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Case Report

A Case of Diabetic Hemichorea Hemiballismus Exacerbated by Hypoglycemia

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ABSTRACT

Objective: We describe an unusual case of diabetic hemichorea hemiballismus (diabetic HCHB) with symptoms resistant to traditional therapy and exacerbated by hypoglycemia.

Case Presentation: A 62-year-old woman with a 3-year history of noninsulin dependent type 2 diabetes presented with left-sided, involuntary, “jerking” movements. History included inconsistent metformin use, peripheral vascular disease, hypertension, and hyperlipidemia. Physical exam was documented as chorea of the left upper and lower extremity. Blood glucose was 776 mg/dL (82–115 mg/dL), and head computed tomography scan was read as asymmetric hyperattenuation of the right lentiform nucleus. The chorea dissipated within 48 hours of basal, bolus insulin and maintenance of blood glucose from 140 to 180 mg/dL. Hyperintensities were not documented on magnetic resonance imaging 4 days later. The patient presented twice in the following weeks for increasing frequency of chorea and hypoglycemia of 62 mg/dL and 40 mg/dL. Repeat magnetic resonance imaging was read as right-sided basal ganglia hyperintensities. Short courses of haloperidol, alprazolam, and tizanidine and a 2-week course of olanzapine yielded no improvement in chorea. Two weeks of tetrabenazine did improve the chorea; however, residual weakness and gait dysfunction persisted.

Discussion: The differential diagnosis for chorea includes hereditary and acquired forms. Diabetic HCHB is a rare, acquired, metabolic form that occurs in older, female, type 2 diabetics with poor glucose control. The patient experienced exacerbations of chorea in the setting of hypoglycemia.

Conclusion: Glycemic control is important in the long-term management of diabetic HCHB, and this case demonstrates hypoglycemia as a potential cause for resistant cases.

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Introduction

Hyperosmolar hyperglycemic nonketotic state (HHS) is a complication of type 2 diabetes marked by a serum glucose greater than 600 mg/dL (82–115 mg/dL) and an effective plasma osmolality greater than 320 mOsm/kg (285–295 mOsm/kg) in the absence of ketoacidosis.¹ The neurological sequelae of HHS are commonly obtundation and coma, but rarely HHS may present with focal chorea in a syndrome known as “diabetic hemichorea hemiballismus” (diabetic HCHB).^{2,3} Diabetic HCHB is caused by a

contralateral basal ganglia insult appearing as hyperattenuation and T1 hyperintensity on computed tomography (CT) and magnetic resonance imaging (MRI), respectively.⁴ We describe an unusual case of diabetic HCHB with prolonged morbidity associated with hypoglycemia and symptoms resistant to traditional therapy.

Case Presentation

A 62-year-old woman with a 3-year history of noninsulin dependent, type 2 diabetes presented to the emergency department with 2 days of “jerking” of her left arm and leg. She reported inconsistent metformin use and had noticed increased urination and a 14 kg weight loss over the past month. Her medical history included hypertension, hyperlipidemia, peripheral vascular disease, bronchiectasis, resolved hepatitis C, and steatohepatitis without cirrhosis. Social history included a 20-pack-year smoking history, alcohol use of 10 drinks per week, marijuana use, and prior intravenous cocaine use. There was no family history of

Abbreviations: CT, computed tomography; HCHB, hemichorea hemiballismus; HHS, hyperosmolar hyperglycemic nonketotic state; MRI, magnetic resonance imaging.

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neurological disorder. Vital signs included a temperature of 98.1 °F, blood pressure of 159/64 mmHg, heart rate of 54 beats per minute, respiratory rate of 19 breaths per minute, and body mass index of 23.6 kg/m². She was oriented with neurological exam significant for circular, nonrhythmic writhing of her left upper and lower extremity with intermittent, ballistic, jerking. These movements were documented as chorea. Pertinent laboratory values included a blood glucose of 776 mg/dL, HbA1c 15.8% (4.8%–5.6%) or 149 mmol/mol (29–38 mmol/mol), venous pH 7.37 (7.35–7.45), bicarbonate 23 mEq/L (20–28 mEq/L), anion gap 13 (6–16), blood urea nitrogen 16 mg/dL (8–20 mg/dL), creatinine 1.48 mg/dL (0.6–1.2 mg/dL), alanine aminotransferase 17 U/L (16–61 U/L), and aspartate aminotransferase 20 U/L (15–37 U/L). The head CT scan was read as asymmetric hyperattenuation of the right lentiform nucleus, sparing the internal capsule, which was likely metabolic in origin (Fig.).

