CASE REPORT

Hyperglycemia-associated Hemichorea-hemiballism: The Spectrum of Clinical Presentation

Phong Ching Lee, Peng Chin Kek and Abel Wah Ek Soh

Abstract

Hyperglycemia rarely manifests as hemichorea-hemiballism (HH), which is characterized by simple partial motor seizures. One of the difficulties in the management of hyperglycemia-induced HH is the failure to recognize this entity due to its relatively uncommon presentation. We herein present a case series of hyperglycemia-associated dyskinesias, highlighting the different possible clinical presentations of this entity. Both hyperglycemia and hyperosmolality are probable predisposing factors, while ketoacidosis has a protective role in preventing the dyskinesias. One of our patients had ketotic hyperglycemia leading to HH, a previously unreported finding. Early recognition of this entity is crucial as prompt glycemic control leads to the resolution of symptoms and signs.

Key words: diabetes, hyperglycemia, hemichorea-hemiballism


Introduction

Hyperglycemia is a rare cause of hemichorea-hemiballism (HH). We herein present a case series examining the various clinical circumstances in which HH can present in individuals with diabetes. We also review the available literature on this phenomenon with respect to its pathogenesis, diagnosis and treatment.

Six patients with diabetes mellitus presented with HH or hemifacial spasm between 2004 and 2013 (Table) to the Singapore General Hospital. All patients presented with hyperglycemia and involuntary movements. Five patients were known to have poorly controlled diabetes, but one had newly diagnosed diabetes. The data from all six patients are shown in Table, and three of the cases are described in more detail below to highlight the different clinical presentations of this entity.

Case Reports

Case 1: Poorly controlled diabetes presenting with hemichorea-hemiballism secondary to non-ketotic hyperglycemia

A 72-year-old Chinese man presented in August 2007 with a two-day history of intermittent involuntary movements of his right arm with each episode lasting approximately 30 seconds. He had poorly controlled insulin-treated type 2 diabetes (diagnosed 7 years prior) complicated by nephropathy and dialysis-dependent end-stage renal failure. The patient noticed that his right arm was “shaking” involuntarily and described having tremors on his right hand. He was otherwise fully alert and responsive. There were no focal neurological signs on the clinical examination.

The initial biochemical data showed an elevated urea level of 11.3 mmol/L and serum creatinine concentration of 318 μmol/L. The patient’s serum glucose level was elevated at 57.7 mmol/L with a corrected serum sodium concentration of 141 mmol/L. The calculated effective serum osmolality was 310 mmol/kg. The HbA1c was 13.4%, the urine ketones were negative, and the calcium and magnesium levels...
47.1 mmol/L with a corrected serum sodium concentration of 22.3 mmol/L. The calculated effective serum osmolality was 297.5 mmol/kg. The HbA1c was >17.6% and CT of the brain did not reveal any intracranial pathology.

The patient was diagnosed with type 2 diabetes mellitus complicated by a hyperglycemic hyperosmolar state and was treated aggressively with intravenous fluid replacement and insulin therapy. Following the resolution of the patient’s hyperglycemia, there were no recurrences of seizures.

Case 3: Ketotic hyperglycemia and hemichorea-hemiballism

A 58-year-old Malay lady presented in December 2011 with witnessed involuntary right arm jerks followed by stiffening of her whole body. The jerking lasted for several minutes. She reported a preceding episode 5 days prior to presentation. There was no loss of consciousness or generalized seizures. The patient had insulin-treated type 2 diabetes (diagnosed 10 years prior to this presentation) with poor glycemic control.

On examination, the patient was lethargic and clinically dehydrated but was still conscious and alert. The neurological examination was unremarkable. The biochemistry results showed a raised urea level of 13.7 mmol/L and creatinine concentration of 191 μmol/L. The patient’s serum glucose level was elevated at 55.7 mmol/L with a corrected serum sodium concentration of 156 mmol/L. The calculated effective serum osmolality was 335 mmol/kg. The HbA1c was >17.6% and CT of the brain did not reveal any intracranial pathology.

The patient was diagnosed with ketotic hyperglycemia and hemichorea-hemiballism.
rum osmolality was 293.7 mmol/kg. The patient’s serum calcium and magnesium levels were normal and HbA1c was 16.3%.

