Hyperglycemia and Hypoglycemia-Related Chorea in an 83-Year-Old Man

JONATHAN SPIEGEL, BS; BRADLEY COLLINS, MD

ABSTRACT

We report a case of a patient who first presented with hyperglycemic chorea, and subsequently with hypoglycemic chorea. The patient's hypoglycemia was thought to be iatrogenic, highlighting the importance of careful glucose management following glycemia- related chorea. Presumably secondary to the patient's chorea, the patient also suffered from new onset shoulder pain, which was managed with gabapentin. Unfortunately, due to the patient's renal failure, the gabapentin, combined with infection, led to encephalopathy in this patient. This report presents and offers useful tips on the management of a unique patient who suffered from hyperglycemic chorea, hypoglycemic chorea, and encephalopathy, all within a few weeks.

KEYWORDS: chorea, movement disorder, hyperglycemia, hypoglycemia

BACKGROUND

Chorea develops from disruptions in the cortico-striato-pallido-thalamic circuit, leading to disinhibition of movement. Chorea is classically said to result from lesions to the subthalamic nucleus (STN), though it is in fact more commonly secondary to striatal[1,2], thalamic,[2] or motor cortex[2] lesions due largely to the higher incidence of strokes in these regions. Further, striatal changes on imaging are nearly universally found in cases of glycemic control related chorea.[1,3]

Chorea is a relatively uncommon syndrome, seen in approximately 1% of patients at some motor disorders clinics.[4] The differential diagnosis for chorea includes over 20 hereditary causes[5] and many acquired ones. While considerable overlap exists, hereditary causes tend to occur in younger patients (<60 years old) and can have accompanying syndromic symptoms. Huntington's disease is the overall most common cause of hereditary chorea, with an estimated prevalence of 1 in 10,000 people,[5] though other hereditary causes may reach similar prevalence within specific ethnic groups, such as dentatorubral pallidoluysian atrophy in Japanese patients.[6]

Acquired causes of chorea can be grouped into cerebrovascular, autoimmune/inflammatory, endocrine, neoplastic, metabolic, infectious, drug-induced, toxic, or other causes, with several etiologies falling under each of these. Among acquired causes of chorea, vascular injury, hyperglycemia or hypoglycemia, drug-induced chorea (particularly secondary to neuroleptics), Syndenham's chorea (secondary to group A beta-hemolytic strep infection), and AIDs-associated chorea (particularly HIV encephalitis and toxoplasma infection) are among the most frequently seen, though the relative frequency of these causes varies widely across case series.[1,4,7] Initial workup of new onset chorea in an older patient with a negative family history and taking no neuroleptic medications should therefore focus on ruling in or out the likely and urgent etiologies of vascular injury and hyper- or hypoglycemia through labs and neuroimaging. Further workup of irreversible, lower likelihood, and/or less urgent causes (e.g. Lyme antibody testing, ceruloplasmin levels, autoimmune panels, etc.) should be reserved for patients whose history and physical exam raise suspicion for these specific etiologies or whose etiology remains unclear after initial workup.

CASE REPORT

An 83-year-old patient presented with large amplitude, left-sided, choreiform movements of the face, arm, and leg. The patient reported that these symptoms began one week prior and worsened while he was receiving hemodialysis for end-stage renal disease (ESRD). He denied any temporal pattern, exacerbators, or alleviators of his symptoms. Additionally, he denied any headache, vision changes, confusion, speech difficulty, nausea, seizures, falls, or new balance or gait disturbances and denied ever smoking or frequent alcohol consumption.

The patient had a past medical history which included: current ESRD treated with hemodialysis, heart failure with reduced ejection fraction (25%, measured eight months prior) status-post NSTEMI, type II diabetes, a one-year prior history of surgically treated colonic malignancy, and a remote history of renal cell carcinoma with nephrectomy. The patient's current medications included: atorvastatin, glimepiride, metformin, acetaminophen, aspirin, and sublingual nitroglycerin.

The patient's vitals and labs are summarized in **Table 1**. On physical exam, he appeared comfortable despite his involuntarily left-sided movements. His cranial nerve exam

