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Case Report

Agraphia with reversible splenial corpus callosum lesion caused by hypoglycemia

Yukari Miyakawa, Tatsuo Fuchigami *, Masako Aoki, Yusuke Mine, Junichi Suzuki, Tatsuhiko Urakami, Shori Takahashi

Department of Pediatrics and Child Health, Nihon University School of Medicine, Tokyo, Japan

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Abstract

Background: Neurological manifestations caused by hypoglycemia range from reversible focal deficits and transient encephalopathy to irreversible coma or death. Recently, high signal intensity lesions in the splenium of the corpus callosum on diffusion-weighted magnetic resonance imaging were reported in adults experiencing hypoglycemia. However, patients presenting with agraphia are rare.

Subject and methods: We examined a 17-year-old left-handed female patient with type 1 diabetes who exhibited transient left agraphia with a reversible splenium lesion of the corpus callosum on diffusion-weighted imaging caused by hypoglycemia, which was improved with blood glucose management alone.

Conclusion: This rare case indicates that agraphia, a sign of callosal disconnection syndrome, can result from a reversible splenial lesion of the corpus callosum caused by hypoglycemia.

Keywords: Hypoglycemia; Agraphia; Splenium of the corpus callosum; Callosal disconnection syndrome; Hypoglycemic encephalopathy; Children

1. Introduction

Recent diffusion-weighted imaging (DWI) studies reported high signal intensity lesions in the splenium of the corpus callosum (SCC) in adults experiencing hypoglycemia, with good outcomes [1–3]. However, patients presenting with agraphia are rare. We examined an adolescent girl with type 1 diabetes exhibiting transient left agraphia and a reversible splenium lesion of the corpus callosum caused by hypoglycemia, which was improved with blood glucose management alone. These findings suggest that agraphia, a sign of callosal disconnection syndrome, may result from a reversible splenial lesion of the corpus callosum caused by hypoglycemia.

2. Case report

A 17-year-old left-handed female patient was admitted to our hospital with visual and writing difficulty. The patient had an 11-year history of type 1 diabetes, receiving ongoing insulin therapy: 30 units of insulin glargine 100 IU/mL once daily at bedtime and 5/7/9 units of insulin glulisine before each meal. The patient's HbA1c (NGSP) was within 8%–9%, with no history of severe hypoglycemia requiring assistance to actively administer carbohydrates. The patient took a low-

* Corresponding author at: Department of Pediatrics and Child Health, Nihon University School of Medicine, 1-6 Kanda-Surugadai, Chiyoda-ku, Tokyo 101-8309, Japan.

E-mail address: fuchigami.tatsuo@nihon-u.ac.jp (T. Fuchigami).

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carbohydrate diet for reducing body weight for 3 months before hospitalization.

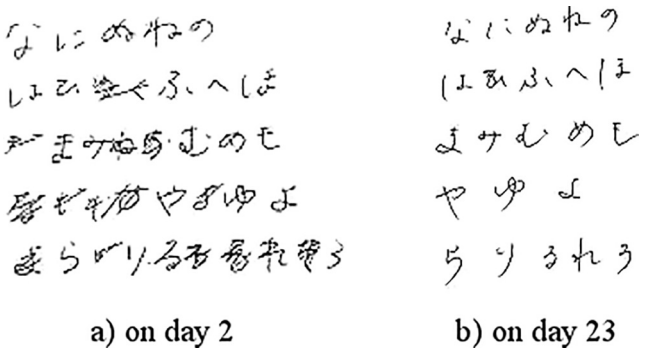
The patient experienced confusion on three consecutive mornings with bedside blood glucose levels of 39–42 mg/dL 8 days before admission. She regained consciousness immediately with glucose supplementation, but noticed writing problems and bilateral visual difficulty.

The patient presented to our hospital with visual and writing difficulties 6 days before hospitalization. Consciousness was clear and brain computed tomography revealed no abnormalities. The dose of insulin glargine was reduced (100 IU/mL from 30 units to 25 units), but symptoms were not improved. She was admitted to our hospital on day 9.

