

## CASE REPORT

## Hyperglycemia-Induced Involuntary Movements: What You Should Know

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### ABSTRAK

*Hemichorea-hemiballismus (HC-HB) adalah gangguan pergerakan tidak terkawal yang melibatkan anggota sebelah badan. Terdapat banyak faktor etiologi yang dijumpai, termasuk strok, jangkitan, dan barah. Walaubagaimanapun, HC-HB yang disebabkan oleh hiperglisemia akut jarang dijumpai. Kami membentangkan dua kes HC-HB yang disebabkan oleh hiperglisemia. Kes-kes yang dibentangkan di sini menunjukkan bahawa HC-HB boleh menjadi antara gejala gangguan neurologi disebabkan diabetes yang tidak dikawal dan boleh dirawat sepenuhnya melalui rawatan bagi hiperglisemia.*

*Kata kunci: chorea, diabetes mellitus, diskinesia, gangguan pergerakan, hiperglisemia, neoplasma, strok*

### ABSTRACT

Hemichorea-hemiballismus (HC-HB) is a movement disorder characterized by involuntary movements involving limbs on one side of the body. Many etiological factors were identified and these included stroke, infection, and neoplasm. However, acute hyperglycemia-induced HC-HB is less well known. We present two cases of non-ketotic hyperglycemia-induced HC-HB. The cases depicted here illustrate that HC-HB can be the sole presentation from among a variety of neurological manifestations of poorly controlled diabetes which can be easily reversed when hyperglycemia is corrected.

**Keywords:** chorea, diabetes mellitus, dyskinesias, hyperglycemia, movement disorders, neoplasm, stroke

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## INTRODUCTION

Hemichorea (HC) is characterized by involuntary rapid and random irregular movements that are not patterned and may be confined to one side of the body, while hemiballismus (HB) is often perceived as a severe type of chorea. Several disease entities other than diabetes can cause HC-HB. Focal lesions from ischemic or hemorrhagic strokes should be considered in elderly patients. Other causes include infection and neoplasm; or a diffuse systemic process such as systemic lupus erythematosus, Wilson's disease and thyrotoxicosis (Block et al. 2006). Although this type of involuntary movement related to hyperglycemia has been described in many case reports, there is paucity of literature in emergency medicine. We report two cases of HC-HB syndrome secondary to hyperglycemia which presented to our Emergency Department (ED).

## CASE REPORT

### *Case 1:*

A 65-year-old male presented with involuntary movements of his left upper and lower limbs of three weeks duration. The symptoms gradually worsened until he had difficulty to walk. His past medical history included poorly controlled diabetes mellitus (DM) and hypertension. He was on subcutaneous injections of biphasic isophane insulin (Mixtard®) 8 units twice daily which he often missed, tablet felodipine 5 mg per day, and atorvastatin 40 mg every night.

There was no history of exposure to any neuroleptic drugs. Neither he nor his family members had any history of movement disorders.

Upon arrival, he was alert and oriented to time, place and, person, and looked dehydrated. There was HC-HB movements of his left upper and lower limbs. The muscle tone, strength, reflexes, and sensation were normal. He occasionally tried to stop these movements using his contralateral hand but the movements were only briefly controlled. Cranial nerve examination was normal and there were no signs of cerebellar dysfunction. His random blood glucose level was 44 mmol/L, corrected sodium concentration was 131 mmol/L, and measured serum osmolality was 285 mOsm/L. Venous blood gas analysis showed pH 7.2, pCO<sub>2</sub> 29.0 mmHg, HCO<sub>3</sub><sup>-</sup> 13.2 mmol/L. No ketones were detected in his urine. The renal profile, liver function test, and other electrolytes were within normal range. Glycated hemoglobin A was 18.2%. The plain computer tomography (CT) of his brain showed cerebral atrophy and no focal parenchymal lesion.

He was started on intravenous fluid for rehydration followed by intravenous insulin infusion. His blood glucose was in the normal range after approximately 10 to 12 hours of admission. He claimed that the involuntary movements had reduced in frequency within a few hours of the initiation of treatment. After two days of admission, the HC-HB had completely disappeared. No other medications were started to suppress the involuntary movements. In the ward, he developed

right forearm thrombophlebitis and blood culture and sensitivity showed methicillin-sensitive *Staphylococcus aureus* (MSSA) bacteremia.

#### Case 2:

A 55-year-old male presented to ED with acute onset of involuntary movements of his right upper and lower limbs three days prior to admission. The movements began abruptly and gradually recurred more frequently. He also complained of weakness of his right hand where he could not fully grip an object. The patient had loss of appetite in the preceding 10 days. He was discharged a month ago from our hospital for pyelonephritis with *Klebsiella sp.* bacteremia. During the current presentation, he had no history of fever or consumption of any neuroleptic drugs. He had underlying diabetes mellitus (DM), hypertension, ischemic heart disease, and end-stage kidney disease. His last hemodialysis was the day before presentation.

On examination, he was conscious and oriented. He looked lethargic and dehydrated. On neurological examination, there was HC-HB of his right upper and lower limbs. Muscle tone was normal throughout. The strength of his right upper and lower limbs was four over five. The sensation over his right upper and lower limbs were diminished, and the deep tendon reflexes of his right upper and lower limbs were depressed. His cranial nerves were normal and there were no signs of cerebellar dysfunction. Investigations on admission revealed a random blood glucose of 53

mmol/L. Venous blood gas analysis showed pH 7.2, pCO<sub>2</sub> 53.7 mmHg, HCO<sub>3</sub><sup>-</sup> 19 mmol/L. Serum ketone was 1.6 mmol/L. Corrected sodium concentration was 141 mmol/L, while the calculated serum osmolality was 363 mOsm/L. The white cell count was 14.7 x 10<sup>9</sup>/L with 93% neutrophils predominant; hemoglobin 7.9 g/dL, platelet 272 x10<sup>9</sup>/L. Potassium was 4.2 mmol/L, urea was 22.1 mmol/L, and creatinine was 727.8 μmol/L. The plain brain CT showed a small hypodense lesion in the left external capsule in keeping with a lacunar infarct and encephalomalacic changes of the left ventricle.

