

CASE REPORT

Uncontrolled Type 2 Diabetes Mellitus - a Rare Cause of Hemiballismus-Hemichorea. A Case Report and Literature Review

Dumitrita-Mirela ILIE¹, Mihaela Livia SELESCU¹, Ioana Andreea NEAGU¹, Dragos Constantin SANDU¹, Delia Adriana PARVU^{1,3}, Gabriela MIHAILESCU^{1,2}

Abstract

Introduction: Chorea, hyperglycemia, basal ganglia syndrome (CHBG) is a rare neurological complication of non-ketotic hyperglycemia which occurs more often in elderly female patients with undiagnosed or poorly controlled diabetes mellitus. **Case report:** We present the case of a 82-year old female, diagnosed with type 2 diabetes mellitus, but untreated, admitted with non-ketotic hyperglycemia and hemiballistic movements in her left limbs, with acute onset, that changed to choreic movements and then disappeared. Brain magnetic resonance imaging (MRI) showed characteristic hyper intensity in the right (contralateral) putamen on the T1-weighted images. Other secondary causes for ballismus and chorea were excluded. Hemiballismus/hemichorea non-ketotic hyperglycemic basal ganglia (CHBG) syndrome was considered and blood glucose was lowered using insulin. As symptomatic treatment, Haloperidol was started but, due to adverse effects, it was stopped and Clonazepam was associated. The movement disorders disappeared in two weeks after glycemic control. **Significance:** Movement disorders, like chorea and/or ballismus (hemichorea/hemiballismus) can be a marker of uncontrolled known diabetes mellitus or a presenting sign for an undiagnosed diabetes mellitus. The chorea hyperglycemia basal ganglia (CHBG) syndrome is rare and likely undiagnosed but, being aware of its existence is of high importance, as normalising blood sugar values severe neurological complications can be avoided.

Keywords: hemiballismus, hemichorea, non-ketotic hyperglycemia, diabetes mellitus, putamen hyperintensity.

Rezumat

Introducere: Sindromul „coree, hiperglicemie, ganglioni bazali” este o complicație neurologică rară a hiperglicemiei non-ketotice, care apare mai frecvent la femei de vârstă înaintată, în condițiile unui diabet zaharat nediagnosticat sau slab controlat. **Prezentare de caz:** Prezentăm cazul unei paciente în vârstă de 82 de ani, diagnosticată cu diabet zaharat tip 2, dar netratată, internată pentru mișcări hemibalice la nivelul membrelor stângi, cu debut acut, în contextul unei hiperglicemii non-ketotice. Mișcările involuntare au devenit ulterior coreice, dispărând în două săptămâni, prin controlul glicemiei cu insulină și sub tratament simptomatic, inițial cu Haloperidol, sistat din cauza efectelor adverse și înlocuit cu Clonazepam. Examenul de rezonanță magnetică cerebrală a evidențiat, în secvențele ponderate T1, hiperintensități caracteristice la nivelul putamenului drept (controlateral). Au fost excluse alte cauze secundare de balism și coree. S-a stabilit diagnosticul de „sindrom hemibalism/hemicoree - hiperglicemie non-ketotică - ganglioni bazali”. **Semnificație:** Tulburările de mișcare, de tip coree și/sau balism (hemicoree/hemibalism) pot reprezenta un indiciu pentru diabetul zaharat necontrolat sau un semn inițial, de debut, al diabetului încă nediagnosticat. Acest sindrom este rar și adesea subdiagnosticat, dar cunoașterea existenței sale, ar putea avea o importanță majoră, normalizarea valorilor glicemice eliminând mișcările involuntare și evitând complicații neurologice severe.

Cuvinte cheie: hemibalism, hemicoree, hiperglicemie non-ketotică, diabet zaharat, hiperintensitate putaminală.

¹ Department of Neurology, Colentina Clinical Hospital, Bucharest, Romania

² „Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

³ Hiperdia - Colentina Clinical Hospital, Bucharest, Romania

Corresponding author:

Dumitrita-Mirela ILIE, Department of Neurology, Colentina Clinical Hospital, 19-21 Stefan cel Mare Avenue, 2nd District, Bucharest, Romania.

