

HEMICHOREA-HEMIBALLISM AS THE FIRST PRESENTATION OF TYPE 2 DIABETES MELLITUS

Andre C. Felicio¹, Claudia V. Chang², Clecio Godeiro-Junior¹, Marina P. Okoshi³, Henrique B. Ferraz¹

Hemichorea-hemiballism (HCHB) can be the solely presentation of a wide range of non-neurological clinical pictures, such as metabolic or hydro-electrolyte derangements. HCHB as the first presentation of type 2 diabetes mellitus has been rarely described¹⁻³.

The case depicted herein reinforces this association highlighting that especially in elder patients with newly diagnosed HCHB, non-ketotic hyperglycemia should promptly be recognized.

CASE

A 70-year-old white man presented with one month history of involuntary movements of the left upper and lower limbs. He also noticed polyuria and polydipsia for the last 2 months and lost 10 kg within this period. His past medical history included controlled hypertension and a heart attack three years before. He used to take on a regular basis and at the time of presentation to our emergency department captopril 50 mg per day, hydrochlorothiazide 25 mg per day, propranolol 120 mg per day, aspirin 200 mg per day, and digoxin 0.25 mg per day. He used to be a heavy drinker (stopped 15 years ago) and smoker (stopped 3 years ago). There was no history of diabetes mellitus, other diseases or exposure to neuroleptic medication. No family history of movement disorders was obtained.

On admission, he was fully alerted and oriented. He had HCHB involving his left upper and lower limb with normal muscle strength, but mild hypotonia. The movements were almost continuous during wakefulness, and disappeared during sleep. Fasting blood glucose was obtained (560 mg/dL) and type 2 diabetes mellitus was diagnosed. Glycosylated hemoglobin A1c was 6.6%. No ketones were detected in urinalysis and urine pH was normal. Corrected sodium concentration was 140 mmol/L, and estimated serum osmolality was 332 mOsm/L. Other routine blood tests including calcium, potassium, magnesium, and phosphate concentrations, and thyroid and parathyroid hormone tests were normal as well liver and kidney functional status. A brain computer tomography (CT) showed a slight hyperdense lesion on the right putamen. T₁-weighted brain magnetic reso-

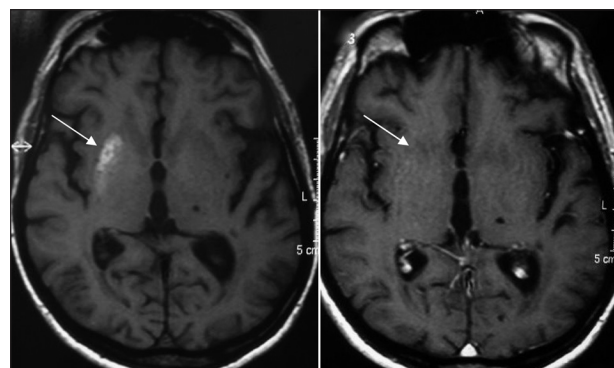


Figure. MRI scan showing a hyperintense lesion in the right putamen on T₁-weighted image (left). A nine-month re-scan (right) shows complete disappearance of the putaminal lesion, even after contrast gadolinium enhancement. Arrow corresponds to the right putamen. A lacunar infarct is also seen on the left thalamic-internal capsular region.

nance imaging (MRI) showed a right hyperintense lesion on putamen with iso-signal intensity on T₂-weighted and Flair images.

With the administration of haloperidol (10 mg per day) and glycemia control (10 IU bed time NPH insulin) and 6 mg per day glimepiride his movement disorder decreased in severity and completely disappeared 15 days after the first medical appointment. A nine-month re-scan with MRI showed a normal putamen without the previously seen hyperintense lesion (Figure).

The patient signed an informed consent to allow his data publication.

DISCUSSION

The underlying mechanisms of brain alterations in patients with non-ketotic hyperglycemia-induced HCHB are not known yet, but they have been attributed to base ganglia cerebral blood flow reduction, petechial hemorrhage, depletion of both GABA and acetylcholine, or metabolic acidosis⁴. Interestingly, among neuronal subtypes, striatal medium spiny neurones are highly vulnerable to energy depletion and this might explain the predilection for lesions situated in the striatum⁴. In a recent case report

HEMICOREIA-HEMIBALISMO COMO PRIMEIRA MANIFESTAÇÃO DE DIABETES MELLITUS TIPO 2

¹ Department of Neurology and Neurosurgery, Movement Disorders Unit, Universidade Federal de São Paulo, São Paulo SP, Brazil (UNIFESP); ² Neuroendocrinology Division, Psychiatry Institute, Faculdade de Medicina da Universidade de São Paulo, São Paulo SP, Brazil (USP); ³ Department of Medicine, Faculdade de Medicina de Botucatu, Universidade Estadual Paulista, Botucatu SP, Brazil (UNESP).

