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Hypoglycemia with focal neurological signs as stroke mimic: Clinical and neuroradiological characteristics

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ABSTRACT

Our aim was to investigate the clinical and radiological features of patients with hypoglycemia with focal neurological signs (HFNS). Among 80 consecutive hypoglycemic patients (blood glucose levels less than 50 mg/dL), who had been admitted between October 2008 and May 2012, we selected 11 patients (6 men and 5 women; mean age, 73.2 ± 12 years) with focal neurological signs. The mean initial blood glucose level was 27.9 mg/dL (range, 13–39 mg/dL). The most frequent symptom was unilateral motor weakness (n = 9), which was usually accompanied with mild or moderate alteration of consciousness. All patients had improved initial neurological signs within 1 h of glucose injection. The initial DWI demonstrated a hyperintense lesion in the contralateral internal capsule with decreased values on the ADC (apparent diffusion coefficient) map in 2 of the patients (18%). The DWI performed one day later shows only faint lesion. The initial DWI in patients with HFNS may display a hyperintense lesion, which was difficult to distinguish from acute cerebral infarction. Hypoglycemia should be considered in cases with DWI showing a disproportionally small lesion in contrast to neurological signs.

1. Introduction

Severe hypoglycemia is known to cause focal neurological signs, such as hemiparesis, aphasia, and blindness. Although focal neurological signs are infrequent among hypoglycemia manifestations [1,2], it can be difficult to distinguish hypoglycemia-related symptoms from stroke, especially in the case of an acute onset or mild consciousness disturbance.

Recently, some authors have reported abnormal findings on magnetic resonance imaging (MRI) of patients with hypoglycemic hemiparesis. In the literature, hyperintense lesions on diffusion-weighted imaging (DWI) have been observed in the internal capsules [3–8]. However, most of the studies have been case reports, and the features of hypoglycemia with focal neurological signs (HFNS) remain to be clarified. The purpose of this study was to investigate the clinical and radiological features of patients with HFNS.

2. Subjects and methods

2.1. Subjects

We retrospectively assessed consecutive hypoglycemic patients who had presented with focal neurological signs and underwent brain MRI in Suiseikai Kajikawa Hospital between October 2008 and May 2012. A diagnosis of hypoglycemia was defined as having a low blood glucose level (less than 50 mg/dL) by a laboratory blood test. We excluded patients who had presented with coma or convulsions, or had comorbidity of acute cerebrovascular disease, epilepsy, traumatic brain injury, or encephalitis. After hypoglycemia was diagnosed, all patients had been treated immediately by injection of 40 mL of 50% glucose. We reviewed medical records to evaluate the following clinical parameters: initial blood glucose level, neurological signs, past history and comorbidity, MRI findings, and outcome of recovery after treatment.

2.2. MRI

MRI, including DWI, was performed within 1 h of arrival and within 7 h after symptom onset. All patients were examined using a 1.5-T clinical MR unit (SIEMENS, MAGNETOM Symphony or MAGNETOM Avanto), with the whole brain scanned at a slice thickness of 5 mm

Abbreviations: HFNS, hypoglycemia with focal neurological signs.

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and a 1.5-mm interslice gap. The imaging protocol consisted of axial DWI with single-shot echo-planar spin-echo sequences, fluid-attenuated inversion recovery imaging (FLAIR), axial T2-weighted gradient-echo sequences, and time-of-flight MR angiography (MRA). Follow-up MRI was performed in cases where the initial DWI showed abnormal findings. One patient (case 2) underwent only DWI. Radiographic image interpretation was confirmed by author who was blinded to clinical data (M. Matsumoto).

This study was approved by the Suiseikai Kajikawa Hospital's Institutional Review Board.