E-mail: iliemirela92@gmail.com

INTRODUCTION

Movement disorders, such as ballismus or chorea can occur as first symptoms in a patient with undiagnosed diabetes mellitus or as a complication of non-ketotic hyperglycemia due to a poor control of the serum glucose in already diagnosed patients, especially with type 2 diabetes mellitus. They are uncommon symptoms, can be seen as complications of diabetes mellitus much more rarely than stroke, seizures, coma or sensory-motor polyneuropathies, but if identified, they should urgently be associated with blood glucose and glycosylated haemoglobin (HbA1C) measurements. From the approximately 200 cases described in the literature, associating non-ketotic hyperglycemia and this type of movement disorders, more frequently adults with a mean age of 71 years were affected, with a sex ratio female: male of 1,8:1, mostly from eastern Asia, but also from other parts of the world like South America, USA and Europe. If this movement disorders affect only one half of the body (as it happened in 90% of the described cases), they are called hemiballismus or hemichorea. Due to the transient changes observed, mainly a hyperintensity in the contralateral putamen and more rarely in the head of the caudate nucleus on the T1 weighted magnetic resonance imaging (MRI), it was considered a functional disturbance of the basal ganglia, induced by non-ketotic hyperglycemia and described for the first time by S.F. Bedwell in 1960 as „Chorea, hyperglycemia, basal ganglia (CHBG) syndrome”, or later by other authors as non-ketotic hyperglycemic hemichorea or diabetic striatopathy¹.

This symptoms may have an acute, subacute or gradually progressive onset. If acute, they can start with ballismus (violent involuntary flinging, fidgety movements, with large amplitude, predominantly affecting the proximal part of the limbs) that can be unilaterally (hemiballismus) or bilaterally (ballismus) and then can switch to chorea (mild/moderate irregular, involuntary, hyperkinetic, dance-like movements, with lower amplitude). The prognosis is good, symptoms improve and disappear in most of the cases after correction of non-ketotic hyperglycemia (in some days to weeks) but can also relapse in a few cases^{2,3,4}.

CASE REPORT

We present the case of a 82-year old right handed woman, who was admitted in the Neurology Department for ballistic movements in her left limbs, with acute onset 2 days before. The patient reported that the invol-

untary ballistic movements were interfering with her daily activities, were present with rest or with attempting purposeful movements, got worse with anxiety and resolved during sleep. She was diagnosed with diabetes mellitus type 2 three months ago (HbA1C = 7.66%) when only diet was recommended. She did not obey the dietary rules. Her past medical history included: atrial fibrillation, one cardio embolic ischemic stroke of the right middle cerebral artery (3 months ago – totally clinically recovered), essential high blood pressure, moderate cognitive impairment (MMSE = 24/30, MoCA = 14/30), pulmonary fibrosis and obesity (BMI = 32,44). She had no personal or family history of movement disorders. She was not exposed to illegal drugs and had no polycythemia and no history of head trauma. Her everyday treatment included: Apixaban 10mg/day (inconstantly), Metoprololum 50mg/day, Atorvastatinum 80mg/day, Candesartan 8mg/day, Furosemide 40mg/day, Memantine 10mg/day and Pantoprazolum 40mg/day.

The neurological examination was normal with four exceptions: she was slightly disoriented, presented ballistic movements involving the left limbs, had mild left hypotonia and her gait was affected by the involuntary movements. The upper limb was more affected than the lower one. The muscle strength was normal. Her blood pressure was 130/80mmHg and she had irregular heartbeats (atrial fibrillation) of 112/minute.

Laboratory testing disclosed non-ketotic hyperglycemia 522 mg/dL (normal ranges 65 – 115 mg/dL) with a high serum level of glycosylated haemoglobin HbA1C = 13.76% (normal ranges 4.8 – 5.9%). There was no acidosis, arterial blood pH = 7.35–7.45 and urine ketones were absent. Liver, kidney, thyroid functions and blood electrolytes levels were in normal ranges.

An emergency brain CT scan was performed which revealed only the stroke sequelae in the territory of the right middle cerebral artery as well as a brain atrophy. No putaminal lesions could be observed (Figure 1). Four days later, a brain 1.5 Tesla MRI without contrast was performed and on the T1 weighted images a hyperintense signal in the right putamen (contralateral to the affected body side), without mass effect or edema and without expression on the other MRI sequences (T2 and DWI) could be identified (Figure 2, Figure 3 and Figure 4).