On admission, vital signs and blood pressure were normal, and body mass index was 22.6. The patient exhibited bilateral subjective visual field abnormalities, including bilateral visual difficulty in the right lower part of the visual field. Perimetry results were normal. Neurological examination revealed no abnormalities except left agraphia. The patient could not accurately write common Japanese characters ("Hiragana") (Fig. 1a) with her left (dominant) hand. She was occasionally unable to remember the shape of the letters, and wrote them incorrectly.

Laboratory blood test results were normal, including complete blood count and serum chemistry. Plasma glucose was 61 mg/dL, HbA1c (NGSP) was 7.5% (reference range: 4.7%–6.2%). Cerebrospinal fluid analysis was unremarkable. DWI on the day of admission revealed a high-intensity lesion only in the SCC, with decreased apparent diffusion coefficient (ADC) (Fig. 2a, b). Magnetic resonance (MR) angiography results were unremarkable. These findings suggested acute hypoglycemic encephalopathy. Left agraphia indicated callosal disconnection syndrome caused by SCC lesions. After admission, the patient received an appropriate diet with a modified insulin regimen: 24 units of insulin glargine 300 U/mL once daily at bedtime, and bolus insulin based on a carbohydrate counting method. The patient's plasma glucose level improved to 70–200 mg/dL, and she exhibited no hypoglycemic events. Left agraphia and visual difficulty gradually improved. DWI revealed remnants of a high signal area in the SCC on day 22. On day 23, the patient's symptoms completely disappeared and she was discharged from our hospital (Fig. 1b). A follow-up MR imaging (MRI) scan on day 46 revealed complete resolution of the SCC lesion (Fig. 2c).

We obtained informed consent from the patient and her mother to publish this case report.



a) on day 2 b) on day 23

Fig. 1. a) Transient agraphia of the left hand on day 2: the patient exhibited difficulty writing "Hiragana" spontaneously. b) Improved writing on day 23.

3. Discussion

In this case, transient left agraphia appeared as a sign of callosal disconnection syndrome in hypoglycemic encephalopathy with a reversible splenial lesion of the corpus callosum. Callosal disconnection syndrome is a rare neurological disorder caused by blocking impulse transmission along a cerebral fiber pathway (mainly in the uncinate temporal-frontal fasciculus and occipito- and temporo-parietal tracts), characterized by left tactile anomia, left ideomotor apraxia, and left agraphia [4]. Left agraphia affecting the non-dominant hand in right-handed patients is typically interpreted as disconnection between the right motor cortex and the language area in the left hemisphere. However, our patient was left-handed, and wrote Hiragana with her dominant left hand. Our findings suggested that the patient exhibited left hemisphere language-dominance. The occipital lobe fiber tracts, which are important for vision, are known to connect through the SCC [5], suggesting that our patient's visual difficulty was caused by a lesion of the SCC. Another study reported that an adult patient with a reversible splenial lesion of the corpus callosum caused by hypoglycemia also exhibited visual difficulty [6].

Brain MRI, particularly DWI, may be useful for diagnosing hypoglycemic encephalopathy and evaluating neurological prognosis. Previous MRI studies have reported various lesions related to hypoglycemic brain damage, including in the cerebral cortex, basal ganglia, hippocampus, posterior limb of the internal capsule, and the SCC [1]. Patients with widespread cortical lesions and bilateral basal ganglia lesions typically have a poor prognosis, while those with focal lesions involving the posterior limbs of the internal capsules, corona radiata, and the SCC typically have a good prognosis, as in the current case [7,8].

The mechanisms underlying the selective vulnerability of the SCC to hypoglycemia are currently unclear. Glucose deprivation is widely assumed to cause severe brain energy failure, reduction of cell membrane ionic pump activity and a consequent shift of cerebral water from the extracellular to the intracellular space [2]. Hypoglycemia has been proposed to perturb cellular fluid mechanics in the SCC, resulting in cytotoxic edema [9]. Reversible splenium lesions of the corpus callosum

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