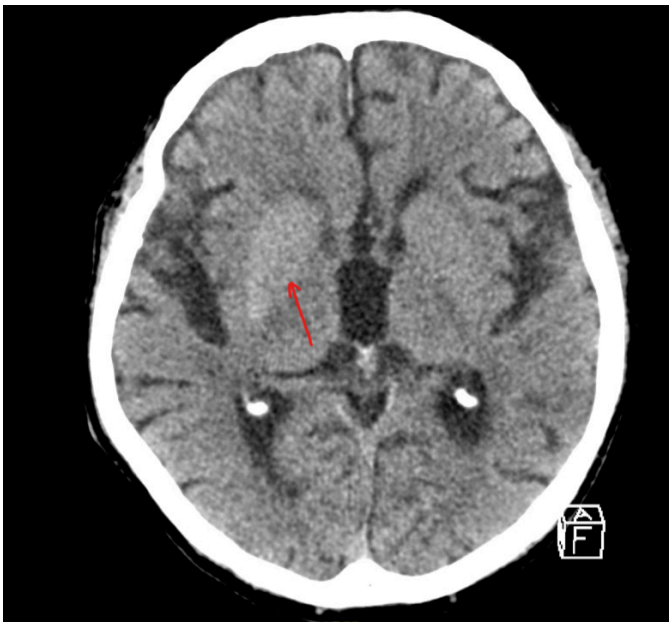
Table 1. Vitals and lab values for the patient at initial presentation for hyperglycemic chorea and at second presentation for hypoglycemic chorea.

	Visit 1	Visit 2
Temperature	36.7°C	37.5°C
Blood Pressure	119/58mmHg	111/52 mmHg
Heart Rate	96	99
Respiratory Rate	16	18
02 Saturation	100% on room air	97% on room air
Glucose	208mg/dl	111mg/dl (44mg/dl prior to arrival at hospital)
Sodium	136mEq/L	133mEq/L
Potassium	3.9mEq/L	3.8mEq/L
Chloride	96mEq/L	93mEq/L
Creatinine	1.74mg/dL	5.39mg/dL
Hemoglobin	10.8g/dL	9.4g/dL

was normal except for difficulty with puffing out his cheeks. Finger to nose was intact, 2+ patellar reflexes, no ankle clonus, and Babinski was down-going. He was able to recall one word on three-word recall and showed unsteady gait. His Romberg was intact with no pronator drift. No abnormalities were noted on HEENT, cardiovascular, respiratory, abdominal, or extremity exams.

CT revealed increased attenuation in the right putamen and globus pallidus (**Figure 1**) as well as small vessel ischemic changes and evidence of a previous left parietal occipital infarction. Subsequent MRI similarly revealed T1 hyperintensity in the right corpus striatum, though image quality was limited by movement. BMP was normal besides a chloride of 96, creatinine of 1.74, glucose of 208, and anion gap of 14. CBC was normal besides a hemoglobin of 10.8, likely secondary to the patients pre-existing renal dysfunction associated anemia. Given the patients plasma glucose of 208 and imaging findings, hyperglycemic chorea was deemed the most likely etiology.

Figure 1. Horizontal CT image showing increased attenuation in the right putamen and right globus pallidus (red arrow).



The first priority in the management of patients with hyperglycemic chorea is glucose and electrolyte control. Until recovery, and in patient's whose symptoms persist, similar agents to those used in Huntington's chorea, including neuroleptics such as olanzapine, risperidone, tiapride, or haloperidol and dopamine depleting agents such as tetrabenazine, deutetrabenazine, or valbenazine, are typically used.[3,8]

In our patient, blood glucose was monitored and controlled, and the patient was treated with olanzapine and a short course of clonazepam. Given the patient's renal failure, metformin was discontinued for the management of his diabetes. Despite potential interactions with the patient's renal failure, glimepiride was continued. At discharge the next day, the patient's face or leg movements were no longer present though occasional large amplitude arm movements persisted.

Approximately two months after discharge, our patient returned to the hospital with a blood glucose of 44, measured at home, and recurrence of his left-sided chorea, accompanied by left-sided shoulder and arm pain (suspected secondary to choreiform movements), and failure to thrive at home. Physical exam revealed tenderness over the left anterior rotator cuff and shoulder MRI showed evidence of inflammation, though image quality was limited by patient movement. 100mg of gabapentin, three times per day, was prescribed to help with the shoulder pain. The hypoglycemia was suspected to be secondary to glimepiride use which was subsequently held, discontinued, and replaced with insulin on a sliding scale with a goal glucose of 120–180. Glucose stabilization led to symptom improvement, albeit without complete remission, and the patient was discharged to a skilled nursing facility. Unfortunately, two weeks later, the patient returned with a clostridioides difficile infection, pneumonia, and urinary tract infection, and accompanying encephalopathy, suspected to be multifactorially secondary to the patient's gabapentin and infections. The patient was treated with antibiotics and his gabapentin dose was decreased to 100mg three times per week and he rapidly recovered.