Taking into account the acute onset of hyperkinetic ballistic, followed by milder choreic movements of the left limbs, on a background of poor glycemic control in a patient diagnosed with type 2 diabetes mellitus,

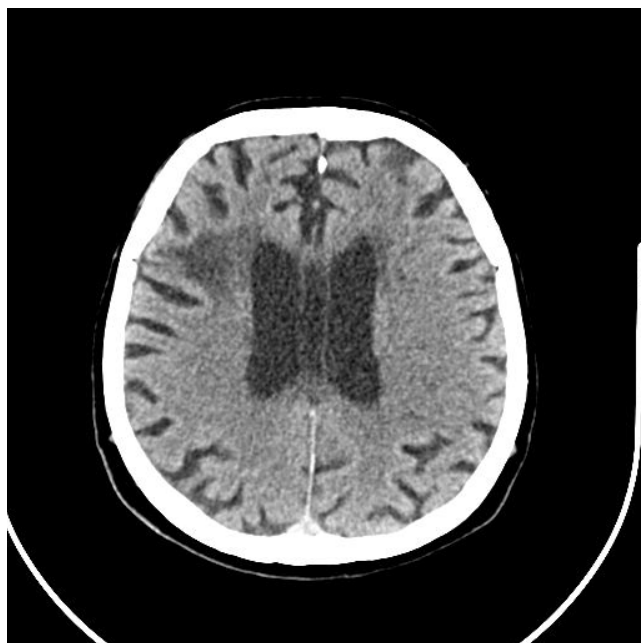


Figure 1. Brain CT scan shows the stroke sequelae in the territory of the right middle cerebral artery and brain atrophy.

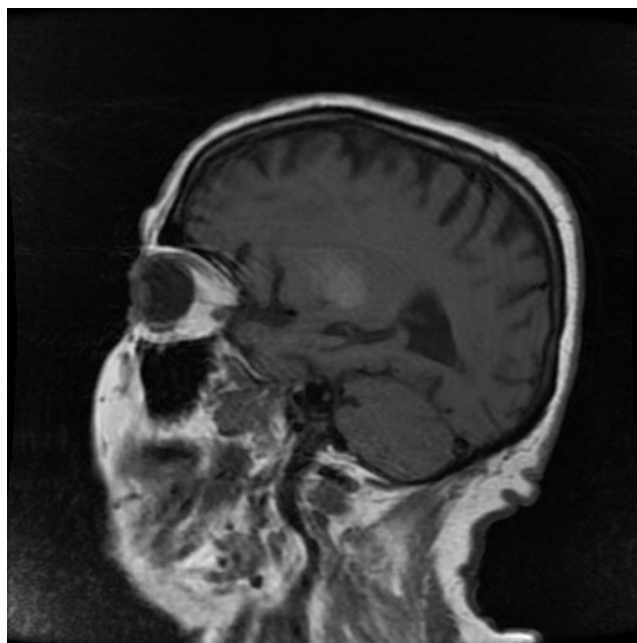


Figure 3. Sagittal T1-weighted MRI shows hyper intensity involving the right putamen.

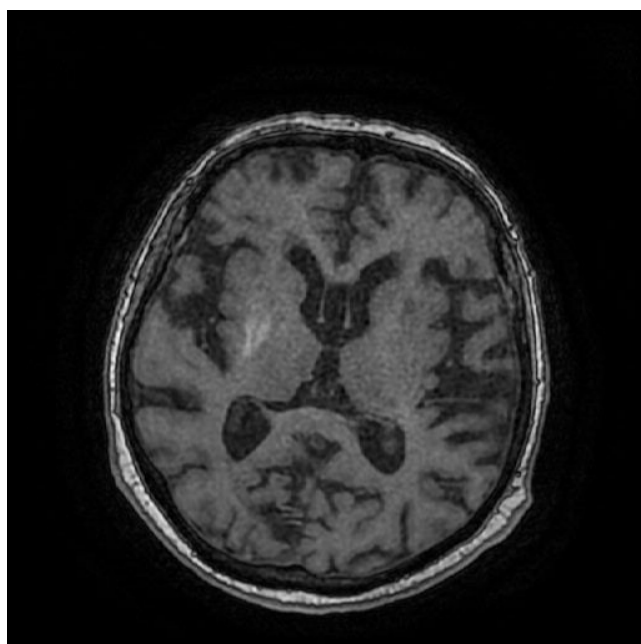


Figure 2. Axial T1-weighted MRI shows hyper intensity involving the right putamen.

