Don't Forget That Chorea!

Lokesh Krishnaji Kolhe (✉ lokesh.kolhe@yahoo.in)

National Healthcare Group <https://orcid.org/0000-0003-2782-0204>

Yumin Audrey Tham

Tan Tock Seng Hospital

Case report

Keywords: Non-ketotic hyperglycaemia, hemichorea-hemiballismus, chorea-ballism

Posted Date: October 20th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-962780/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Hemichorea-hemiballismus is a spectrum of involuntary, continuous non-patterned movement involving one side of the body. Possible causes of hemichorea-hemiballismus include haemorrhagic or ischemic stroke, neoplasm, systemic lupus erythematosus, NHH (non-ketotic hyperglycaemic hemichorea), Wilson's disease, and thyrotoxicosis. Amongst the metabolic causes, chorea associated with NHH is noteworthy and is mainly reported in elderly Asian women. The pathophysiology of this syndrome remains controversial. It is likely that a combination of hyperglycaemia induced basal ganglia metabolic derangement and failure of cerebral blood flow autoregulation contribute to the syndrome.

Case presentation: A 45-year-old Malay gentleman presented to our Emergency Department with right upper and lower limb weakness associated with hemichorea for 3-4 days. His initial blood glucose level was 22 mg/dl with normal serum ketone and bicarbonate levels. CT brain showed a hyperdensity in the left caudate nucleus and globus pallidus region. Subsequent brain MRI revealed an asymmetric T1 hyperintensity of the left putamen. This specific finding was compatible with hyperglycaemia-induced hemichorea-hemiballismus syndrome. The hemiballismus/hemichorea improved rapidly within the next day.

Conclusions: This unusual clinical presentation is often accompanied by severe hyperglycaemia. Appropriate blood glycaemic control is important because it is reversible with correction of hyperglycaemia. Thus, prompt recognition and treatment is essential to avoid adverse outcomes.

Background

Chorea-ballism is an irregular, poorly patterned, involuntary movement disorder mainly involving unilateral, or sometimes bilateral extremities. Various conditions such as cerebrovascular insufficiency, neurodegenerative diseases, neoplastic diseases, immunologic diseases, infectious diseases and metabolic diseases are known secondary causes of this uncommon disorder(1). A recent study by Ryan et al observed that chorea/ballism developing in the context of non-ketotic hyperglycemia (NKH) is frequently misdiagnosed or under-recognised. This condition is often associated with imaging findings such as T1 MRI hyperintensity of the contralateral striatum/putamen which is sometimes misinterpreted as striatal hemorrhage(2, 3). The pathophysiology of NKH is not clearly elucidated but is more commonly observed in elderly Asian females who have type 2 Diabetes Mellitus (T2DM)(4). In this report, we describe such a case in a middle-aged gentleman, initially misdiagnosed as intracranial haemorrhage, which, to our knowledge, is the first such publication locally.

Case Presentation

A 45-year-old Malay man with a past medical history of poorly controlled T2DM, previous deep vein thrombosis with extensive pulmonary embolism and right foot Charcot arthropathy presented to the

Emergency Department with complaints of slurring of speech, right upper and lower limb weakness and numbness for a week. He also reported that his right upper limb was 'restless' and had been continuously moving involuntarily for one day. The patient reported that his capillary blood glucose (CBG) had been ranging between 30-31 mmol/L a day before presentation, significantly higher than his usual range of 10-12 mmol/L. He reported no preceding head injury, seizure, headache or infective symptoms. On presentation, the patient was obese, vital signs were: blood pressure of 192/119 mmHg, heart rate of 65 beats per minute, respiratory rate of 18 breaths per minute, and normal oxygen saturation without respiratory distress. Neurological examination was notable for slurred speech, with a positive pronator drift and marginally reduced power of his right upper and lower limbs. Irregular, non-purposeful jerking movements of the right upper and lower limbs were also observed. Rest of the physical examination was largely unremarkable. Bedside capillary blood glucose was 21.5 mmol/L. Laboratory investigations revealed mild hyponatremia of 130 mmol/L, creatinine 159 μ mol/L, white blood cells 11.8×10^9 /L, hemoglobin 12 g/dL. Plain CT Brain (Figure 1) imaging showed an area of hyperdensity in the left caudate nucleus.

