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Case Report

A Case of Bilateral Hyperglycemic Nonketotic Chorea in an 83-year-old Woman With Normal Brain Imaging

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Abstract

Bilateral hyperglycemic nonketotic chorea is a rare complication of hyperglycemia. In most cases, the literature illustrates patients presenting with unilateral chorea with image findings significant for hyperintense lesions in the basal ganglia on magnetic resonance imaging (MRI) or hyperdensities on computerized tomography (CT). Here, we present a case of an 83-year-old patient who was admitted to the hospital due to acute onset of orofacial and bilateral upper extremity chorea. She had no previous history of infection, genetic mutation, neoplasms, neurodegeneration, stroke, metabolic disease, drug exposure, or autoimmune disease. Surprisingly, her MRI showed only chronic microvascular changes in periventricular white matter without basal ganglia abnormalities. However, she was noted to have marked worsening of her glycemic control over the preceding 12 months based on worsening glycated hemoglobin (HbA1c) levels and elevated serum glucose on presentation. A literature review indicates that chorea caused by hyperglycemia is at times reversible with glycemic control, but as demonstrated in our patient, this is not always necessarily the case. A similar course has only been elaborated in a few other cases in the literature. We will also review the pathogenesis, the usual disease clinical course and standard treatment from the literature.

Key Words: bilateral hyperglycemic chorea, hyperglycemic nonketotic chorea, metabolic chorea, uncontrolled diabetes complication

Abbreviations: GABA, gamma-aminobutyric acid; HbA1c, glycated hemoglobin; MRI, magnetic resonance imaging.

Introduction

Chorea can be caused by genetic, acquired, or metabolic causes. Huntington disease, spinocerebellar ataxia, dentatorubral-pallidoluysian atrophy, and paroxysmal exertional dyskinesia are some of the widely recognized genetic causes of chorea [1]. Cerebrovascular accidents affecting the basal ganglia or space-occupying lesions are some of the acquired causes of chorea. Metabolic causes include disorders of copper metabolism (Wilson disease) and, rarely, hyperglycemia. Nonketotic hyperglycemic chorea is an uncommon metabolic cause of chorea as well as a metabolic neurological complication of uncontrolled diabetes. Few cases of bilateral hyperglycemic nonketotic chorea have been presented over the years; however, data on the exact numbers of cases seen are sparse—an analysis of all cases of chorea at Mayo Clinic Rochester for a 15-year period from the year 2000 to 2014 indicated that hyperglycemia-related chorea only accounted for 1% of cases of chorea [2]. In general, better glycemic control along with neuropsychiatric medications such as haloperidol can improve cases presenting with unilateral nonketotic chorea [3, 4]. In contrast, bilateral hyperglycemic nonketotic chorea seems to persist despite achieving glycemic control, which has been attributed to other confounding factors, such as other underlying basal ganglia abnormalities from previous ischemic injury as a likely primary cause of chorea and hyperglycemia possibly aggravating the chorea even further [5]. However, Saleh et al suggested that bilateral chorea due to hyperglycemia actually has a longer natural course, possibly lasting months despite glycemic control. This might especially be true in cases where no lesions were identified on extensive brain imaging [6], as was the case in our patient. Similarly, we present a case of an 83-year-old female with acute onset choreoathetoid orofacial and bilateral upper extremity movements and tremors with poor glycemic control suspected of having hyperglycemic nonketotic chorea and whose symptoms did not resolve completely with known standard treatment.

Case Presentation

An 83-year-old woman with a past medical history significant for essential hypertension, depression, anxiety, hyperlipidemia, and noninsulin-dependent type 2 diabetes mellitus was admitted to the hospital due to abnormal movements of her extremities. Her symptoms had started approximately a week prior to her hospitalization with uncontrollable nonpurposeful involuntary writhing movements involving her left upper extremity that progressed to involve her right upper extremity and orofacial muscles followed by bilateral lower extremities. She denied any previous history of cerebrovascular accident/transient ischemic attack or movement disorders. Her family history was also negative for movement disorders. She was on sertraline for the treatment of depression for approximately 2.5 years and stopped it after the onset of her symptoms. Of note, her glycated hemoglobin (HbA1c) worsened from 7.2% (7.2% of hemoglobin or 55 mmol/mol) to

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13.6% (114 mmol/mol) over the course of the last year prior to her presentation.

