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Case Reports

Persistent hemichoreoathetosis-hemidystonia after nonketotic hyperosmolar hyperglycemia

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A B S T R A C T

Most commonly, hemichorea associated with nonketotic and ketotic hyperglycemia resolves with normalization of blood glucose. Herein, we present a case of hyperosmolar hyperglycemic left hemichoreoathetosis-hemidystonia that has persisted for over 1 year. The subject presented to the emergency room with dysarthria and manifested left hemichoreoathetosis-hemidystonia within 36 h of admission. Initial computed tomography (CT) showed hyperdensity in the right putamen and left caudate. Magnetic resonance imaging (MRI) showed T1 hyperintensity within the right putamen. Failure to detect these classic imaging abnormalities during hospitalization resulted in a delayed etiologic diagnosis. Modest symptomatic improvement in the severity of hemichoreoathetosis-hemidystonia has been noted with low dose tetrabenazine.

1. Case report

An 82-year-old right-handed female presented to the emergency room (ER) with "dysarthria" of approximately 8 h duration per notes from the treating ER physician. Initial laboratory studies showed hyperglycemia (serum glucose = 661 mg/dL, range = 70–110 mg/dl), acute on chronic kidney insufficiency (creatinine = 3.21 mg/dl, range = 0.60–1.30 mg/dl), hyponatremia (sodium = 126 mmol/L, range = 135–145 mmol/L), anemia (hematocrit = 33.2 %, range = 37.0–47.0 %), normal carbon dioxide (22 mmol/L, range = 21–32 mmol/L), anion gap = 12 mEq/L (range = 6–12 mEq/L), and markedly elevated hemoglobin A1C (>14.0). Venous blood gas was normal: pO2 = 26 (range = 25–29 mmHg), pCO2 = 45 (range = 41–54 mmHg), HCO3 = 23.8 (range = 22.0–26.0 mmol/L), and pH = 7.37 (range = 7.31–7.41). Osmolality was markedly elevated at 327 mOs/kg (range = 285–295 mOs/kg). β-hydroxybutyrate level was mildly elevated at 1.483 (range = 0.019–0.269 mmol/L). Urinalysis showed trace ketones. The subject was hypertensive (176/103 mm Hg) upon admission to the ER. Unenhanced computed tomography (CT) of the head, which was obtained approximately 9 h after onset of neurological dysfunction and 1 h after admission to the ER, showed no evidence of an acute infarction, mild-to-moderate cortical atrophy, and moderate angiopathy. In the radiology report, no mention was made of hyperdensity in the right putamen and left caudate (Fig. 1A). CT angiogram showed no high-grade stenosis of the extracranial vasculature, high-grade stenosis of the proximal P2 segment of the right posterior cerebral artery, and a right dominant vertebral artery with hypoplastic left V4 segment.

Hyperglycemia was corrected with insulin and hydration to 317 mg/dl within 12 h of admission, and 179 mg/dl within 24 h of admission. Sodium was corrected to 139 mmol/L within 32 h of admission. Sodium was not assessed in the interval between the admission value of 126 mmol/L and the value of 139 mmol/L obtained 32 h later. Osmolality was not repeated during the hospitalization. Magnetic resonance imaging (MRI) of the brain obtained 48 h after the ER CT showed slight T1 hyperintensity in the right putamen and no evidence of a recent ischemic or hemorrhagic stroke (Fig. 1B). There was no evidence of osmotic demyelination syndrome, or more specifically, central pontine myelinolysis, on CT or MRI. Involuntary movements progressed to affect the left face, arm, and leg over the course of 72 h while hospitalized. Information from family suggests that the initial "dysarthria" was likely due to dystonia and chorea affecting left-sided oral-buccal-lingual structures. The subject was initially treated with low-dose clonazepam with minimal benefit.

The involuntary movements stabilized upon discharge from the hospital and remained largely unchanged over a period of 2.5 months. Left hemichoreoathetosis-hemidystonia affecting the face, arm and leg was noted on initial examination in my outpatient movement disorders clinic (Video – 2.5 months after onset). The face and arm were more severely affected than the leg. There was minimal effect on gait, swallowing or speech. There was no loss of motor power. There was modest improvement with tetrabenazine (12.5 mg PO TID, Video – 6 months after onset, 4 h after last dosage of tetrabenazine). Higher dosages of tetrabenazine were not tolerated due to sedation. The movement disorder has remained largely unchanged a year after onset. The subject

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reports that if she misses a dosage of tetrabenazine, the severity of her involuntary movements is like that present at 2.5 months after onset. She has not been interested in pursuing alternative pharmacological or surgical treatments. Moreover, use of D2 receptor blockers has been avoided due to the risk of tardive dyskinesias and worsening control of diabetes.

2. Discussion

Diabetic ketoacidosis (DKA) is characterized by moderate elevation of serum glucose (>250 mmol/L), anion gap > 10 mEq/L, variable osmolality, blood pH < 7.30, and elevated urine and serum ketones. In contrast, nonketotic or hyperosmolar hyperglycemia is associated with higher elevations of blood glucose (>600 mmol/L), serum osmolality > 320 mOsm/kg, small or absent serum and urine ketones, and variable anion gap. β-hydroxybutyrate, the most abundant ketone in DKA, has been used as a sensitive and reliable diagnostic marker [1,2] in the ER and intensive care unit. The threshold values for DKA range from 1.5 mmol/L to 3.5 mmol/L [3]. Hence, our subject's clinical profile was most consistent with a diagnosis of nonketotic, hyperosmolar hyperglycemia. In the strictest sense though, the use of "nonketotic" is a misnomer given the presence of trace ketones and mildly elevated β-hydroxybutyrate as seen in our case.

