

Comparison of Hemichorea-Hemiballism between Acute Stroke and Nonketotic-Hyperglycinemia in the Clinical Scenario: Report of a Rare Diabetic Complication

CASE REPORT

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Abstract

Hemichorea-hemiballism is a rare manifestation of stroke, characterized by involuntary arrhythmic motions in one side of the body, which results from focal lesions in the contralateral subthalamic nucleus. Here, we reported a 74-year-old man with sudden onset violent involuntary rapid and irregular movements of left limbs after nap, since 6 hours prior to emergency department. The diagnosis of acute subthalamic nucleus infarction related hemichorea-hemiballism was confirmed by brain magnetic resonance image (MRI). Additionally, newly diagnosed type 2 diabetes mellitus without control was made based on high blood sugar and glycated hemoglobin (HbA1c). Medications including oral hypoglycemic agents, dual antiplatelet drugs and neuroleptics plus dopamine receptor antagonists were administered. The patient showed no obvious involuntary movements of left limbs after 3-month follow-up.

Keywords

Hemichorea-Hemiballism; Stroke; Nonketotic Hyperglycemia; Diabetes Mellitus.

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Introduction

Hemiballism is an unusual excessive movement disorder characterized by high amplitude arrhythmic motions, especially in the shoulder and

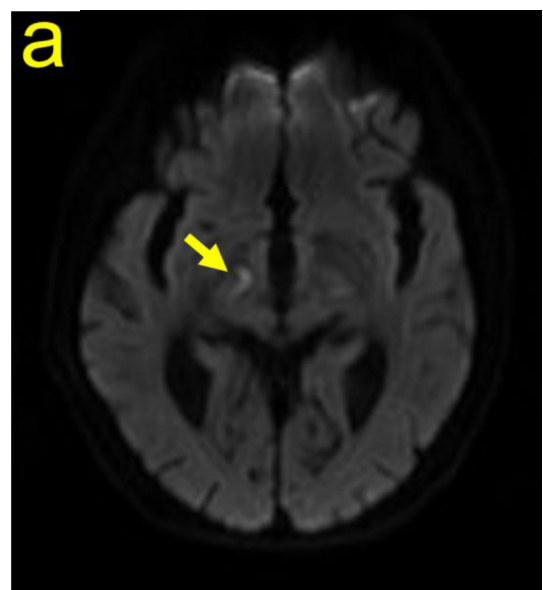
hip regions. Moreover, hemiballism usually evolves into hemichorea that there lower in amplitude, less frequent and more distal. Acute development of hemichorea-hemiballism is often caused by focal lesions in the contralateral subthalamic nucleus [1-3]. The insult of subthalamic nucleus causes reduced internal globus pallidus (GPi) inhibitory input to the motor component of the thalamus, resulting in amplified excitatory output to the motor cortex from the thalamus and excessive movement [4]. Type 2 diabetes mellitus is the major cause of microvascular and macrovascular complications. Vascular causes and nonketotic hyperglycemia are the most common etiologies for this rare disorder. Left subclavian steal syndrome, severe stenosis of right internal carotid artery and atherosclerosis of basilar artery may worsen the insufficient cerebral vessel supply to subthalamic nucleus [1-5]. The prognosis of hemichorea-hemiballism varies significantly by the etiology; however, the majority of patients usually have response to medical treatment. Including detailed medical history, neurologic examination and radiographic findings are helpful for the rapid and accurate diagnosis.