Received 11 September 2007, received in final form 5 December 2007. Accepted 7 February 2008.

Dr. Andre C. Felicio – Disciplina Neurologia - Rua Pedro de Toledo 650 - 04039-002 São Paulo SP - Brasil. E-mail: cf.andre@gmail.com

study, it was suggested that petechial hemorrhage secondary to erythrocyte diapedesis due to hyperglycemia-induced blood-brain barrier dysfunction might also have a role in the syndrome⁵.

Typically, the neuroimaging abnormalities seen in patients with HCHB last several months to years disappearing much later than the movement disorder. The characteristic features are high signal intensity lesions on T₁-weighed brain MRI, and these alterations are not yet fully understood. There is, however, hyperglycemia-induced HCHB without MRI abnormalities², and therefore these unique imaging alterations should not be taken as a clear-cut surrogate marker for putaminal dysfunction associated to an hyperglycemic insult.

Elder female diabetic patients from East Asian origin are more prone to develop HCHB, but whether this is related to a particular genetic predisposition is still a matter of debate. Recently, it was suggested that the presence of acanthocytes in circulating peripheral blood might render diabetic patients prone to develop HCHB⁶. In our case we did not search for acanthocytes on the peripheral blood since a good relief of symptoms was obtained with glycemia control and the use of neuroleptics.

The prognosis of non-ketotic hyperglycemia-induced HCHB is favorable and depends on the prompt identification of undiagnosed diabetes or the compensation of previously diagnosed patients. Additionally, typical neuroleptics and sometimes benzodiazepines are useful in the management of the choreic movements. Topiramate⁷, levetiracetan⁸ and tetrabenazine⁹ have also been tried in selected cases with favorable outcomes.

We recently reported three other cases (2 men, 1 woman) of new onset HCHB in elder patients attributed to non-ketotic hyperglycemia³. One of these patients, similarly to this case, was unaware of having type 2 diabetes mellitus. The mean time for their movement disorder to fully recover was approximately 12 days and they all took haloperidol in a long-term basis without side effects. Two of the patients had concurrent infection (pneumonia

and meningitis) suggesting that this might play as a trigger factor for HCHB in predisposed patients. The characteristic T₁-weighed hyperintense lesions in the striatum were found in all patients especially contralateral to the affected limb. Cupidi and coworkers also described a diabetic patient mild uremia that developed an acute but reversible form of parkinsonism, emphasizing that acute extrapyramidal syndromes may occur in diabetic patients with concurrent decompensated metabolic diseases and that this clinical syndrome is likely independent from racial and/or genetic variables¹⁰.

In conclusion, this case report underscores the non-ketotic hyperglycemia-induced HCHB syndrome as an unusual presentation of type 2 diabetes mellitus, highlighting that its recognition and stringent glycemia control associated to the use of neuroleptics hasten the patient recovery. Moreover HCHB syndrome should be regularly included in the differential diagnosis of acute movement disorders, especially in the elder population.

REFERENCES

1. Ifergane G, Masalha R, Herishanu YO. Transient hemichorea/hemiballismus associated with new onset hyperglycemia. *Can J Neurol Sci* 2001;28:365-368.
2. Branca D, Gervasio O, Le Piane E, et al. Chorea induced by non-ketotic hyperglycaemia: a case report. *Neurol Sci* 2005;26:275-277.
3. Chang CV, Felicio AC, Godeiro-Junior CO, et al. Chorea-ballism as a manifestation of decompensated type 2 diabetes mellitus. *Am J Med Sci* 2007;333:175-177.
4. Oh S-H, Lee K-Y, Im J-H, et al. 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;200:57-62.
5. Mestre TA, Ferreira JJ, Pimentel J. Putaminal petechial haemorrhage as the cause of non-ketotic hyperglycaemic chorea: a neuropathological case correlated with MRI findings. *J Neurol Neurosurg Psychiatry* 2007;78:549-550.
6. Pisani A, Diomedei M, Rum A, et al. Acanthocytosis as a predisposing factor for non-ketotic hyperglycemia induced chorea-ballism. *J Neurol Neurosurg Psychiatry* 2005;76:1717-1719.
7. Driver-Dunckley E, Evidente VG. Hemichorea-hemiballismus may respond to topiramate. *Clin Neuropharmacol* 2005;28:142-144.
8. Zesiewicz TA, Pathak A, Sullivan KL, Shamayev M, Hauser RA. Treatment of chorea with levetiracetam. *Eur J Clin Pharmacol* 2006;62:87
9. Sitburana O, Ondo WG. Tetrabenazine for hyperglycemic-induced hemichorea-hemiballismus. *Mov Disord* 2006;21:2023-2025.
10. Cupidi C, Piccoli F, La Bella V. Acute reversible parkinsonism in a diabetic-uremic patient. *Clin Neurol Neurosurg* 2006;108:601-603.