3. Results

3.1. Clinical findings

Among 80 patients admitted for hypoglycemia, 11 patients (6 men and 5 women; mean age, 73.2 ± 12 years) were selected for this study as HFNS. Other type of hypoglycemia included no consciousness disturbance (dizziness or feeling of weakness in the limbs, n = 4), only mild alteration of consciousness disturbance (confusion or drowsiness, n = 33), coma (n = 33), and coexistence with acute cerebral infarction n = 4). Five of the coma patients had convulsion on admission. Among the comatose group, 2 patients died, and 1 patient remained in a vegetative state. The clinical characteristics of HFNS are shown in Table 1. The mean initial blood glucose level was 27.9 mg/dL (range, 13–39 mg/dL). Nine of the 11 patients had diabetes mellitus. Seven of 9 diabetes mellitus patients were treated with sulfonylurea (SU). The mean time duration from the last SU taking time was 8.4 h. Two of 8 DM patients were not treated with SU. One of these was treated with metformin (case 3), and the other was treated with glinide (case 8). In these 2 patients, it was considered that hypoglycemia was caused by the continuation of antidiabetic drugs in spite of decreased dietary intake. None were treated with insulin. In regard of non-diabetic patients, the cause of hypoglycemia about case 5 was excessive alcohol consumption. The cause of case 10 was unknown. Four patients had previous cerebral infarction, one of whom having left-sided hemiparesis (case 6). Nine patients showed newly-acquired motor weakness such as hemiparesis (n = 7), and monoparesis (n = 2). Eight patients had mild or moderate alteration of consciousness; however, all patients were able to sense or respond to verbal or painful stimuli. Other neurological signs included dysarthria (n = 4), hemiparesthesia (n = 1), hemispatial neglect (n = 1), and ideomotor apraxia (n = 1). None of them showed seizure attack. No episode of transient neurological signs had preceded prior to admittance. All patients had improved neurological signs within 1 h of glucose injection. (The average improving time after glucose injection was about 10 min.)

3.2. MRI findings

In 2 of the 11 patients (18%), the initial DWI showed a hyperintense lesion in the contralateral internal capsule with a decrease of values on the ADC map (Fig. 1). The DWI performed one day later shows only faint lesion. MRA showed severe stenosis or occlusion of the intracranial cerebral artery in 4 patients.

4. Discussion

The present study investigated features of HFNS in a consecutive case series. First, the most frequent symptom observed was unilateral motor weakness, which was usually accompanied with mild or moderate alteration of consciousness. Second, complete recovery was obtained after supply with glucose administration in all the patients including patients treated several hours after the onset. Third, 18% of patients showed brain abnormalities on DWI. To the best of our knowledge, this is the first study of a case series of HFNS.

Table 1
Summary of clinical and radiological features of hypoglycemic patients with focal neurological signs.

No.	Age	Sex	Comorbidity			Previous cerebral infarction	Blood glucose (mg/dL)	Neurological signs			Onset – MRI interval (hrs.)	DWI hyperintense lesion	MRA	Outcome
			DM	SU	Other comorbidities			Motor weakness	Consciousness	Other			Severe stenosis /occlusion	
1	61	F	+	+			38	None	Normal	Right hemispatial neglect, ideomotor apraxia, dysarthria	3	None	Severe stenosis (bilateral ICA·MCA)	CR
2	62	M	+	+	IHD		23	None	Normal	Right hemiparesthesia	3	None	N.A.	CR
3	69	M	+		Gastrectomy	+	19	Monoparesis (right upper limb)	Confusion		1	None	Normal	CR
4	85	M	+	+	HT, CKD, dyslipidemia	+	38	Monoparesis (left lower limb)	Normal		6	None	Severe stenosis (left ICA·bilateral MCA·BA)	CR
5	54	M			Alcohol abuse		13	Hemiparesis (right)	Drowsiness		1	None	Normal	CR
6	61	F	+	+	Pancreatic cancer	+	39	Hemiparesis (right)	Drowsiness		5	IC (Left)	Severe stenosis (bilateral MCA)	CR
7	76	F	+	+	Colon cancer	+	21	Hemiparesis (left)	Drowsiness	Eye deviation (to right side)	3	IC (right)	Normal	CR
8	76	F	+		HT, CKD		39	Hemiparesis (right)	Confusion	Dysarthria	6	None	Normal	CR
9	82	F	+	+	IHD, HT, CKD, hypothyroidism		29	Hemiparesis (left)	Confusion	Dysarthria	1	None	Normal	CR
10	86	M					19	Hemiparesis (left)	Confusion		7	None	Occlusion (left ICA)	CR
11	92	M	+	+	HT		29	Hemiparesis (right)	Drowsiness	Dysarthria	1.5	None	Normal	CR