Case Report

A 74-year-old man presented with sudden onset continuous, involuntary flailing, violent, and undesired movements of left entire limbs after nap, since six hours prior to emergency department. His family history was unremarkable. He had history of hypertensive cardiovascular disease without regular medications control. His body temperature was 36.5°C, blood pressure was 147/71 mmHg and pulse rate was 85 beats/min. Neurological examination demonstrated alert consciousness with well orientation, left nasolabial fold defect, and weakness in left limbs. The Medical Research Council (MRC) score in this patient was 4 of 5 over left limbs and 5 of 5 over right limbs. Blood laboratory investigation revealed white blood count: 5410 / μ L

(normal range, 4800-10800), serum glucose: 412 mg/dL (normal range, 70-110), blood urea nitrogen: 11.5 mg/dL (normal range, 6-24), serum creatinine: 0.74 mg/dL (normal range, 0.5-1.4), sodium: 130 mmol/L (normal range, 137-145), potassium: 4.39 mmol/L (normal range, 3.1-5.3), magnesium: 2.16 mg/dL (normal range, 1.8-2.55), phosphate: 4.21 mg/dL (normal range, 2.6-4.4), calcium: 9.6 mg/dL (8.8-10.6) and elevated NT-proBNP 967 pg/mL (normal range, <300). Electrocardiogram showed sinus rhythm and T-wave inversion in V1-5. An urgent brain computed tomography (CT) revealed generalized cerebral atrophy combined old lacunar infarctions of bilateral corona radiata and basal ganglia. However, there is no active lesion in this CT study. Followed brain magnetic resonance image (MRI) disclosed hyperintensity within the right subthalamic nucleus in diffusion-weighted image sequence (**Figure 1a**) and hypointensity in apparent diffusion coefficient sequence (**Figure 1b**). MR angiography (MRA) revealed segmental stenosis of bilateral middle cerebral artery (MCA),

Figure 1: Right subthalamic nucleus (arrow) of brain MRI.



a) Hyperintensity in MRI diffusion-weighted image sequence.

Figure 1: Right subthalamic nucleus (arrow) of brain MRI.



b) Hypointensity in MRI apparent diffusion coefficient sequence.

posterior cerebral artery (PCA), internal carotid artery (ICA) and basilar artery (BA). Transcranial Doppler ultrasound and carotid Dopscan showed severe stenosis of right internal carotid artery (70%) and left subclavian steal syndrome. The diagnosis of subthalamic nucleus infarction related hemichorea-hemiballism was impressed based on the clinical and radiological manifestations. Thus, dual anti-platelet agents were administered. Newly diagnosed type 2 diabetes mellitus was confirmed and oral hypoglycemic agents were prescribed for high glycated hemoglobin (HbA1c) 12.4% (normal range, 4-6). Medications including haloperidol, risperidone and trihexyphenidyl were also used for symptomatic treatment. There was improvement in his involuntary movements of left limbs after 3-month follow-up.

Discussion

The first and second most common causes of hemichorea-hemiballism are stroke and nonketotic hyperglycemia [3, 4, 6]. The incidence of poststroke

and nonketotic hyperglycemia related hemichorea-hemiballism are around 0.08% and 0.001%, respectively [5, 6]. Other origins, including demyelinating plaque, amyotrophic lateral sclerosis, traumatic brain injury, Wilson's disease, metabolic derangements, autoimmune disorders, endocrine, infection, neoplasm, drugs and toxin have been reported [6-8]. These movement disorders usually develop while awake and disappear during sleep. Up to now, the detail pathophysiology is not comprehensively understood [8-10].

Current theories advocate that the deficiencies in functional connectivity rather than a single basal ganglia lesion account for these disorder. The interruption of the connections between internal globus pallidus, subthalamic nucleus, and thalamus may further cause a disturbance in the basal ganglia-cortical circuit. This could further result in a reduced inhibition of thalamocortical excitatory (glutamatergic) neurons and eventually in hyperkinetic movements [11]. In general, the vascular supply to the subthalamic nucleus is from two branches of the internal carotid artery, including perforating branches of the anterior choroidal artery and posterior communicating artery as well as posteromedial choroidal arteries which are part of posterior circulation. The contribution of each vessel to the blood supply of the subthalamic nucleus is variable and their vascular territories intermix [12]. In our patient, the condition of segmental stenosis of bilateral MCA, PCA and severe right internal carotid artery stenosis (70%) in addition to left subclavian steal syndrome, decreased blood flow of basilar artery, which may further attribute the loss of blood circulation to subthalamic nucleus and cause ischemic infarction.