A presumptive diagnosis of left basal ganglia haemorrhage was made by the treating physician. Subsequently the CT brain report raised a suggestion that the hyperdense appearance of the left basal ganglia structures without any mass effect may be related to non-ketotic hyperglycaemia with a less likely differential of subacute infarct with petechial haemorrhagic conversion. Despite the above report, our neurosurgical colleague opined that intracranial haemorrhage was a more likely diagnosis and proceeded with admission to the neurosurgical ward. An MRI brain (Figure 2) was subsequently performed, which showed hyperintense appearance of the left caudate head and lentiform nucleus on T1-weighted images and iso- to slightly hypointense on T2-weighted images. Similar signal changes extended to the posterior limb of internal capsule and left cerebral peduncle.

The above findings were deemed to be related to a toxic/metabolic process for which non-ketotic hyperglycaemia was the primary consideration. The patient was then referred to inpatient endocrine and neurology services for optimization of treatment. With intensive glucose control and oral haloperidol as needed, the patient's chorea appeared to improve significantly.

Discussion

Hemiballism-hemichorea (HC-HB) caused by non-ketotic hyperglycaemia was first reported by Bedwell in 1960. He described a 65 year old woman who developed ballistic movements in all four limbs during three episodes of hyperglycaemia(5). NKH is the most common metabolic cause of HC-HB and is often a reversible condition. HC-HB is a disease with a low prevalence and mainly described in case reports or case series involving individuals of Asian descent, females, and the elderly. The slightly increased incidence in the Asian population may suggest an underlying genetic predisposition(6). Besides an abnormal metabolic panel, it is associated with noticeable changes in neuroimaging. CT and MRI scans of several affected patients show hyperdensities and hyperintense signals respectively on the contralateral striatum(7). A meta-analysis of 53 cases conducted by Oh et al showed that 89% of the

cases had hemichorea with contralateral putaminal hyperintensity and 11% had generalised chorea with bilateral putaminal changes on MRI(8). Findings on MRI include unilateral hyperintensity on T1-weighted images without the corresponding hyperintensities on T2-weighted images that characterize basal ganglia haemorrhage(9).

The pathophysiology of NKH-induced chorea is not clearly understood, with several competing hypotheses. The most commonly invoked theory suggests that depletion of gamma-aminobutyric acid (GABA) and acetylcholine, which are needed as an alternative energy source during nonketotic hyperglycaemia, leads to a decreased inhibitory signal to the thalamus resulting in hyperactive movement(1, 10). Another potential mechanism suggested, is acute putaminal dysfunction secondary to hyperglycaemic or hyperosmolar insult, associated with some degree of Wallerian degeneration of the internal white matter of the putamen have been considered to play a pathogenetic role in NKH patients with putaminal MRI abnormalities(11). As such, the rapid reversibility of the neurological signs with correction of the metabolic disturbance suggests a direct causal relation between hyperosmolar hyperglycaemia and the neurological signs.

Following recognition, NKH should be treated with aggressive glucose control, which typically leads to resolution of the hemichorea and imaging findings. Most patients with HC-HB show partial or complete resolution after treatment with neuroleptic drugs, and in most case reports there was complete resolution of symptoms at three months of follow up(11)(12)(6)(13). In the case series reported by Ryan et al, the treatment of six patients with typical or atypical neuroleptics was maintained throughout the follow up period of one month to five years. In four of these cases, mild chorea persisted on treatment(3).

Our patient was discharged on day four of admission with improved symptoms and optimisation of DM management. A review of the electronic records showed that he reported worsening chorea two weeks after discharge. After regular doses of haloperidol, he reported symptom resolution in his lower limb but persistent symptoms in his upper limb. This corroborates with our earlier literature review suggesting that some patients show partial resolution of their symptoms and require prolonged treatment.

In conclusion, although NKH is uncommonly caused by a dysfunction of glucose metabolism, we advise checking blood glucose in patients presenting with hyperkinesia, as the condition may rapidly resolve with hydration and resolution of the hyperglycaemia. It is also advisable to be cognisant that this movement disorder may be the initial presenting symptom of diabetes mellitus(14).

We would like to reiterate the importance of early recognition of this uncommon condition. In our case, thankfully, the mistaken first impression of treating the above patient for an intracranial haemorrhage did not result in adverse outcomes. Prompt diagnosis and appropriate glycaemic control would improve symptoms in such patients, which would in turn minimize discomfort as well as avoid unnecessary investigations and interventions.