The patient was admitted, and blood glucose was maintained between 140 and 180 mg/dL with basal, bolus insulin. Within 48 hours, the patient's jerking and writhing of the left upper and lower extremity were suppressible with concentration. An MRI 4 days later was read as chronic microvascular, ischemic changes with no focal abnormality to correspond to the prior head CT. At discharge, the writhing motion had improved from constant to intermittent. She was prescribed insulin lispro, 8 units, 3 times daily and insulin glargine 18 units daily. Metformin was resumed at 500 mg, daily. The discharge diagnosis was diabetic HCHB.

The patient returned to the hospital 1 month later with increased frequency of left-sided “jerking” motions and ambulatory dysfunction. Neurological exam was documented as chorea and described as continuous, circular hemi-ballistic movements of the left upper and lower extremity. Blood glucose was 62 mg/dL and HbA1c was 9.9% (85 mmol/mol). She was admitted and treated with alprazolam, 1 mg, 3 times daily, tizanidine, 4 mg, 3 times daily, and a dose of intramuscular haloperidol, 12.5 mg, with no change in chorea. Paraneoplastic autoantibody and antinuclear antibody testing were negative. Ceruloplasmin was 36 mg/dL (17–61 mg/dL), and copper was 157 µg/dL (70–175 µg/dL). It was documented that

the patient's left upper and lower extremity chorea dissipated when not being examined. She was discharged with a diagnosis of conversion disorder. Discharge medications included alprazolam, 1 mg, 3 times daily for anxiety and tizanidine, 4 mg, 3 times daily for muscle spasms. Metformin and lispro were continued at the same doses, and glargine was decreased to 14 units daily.

Within 24 hours, she presented with continuing chorea. Blood glucose was 200 mg/dL. She was again diagnosed with diabetic HCHB and discharged with olanzapine 5mg daily. She presented 2 days later with increased frequency of chorea and a blood glucose of 40 mg/dL. Repeat MRI was read as hyperintensity in the right lentiform and caudate nuclei with corresponding intrinsic T1 hyperintensity. Her olanzapine was increased to 15 mg daily. Lispro was adjusted to 5 units, 3 times daily, and glargine was increased to 22 units daily.

Two weeks later at an outpatient visit she reported no improvement with olanzapine therapy. Her HbA1c was 5.0% (39 mmol/mol). She was prescribed tetrabenazine 12.5 mg twice daily and experienced resolution of the involuntary movements in her left arm and leg over a 2-week period. She still has residual weakness in the left arm and leg resulting in gait dysfunction.

Discussion

In summary, we describe the case of a 62-year-old female with type 2 diabetes presenting with chorea, hyperglycemia, and radiologic imaging consistent with diabetic HCHB. The involuntary movements began to dissipate within 48 hours of glucose normalization, and the hyperintensities of the basal ganglia were not documented on MRI. Her chorea worsened in the following weeks during episodes of hypoglycemia including redemonstration of basal ganglia hyperintensities on MRI. Short courses of multiple agents yielded no improvement in movements. Tetrabenazine therapy did improve the movements after 2 weeks; however, residual weakness and gait dysfunction persisted.

Chorea is a hyperkinetic movement disorder originating from basal ganglia pathology.⁵ Hereditary forms of chorea include Huntington and Wilson disease.⁵ The patient had no family history of neurologic or Huntington disease. Ceruloplasmin and copper levels were normal, making Wilson disease unlikely. Vascular hemichorea is another consideration given the patient's history of peripheral vascular disease. Vascular hemichorea is associated with an ischemic or hemorrhagic stroke involving the basal ganglia.⁶ In this case, the head CT scan and subsequent MRI reports documented no ischemic or hemorrhagic stroke.