Initially reported in nonketotic hyperosmolar hyperglycemia with marked elevations of glucose, unilateral choreoathetosis or ballism has also been associated with modest elevations of glucose (250–500 mg/dl) and variable degrees of ketosis. The involuntary movements typically resolve with normalization of serum glucose but, in rare cases, may persist for months or even years [4,5]. In one report, hemichorea-hemiballism affecting the arm and leg developed with hemoglobin A1C of 17.0 %, serum glucose of 296 mg/dl, and osmolality of 296 mOsm/L, and persisted for 10 months after normalization of glucose [6]. The condition may be more common in women [5–7], Asians and the elderly, and can present with variable combinations of positive [chorea, dystonia [8], and athetosis] and negative motor manifestations [9]. Occasionally, involuntary movements are bilateral.

Imaging abnormalities usually resolve within days or weeks of glucose normalization but, in some cases, may persist for months or even years [9]. Given the common use of ER CT to exclude a hemorrhagic stroke in patients with acute onset of neurological dysfunction, hyperintensity of the striatum (putamen +/− caudate) is often the first imaging abnormality noted and should immediately point out the correct diagnosis. Our patient's MRI was delayed during transition through the ER but did show T1 hyperintensity, the most consistent finding of the disease. Some patients also show other MRI abnormalities including T2 hypointensities [10].

Certain authors have deemed this disorder a diabetic striatopathy [9]. Based on post-mortem pathological analyses and functional imaging studies including proton MR spectroscopy, it has been suggested that the CT and T1 MRI imaging abnormalities are due to regional energy depletion with increased lactic acid, acetate, and lipids, and decreased N-acetylaspartate and creatine [11]. Gemistocytes have been seen in post-mortem tissue from the affected striatum [11].

This case report points out and underscores several important issues relevant to the diagnosis and treatment of acute dyskinesias in the setting of diabetes and hyperglycemia. First, the presence of small amounts of ketones or mild elevations of β-hydroxybutyrate should not confound the correct clinical diagnosis of nonketotic hyperglycemia. Second, careful interpretation of CT and MRI imaging is critical. In this case, the CT and MRI abnormalities characteristic of nonketotic hemichorea were not recognized during the subject's hospitalization and were only detected by retrospective review of imaging 2.5 months later. Third, in addition to chorea/ballism, clinical manifestations may include other abnormal movements such as athetosis and chorea. Fourth, this movement disorder may persist for months or years after correction of hyperglycemia. Lastly, central to patient management is correction of hyperglycemia, along with co-existent metabolic abnormalities including hyponatremia and hyperosmolality. It is not known if the time course of correcting hyperglycemia, and commonly associated metabolic, renal, and cardiovascular abnormalities (i.e., hyponatremia, hyperosmolality, volume depletion, renal insufficiency, and hypertension) is associated with long-term persistence of hemichorea. In general, rapid correction of osmolality and glucose levels are associated with lower mortality and more favorable neurologic outcomes in all cases of hyperosmolar hyperglycemia [12]. However, slower corrections of sodium may be advisable in patients with co-morbid hyponatremia. Acute management of acute diabetic striatopathy and associated metabolic and multi-system dysfunction demands further study.

3. Financial disclosures

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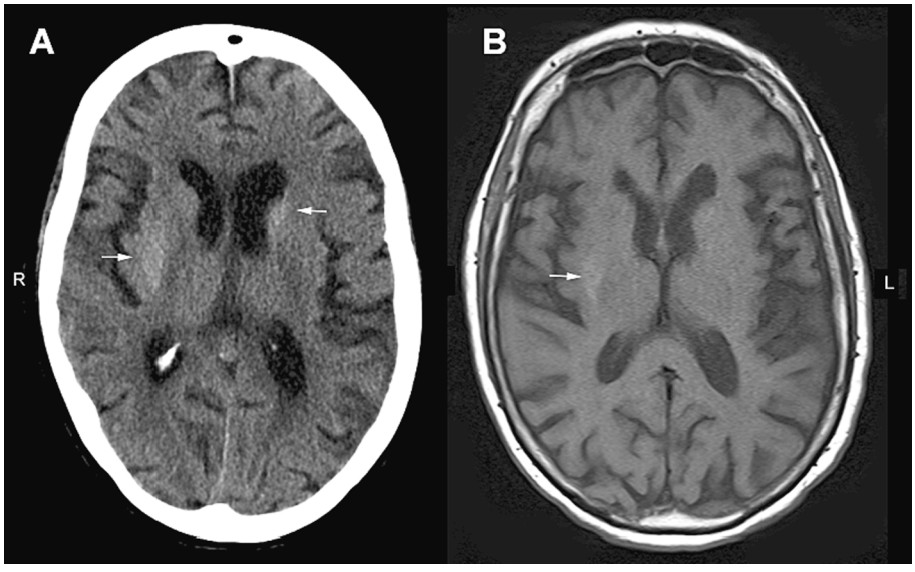

Fig. 1. Brain CT (A) obtained during emergency room visit and 9 h after onset of neurological dysfunction shows hyperintensity in the right putamen and left caudate. Brain MRI (B) obtained 48 h after the CT shows T1 hyperintensity in the right posterior putamen. R, right. L, left.

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Ethical statement

The subject of this case report provided written informed consent for publication of her clinical history, radiographic images, and Video.

Declaration of Competing Interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.prdoa.2023.100221.

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