Abbreviations

CBG	capillary blood glucose
DM	diabetes mellitus
GABA	gamma-aminobutyric acid
HC-HB	hemichorea-hemiballismus
NKH	non-ketotic hyperglycaemia
T2DM	type 2 diabetes mellitus

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Informed written consent obtained from the patient

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests

Funding

Not applicable

Authors' contribution

KLK drafted the manuscript, which was revised by TYA. All authors read and approved the final manuscript.

Acknowledgements

We thank the patient for allowing us to share details of his case. We also thank the doctors involved in the management of the patient in the Emergency Department as well as the inpatient ward.

References

1. Lee S-H, Shin J-A, Kim J-H, Son J-W, Lee K-W, Ko S-H, et al. Chorea-ballism associated with nonketotic hyperglycaemia or diabetic ketoacidosis: Characteristics of 25 patients in Korea. *Diabetes Res Clin Pract.* 2011 Aug;93(2):e80–3.
2. Chang K-H, Tsou J-C, Chen S-T, Ro L-S, Lyu R-K, Chang H-S, et al. Temporal features of magnetic resonance imaging and spectroscopy in non-ketotic hyperglycemic chorea-ballism patients: MRI and MRS features of non-ketotic hyperglycemic chorea-ballism. *Eur J Neurol.* 2010 Apr;17(4):589–93.
3. Ryan C, Ahlskog JE, Savica R. Hyperglycemic chorea/ballism ascertained over 15 years at a referral medical center. *Parkinsonism Relat Disord.* 2018 Mar;48:97–100.
4. Cosentino C, Torres L, Nuñez Y, Suarez R, Velez M, Flores M. Hemichorea/Hemiballism Associated with Hyperglycemia: Report of 20 Cases. *Tremor Hyperkinetic Mov* [Internet]. 2016 Jul 19 [cited 2021 May 31];6. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4955070/>.
5. Bedwell SF. Some observations on hemiballismus. *Neurology.* 1960 Jun;10:619–22.
6. Hernandez GT. Chorea. Hyperglycemia, Basal Ganglia Syndrome (C-H-BG) in an uncontrolled diabetic patient with normal glucose levels on presentation. *Am J Case Rep.* 2014;15:143–6.
7. Bendi VS, Matta A, Torres-Russotto D, Shou J. Bilateral chorea/ballismus: detection and management of a rare complication of non-ketotic hyperglycaemia. *BMJ Case Rep.* 2018 Jun 19;bcr-2018-224856.
8. Oh S-H, Lee K-Y, Im J-H, Lee M-S. Chorea associated with non-ketotic hyperglycemia and hyperintensity basal ganglia lesion on T1-weighted brain MRI study: a meta-analysis of 53 cases including four present cases. *J Neurol Sci.* 2002 Aug 15;200(1–2):57–62.
9. Hansford BG, Albert D, Yang E. Classic neuroimaging findings of nonketotic hyperglycemia on computed tomography and magnetic resonance imaging with absence of typical movement disorder symptoms (hemichorea-hemiballism). *J Radiol Case Rep.* 2013 Aug;7(8):1–9.
10. Abdelghany M, Massoud S. Nonketotic hyperglycemic chorea. *Case Rep Neurol Med.* 2014;2014:128037.
11. Branca D, Gervasio O, Le Piane E, Russo C, Aguglia U. Chorea induced by non-ketotic hyperglycaemia: a case report. *Neurol Sci.* 2005 Oct;26(4):275–7.
12. Dhull P, Upreti V, Kumar KVSH, Patnaik S. Hemichorea-hemiballismus in nonketotic hyperglycemia. *J Acad Med Sci.* 2012;2(2):82.
13. Al-Quliti KW, Assaedi ES. Hemichorea with unilateral MRI striatal hyperintensity in a Saudi patient with diabetes. *Neurosciences.* 2016 Jan;21(1):56–9.
14. Lin JJ, Chang MK. Hemiballism-hemichorea and non-ketotic hyperglycaemia. *J Neurol Neurosurg Psychiatry.* 1994 Jun;57(6)(1):748–50.

Figures

Figure 1

Plain CT brain showing hyperdensity in the patient's left caudate nucleus

Figure 2

T1 weighted MRI brain of the patient showing hyperintense left caudate head and lentiform nucleus