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Short communication

Hyperglycemic chorea/ballism ascertained over 15 years at a referral medical center

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ABSTRACT

Objective: To describe chorea/ballism triggered by a hyperglycemic event.
Methods: We used the electronic records system at Mayo Clinic—Rochester to identify patients diagnosed with chorea or ballism from January 1st, 2000 through December 31st, 2014. Each record was reviewed to confirm chorea/ballism. From these cases we selected those that developed chorea/ballism within a month after a hyperglycemic episode (blood glucose >300 mg/dL). Clinical, laboratory, and imaging findings were analyzed.
Results: Of the 596 chorea cases, we identified 7 patients (5 women) whose chorea was preceded by a hyperglycemic episode (range 3—30 days) during 15 years of surveillance, including new-onset diabetes in four cases. Median age was 80 years (range, 53—86). The chorea/ballism was unilateral in 6/7 cases and half of these unilateral cases had contralateral putamen T1-hyperintensity on brain MRI. After glucose correction, the chorea resolved within one week without recurrence in only one case. Among the 6 cases with persistent chorea, it was controlled with dopamine blocking/depleting medications.
Conclusions: Chorea triggered by hyperglycemia is a rare complication of diabetes, with only seven cases identified at our tertiary medical center during 15 years of surveillance. This comprised about 1% of all chorea cases at our center during this time. Hyperglycemic chorea primarily developed in later life, with new-onset diabetes in the majority (4/7). Although MRI putamen T1-hyperintensity is reportedly typical, it was only seen in 3/6 cases. This MRI appearance may be mistaken for a hemorrhagic stroke, given the usual unilateral presentation. The chorea was controlled with dopamine blocking/depleting medications.
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1. Introduction

Acquired, adult-onset chorea/ballism that is unrelated to medications or stroke has a relatively limited differential diagnosis, such as chorea associated with circulating lupus anticoagulant, JAK2-polycythemia vera or a paraneoplastic syndrome (e.g., CRMP-5).

A distinctive syndrome of chorea/ballism developing during or shortly after an episode of non-ketotic hyperglycemia may be initially overlooked or misdiagnosed [1–4]. This is often associated with T1 MRI hyperintensity of the striatum/putamen [1,2,4,5], sometimes misinterpreted as striatal hemorrhage [6,7]. The presentation of the chorea/ballism may be dramatic, with the chaotic, hyperkinetic movements impairing normal motor function. The purpose of this study is to ascertain the frequency of this uncommon condition at a large referral center (Mayo Clinic - Rochester), and characterize the demographics, treatment responses and outcomes.

2. Methods

We used the electronic records system at Mayo Clinic—Rochester to identify patients diagnosed with chorea or ballism during a 15 year epoch, from January 1st, 2000 through December 31st, 2014. This would have included reviews of all in-patient and outpatient evaluations from the entire Mayo Clinic database. Each medical record was individually reviewed to confirm chorea/ballism. We then selected those cases where chorea/ballism was time-locked to hyperglycemic episodes (i.e., within 30 days; blood glucose >300 mg/dL). None of these cases were previously described in the literature.

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3. Results

During the 15 year study period, 740 Mayo Clinic patients matched our search criteria. After chart review, 596 cases were confirmed as having chorea/ballism. We then identified patients where chorea/ballism subacutely developed in association with a discreet episode of marked hyperglycemia (glucose >300 mg/dL), totaling seven cases. These seven cases reflected approximately 1% of all Mayo Clinic chorea cases during the 15 years of study. Of the seven patients, four were also given a new diagnosis of type 2 diabetes mellitus (DM2) at the time of this episode. Table 1 shows the glucose values at the time of the hyperglycemic episode. Two patients, both with known diabetes, had glucose levels of 300–599 mg/dL (one with HbA1c >17%), whereas the remaining five had glucose levels greater than 600 mg/dL. One patient presented in nonketotic hyperglycemic hyperosmolar coma. Other metabolic/systemic causes were excluded. A complete blood count, electrolyte panel, creatinine level, liver function tests, erythrocyte sedimentation rate, and thyroid stimulating hormone level were unremarkable in all seven patients. CRP, ANA, rheumatoid factor, ANCA, antiphospholipid antibodies, anti-streptolysin O, anti-DNAase B, syphilis, Lyme, HIV, hepatitis B and C, homocysteine, ceruloplasmin, and protein electrophoresis were checked in some, and were negative. CSF studies, when obtained (2 cases), were unremarkable. All of these patients had brain imaging, which did not disclose any relevant clues.

