Clinical Case Report

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

A case report

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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

Editor: Jun Shuen Chen.

P-JH and C-CK contributed equally to this work (co-first author).

M-HC, J-SC, and C-PC also contributed equally to this work (co-correspondence author).

CPC, CCK, JSC, and PJH were involved in the article concept. CPC, PJH, JSC, TYK, MHC, and YHK participated in the sequence alignment and drafted the manuscript. PJH, CCK, CPC, MHC, and JSC contributed to finish the final manuscript. All authors revised the article for intellectual content and approved the final version.

This study was supported by the grants of AF-TYGH-10801, Taoyuan Armed Forces General Hospital, Taiwan.

The authors declare that they have no competing interests.

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Medicine (2019) 98:28(e16255)

Received: 16 January 2019 / Received in final form: 2 May 2019 / Accepted: 7 June 2019

http://dx.doi.org/10.1097/MD.0000000000016255

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, 115 mmHg (normal range, 75–100); $PaCO_2$, 34.3 mmHg (normal range, 35–45); HCO_3, 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,

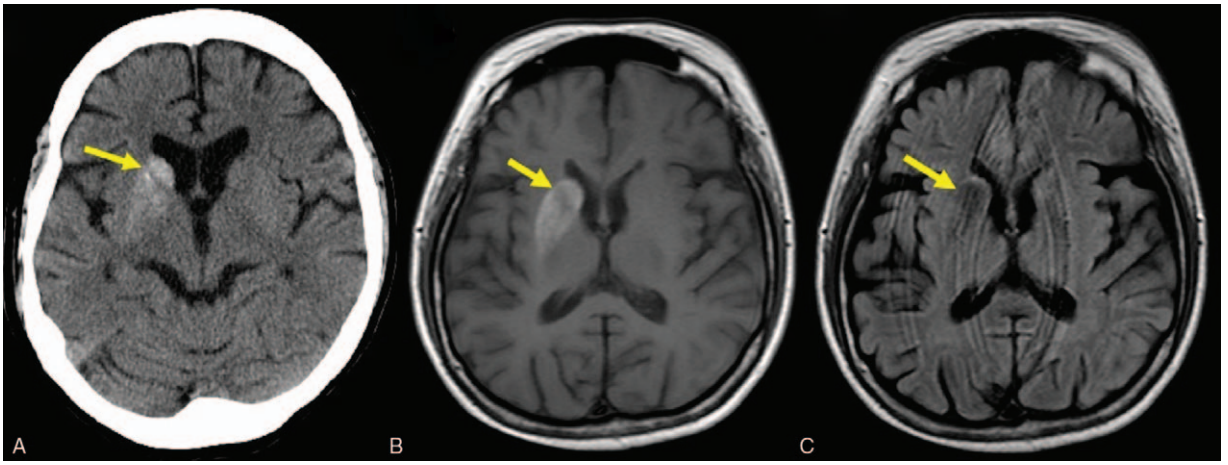

Figure 1. Right caudate nucleus and putamen of brain (arrow). Hyperintensity in brain CT, Hyperintensity in MRI T1-weighted sequence, (c) Hypointensity in MRI T2-weighted sequence.

Table 1

The common causes of hemichorea-hamiballism.

Primary (inherited)	Secondary (acquired)	
Huntington disease	Vascular	Nonketotic hyperglycemia
Amyotrophic lateral sclerosis	Drugs	Vitamin B12 deficiency
Demyelinating disease	Endocrine	Post-heart operation
Wilson's syndrome	Infection	Brain trauma or tumor
Multiple sclerosis	Autoimmune	Toxins

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).[3–6] 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 regional 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 hyperintensed putamen usually present gliotic changes with gemistocytes (swollen astrocytes) and selective neuronal loss but no evidence of infarction or hemorrhage.[7–10,12]

Previous case reports have revealed that diabetic non-ketotic hemichorea-hemiballism can develop a few weeks after blood glucose levels have been controlled.[13–15] 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 this disease usually coincides with that of severe hyperglycemia and tracks the relationship between the restoration of serum sugar levels and improvement of hemichorea. Oh et al performed a study including a meta-analysis of 53 cases with diabetic non-ketotic hemichorea-hemiballism. Their study showed that the mean serum glycemic level at the onset of hemichorea was 481.5 mg/dL (range, 169–1264), HbA1c level was 14.4% (range, 9.9–19.2), and serum osmolarity was 305.9 mmol/kg (range, 291–335). The mean age at the onset was 71.1 years (range, 22–92 years), and women were affected more frequently than men (men/women = 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 manganese, 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 pallidoluysian 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.[23,26,27] 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.[23–25] 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.

Acknowledgments

Informed written consent was obtained from the patient for publication of this case report and accompanying images. We thank the patient's consent to publish the clinical information.

