ACUTE CHOREO-DYSTONIA IN A NEWLY DIAGNOSED PATIENT WITH DIABETES MELLITUS: A CASE REPORT AND REVIEW OF LITERATURE

T.O. Akande[1], O.V. Olalusi[1], D.I. Olulana[2]

1. Department of Medicine, University College Hospital, Ibadan, Nigeria.
2. Department of Surgery, University of Ibadan and University College Hospital, Ibadan, Nigeria.

Correspondence:
Dr. O.V. Olalusi
Dept. of Medicine,
University College Hospital,
Ibadan.
E-mail: oladotunvolalusi@gmail.com

Submission Date: 16th Jan., 2023
Date of Acceptance: 30th Oct., 2023
Publication Date: 1st Nov., 2023

ABSTRACT

Introduction: **Diabetes mellitus is a disease with diverse macrovascular and microvascular consequences. One of the unusual effects of hyperglycemia is involuntary movement, termed hyperglycemia-induced involuntary movement. This could range from hemibalismus, chorea, choreo-atethosis, tremors to dystonia. Chorea associated with dystonia is a less commonly reported manifestation. When it is focal, it can be misdiagnosed as stroke or seizure disorder. To the best our knowledge, there is hitherto no case report in sub-Saharan Africa describing the occurrence of focal choreo-dystonia in type 2 Diabetes Mellitus.**

Case presentation: **Here, we present a case of a middle-aged Nigerian woman with focal choreo-dystonia of the right upper limb accompanying the diagnosis of type 2 diabetes. Achieving euglycemia with insulin resulted in complete resolution of the choreo-dystonia.**

Conclusion: **Doctors in resource-constrained settings should be aware of this presentation to avoid misdiagnosis and to provide prompt and goal-oriented management with a view to reducing morbidity and attendant health-care costs.**

Keywords: Diabetes mellitus, Choreo-dystonia, Case report, Hyperglycemia, Involuntary movement

BACKGROUND

Diabetes mellitus (DM) is a disease of public health concern with rapidly worsening epidemiologic indices.[1] It affects over 400 million patients worldwide with devastating macrovascular and microvascular complications.[2] However, involvement of the nervous system and the spectrum of movement abnormalities in patients with DM are often under-recognised and under-reported.[3] These neurologic features can result from hyperglycemia, vascular complications or the treatment of the DM itself. Early recognition and diagnosis however remain a challenge in resource-limited settings. One of the unusual effects of hyperglycemia is involuntary movement, termed hyperglycemia-induced involuntary movement (HIIM).[4]

Chorea is a hyperkinetic movement disorder characterized by rapid non-purposeful dance-like movements of distal limbs and can involve the face and trunk while dystonia is a sustained contraction of both agonistic and antagonistic muscles giving rise to abnormal posturing.[5] Chorea, dystonia, athetosis, and ballism are some of the involuntary movements of the choreiform spectrum that have been described in literature[6,7]. Bedwell[8], in 1960, first reported chorea as a rare clinical entity but it is now known to encompass a triad of chorea, hyperglycemia, and basal ganglia hyperintensity. The prevalence of hyperglycemia-induced chorea in resource-limited settings is unknown and this could be due to under-recognition and late diagnosis. Dystonia associated with chorea is rare and, to the best of our knowledge, yet unreported in sub-Saharan Africa. Here, we present a case of a middle-aged woman with focal choreo-dystonia of the right upper limb heralding the diagnosis of type 2 diabetes. Prompt recognition and attainment of euglycemia with insulin resulted in complete resolution of the choreo-dystonia.

CASE PRESENTATION

A 64-year-old right-handed Nigerian female was admitted on account of sudden onset of involuntary movement of the right upper limb a week prior to presentation. She described involuntary movement of the right upper extremity with associated abnormal posturing. The abnormal movement was precipitated by attempts to use the hand, starting as abnormal twisting involving the wrist and then jerky movements of the forearm, resolving spontaneously within five minutes. Symptoms occurred during the day and she had no preceding numbness and paresthesias. She had no prior history of similar symptoms, involvement of other body parts, limb weakness or gait abnormality. There was no loss of consciousness during episodes, alteration in sensorium or personality change. She had received a diagnosis of diabetes

mellitus at a private health facility two weeks before presentation following a month's history of increased urination and thirst. She had no known family history of DM. She had been commenced on tabs metformin 500mg three times daily and glibenclamide 5 mg daily to which she was not compliant.

