Nonketotic hyperglycemia (NKH) is defined as absence of ketoacidosis in the presence of significant hyperglycemia, typically levels exceeding 800 mg/dl, and hyperosmolality. NKH is more common in older women, over age 50, with diabetes mellitus (DM). Precipitating factors that may increase risk of developing NKH include infection, surgery, dialysis, tube feedings, stress, and certain drugs that impair glucose tolerance, such as diuretics, β-blockers, corticosteroids, phenytoin and diazoxide.¹ Neurological manifestations of NKH include delirium, partial or generalized seizures, hemichorea-hemiballism (HC-HB), dysphagia, aphasia, hemianopsia, hemiparesis, and hemisensory loss.² HC-HB is a movement disorder reported as a rare complication of NKH. Clinical awareness of the variety of neurological manifestations associated with NKH has become increasingly important in order to implement the appropriate treatment.

Case Report

A 67-year-old woman with history of congestive heart failure, hypertension, coronary artery disease, hyperlipidemia, arthritis, and impaired glucose tolerance presents to clinic for evaluation of confusion, polyuria, polydipsia and generalized weakness. She takes lisinopril, furosemide, spironolactone, carvedilol, simvastatin, clopidogrel, and aspirin. She reports no smoking or drinking alcohol. Her family history is significant for DM and heart disease. Physical examination revealed blood pressure of 80/50 mmHg, dry mucous membranes and grade 2/6 systolic murmur. Neurological examination was unremarkable except for confusion. Serum glucose was 801 mg/dL with bicarbonate 20 mEq/L. Calculated
serum osmolality was 308mOsm/Kg with sodium 129mEq/L, potassium 4.2mEq/L, chloride 94mEq/L, BUN 15mg/dL and creatinine 1.16mg/dL. Diagnosis of hyperosmolar NKH was made and she was admitted for IV fluids and insulin.

Within 24 hours after admission she developed involuntary, uncontrollable jerky-like movements and medium amplitude swings predominantly involving her left upper and, to lesser extent, left lower extremity, consistent with HC-HB. She was placed on sinemet 25/100mg three times daily without improvement. CT of the brain without contrast on day two of admission revealed hyperdensity in right putamen, and T1-weighted brain MRI showed increased signal in the same area. (Fig.1 A, B) With insulin administration, glucose readings initially ranged from 205-399mg/dL gradually trending downward to 101-243mg/dL during the 10-day hospital course. Areas of erythema were detected over her left arm from constant friction secondary to rubbing due to severe uncontrollable movements. After being discharged on insulin and metformin, she continued to experience involuntary, uncoordinated jerky movements of her left upper extremity that gradually resolved over a period of approximately four months with strict glycemic control.

Discussion

HC-HB is a movement disorder typically characterized by rapid involuntary jerky movements and periodic uncoordinated swings involving a unilateral limb, as manifested in this patient. It is more common in older diabetic women of Asian descent and occurs most commonly from ischemia or stroke in the contralateral basal ganglia and less commonly with NKH. Other causes include tumors, vascular malformations, neurodegenerative disorders (Huntington’s), infections (HIV), toxins, systemic lupus erythematosus and thyrotoxicosis.1 This rare dyskinetic syndrome of HC-HB with NKH resolves at variable rates after correcting hyperglycemia, although cases of unresolved symptoms several months after achieving glycemic control have been reported.2,3 Medications that have been used with the most benefit in trying to reduce involuntary movements, during the process of lowering glucose levels, include antipsychotics, benzodiazepines, anti-convulsants such as topiramate, and dopamine depletor tetrabenazine.4

Patients with HC-HB and NKH demonstrate characteristic neuroradiological findings on T1-weighted MRI of the brain, consisting of hyperintensity signal in the contralateral putamen, sometimes also involving caudate nucleus and globus pallidus, usually reversing within a few months on follow-up neuroimaging. Non-contrast CT of the brain in these patients reveals hyperdensity in contralateral basal ganglia.5,6 (Fig.1) The precise mechanism of HC-HB in NKH is presently unknown, although several theories have been proposed.2,3,5-8 Hyperglycemia has been shown to reduce regional cerebral blood flow, causing ischemia; in the absence of ketoacidosis, there is a shift from aerobic to anaerobic glucose metabolism, subsequently attenuating the Kreb’s cycle. The resulting increase in GABA metabolism and depletion, via the succinic semialdehyde pathway, leads to disinhibition of dopamine (DA) pathways in the basal ganglia. This consequently disrupts DA balance toward a state of dopaminergic hyperactivity. Also, it is suggested that astrocytes, which normally regulate extracellular K+ homeostasis, become swollen, reactive and dysfunctional (known as gemistocytes), leading to dysregulation of neuronal transmission.9 Lack of estrogen, during postmenopausal state, has been suggested to cause dopamine hypersensitivity, which may explain why continued on pg.38
Meningo-Vascular Syphilis

24. Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines, 2006. MMWR. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5511a1.htm

Case Report: Hemichorea-Hemiballism

older woman are at higher risk of developing this rare form of dyskinesia. Another proposed hypothesis is that of petechial hemorrhages resulting from blood-brain barrier disruption due to hyperglycemia and cerebral ischemia, along with underlying diabetic small vessel disease. This case emphasizes the importance of recognizing neurological sequelae of NKH, such as HC-HB, which is reversible and resolves after normalization of glucose.

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continued from pg.31