BA indicates basilar artery; CKD, chronic kidney disease; CR, complete recovery; DM, diabetes mellitus; HT, hypertension; IC, internal capsule; ICA, internal cerebral artery; IHD, ischemic heart disease; MCA, middle cerebral artery; N.A., not available; SBP, systolic blood pressure; and SU, sulfonylureas.

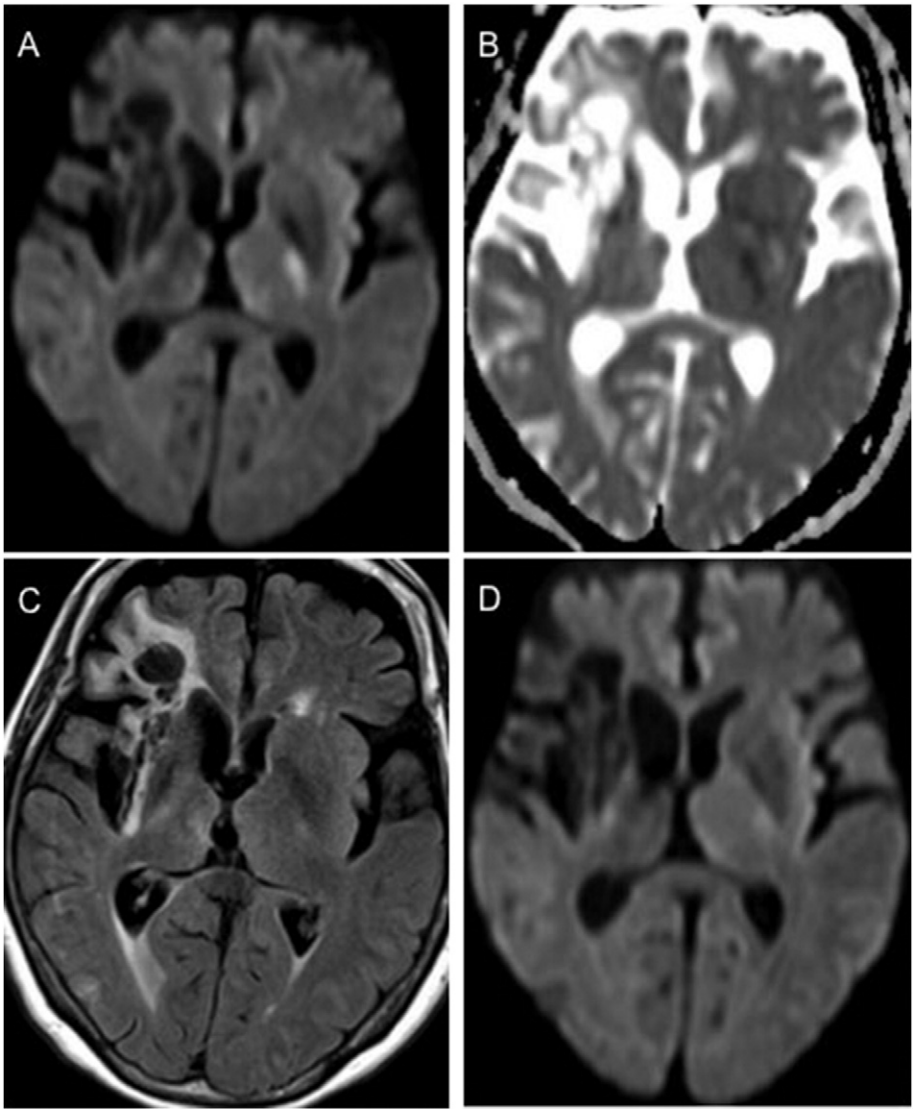

Fig. 1. Example of a hypoglycemic patient on MRI (case 6). DWI on admission shows a hyperintense lesion in the left internal capsule (A) with decreased ADC (B). This lesion appears normal on FLAIR (C). The DWI performed one day later shows only faint lesion (D).