Autoimmune conditions associated with chorea include systemic lupus erythematosus and paraneoplastic syndromes.^{5,7} The negative antinuclear antibody test made systemic lupus erythematosus unlikely. Paraneoplastic chorea most commonly occurs in the setting of small cell lung carcinoma or adenocarcinoma.⁷ This patient did have risk factors for malignancy; however, a paraneoplastic autoantibody panel was negative.⁷

Metabolic derangement is an additional etiology for acquired chorea. Carbon monoxide, cyanide, and methanol are cellular-respiratory toxins that affect the basal ganglia.⁴ These poisons generally result in bilateral lesions and present as altered mental status or coma.⁴ Hyperammonemia and hyperglycemia can both cause hyperattenuation and T1-weighted hyperintensity isolated to the basal ganglia on CT and MRI, respectively.⁴ This patient had multiple risk factors for cirrhosis including prior hepatitis C infection and steatohepatitis. Although ammonia was not measured, the alanine aminotransferase and aspartate aminotransferase were normal, and signs of cirrhosis were not documented. This leaves hyperglycemia as the most likely etiology and diabetic HCHB as the probable diagnosis.



Fig. Computed tomography scan of the head without contrast (sagittal view) showing asymmetric hyperattenuation of the right lentiform nucleus with sparing of the internal capsule.

The prevalence of diabetic HCHB is 1 in 100 000.⁸ Predisposing factors include long-standing diabetes with poor glucose control, female gender, and advanced age.⁸ Underlying vascular disease makes this patient uniquely susceptible, as the basal ganglia is rich in vascular supply and neurotransmitters and subsequently has high metabolic demands.⁴ The hyperviscosity induced during severe hyperglycemia is believed to have synergistic effects with vascular insufficiency.^{9,10} The result is transient dysfunction of the striatum, leading to alterations in neurotransmitter metabolism.^{9,10} Ischemia-induced dysfunction of γ aminobutyric acid-ergic projection neurons is a proposed mechanism for loss of basal ganglia tonic inhibition and subsequent chorea.¹⁰

Pharmacologic therapy for cases of diabetic HCHB resistant to glycemic control involves modulation of γ aminobutyric acid-ergic and dopaminergic transmission. D2 receptor antagonists are the mainstay of therapy and include typical and atypical antipsychotics.¹¹ Tetrabenazine is a monoamine oxidase inhibitor utilized in Huntington chorea that is also believed to act through dopamine depletion.¹¹ Resistant cases may require weeks to months of therapy.^{12,13}

One unique aspect of this case is the patient's exacerbations during hypoglycemic episodes. This has not been previously reported in cases of diabetic HCHB, although exacerbations have been described with repeat episodes of hyperglycemia.¹² One case report does describe a dialysis patient with recurrent, bilateral chorea in the setting of hypoglycemia.¹⁴ Hypoglycemia is known to cause hyperintensities within the basal ganglia on MRI; however, internal capsule, corpus callosum, and diffuse cortical abnormality are usually observed as well.⁴ Our patient had 2 documented hypoglycemic episodes. She was likely experiencing more frequent, less overt hypoglycemic episodes as her HbA1c decreased from 15.8% (149 mmol/mol) to 5.0% (31 mmol/mol) over 2 months.

Conclusion

In conclusion, diabetic HCHB is a rare complication of type 2 diabetes that occurs in older, female patients with poor glycemic control and chronic vascular disease.^{4,8,9} The initial differential for evaluating chorea is broad and includes conditions that impact the basal ganglia, including hereditary, autoimmune, and paraneoplastic syndromes, cerebral vascular accident, and metabolic disturbance.^{5,7} Glycemic control is important in the long-term management of diabetic HCHB, and this case demonstrates hypoglycemia as a potential cause for resistant cases. Cases resistant to

glycemic control should be managed with dopamine antagonists, with the expectation of gradual rather than immediate resolution of symptoms.^{11–13} Tetrabenazine is another option for patients who fail to respond to the aforementioned therapies.¹¹

Disclosure

The authors have no multiplicity of interest to disclose.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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