Vital signs were normal on admission. Other than moderate dehydration and choreo-dystonic hyperkinetic movement involving the right hand, the other aspects of the physical findings were unremarkable. Admitting fasting blood glucose was 400mg/dl. The Hemoglobin A1c was 14.5%. The complete blood count was normal. Assessment was acute focal choreo-dystonia from severe hyperglycemia to exclude a stroke and focal-onset seizure disorder. An axial section of the computed tomography (CT) scan of the brain showed hyperdense signals within the Globus pallidi**,** the falx and choroid plexus in keeping with calcification (likely age-related) figure 1. A brain MRI was not done due to financial constraints, the electroencephalogram (EEG) was otherwise not remarkable. Serum electrolytes, calcium, magnesium as well as albumin were essentially normal. Dipstick urinalysis showed 1+ ketonuria, 2+ glycosuria and trace leucocytes. The serum osmolality was 343mosm/l.

the abnormal movements completely resolved on day five of in-patient care. She was discharged home 9 days after admission. Medications at discharge were to tabs gliclazide 30mg daily, sitagliptin 50mg daily, metformin 1000 mg twice daily, glargine insulin 14 units at bed time and levetiracetam 500 mg twice daily. She was followed up at the clinic 2 weeks, 1 month, 3 months and 6 months post-discharge and had no repeat dystonia. The glycemic control remained satisfactory. Blood pressure remained normal, fasting plasma glucose ranged between 111-141 mg/dl, 2 hours post prandial ranged between 119-148mg/dl. Levetiracetam was discontinued and there was still no recurrence of the abnormal movements. She continued to do well on anti-diabetic medications till date. In one of her clinic sessions, she was thankful that the diagnosis was not stroke and particularly glad that her symptoms had resolved without any neurologic sequalae or disability.

DISCUSSION

We have presented a middle-aged woman with focal choreo-dystonia involving the right upper limb having recently received a diagnosis of type 2 diabetes mellitus. Her symptoms resolved completely after 5 days following treatment of severe hyperglycemia. The brain