Diagnostic Assessment

On physical exam, she was noted to have right more than left choreiform, writhing movements. She was unable to consciously control her chorea with active movements. In addition to her upper extremities, she also had lip/mouth movements with automatisms. The movement was nonsuppressible and ceased only during sleep. No other remarkable neurological abnormalities were noted, and no muscle weakness was present in either the upper or the lower limbs.

Laboratory examinations reported normality in full blood count, liver function tests, renal function, thyroid function tests, urine toxicology, and iron studies, and vitamin B12 was unremarkable. Bicarbonate level on admission was noted to be 22 mEq/L or mmol/L and anion gap was 9 mEq/L or mmol/L. The patient had translocational hyponatremia with sodium of 132 mEq/L or mmol/L (reference range: 136-145 mEq/L or mmol/L) (corrected sodium 137 mEq/L or mmol/L) secondary to hyperglycemia of 443 mg/dL or 24.59 mmol/L and significantly elevated HbA1c of 13.6% or 114 mmol/mol (reference range: 4%-5.6% or 20-38 mmol/mol). Radiological images on admission showed unremarkable computerized tomography (CT) of the brain and magnetic resonance imaging (MRI) of the brain with and without contrast remarkable for periventricular deep cerebral white matter advanced chronic microvascular ischemic changes without any other abnormalities, including acute strokes, bleeding, or mass effects (Fig. 1).

The patient was evaluated by the neurologist, and workup was performed to rule out other causes, such as autoimmune diseases, including systemic lupus erythematosus (normal immune indices and no discomfort, such as dry mouth, dry eyes, malar rash, joint swelling, and pain), and drug-induced chorea was excluded (normal drug screen). Intracranial tumors were excluded (no abnormal lesions were found on brain MRI). Likelihood of Huntington disease was excluded due to no family history of the disease (no genetic variation associated with clinical phenotype/initial diagnosis was found in monogenic disease screening, that is, Huntington disease DNA testing). The patient was an elderly diabetic female patient with poor blood glucose control, and the urinary ketone bodies and serum ketone bodies were negative at the time of onset. Her clinical manifestation was bilateral gradual dance-like autonomic movement. Therefore, together with a neurologist, after ruling out other potential causes of chorea, a consensus was reached on hyperglycemic basal ganglia syndrome and hyperglycemic nonketotic chorea as the most likely culprit for her presentation.

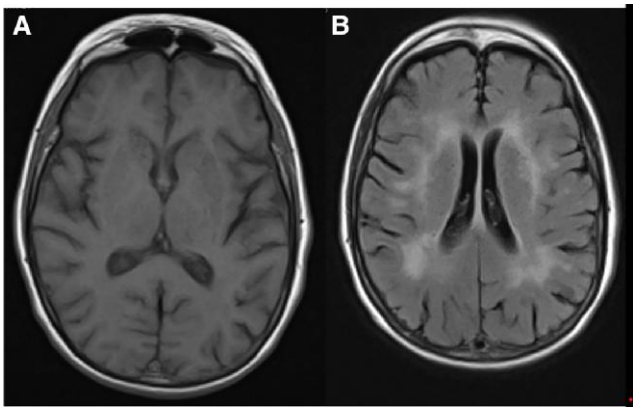

Figure 1. A, T1-weighted MRI brain showing no apparent pathology in the basal ganglia. B, FLAIR AX MRI brain showed hyperintense changes in the cerebral white matter indicating chronic microvascular ischemic change.

Treatment

During hospitalization, her blood glucose was actively controlled with insulin, while haloperidol was initiated for the extrapyramidal symptoms. Insulin dose was adjusted based on glucose monitoring subsequently discharged on Levemir 16 units twice a day, Novolog 12 units with meals 3 times a day.

