Investigation of the relationship between non-ketotic hyperglycemia and hemichorea-hemiballism

A case report

Po-Jen Hsiao, MDa,b,c, Chih-Chun Kuo, MDa,d, Tai-You Kuo, MDa,e, Yung-Hsi Kao, PhDc, Jenq-Shyong Chan, MDa,b, Yen-Yue Lin, MDc,f, Ming-Hua Chen, MDg,∗ Jin-Shuen Chen, MD, PhDh,i,∗ Chih-Pin Chuu, PhDh,i,

Abstract

Rationale: Hemichorea-hemiballism, a rare manifestation of non-ketotic hyperglycemia, characterized by involuntary arrhythmic motions involving one side of the body, results from focal lesions in the contralateral caudate nucleus and putamen. Hyperkinetic disorders can be complications of uncontrolled diabetes mellitus and should not be ignored.

Patient concerns: We present the case of a 39-year-old woman who presented to the emergency department with a 3-day history of left-sided hemichorea-hemiballism. She had type 2 diabetes mellitus with poor control and maintenance of regular hemodialysis.

Diagnoses: The patient was diagnosed as hyperglycemia, normal ketone body and hemichorea-hemiballism based on laboratory examination, computed tomography (CT) scan, and brain magnetic resonance image (MRI).

Interventions: Intensive glycemic control via insulin injection was prescribed for correction of hyperglycemia.

Outcomes: The unilateral involuntary movements subsided progressively over four weeks. The patient’s hemichorea had completely resolved at the three-month follow-up.

Lessons: This unusual clinical presentation is often accompanied by severe hyperglycemia. Appropriate blood glycemic control is important. If physicians recognize and provide early treatment for this disease, it is usually treatable and has a good prognosis.

Abbreviations: BBB = blood brain barrier, CT = computed tomography, DNA = deoxyribonucleic acid, GABA = gamma-aminobutyric acid, Hba1C = glycated hemoglobin, MELAS = mitochondrial myopathy, encephalopathy, lactic acidosis, and strokes syndrome, MRC = Medical Research Council, MRI = magnetic resonance image.

Keywords: diabetes mellitus, hemichorea-hemiballism, non-ketotic hyperglycemia
1. Introduction
Chorea is a condition characterized by involuntary irregular movements that are repetitive or not rhythmic. Hemichorea is a hyperkinetic disorder involving one side of the body. Hemiballism is an unusual hyperkinetic movement disorder characterized by high-amplitude arrhythmic motions, especially at the shoulder and hip. Hemiballism often evolves into hemichorea, in which movements are lower in amplitude, less frequent, more distal, and more flowing. The acute development of hemichorea-hemiballism is often caused by focal lesions in the contralateral caudate nucleus and putamen. Acute stroke and non-ketotic hyperglycemia are the most common etiologies.[1–3]

The characteristic radiographic high-density changes in the contralateral caudate nucleus and putamen may initially be misinterpreted as hemorrhage when considering computed tomography (CT) scans.[3–5] The rapid and accurate differential diagnosis of hemichorea-hemiballism is challenging in clinical practice.

Here we present a rare case of acute unilateral involuntary movements mimicking acute stroke. The final diagnosis of diabetic non-ketotic hemichorea-hemiballism was made based on medical history, radiography, and laboratory findings. The symptoms were minimized after correction of hyperglycemia.