DISCUSSION

While approximately 85% of patients will recover from hyperglycemic chorea within the first month,[3] outcomes vary widely. One review, for example, reported patients ranging in their length of symptom duration from <2 days to

>5 years.[1] While their results did not reach significance, in reviewing the literature, this same study found preliminary indications that extension of neuroimaging findings beyond the putamen as well as female sex predicted longer symptom persistence. When these same analyses included stroke patients with chorea in addition to hyperglycemic chorea cases, increasing the power of the analyses without substantially shifting the effect sizes, these same predictors offered significant prognostic value. While no prior reports have documented a single individual suffering from both hyper- and hypo-glycemic chorea, their review did note symptom recurrence to occur in 11/236 (5%) cases they reviewed as well as in 3/11 (27%) of their original cases.[1]

Interestingly, extreme variation in glucose is not necessarily required for symptoms to emerge. In Lee et al's case series of 14 patients for example, two (14%) had euglycemia (blood glucose between 90mg/dl and 150mg/dl) at time of glucose measurement and five (36%) had glucose measured between 150mg/dl and 250mg/dl. Only 3/14 (21%) of their patients had glucose >400mg/dl.[1] Our patient's presentation with a blood glucose of 208 is therefore not atypical of patients with hyperglycemic chorea.

The precise mechanisms underlying glycemic control-related chorea remain unclear, though several theories have been proposed including hyperglycemia causing alterations in gamma-aminobutyric acid (GABA) metabolism, osmotic changes, ischemia, calcification, petechial hemorrhages, and gemistocytes formation (reactive swollen astrocytes).[8] Interestingly, the theory that the brain may metabolize GABA under energy restricted conditions, disinhibiting the thalamus and causing chorea, may explain why an estimated 91% of hyperglycemic chorea cases specifically involve non-ketotic hyperglycemia (NKH),[3] though it does not explain hypoglycemic or hyperglycemic hyperketotic chorea. These theories also leave many questions unanswered, such as why the vast majority of cases of glycemia-related chorea lead to unilateral symptoms or why only a very small subset of patients with hyperglycemia develop symptoms.

The present case presents a patient who suffered first from hyperglycemic chorea but whose glucose control subsequently led to iatrogenic hypoglycemia which provoked recurrence of his chorea symptoms, highlighting the importance of careful glucose management in patients who have suffered from hyperglycemic chorea. This case also highlights the potential for joint irritation secondary to choreiform movement as well as the importance of adjusting gabapentin dosing in patients with renal failure.

References

1. Lee D, Kwon YN, Shon SH, Lee JH, Ahn TB. Glycemic and vascular choreoballism as main causes of secondary choreoballism involving the putamen. Park Relat Disord [Internet] 2016 [cited 2021 Feb 9];30:29–35. Available from: https://pubmed.ncbi.nlm.nih.gov/27353422/
2. Chung SJ, Im JH, Lee MC, Kim JS. Hemichorea after stroke: Clinical-radiological correlation. J Neurol [Internet] 2004 [cited 2021 Feb 9];251(6):725–9. Available from: https://pubmed.ncbi.nlm.nih.gov/15311349/
3. Gómez-Ochoa SA, Espín-Chico BB, Pinilla-Monsalve GD, Kaas BM, Téllez-Mosquera LE. Clinical and neuroimaging spectrum of hyperglycemia-associated chorea-ballism: Systematic review and exploratory analysis of case reports. Funct Neurol 2018;
4. Dewey RB, Jankovic J. Hemiballism-Hemichorea: Clinical and Pharmacologic Findings in 21 Patients. Arch Neurol [Internet] 1989 [cited 2021 Feb 9];46(8):862–7. Available from: https://pubmed.ncbi.nlm.nih.gov/2757526/
5. Mencacci NE, Carecchio M. Recent advances in genetics of chorea [Internet]. Curr. Opin. Neurol. 2016 [cited 2021 Feb 9];29(4):486–95. Available from: https://pubmed.ncbi.nlm.nih.gov/27257945/
6. Yanagisawa H, Fujii K, Nagafuchi S, et al. A unique origin and multistep process for the generation of expanded DRPLA triplet repeats. Hum Mol Genet [Internet] 1996 [cited 2021 Feb 9];5(3):373–9. Available from: https://pubmed.ncbi.nlm.nih.gov/8852663/
7. Piccolo I, Defanti CA, Soliveri P, Volontè MA, Cislaghi G, Girotti F. Cause and course in a series of patients with sporadic chorea. J Neurol [Internet] 2003 [cited 2021 Feb 9];250(4):429–35. Available from: https://pubmed.ncbi.nlm.nih.gov/12700907/
8. Bendi VS, Matta A, Torres-Russotto D, Shou J. Bilateral chorea/ballismus: Detection and management of a rare complication of non-ketotic hyperglycaemia. BMJ Case Rep [Internet] 2018 [cited 2021 Feb 9];2018. Available from: https://pubmed.ncbi.nlm.nih.gov/29925556/

Authors

Jonathan Spiegel, BS, Warren Alpert Medical School of Brown University, Providence, RI; Brain Health Imaging Institute at Weill Cornell Medicine Department of Radiology, New York, NY.

Bradley Collins, MD, Department of Medicine, The Miriam Hospital; Warren Alpert Medical School of Brown University, Providence, RI.

Correspondence

jonathan_spiegel@brown.edu