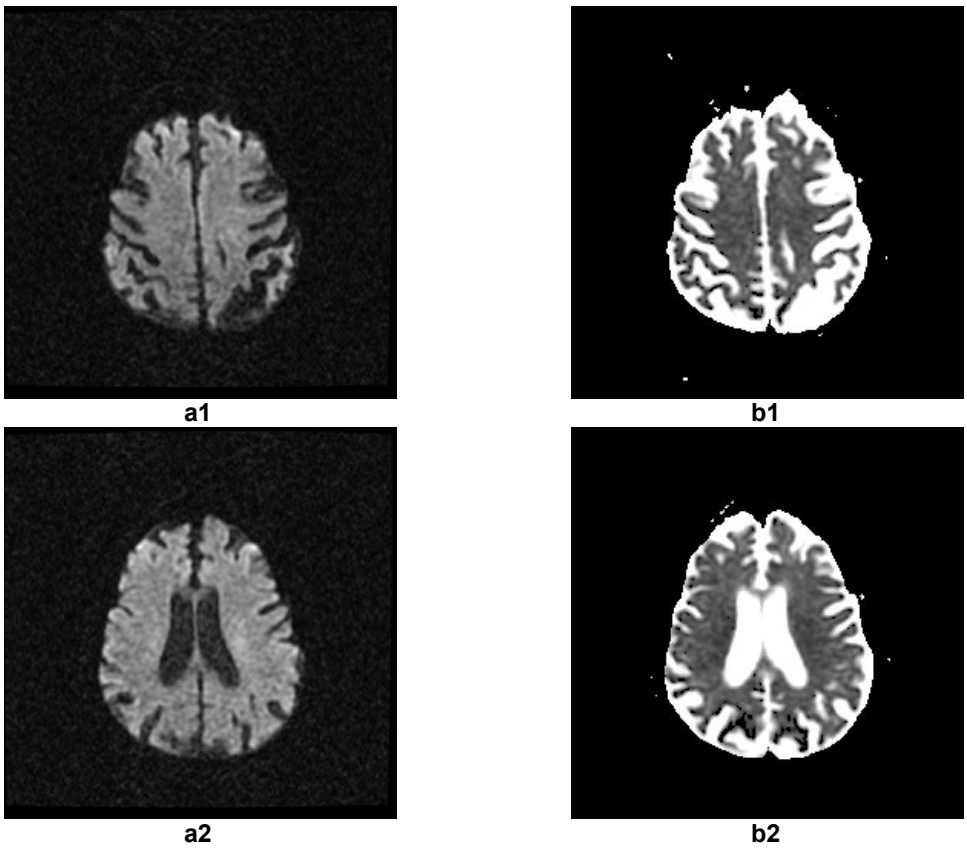

Fig. 2. Second MRI of brain performed 7 days later hospitalization showed resolution of diffusion restriction without any sequel changes behind (Figs. 2; 2a1, 2a2, 2b1, 2b2)

pattern and clinical outcome either. We have found that there were diffuse lesions involving bilateral hemispheric white matter, including perirolandic regions and posterior aspects of the corona radiata representing diffusion restriction in our patient with coma. A new conventional MRI with DWI repeated after 7 days revealed that the lesions were recovered (Fig. 2). The moderately sized MRI-lesions in this case could explain the coma, but it was surprising that the vanishing of the lesions did not correlate with clinical improvement. There was not any possible explanation of the persistent coma status except unknown duration of hypoglycemia and old age. Additionally, there was not any reasonable explanation for the discrepancy between resolved diffusion abnormality and poor clinical outcome.

4. CONCLUSION

Hypoglycemia causes transient cytotoxic edema. Neurological manifestations complicating profound hypoglycemia range of reversible focal deficits to irreversible comas. The early reversible diffusion restriction does not correlate with clinical symptoms and the disappearance of diffusion abnormality does not always indicate a clinical recovery. The relationships of cell damage, clinical findings and radiological changes because of the decreased blood glucose level are still waiting for investigation.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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