2. Case report
A 39-year-old woman presented to our emergency department with severe continuous, involuntary flailing, violent, and undesired movements of the left limbs, which lasted for 3 days. Her family history was unremarkable, except for type 2 diabetes mellitus. She had history of type 2 diabetes mellitus with poor control and maintenance regular hemodialysis. Her body temperature was 35.9°C, blood pressure was 166/96 mmHg, and pulse rate was 106 beats/minute. Neurological examination demonstrated alert consciousness with good orientation, no facial droop, and score of Medical Research Council (MRC) for muscle strength was 5. Blood laboratory investigation revealed a white blood count of 5480/μL (normal range, 4800–10800), serum glucose level of 765 mg/dL (normal range, 70–110), blood urea nitrogen level of 38.8 mg/dL (normal range, 6–24), serum creatinine level of 7.94 mg/dL (normal range, 0.5–1.4), sodium level of 125 mmol/L (normal range, 137–145), potassium level of 4.13 mmol/L (normal range, 3.1–5.3), magnesium level of 2.05 mg/dL (normal range, 1.8–2.55), phosphate level of 4.7 mg/dL (normal range, 2.6–4.4), calcium level of 8.3 mg/dL (normal range, 8.8–10.6), ketone body level of 0.1 mmol/L (normal range, 0.0–0.6), lactate level of 0.6 mmol/L (normal range, 0.5–2.2), and arterial blood gas level of pH: 7.465 (normal range, 7.35–7.45); PaO2, 113 mmHg (normal range, 75–100); PaCO2, 34.3 mmHg (normal range, 35–45); HCO3, 24.9 mmol/L (normal range, 22–26). An urgent brain CT showed hyperintensity within the right caudate nucleus and putamen (Fig. 1a), which we initially believed was acute hemorrhage. A follow-up brain magnetic resonance image (MRI) disclosed hyperintensity within the right caudate nucleus and putamen in the T1-weighted sequence (Fig. 1b) and hypointensity in the T2-weighted sequence (Fig. 1c). Acute cerebral hemorrhage was excluded, and the diagnosis of non-ketotic hyperglycemia-related hemichorea-hemiballism was established based upon the clinical and radiological manifestations. Intensive glycemic control via insulin injection was prescribed for the high glycated hemoglobin (HbA1c) level of 13.4% (normal range, 4–6). Medications including clonazepam and risperidone were also administered for symptomatic treatment. Four weeks later, the symptoms of unilateral involuntary violent and wide-amplitude movements of shoulder and hip had improved, apparently owing to tight serum glycemic control. The patient’s hemichorea had resolved completely at the 3-month follow-up.

3. Discussion
Hemichorea-hemiballism presents clinically as continuous, involuntary, violent, wide-amplitude movements involving one side of the body. The prevalence of hemichorea-hemiballism is less than 1 in 100,000, and majority of individuals affected are Asian women in their seventh decade.[4] The most common cause is ischemic/hemorrhagic stroke, followed by non-ketotic hyperglycemia. Other factors, such as traumatic brain injury; amyotrophic lateral sclerosis; demyelinating plaque; metabolic derangements in levels of sodium, manganese, magnesium,
calcium, and glucose; uremia; thiamin deficiency; endocrine disorders; autoimmune problems; neoplasms; infections; Wilson disease; drugs such as levodopa, oral contraceptives, anticonvulsants, and neuroleptics; and toxins such as carbon monoxide, alcohol, aluminum, and lead have been reported (Table 1).[1–6]

These movement disorders develop while awake and disappear during sleep. To date, the detailed pathophysiology of hemichorea-hemiballism is not well understood.

In our patient, the possible mechanisms of non-ketotic hyperglycemia-related hemichorea-hemiballism are the disruption of the blood brain barrier (BBB) owing to hyperglycemia-induced blood hyperviscosity; anaerobic metabolism of brain cells resulting from decreased cerebral blood flow and glucose metabolism failure; augmented sensitivity of dopaminergic receptors in postmenopausal women owing to declined estrogen concentration; or decreased gamma-aminobutyric acid (GABA) availability in the striatum secondary to the non-ketotic state.[6–11] Disrupted BBB causes transient ischemia of vulnerable striatal neurons. Imbalanced dopamine and GABA systems and vascular insufficiency could further contribute to movement disorders. Histological findings of the hypertensured putamen usually present gliotic changes with gemistocytes (swollen astrocytes) and selective neuronal loss but no evidence of infarction or hemorrhage.[7–12]

Previous case reports have revealed that diabetic non-ketotic hemichorea-hemiballism can develop a few weeks after blood glucose levels have been controlled.[14–15] This response indicates a delayed reaction to severe hyperglycemia. Most patients with diabetic non-ketotic hemichorea-hemiballism usually have a benign clinical course that can be treated medically. The time of resolution of the blood glucose levels has been controlled.[13] In our patient, involuntary movements existed from 17:30. Follow-up brain MRI studies were performed for 22 patients. In most patients, the symptoms of hemichorea improved along with the disappearance of the MRI lesions. In 39 patients, hemichorea was completely ameliorated. The remaining 14 patients revealed gradual improvement during the follow-up period. Hemichorea recurred in 7 patients.[16] Its management comprises aggressive glycemic control with either partial or complete resolution. Clinical symptoms usually take approximately five to six months to resolve after the hyperglycemia is controlled.[16–18] Therefore, the most important treatment for diabetic non-ketotic hemichorea-hemiballism is the achievement of appropriate blood glycemic control. Dopamine receptor antagonists and GABA_A receptor agonists can be used to control these movement disorders. Prompt recognition of diabetic non-ketotic hemichorea-hemiballism is important because normalization of glycaemia can reverse the symptoms and minimize complications. Delayed diagnosis and treatment may cause irreversible neurologic sequelae.[6,16–18]