A literature review of case reports of hypoglycemic hemiparesis revealed that the average glucose level was about 30 mg/dL [9], which is similar to our findings. Recent case reports of hypoglycemic hemiparesis have described hyperintense lesions on DWI with reduced ADC values in the white matter, most common in the contralateral internal capsule [3–8]. A few cases showed these lesions on the splenium of the corpus callosum [5–8,10] and corona radiata [10]. After correction of hypoglycemia, all lesions disappeared on the following DWI with recovery of neurological signs. The characteristics of the DWI hyperintense lesions in our case series were similar to the previous case reports.

Two recent studies of large case series of hypoglycemic coma have reported the following findings: incidence of complete recovery after treatment was not high (64–72%); mean blood glucose levels on arrival ranged from 19.6 to 35 mg/dL; DWI within 72 h after onset showed abnormal hyperintense signals with reduced ADC values [8,11]; DWI hyperintense lesions were located mainly in the bilateral internal capsules, subcortical white matter, and cerebral cortex [8,11]; and the occurrence of DWI abnormalities was high (64–100%). Johkura et al. suggested that limited internal capsule lesions were associated with good prognosis [8]. Compared to the case series of hypoglycemic coma, patients with HFNS showed a better prognosis and a milder decline of blood glucose levels, and lesions on DWI were limited in the white matter to the unilateral internal capsules. In addition to these findings, the occurrence of DWI abnormalities was relatively infrequent in our series. The clinical and radiological features of HFNS could be considered as a milder form of hypoglycemic coma. The reason why laterality is shown in hypoglycemic attack is not yet clear. The presence of intracranial major artery stenosis/occlusion is considered as one of the causes. However, there is no relation between major vessel lesion and focal symptom in our case-series. Asymmetry of ADC changes and isoelectric electroencephalogram was observed in 40% of the experimental animals in the early phase of the progression of hypoglycemia [12]. A less severe form might explain asymmetry of lesion in HFNS.

The pathogenesis of reversible DWI abnormalities of hypoglycemia is not fully understood. The hyperintense lesions in DWI with decreased ADC values, which are reversible, have also been observed in other diseases such as seizures, viral encephalitis, multiple sclerosis, and toxic metabolic disease [13–16]. It has been suggested that excitotoxic brain injury may be one of the mechanisms of this type of DWI abnormality, which occurs due to increased extracellular excitatory amino acids, such as glutamate and aspartate, in different neuropathological

conditions [14]. Recently, it has been demonstrated that aglycemic white matter injury arose from N-methyl-D-aspartate receptors (NMDAR) activated by aspartate, not glutamate, in animal experiments (NMDAR 'excitotoxic' injury). DWI lesions in white matter may be caused by NMDAR activated by aspartate in hypoglycemia [17].

Our study has several limitations: recall or selection bias may exist due to being a retrospective study, and the number of patients was small.

5. Conclusions

To the best of our knowledge, this is the first reported study of a case series of HFNS. DWI may reveal a hyperintense lesion which is difficult to distinguish from acute cerebral infarction. Hypoglycemia should be considered in the case of DWI showing a disproportionally small lesion in contrast to neurological signs.

Authors' contribution

Ohshita: drafting the manuscript, study concept and design, analysis and interpretation of data.
Imamura: analysis and interpretation of data, acquisition of data
Nomura: analysis and interpretation of data, acquisition of data.
Wakabayashi: revising the manuscript, acquisition of data.
Kajikawa: revising the manuscript, study supervision.
Matsumoto: revising the manuscript, study supervision.

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Conflicts of interest

There are no known conflicts of interest associated with this publication.

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