Resolving the Dance: A Case Study on Non-Ketotic Hyperglycemic Hemichorea-Hemiballismus in a Patient with Long-Standing Type 2 Diabetes

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Patient: Male, 53-year-old
Final Diagnosis: Non-ketotic hyperglycemic hemichorea-hemiballism
Symptoms: Hemichorea
Clinical Procedure: —
Specialty: Endocrinology and Metabolic

Objective: Rare disease
Background: Non-ketotic hyperglycemic hemichorea-hemiballism (HCHB) is a rare complication of diabetes, which is mainly described in case reports. This condition occurs more commonly in older women and is known to be associated with T1 hyperintensity basal ganglia lesions on magnetic resonance imaging (MRI). The pathophysiology of non-ketotic hyperglycemic HCHB is not well defined, although a combination of regional metabolic failure and ischemia due to hyperglycemia is suspected to occur. Treatment entails tight blood glucose control, although antipsychotic medications such as risperidone may be helpful in refractory cases.

Case Report: We describe a case of a middle-aged man with long-standing type 2 diabetes who experienced 3 weeks of progressive unilateral arm, leg, and face choreiform movements. Laboratory testing performed just prior to symptom onset was notable for a hemoglobin A1C of >15% and a serum blood glucose of 566 mg/dl. MRI revealed diffuse T1 hyperintensity in the left lentiform nucleus. Our patient's insulin regimen was adjusted, resulting in improvement in average serum glucose (A1C of 9.4%). However, his symptoms did not improve significantly. A trial of benzodiazepine was attempted, without success. When risperidone was started, the patient experienced resolution of symptoms. Recurrence of non-ketotic hyperglycemic HCHB while off risperidone has not occurred to date.

Conclusions: Non-ketotic hyperglycemic HCHB is a rare but important diagnosis to consider in patients with hyperglycemia and new-onset choreiform movements. Patients with long-standing type 2 diabetes may be affected, especially when glycemic control worsens. When tight blood glucose control does not resolve symptoms, a short course of antipsychotic agents may provide relief.

Keywords: Chorea • Diabetes Complications • Dyskinesias • Hyperglycemia

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Background

Hemichorea-hemiballismus (HCHB) is a hyperkinetic movement disorder that results from disturbances within the basal ganglia [1]. Ischemia, infection, and malignancy are common causes of such disruptions, whereas genetic syndromes, such as Huntington's and Wilson's disease, or endocrinopathies, such as thyrotoxicosis, are more rare causes [1]. Non-ketotic hyperglycemia is one such rare cause of HCHB, described mainly in case reports [1]. It is most commonly seen in elderly women of Asian descent with diabetes and can occur in patients both with new-onset and pre-existing diabetes [2,3]. Prompt recognition of this condition is important as blood glucose control will often result in resolution of this disorder [3]. However, this case report offers an overview of a less conventional treatment strategy, as the described patient's HCHB did not completely resolve with improved glycemic control alone, requiring initiation of an antipsychotic agent.

Case Report

A 53-year-old man with a past medical history significant for long-standing type 2 diabetes mellitus (T2DM), hypertension, transient ischemic attack a decade ago, and chronic kidney disease stage 3, presented to our primary care clinic for evaluation of progressively worsening choreiform movement of his right arm, leg, and, later, face that started 3 weeks ago. The movements were non-suppressible, improved with sleep, and did not affect his left side. There was no trauma or any recent strokes. Laboratory testing performed at a routine primary care visit prior to the onset of these movements demonstrated that his hemoglobin A1C had increased from 8% to greater than 15%; his serum blood glucose was 566 mg/dL, CO₂ was 26 mmol/l, anion gap was 12, and creatinine was 2.01 mg/dL. This worsened glycemic control occurred in the setting of increased depression after the death of a family member and consequent decreased medication adherence. Two weeks prior to his presentation, his psychiatrist addressed his depression by stopping his sertraline 200 mg and adding duloxetine 60 mg. When this failed, he was transitioned back to sertraline but the choreiform movements of his right arm persisted and advanced to his right leg and right face. He had no family history of movement disorders. He denied alcohol use.