The characteristic radiographic manifestations of non-ketotic hyperglycemia-related hemichorea-hemiballism are high-density changes in brain CT, high signal changes in brain MRI T1-weighted sequences, and equal or low signal in MRI T2-weighted sequences of the contralateral striatum.[14–17] Clinicians may interpret the initial high-density lesion of brain CT as acute hemorrhage. The hyperglycemic state promotes deposition of a T1-intense mineral, such as calcium or magnesium, which recovers after glucose is normalized.[16–18] Only a few case reports with negative imaging have been reported.[14,19,20]

Other neurodegenerative diseases should be ruled out in these patients. These conditions include brain lesions in the basal ganglia, including Huntington disease, spinocerebellar degenerations such as Creutzfeldt-Jakob disease, and dentatorubral pallidolysian atrophy, which can involve marked increase of ubiquitin levels.[21,22] These neurological diseases are usually progressive. These diseases were ruled out in this case because our patient’s symptoms were relieved after medical treatment. In these conditions, lesions present as areas with low signal intensities on T1-weighted images and high signal intensities on T2-weighted images.

Some diseases specifically associated with diabetes mellitus are mitochondrial disorders, including Stiff-person syndrome caused by decreased GABA activity, and myoclonus owing to diabetic muscle atrophy.[23–25] Therefore, it is necessary to consider mitochondrial disorders as a potential differential diagnosis. A 3243-point mutation in the nucleotide sequence of mitochondrial DNA, which is associated with a family history of diabetes mellitus, has also been observed in mitochondrial myopathy, encephalopathy, lactic acidosis, and strokes syndrome (MELAS). Ataxia has been reported in MELAS with diabetes mellitus. Nevertheless, MELAS presents as a cerebral infarct-like lesion in the occipital region and is reported to be associated with macroangiopathy.[23,25] Stiff-person syndrome manifests as epileptic muscle spasms of the trunk and limb proximal muscles, spreading throughout the whole body over the course of a few months.[24–25] In our patient, involuntary movements existed only in the left upper and lower extremities, and no lactic acidosis was noted. Consequently, the diagnosis of mitochondrial disorders was unlikely in this case. Moreover, diabetic muscular atrophy is included in the concept of diabetic peripheral neuropathy. The possibility of diabetic peripheral neuropathy related motor dysfunction was less likely in our patient.

In conclusion, when a diabetic patient presents with acute unilateral involuntary movements, the diagnosis of diabetic non-ketotic hemichorea-hemiballism should be considered. If physicians make an early diagnosis and provide prompt treatment, this disease is usually treatable and has a good prognosis.

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Author contributions

Conceptualization: Po-Jen Hsiao, Chih-Chun Kuo, Tai-You Kuo, Jenq-Shyong Chan, Ming-Hua Chen, JIn-Shuen Chen, Chih-Pin Chuu.

Data curation: PO-JEN HSIAO, Tai-You Kuo, Yung-Hsi Kao, Yen-Yue Lin, JIn-Shuen Chen.

Investigation: PO-JEN HSIAO, Chih-Chun Kuo, Tai-You Kuo, Yung-Hsi Kao, Jenq-Shyong Chan, Yen-Yue Lin, Ming-Hua Chen, JIn-Shuen Chen, Chih-Pin Chuu.

Methodology: PO-JEN HSIAO, Yung-Hsi Kao, JIn-Shuen Chen, Chih-Pin Chuu.

Project administration: Yung-Hsi Kao, Chih-Pin Chuu.

Supervision: Yen-Yue Lin.

Validation: JIn-Shuen Chen.

Writing – original draft: PO-JEN HSIAO, Chih-Chun Kuo.

Writing – review & editing: PO-JEN HSIAO, Tai-You Kuo, JIn-Shuen Chen, Chih-Pin Chuu.

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