CT of the brain did not reveal any intracranial abnormality. Magnetic resonance imaging (MRI) of the brain showed scattered non-specific T2 hyperintensities in bilateral subcortical white matter. The patient did not have any further seizures after receiving appropriate fluid replacement therapy and correction of her metabolic disorder by intravenous insulin therapy.

Discussion

Hyperglycemia is most commonly associated with HH, although generalized tonic-clonic seizures may also occur (1). The cases described above highlight that HH can occur in both patients with well-established diabetes mellitus presenting with hyperosmolality and also as the initial presenting symptom of diabetes mellitus (1, 2). In a previously published case series of 21 patients with non-ketotic hyperglycemic induced seizures, more than half (61.9%) of the patients had never been diagnosed as having diabetes mellitus (3).

Pathogenesis

HH may be induced by non-ketotic hyperglycemia with hyperosmolality and dehydration, although the pathogenesis is not completely understood. The hyperosmolar gradient between the intra- and extracellular neuronal environments can cause intracellular dehydration, thereby inducing seizures (4). However, the contribution of hyperosmolality in the pathogenesis of HH is still unclear as demonstrated by the wide range of serum osmolality seen in our patients (from 293.7 to 335.1 mmol/kg).

We postulate that the magnitude of hyperglycemia plays an important role, given that 4 out of 6 of the patients in our series had a glucose level >40 mmol/L on admission. One hypothesis is that hyperglycemia increases the metabolism of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter in the central nervous system (2). This results in decreased GABA levels and a reduction of the epileptic seizure threshold. Of note, Case 4 in our series presented with a serum glucose of 22.9 mmol/L. This suggests that it is not just the degree of hyperglycemia alone that causes HH, and the underlying pathogenesis is likely multifactorial.

Most of the previously published literature has focused on non-ketotic hyperglycemia and HH; however, there have been no published reports thus far describing HH in ketogenic hyperglycemia. Ketone bodies increase GABA synthesis and have an almost immediate protective effect against epilepsy (5). Interestingly, Case 3 from our series illustrated that HH may still occur in the presence of ketosis without biochemical acidosis. Another hypothesis suggests that intracellular acidosis elevates the GABA levels, thus increasing the seizure threshold (2). It is possible that acidosis, rather than ketosis, plays a pivotal role in protecting against HH in diabetic ketoacidosis and hence seizures may still occur in patients presenting with ketogenic hyperglycemia.

Diagnosis

One of the difficulties in the management of hyperglycemia-induced HH is failure to recognize the association due to its relatively uncommon presentation. The diagnosis becomes even more complicated in cases with no previous history of diabetes, with HH being an initial presentation of diabetes mellitus. An early diagnosis would decrease the associated morbidity and mortality in individuals who present with a hyperglycemic hyperosmolar state and HH. Hence, the serum glucose should always be checked in patients presenting with HH.

Electroencephalography (EEG) has not been very useful and only focal slow wave abnormalities or asymmetrical activity may be present over the involved region (6). In some cases, periodic lateralized epileptiform discharges on the EEG correlated with clonic contractions (7) whereas no paroxysmal activity is noted in others (8). Three patients in our series had EEGs performed; all showed slow wave abnormalities suggestive of diffuse encephalopathy.

High signal changes over the basal ganglia region on T1-weighted MRI has also been reported in hyperglycemia-associated HH (9). The MRI image of Case 4 is shown in Figure below and demonstrates the characteristic basal ganglial T1 hyperintensity on MRI.

Treatment

Hyperglycemia-associated HH is generally resistant to antiepileptic drugs but typically resolves spontaneously with the resolution of hyperglycemia (2). Hyperglycemia should be treated with intravenous insulin and hydration with close glucose and electrolyte monitoring; furthermore, potassium should be replaced as necessary.
Recurrence of seizures

The maintenance of good glycemic control is important as patients with poor control (HbA1c >9%) on follow-up are at a higher risk of seizure recurrence (44.8% vs. 8.3%) (10). Following the normalization of hyperglycemia and maintenance of good glycemic control, none of the patients in our series had recurrence of HH.

Hyperglycemia rarely manifests as HH, and it may be difficult to identify hyperglycemia-induced seizures, particularly in individuals with previously undiagnosed diabetes mellitus. Our case series has demonstrated the various ways this entity can present, including in ketotic hyperglycemia, and the importance of clinical recognition as the seizures tend to resolve with the normalization of blood glucose levels.

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References