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References

[1] Martin JP. Hemichorea resulting from a local lesion of the brain. Brain 1927;50:637–51.
[2] Matsuzono K, Suzuki M, Furuya K, et al. Hemichorea-hemiballism by branch atheromatous disease with a unique cerebral blood flow abnormality. J Neurol Sci 2018;393:113–5.
[3] Hawley JS, Weiner WJ. Hemiballismus: current concepts and review. Parkinsonism Relat Disord 2012;18:125–9.
[4] Jaafar J, Rahman RA, Draman N, et al. Hemiballismus in uncontrolled diabetes mellitus. Korean J Fam Med 2018;399:200–3.
[5] Kiryluk K, Khan F, Valeri A. Acute chorea and bilateral basal ganglia lesions in a hemodialysis patient. Kidney Int 2008;73:1087–91.
[6] Mihai CM, Catrinoiu D, Stoicescu RM. Atypical onset of diabetes in a teenage girl: a case report. Cases J 2008;1:425.
[7] Nakajima N, Ueda M, Nagayama H, et al. Putaminal changes before the onset of clinical symptoms in diabetic hemichorea-hemiballism. Intern Med 2014;53:489–91.
[8] Lin JJ, Chang MK. Hemiballism-hemichorea and non-ketotic hyperglycaemia. J Neurol Neurosurg Psychiatry 1994;57:748–50.
[9] Cheema H, Federman D, Kam A. Hemichorea-hemiballismus in non-ketotic hyperglycaemia. J Clin Neurosci 2011;18:293–4.
[10] Qi X, Yan Y, Gao Y, et al. Hemichorea associated with non-ketotic hyperglycaemia: a case report. Diabetes Res Clin Pract 2012;95:e1–3.
[11] Ruhangisa F, Stephen H, Senkondo J, et al. Acute hemichorea in a newly diagnosed type II diabetes patient: a diagnostic challenge in resource-limited setting: a case report. BMC Res Notes 2016;9:413.
[12] Pahalagamage SP, Senanayake S. Herath HMMTBCase report of hyperglycemic nonketotic chorea with rapid radiological resolution. BMC Med Imaging 2017;17:54.
[13] Bizet J, Cooper CJ, Quansah R, et al. Chorea, hyperglycemia, basal ganglia syndrome (C-H-BG) in an uncontrolled diabetic patient with normal glucose levels on presentation. Am J Case Rep 2014;15:143–6.
[14] Chang X, Hong W, Yu H, et al. Chorea associated with nonketotic hyperglycemia: a case report with atypical imaging changes. Medicine (Baltimore) 2017;96:e8602.
[15] Taboada GF, Lima GA, Castro JE, et al. Dyskinesia associated with hyperglycemia and basal ganglia hyperintensity: report of a rare diabetic complication. Metab Brain Dis 2013;28:107–10.
[16] Oh SH, Lee KY, Im JH, et al. Chorea associated with non-ketotic hyperglycemia and hyperintensity basal ganglia lesion on T1-weighted brain MRI study: a meta-analysis of 53 cases including four present cases. J Neurol Sci 2002;200:57–62.
[17] Hwang KJ, Hong IK, Ahn TB, et al. Cortical hemichorea-hemiballism. J Neurol 2013;260:2986–92.
[18] Patel B, Ladva ZR, Khan U. Hemichorea-hemiballism: a case report. Pract Neurol 2015;15:222–3.
[19] Tocco P, Barbieri F, Bonetti B, et al. Hemichorea-hemiballismus in patients with non-ketotic hyperglycemia. Neurol Sci 2016;37:297–8.
[20] Branca D, Gervasio O, Le Piane E, et al. Chorea induced by non-ketotic hyperglycaemia: a case report. Neurol Sci 2005;26:275–7.
[21] Hashimoto K, Ito Y, Tanahashi H, et al. Hyperglycemic chorea-ballism or acute exacerbation of Huntington's chorea? Huntington's disease unmasked by diabetic ketoacidosis in type 1 diabetes mellitus. J Clin Endocrinol Metab 2012;97:3016–20.
[22] Manaka H, Kato T, Kurita K, et al. Marked increase in cerebrospinal fluid ubiquitin in Creutzfeldt-Jakob disease. Neurosci Lett 1992;139:47–9.
[23] Nakamura S, Yoshinari M, Wakisaka M, et al. Ketoacidosis accompanied by epileptic seizures in a patient with diabetes mellitus and mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS). Diabetes Metab 2000;26:407–10.
[24] Sharma CM, Pandey RK, Kumawat BL, et al. A unique combination of autoimmune limbic encephalitis, type 1 diabetes, and Stiff person syndrome associated with GAD-65 antibody. Ann Indian Acad Neurol 2016;19:146–9.
[25] Zaidi SA, Chhetri SK, Lekwuwa G, et al. An unusual presentation of diabetic amyotrophy: myoclonus. BMJ Case Rep 2013;2013:pii: bcr2012008245.
[26] Finsterer J, Zarrouk-Mahjoub S. Macroangiopathy is a typical phenotypic manifestation of MELAS. Metab Brain Dis 2017;32:977–9.
[27] Zhu K, Li S, Chen H, et al. Late onset MELAS with m.3243A > G mutation and its association with aneurysm formation. Metab Brain Dis 2017;32:1069–72.