All of the seven affected patients were white-Caucasian of European heritage; five were female. As shown in Table 1, these patients tended to be elderly, with the median age, 80 years (range 53–86); four patients were over 80 years old (3 of these 4 had a new diagnosis of diabetes). Most patients were not obese, with the BMI <25 kg/meter-squared in four patients; mild obesity was present in the remaining three patients, with BMI values of 30–32. The most common comorbidities were hypertension (5/7), hyperlipidemia (4/7), hypothyroidism (3/7), depression (2/7), coronary artery disease (2/7), congestive heart failure (2/7), and atrial fibrillation

Table 1
Summary of patients.

Patient	1	2	3	4	5	6	7
Age	86	80	83	77	53	84	68
Gender	F	F	M	M	F	F	F
BMI	24.7	19.4	31.6	30.4	24.1	22.9	31.4
Admission glucose	710	>600 ^	>600	400–599	305 HbA1c >17%	982	1004
Type 2 DM	New onset	Chronic	New onset	Chronic	Chronic	New onset	New onset
Comorbidities	Possible restless legs syndrome	DM2, HL, HTN, hypothy-roidism, depr/anx.	HL, HTN, CAD, CHF, A-fib, depr.	HTN, DM2, A-fib	DM2, HL, HTN, hypothyroid-ism, breast cancer	HL, HTN, CAD, CHF, CKD, hypothyroid-ism	Not Available
Onset of chorea/ballism	<2 week onset	After coming out of HHN coma.	Over 3 days; over 2 weeks for recurrence.	Over 1 week	Over 1 month	Over 6 days. Starting 3 weeks after event.	Over 5 days
Chorea	RUE moderate, RLE mild	Moderate in legs (L > R), mild in arms and trunk	LLE severe, LUE moderate	RLE moderate, RUE mild, R face mild	LUE and L face	RUE, RLE	LUE
Severity	Impacted her functioning	Greatly limited ADL	Unable to perform ADL	Cannot drive, but can walk and use arms	Unknown	Great distress and discomfort	Severe, slapping herself in face
MRI available	Yes	Described in report (no images)	Yes	Yes	Described in neurologist's note (no images)	No (not performed due to AICD)	Yes
T1	Normal	Normal	Hyperin-tense in right putamen	Hyperintense in left putamen	Hyperintense in right putamen	–	Normal
T2	Hypoin-tense in both basal ganglia	Normal	Hyperin-tense in right putamen	Hypointense in left putamen	Normal	–	Normal
Other imaging comments	–	Limited sequences performed	Initially diagnosed as hemorrhage	Initially diagnosed as hemorrhage	Initially diagnosed as hemorrhage	Head CT was unremark-able	–
Treatment	Quetiapine partially effective	Lorazepam ineffective, it gave excessive sedation. Haloperidol effective.	Self-resolved within 1 week, then recurred 2 weeks later. Haloperidol effective.	Risperidone partially effective, so reserpine was added.	Clorazepate, gabapentin, carbamaze-pine were ineffective. Fluphenazine partially effective, so reserpine was added.	Haloperidol effective. She died 15 months later.	Self-resolved within 1 week of glucose correction.
Last follow up visit	5 years	3 months	1 month	2 months	2 years	15 months	11 months
Outcome	Improved chorea on quetiapine.	Minor chorea on haloperidol, doing well.	Minor chorea on haloperidol, doing well.	No follow up after adding reserpine.	Chorea controlled, but recurred when neuroleptic was weaned. She developed tardive dyskinesia and drug-induced parkinsonism	Chorea was controlled on haloperidol until death 15 months later (cause not investigated but pancreatic and renal masses were present).	She died from pancreatic cancer 11 months after the hypergly-cemic event. Cancer diagnosis was made 1 month after the hypergly-cemic event.

Abbreviation legend: HHN (Hyperosmolar hyperglycemic nonketotic), DM2 (type 2 diabetes mellitus), HL (hyperlipidemia), HTN (hypertension), CAD (coronary artery disease), CHF (congestive heart failure), a-fib (atrial fibrillation), depr/anx (depression/anxiety), CKD (chronic kidney disease), RUE/RLE/LUE/LLE (right/left upper/lower extremity), ADL (activities of daily living), AICD (automatic implantable cardioverter-defibrillator).

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