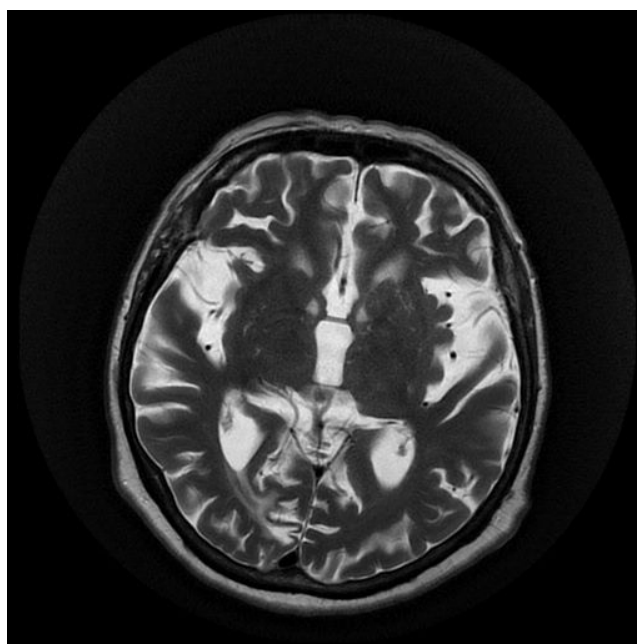


Figure 4. Axial T2-weighted MRI - no lesions in the right putamen.

absent ketones in the urine and typical hyper intense right putaminal T1 weighted MRI changes, we considered the rare entity „chorea, hyperglycemia, basal ganglia (CHBG) syndrome” as the diagnosis of this patient. Treatment with rapid acting insulin (Humulin R) administered intravenously and subcutaneously was started, in order to progressively lower blood glucose.

As symptomatic treatment Haloperidol was prescribed, but the patient had adverse effects, so it was stopped and Clonazepam 2mg/day was the second option to continue the treatment.

During the second day of hospitalization and treatment, hemiballismus changed into hemichorea, which then slowly improved after blood sugar levels were

lowered and disappeared in the 12 following days. No control brain MRI was performed before she was discharged.

DISCUSSION

Chorea and/or ballismus associated with non-ketotic hyperglycemia accounts for 1% of the total cases presenting with this type of movement disorders and have an estimated prevalence of less than 1/100000. Other causes of secondary chorea can be drugs, neurodegenerative disorders, cerebrovascular lesions, paraneoplastic, immunological, other metabolic or infectious diseases^{3,5,6}.

The chorea hyperglycemia basal ganglia syndrome (CHBG) is defined like a triad represented by involuntary movements chorea and/or ballismus (uni- or bilateral), contralateral (rarely bilateral) neuroimaging basal ganglia abnormalities (especially high signal in T1 weighted MRI) and non-ketotic hyperglycemia in a patient with unknown diabetes mellitus being a presenting sign, or in a patient diagnosed with diabetes mellitus but with poorly controlled glycemic values for some months⁷. More frequent one side of the body is affected. Upper limbs are more involved than the lower ones and in some cases the face can also be affected. Bilateral ballistic and/or choreic movements occur in less than 10% of cases^{4,7,8}.

Other neurological abnormalities that can accompany non-ketotic hyperglycemia are: seizures, delirium, aphasia, nystagmus, hemiparesis, hemisensory loss, hemianopia and coma⁹.

Most of the cases described in the literature had typical radiographic changes. Brain CT scan could be normal or it could reveal striatal hyper density, contralateral to the body side affected by hemichoreic movements. Brain MRI is the method of choice to assess the self-limited basal ganglia lesions induced by non-ketotic hyperglycemia. The typical and most consistent feature of this syndrome is the T1 weighted hyper intense signal in the putamen, sometimes affecting also the head of the caudate nucleus, always well delineated and not respecting a vascular territory. In the majority of cases, lesions were reported to be contralateral to the affected body side, but there were also some cases described with bilateral lesions. The findings in T2 weighted images varied, being absent or hyper- iso- or hypo intense. The diffusion-weighted images (DWI) excluded a recent infarction, hidden ischemia or a hemorrhagic lesion. In contrast MRI,