Outcome and Follow-up

On subsequent follow-up with endocrinology and neurology, she showed improvement of her chorea with continued improved glycemic control and haloperidol but still continued to have some degree of chorea. Her chorea remained persistent at the follow-up visit approximately 3 months post discharge. Her HbA1c was 5.4% on a follow-up visit with endocrinology at 6 months post discharge and she was not seen to have any significant chorea. No follow-up MRI of the brain was performed in the outpatient setting as of writing of this case report.

Discussion

A meta-analysis of 53 cases of hyperglycemic nonketotic chorea in 2002 found that the majority of patients affected with hyperglycemic chorea were women relative to men, and the mean age of onset was 71. At 1 year, the mean serum glucose level at the time of onset of chorea was 481 mg/dL or 26.7 mmol/L, and the average glycosylated hemoglobin level was 14.4% (range 9.9% to 19.2%). The majority of cases had unilateral chorea (88.6%), and only 6 of the 47 (11.4%) presented with bilateral chorea, similar to our patient [3]. Interestingly, in all of the cases reviewed in the meta-analysis, imaging elaborated clear involvement of the putamen in all the cases at least to some extent without involvement of the caudate or globus pallidus [3]. In contrast, our patient did not have any basal ganglia abnormalities noted on her MRI. Mechanisms hypothesized to provide some sort of explanation for hyperglycemic chorea include a shift in cerebral metabolism to the consumption of gamma-aminobutyric acid (GABA) and acetate during the hyperglycemic state, which leads to metabolic acidosis, as GABA cannot meet the energy needs of the brain along with depletion of GABA and acetate during nonketotic hyperglycemia [7]. Depletion of acetate in turn causes insufficient synthesis of acetylcholine, decreased GABA and acetylcholine along with intracellular acidosis, and low energy stores in the basal ganglia might be responsible for the chorea observed in nonketotic hyperglycemic states [7]. A similar explanation was presented in another study which found that decreasing GABA concentrations decrease the level of thalamic inhibition of the basal ganglia, which might explain hyperglycemia-induced chorea [4]. This hypothesis fails to provide

an adequate explanation for the persistence of chorea after the initial glucose abnormality has been corrected. Another alternative explanation is hypoperfusion of the basal ganglia leading to metabolic abnormalities from either ischemia, hyperglycemia, or a combination of these might be a possible explanation for the chorea seen from hyperglycemia [3]. Some older literature also implicated possible upregulation of dopamine receptors and dopamine hypersensitivity as a possible explanation for chorea from hyperglycemia [8].

Current standard treatment measures have included achieving glycemic control as well as simultaneous use of neuropsychiatric medications such as haloperidol. One study indicated resolution of chorea within 1 week of achieving better glycemic control in only 1 out of 7 cases identified with persistence of chorea in the other 6 remaining cases, and resolution of chorea in these remaining cases was achieved with the use of dopamine antagonistic agents such as haloperidol, quetiapine, and reserpine [2]. In general, based on a review of the current literature, the average duration of chorea prior to patient evaluation ranged from 3 days to over 1 month [7], and after initiation of treatment, either resolution or improvement of chorea occurred in 4 to 6 weeks on average (range of 3 days at the minimum to 5 years in the longest instance) [3].

In our patient, along with insulin for glycemic control, haloperidol was initiated with slight improvement in her symptoms. Though symptoms continued to improve at subsequent follow-up visits with neurology, her chorea persisted at 3 months after initial presentation. The course of our patient appears similar to the case presented by Saleh et al, and we agree with their postulation of a possible longer natural course in cases of bilateral hyperglycemic nonketotic chorea and without significant noticeable basal ganglial changes on imaging compared with the most rapid resolution that is seen in most cases of unilateral hyperglycemic chorea.

Learning Points

- Hyperglycemia was considered a possible cause of acute onset bilateral chorea.
- Basal ganglial abnormalities are not always seen in cases of hyperglycemia chorea, and the absence of such findings should not discount the diagnosis.
- Bilateral hyperglycemic nonketotic chorea might have a longer natural course to achieve improvement/resolution compared with cases of hemichorea secondary to hyperglycemia.

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Informed Patient Consent for Publication

Informed consent was obtained directly from the patient.

Data Availability Statement

Data sharing is not applicable to this article, as no datasets were generated or analyzed during the current study.

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