He was treated for hyperosmolar-hyperglycemic state (HHS). The patient was started on intravenous fluid for rehydration and the response was carefully monitored by the ultrasound of inferior vena cava diameter. He was then started on intravenous insulin infusion. His glucose normalized over the next 10 to 15 hours. He was also referred to the nephrology unit for his regular hemodialysis. The involuntary movements completely disappeared after three days. No other medications were started to suppress the movements. He had a prolonged stay due to sepsis secondary to a renal abscess which was contributed by the previous infection during his last admission.

## DISCUSSION

It is uncertain why only a small number of hyperglycemic patients develop HC-HB. While both of our patients were males, previous reported cases involved

women with a mean age of 71 years (Oh et al. 2002). The Asians seemed to be more predisposed to HC-HB (Lin et al. 2001), and this suggests a possible genetic predisposition. In Malaysia, 70% of diabetics develop neuropathy (Ministry of Health Malaysia, 2013). A study by Rahmah et al. (2011) showed that the prevalence of good clinical control among elderly diabetics was still low and this predisposed them to a higher risk of diabetic complications.

The involuntary movements could begin acutely, and often worsen over several days. Most of the published case reports used the terms hemichorea or hemiballismus as symptoms were described to occur on one side of the body; involving the upper and/or the lower extremities, with occasional facial involvement (Oh et al. 2002). Nevertheless, Cosentino et al. (2016) reported that 15% of their cohort had bilateral involvement.

Various theories were proposed to describe the basic pathophysiology leading to basal ganglia dysfunction and development of hyperglycemia associated HC-HB. Metabolic diseases such as DM provide the basis of blood-brain-barrier dysfunction, with a synergistic effect during hyperglycemic crisis. Previous studies have demonstrated that acute and chronic hyperglycemia may induce a decrease in regional cerebral blood flow that results in ischemia. Hypoxic-ischemic damage induces metabolic derangements that can further worsen clinical manifestations (Cheema et al. 2011).

Ifergane et al. (2001) postulated that in non-ketotic hyperglycemia, the

hypertonicity causes a shift of Krebs cycle toward the anaerobic pathway with consequent depletion of the neuroinhibitory transmitter gamma aminobutyric acid (GABA), thereby increasing the pallidal activity with resultant dyskinesia. On the contrary, patients with diabetic ketoacidosis (DKA) rarely develop HC-HB as ketones become the energy source and GABA can be resynthesized.

The modality of choice for assessing suspected non-ketotic hyperglycemic HC-HB would be the magnetic resonance imaging (MRI). Patients with normal CT findings have had abnormal MRI results, according to Nagai et al. (1995). Advanced imaging analysis, in one study, demonstrated that the basal ganglia in patients with HC-HB are hyperintense on the T1-weighted brain magnetic resonance imaging (MRI) and this change was reversible after clinical improvement in hyperglycemia and chorea (Oh et al. 2002), suggesting that hyperglycemia may induce reversible focal ischemia (Sung & Lu 2007). However, this radiology modality may not be widely available and costly. Therefore, CT can be utilized more by the emergency doctors. No MRI was carried on our patients during admission. This is likely because the hyperkinesia resolved dramatically after control of the hyperglycemia.

While our first patient's brain CT scan did not show signs of acute ischemia, the CT of our second patient showed lacunar infarction. The HC-HB in our second patient was probably due to combination of infarct and HHS. The cornerstone of the treatment in both our patients is aggressive glucose

management. The management of our second patient was slightly more complex as the patient had underlying end stage renal failure, ischemic heart disease, and initial blood investigations demonstrated HHS. Therefore, fluid resuscitation was limited by his underlying illness. Both of our patients were started on insulin infusion. The involuntary movements gradually reduced in frequency after a few hours of glucose normalization and completely resolved after two to three days of admission. Nevertheless, Roy et al. (2016) reported a case of irreversible HC-HB despite achieving blood sugar control and it was postulated that the prolonged and untreated course of hyperglycemia may have resulted in true infarction with an irreversible neurological syndrome.

In the ED, it is critical to identify hyperglycemia as a reversible cause of involuntary movements to prevent early unnecessary etiological workup, while preventing progression to life-threatening conditions such as HHS and DKA. Besides that, a proper diagnosis of hyperglycemia induced HC-HB can avoid unnecessary initiation of anti-epileptics especially phenytoin to suppress the jerky movements in cases where epileptic seizures are mistakenly diagnosed. This is because, involuntary movements secondary to hyperglycemia is refractory to phenytoin as phenytoin may inhibit insulin secretion and worsens hyperglycemia (Carter et al. 1981). However, there were case reports on the use of haloperidol, benzodiazepines, topiramide, and levetiracetam in the management of

choreic movements which showed favorable outcomes (Pena et al. 2002; Driver-Dunckley & Evidente 2005; Zesiewicz et al. 2006).

## CONCLUSION

Non-ketotic hyperglycemic HC-HB is an interesting and important differential diagnosis in patients presenting to ED with abnormal involuntary movements. Early recognition of the clinical and radiological features is essential, as the treatment should be aimed primarily at the reversal of the hyperglycemia and the accompanying metabolic disturbances. The prognosis would be excellent and often resolving within hours to days of glucose normalization.

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