these lesions were mostly no enhancing. Differential diagnosis of the basal ganglia T1 weighted MRI hyper intensity include: idiopathic calcification, calcium and phosphate abnormalities, Wilson's disease, manganese deposition (globus pallidus is usually affected), global hypoxia, methaemoglobin in intracranial hemorrhage, Japanese encephalitis, hamartoma in type 1 neurofibromatosis. What is also important to be taken into account, in comparison to this other causes, is that the described images disappeared in most of the cases in weeks or months after the movement disorder was cured. There is also an uncommon type of patients with CHBG syndrome that don't have typical CT or MRI images, but hemichorea and/or hemiballismus are present^{2,4,6,7,10}.

Magnetic resonance spectroscopy may reveal low N-acetylaspartate to creatinine ratio, high choline to creatinine ratio and associated lactate peak⁶. The single-photon emission computerized tomography (SPECT) showed in most of the cases hypoperfusion in the corresponding areas, but also normal or hyperperfusion in some other cases. Positron emission tomography (PET) revealed markedly reduced rates of cerebral glucose metabolism in the areas corresponding to the lesions with hyperintensity in the T1 weighted images on MRI, suggesting evidence of regional metabolic failure^{11,12}.

Although the pathophysiology of this rare syndrome is still not fully understood, it is considered that it is an ongoing dynamic process that transiently affects the function of the basal ganglia. Some hypothesized mechanisms are more frequently cited: hyper viscosity secondary to hyperglycemia leading to regional blood-brain barrier disruption and metabolic damage, hyperglycemia induced intracellular hyperosmolality and hypo perfusion in the putamen, anaerobic glucose metabolism leading to depletion of GABA and secondary to acetylcholine depletion in the basal ganglia due to the non-ketotic state, disinhibition of the thalamocortical pathway leading to motor cortical hyperexcitability, microhemorrhages or some infections which could be triggers. Besides, the higher predisposition in postmenopausal woman could be explained by the dopaminergic receptors hypersensitivity state and changes in estrogen levels, which affect interactions with GABA. Histological findings are characterized by selective neuronal loss, gliosis and reactive astrocytes, without any evidence of hemorrhage or infarction within the striatal areas^{2,5,6,8,9}.

As more cases in the Asian population were described, genetic, inadequate diabetes control in that area and/or environmental factors were suspected, but not yet demonstrated^{3,6}.

The mainstay of treatment involves optimal glyce-mic control associated or not with symptomatic treat-ments as: postsynaptic dopamine receptor blockers (dopamine antagonists) - antipsychotics, neuroleptics (Haloperidol, Risperidone, Tiapridal, Chlorpromazine, Tetrabenazine), with GABA-ergic anticonvulsants (Topiramate, Valproate, Pimozide) or with benzodia-zepines (Clonazepam, Diazepam) in order to control the hyperkinetic movements. Most cases have a benign outcome and a good prognosis which depends on the prompt recognition of the syndrome and the optimal blood sugar control. According to a meta-analysis of 54 patients with CHBG syndrome, most people recovered after some days to some months, but the T1-weighted MRI changes sometimes persisted longer, despite the clinical improvement, but most of them finally dis-appeared after a median of 6 months^{3,8,11,13,14}. For per-sistent chorea, refractory to medical treatment, neuro-surgical ventrolateral thalamotomy was used with good clinical results.

Hemichorea-hemiballismus syndrome is a rare mo-vement disorder, involving one side of the body. Some-times, during the recovery, there is a transition from hemiballismus to hemichorea. It is caused by lesions in the basal ganglia due to: Wilson's disease, stroke, tumor, vascular malformation, demyelination, non-ketotic hyperglycemia (CHBG syndrome), vasculitis (systemic eritematous lupus), trauma, infection (tuberculoma, toxoplasmosis) and thyrotoxicosis².