On physical exam, the patient had abnormal, non-suppressible dance-like movements of his right arm and right leg consistent with hemiballismus and hemichorea. There was also a non-rhythmic twitching movement involving the right side of his face. His blood glucose level was 163 mg/dL, antinuclear antibody screen was negative, hepatic function panel and ceruloplasmin level were normal, and human immunodeficiency virus testing was nonreactive. MRI head was obtained and showed diffuse T1 hyperintensity in the left lentiform nucleus (Figure 1). In conjunction with his recently worsened glycemic control, he was diagnosed with non-ketotic hyperglycemic HCHB. His glyemic control was optimized with adjustment of his insulin regimen (A1C decreased to 9.4%), but his symptoms only minimally subsided. With collaboration with the neurology team, he was started on lorazepam 0.5 mg every 6 hours as needed, which did not improve his symptoms at his 2-week follow-up visit despite blood glucose improving to 112 to 120 mg/dL on his home glucometer. The lorazepam dose was subsequently increased to 1 mg every 6 hours as needed, but his symptoms persisted. One week later, he was transitioned to risperidone 0.25 mg twice daily as needed, which was highly effective, as he had a 95% reduction in non-suppressible movements. In subsequent weeks, he occasionally experienced mild choreiform hand movements when due for his dose of risperidone. The risperidone was eventually discontinued 6 months later after the abnormal movements ceased completely. He has not had any subsequent recurrence of HCHB to date.

Discussion

Non-ketotic hyperglycemic HCHB was first described in 1982 by Rector, who identified 3 patients with this condition whose symptoms improved with resolution of hyperglycemia [4]. Since

Figure 1. MRI head demonstrating diffuse T1 hyperintensity within the left lentiform nucleus (white arrow).
that time, 153 case reports on this condition have been published according to a 2022 comprehensive literature review by Cincotta and Walker [4]. Their analysis demonstrated that non-ketotic hyperglycemia may be the second leading cause of hemichorea, after stroke [4]. However, this remains a rare condition; for instance, at a large referral center, only 7 cases of non-ketotic hyperglycemic hemichorea-hemiballismus were identified after the authors chart-reviewed 596 cases of chorea/ballism over a 15-year period [5].

The etiology of non-ketotic hyperglycemia HCHB is not fully defined in the literature. Regional metabolic failure as a result of hyperglycemia causing a hyperviscous state is one proposed hypothesis [2,6]. This hypothesis is supported by the fact that hemichorea has also been observed in patients with polycythemia vera, in which hyperviscosity is thought to cause venous stasis and inadequate perfusion [4]. T2 hyperintensities have been observed in patients with polycythemia vera presenting with hemichorea, similar to imaging findings seen in non-ketotic hyperglycemia HCHB [4]. Increased sensitivity of dopamine receptors in a postmenopausal state is another possible etiology, and perhaps helps to explain the higher incidence of this syndrome in female patients [2]. An additional hypothesis is that production of gamma-aminobutyric acid (GABA), the main inhibitory neurotransmitter in the brain, is altered in non-ketotic states due to diminished acetoacetate production [2,6]. However, these hypotheses involve global metabolism processes and do not explain why cases almost always result in unilateral, rather than bilateral, insults [4].

MRI is the imaging modality of choice in this condition. Diffuse T1 hyperintensity in the lentiform nucleus on MRI is consistently identified in patients with non-ketotic hyperglycemia HCHB [1]. Most case reports describe unilateral imaging findings, which correlate to the body side affected by chorea and ballism [1]. Bilateral lesions are rare [1]. It is important to note that the radiographic signature of this condition mimics that of basal ganglia hemorrhage on MRI and thus may lead to misdiagnosis [7]. Because treatment of basal ganglia hemorrhage is vastly different than treatment of non-ketotic hyperglycemic HCHB, increasing knowledge of this condition among clinicians is important.

The mainstay of treatment is correction of hyperglycemia, which in most cases results in resolution of symptoms [3]. Both rapid resolution and subacute resolution after euglycemia have been described in the literature [2,3]. However, in refractory cases antipsychotics, GABA-receptor agonists, selective serotonin reuptake inhibitors, or dopamine-depleting agents may be required [8]. For our patient, 3 weeks of euglycemia did not improve symptoms and risperidone was started, resulting in prompt improvement. To date, the described patient has not experienced recurrence of symptoms. Nonetheless, continued monitoring may be important, as cases of recurrent non-ketotic hyperglycemia HCHB have been described in the literature [9].

Conclusions
This case report demonstrates non-ketotic hyperglycemia HCHB as a rare but potential manifestation of poorly controlled diabetes mellitus. Early recognition and aggressive treatment of hyperglycemia is important to address this reversible condition. In refractory cases, antipsychotic therapy may be warranted.

Statement
The majority of the work and patient care was done at the University of Rochester Medical Center, Department of Medicine. Part of the authorship was completed while KT was at NYU Langone, Department of Medicine.

Declaration of Figures’ Authenticity
All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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