Diabetes mellitus is one of the most potent independent risk factors for the development of diabetic cerebral vascular disease (CVD). Hyperglycemia itself could cause insulin resistance, oxidative stress, loss of endothelium-derived nitric oxide, endothelial dysfunction, abnormal release of en-

dothelial vasoactivators, excess free fatty acids, prothrombotic state, vascular smooth muscle dysfunction, and the down-regulation of MicroRNAs participated in the balance of endotheliocytes as well as vessel generation and recovery. These abnormalities, mainly *via* mitogen-activated protein kinase, phosphatidylinositol 3-kinase, hexosamine, polyol, protein kinase C activation, and increased generation of advanced glycosylation end products pathway, play a significant role in diabetic CVD complications [13].

However, nonketotic hyperglycemia related hemichorea-hemiballism could have hyperintensity lesion in striatum and subthalamic nucleus in brain CT and MRI T1 weighted sequence [14]. This rare diabetic complication should be also in the differential diagnosis in our patient. The possible mechanisms may be disruption of blood brain barrier (BBB) due to hyperglycemia induced blood hyperviscosity. The anaerobic metabolism of brain cell resulting from decreased regional cerebral blood flow and glucose metabolism failure, which could further aggravate decreased gamma-aminobutyric acid (GABA) availability in the nonketotic state. Disrupted BBB causes transient ischemia of vulnerable neurons [8-10]. The imbalanced GABA system and vascular insufficiency could further contribute to movement disorder. The hyperglycemic state promotes deposition of a T1-intense mineral, such as calcium or manganese and recovered after glucose normalized [15].

For non-symptomatic management, the most importance is to search for reasons that required etiology-specific treatment. Dehydration and rhabdomyolysis maybe the medical complications in the patients with severely hyperkinetic movement, which can be prevented by good support care. Pharmacological therapy is not essential in all cases, since many patients have a mild and self-limited disorder. If drugs are needed, there are many options. Antidopaminergic therapy remains the mainstay of all pharmacological treatment. In

most series, such treatment has provided valuable advantage in about 90% of patients. However, one unique therapeutic challenge with dopamine-antagonist treatment of hemiballism (predominantly in older patients) is the development of dose-limiting and drug-induced parkinsonism on the non-ballistic side. Thus, we added trihexyphenidyl, an anticholinergic agent used mainly in the symptomatic therapy of parkinson disease and movement disorders. Typical neuroleptics such as pimozide, haloperidol, chlorpromazine, and perphenazine were the first to be used. Atypical antipsychotics (olanzapine, risperidone) are also effective drugs. These agents, in common with the older typical neuroleptics, block striatal D2 dopamine receptors. Clozapine, however, absences of substantial D2 blockade and yet it too has been described to improve hemiballism in a trivial number of patients. Tetrabenazine, which depletes dopamine, can be an effective treatment of bemiballism. Because of the risk of drug-induced parkinsonism and tardive dyskinesias, tetrabenazine is preferred over haloperidol [16]. There are other effective drugs including antiepileptics (valproate, topiramate) and benzodiazepines.

Conclusion

Natural history of hemichorea-hemiballism varies depending on etiology. The prognosis is usually benign in most cases. The mainstay of management strategy is to determine the etiology and then correct underlying disorder.

Statements

Contributorship Statement

- Tai-You Guo, Chih-Chun Kuo, Po-Jen Hsiao & Hann-Yen Shyu: participated in drafted the manuscript and revised the manuscript.
- Tai-You Guo & Chih-Chun Kuo: contributed equally to this work (co-first author).

- Chih-Chun Kuo, Ming-Hua Chen, Ching-I Lin & Jenq-Shyong Chan: participated in collect the data.
- Hann-Yen Shyu & Po-Jen Hsiao: participated in organized and revised the final manuscript. Contributed equally to this work (co-corresponding author).

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Competing interests

None declared.

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