CONCLUSIONS

Chorea and/or ballismus – most commonly seen as he-michorea and/or hemiballismus with acute onset can bring a patient in the neurology department and the neurological assessment combined with a screening for blood glucose and HbA1C can discover a new or an

old and poorly controlled diabetes mellitus! As diabe-tes mellitus is a widely prevalent disease and this type of complication is amenable, by controlling glyce-mic values, it is important for clinicians to be aware of this condition. The differential diagnosis in a patient with a history of diabetes mellitus, associating involuntary movements of the limbs such as hemiballismus/hemi-chorea and T1 hyperintensity of the basal ganglia con-tralateral to the body side affected by these movement disorders, should start with non-ketotic hyperglycemia-induced hemichorea/hemiballismus syndrome, even if it is a likely underdiagnosed rarity. It is important to be aware of the CHBG syndrome and distinguish it from other central nervous system disorders, as it is reversi-ble after blood sugar levels correction and an adequate control of diabetes mellitus. A rapid recognition and treatment of this syndrome can avoid a bad outcome, such as an irreversible damage of the basal ganglia or other parts of the central nervous system.

Abbreviations

CT – Computed Tomography

MRI – Magnetic resonance imaging

DWI – diffuse weighted images

MMSE – Mini Mental State Examination

MoCA – Montreal Cognitive Assessment

HbA1C – glycosilated hemoglobin

GABA – gamma amino butyric acid

CHBG – chorea hyperglycemia basal ganglia

SPECT – single-photon emission computerized to-mography

PET – positron emission tomography

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Hel-sinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

References

1. Bedwell SF. Some observations on hemiballismus. *Neurology* 1960;10:619-622.
2. Su S, Gaillard FR. Non-ketotic-hyperglycaemic-hemichorea. www.radiopaedia.org
3. Pham K, Meegada S et al. Hemichorea Induced by Non-ketotic Hyperglycemia in a Caucasian Woman. *Cureus Journal of Medical Science*, 2020;12(2): e6866.doi 10.7759/cureus.6866
4. Danve A, Kulkarni S, Bhoite G. Non-ketotic hyperglycemia unmasks hemichorea. *Journal of Community Hospital Internal Medicine Perspectives*. Sep. 2015; 5(4):1-5. 27825, DOI: 10.3402/jchimp.v5.27825
5. Abdelghany M, Massoud S. Nonketotic Hyperglycemic Chorea. *Case Reports in Neurological Medicine*. Hindawi Publishing

- Corporation Volume 2014, Article ID 128037:1-3. <http://dx.doi.org/10.1155/2014/128037>.
6. Dwarak S, Prabhakar K et al. Chorea, Hyperglycemia, Basal Ganglia Syndrome in Diabetes – Two Rare Case Reports. *MAEDICA – A Journal of Clinical Medicine*. 2019; 14(1): 59-62. <https://doi.org/10.26574/maedica.2019.14.1.59>
 7. Cosentino C, Torres L et al. Hemichorea/Hemiballism Associated with Hyperglycemia: Report of 20 Cases. *Tremor and Other Hyperkinetic Movements*. 2016;6:1-4. <http://www.tremorjournal.org>
 8. Sperling M, Bhowansingh R. Chorea Hyperglycemia Basal Ganglia Syndrome in a 63-Year-Old Male. *Case Reports in Medicine*. Hindawi. Volume 2018; Article ID 9101207:1- 4. <https://doi.org/10.1155/2018/9101207>
 9. McCullen MK, Miller J et al. Expert Opinion: Chorea in the Setting of Hyperglycemia – A Case Report and Review of the Literature. *Practical Neurology*. March/April 2010: 16-19.
 10. Chang X, Hong W, Yu H, Yao Y. Chorea associated with nonketotic hyperglycemia. A case report with atypical imaging changes. *Medicine (Baltimore)*. 2017; 96(45):1-2.
 11. Oh SH, Lee KY 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*. Aug 2002; 200(1-2):57-62.
 12. Hsu JL, Wang HC, Hsu WC. Hyperglycemia-induced unilateral basal ganglia lesions with and without hemichorea: a PET study. *J. Neurol* 2004; 251: 1486-90.
 13. Bizet J, Cooper CJ et al. Chorea, Hyperglycemia, Basal Ganglia Syndrome (C-H-BG) in an uncontrolled diabetic patient with normal glucose levels on presentation. *The American Journal of Case Reports*. 2014; 15: 143–146. doi: 10.12659/AJCR.890179
 14. Padmanabhan S, Zagami AS, Poynten AM. A Case of Hemichorea-Hemiballismus Due to Nonketotic Hyperglycemia. *Diabetes Care*. Apr 2013; 36(4): e55-e56.