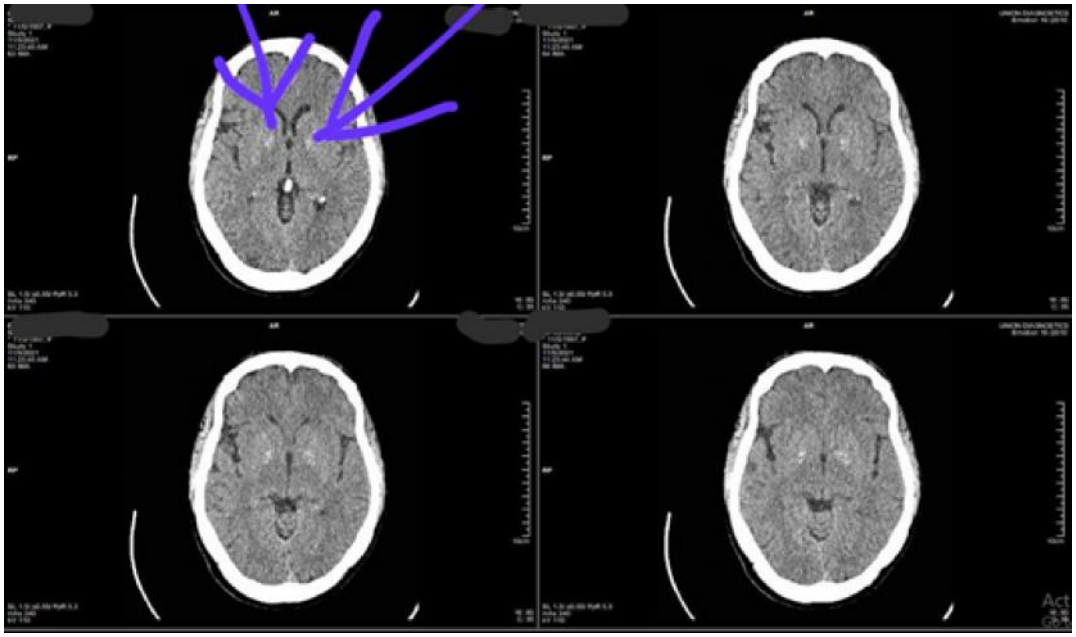

Fig. 1: An axial section of the computed tomography (CT) scan of the brain showed hyperdense signals within the Globus pallidi (arrows)**,** the falx and choroid plexus in keeping with calcification (likely age-related)

She was placed on intravenous fluids normal saline (one litre every 8 hours), basal-bolus insulin regimen (soluble insulin 8 units 30 minutes before meals and Glargine 14 units at night) and tabs levetiracetam (Keppra) 500 mg daily. She was managed by the endocrinology and neurology teams while on admission. Following control of the hyperglycemia, CT scan, done seven days after symptom onset, excluded acute vascular or infective lesions. The rapid resolution of symptoms with attainment of euglycemic state and the otherwise normal brain imaging made the possibility of stroke or seizure disorder less likely. Besides, she had no recurrence of symptoms or sequelae on follow-up visits, several months after

discharge. While there have been sparse reports of acute hemichorea[9] and dystonia in type 2 diabetes mellitus, chorea associated with dystonia is rare[10] and yet to be reported in sub-Saharan Africa.[10,11,12,13] Prompt recognition, diagnosis and attainment of euglycemia in this case was key to limiting morbidity and attendant health-care cost.

Chorea and dystonia are hyperkinetic movement disorders which can be seen in a wide array of disease conditions.[14] Approximately 25% of dystonias and essentially all choreas are symptomatic, the underlying cause being an identifiable neurodegenerative disorder, hereditary metabolic defect, or acquired systemic medical disorder.[14] The most common aetiologies are hypoxia-ischaemia and medications, while infections, autoimmune and metabolic disorders are less frequent causes. Not uncommonly, a given systemic disorder may induce more than one type of dyskinesia by more than one mechanism.[6] Diabetes is one of such systemic disorders with ravaging metabolic manifestations. It can affect both the peripheral and central nervous systems (CNS). Our patient had involvement of the CNS manifesting as abnormal twisting movements of the right hand (dystonia) with irregular dance-like jerks (chorea). She had a high serum osmolality (343 mosm/kg) and her symptoms resolved with rehydration and insulin administration. She had received anti-seizure medications with no relief.

Hyperglycemia-induced involuntary movement disorder includes hemichorea, hemiballismus, tremors, or dystonia, most of which resolve completely after normalizing blood glucose levels.[7] Ruhangisa and colleagues[9] in Tanzania reported hemichorea in a newly-diagnosed diabetic. The case was very similar to ours with a normal brain imaging and complete resolution of symptoms within 6 days of commencement of insulin therapy. However, unlike our case, there was no finding of dystonia. Dystonia associated with chorea is a less commonly reported manifestation[9], and to the best of our knowledge, this has yet to be reported in sub-Saharan Africa.[11,12,13] Outside the shores of Africa, authors have described cases of hemidystonia, hemichorea and hemi-choreodystonia in patients with long-standing uncontrolled DM.[15,16,17] Majority of these cases required antipsychotics, benzodiazepines and antiseizure medications and were refractory to treatment. Very few of these cases resolved within days of treatment of the hyperglycemia with insulin, as seen in our case. In a recent case series of 59 patients reviewing the clinico-radiologic spectrum of acute onset movement disorders in DM, ballism was the most common movement disorder (30.5%), followed by pure chorea (25.4%), choreoathetosis (13.6%), tremor (8.5%), hemifacial spasm (5.1%), parkinsonism (5.1%), myoclonus (5.1%), dystonia (3.4%), and restless leg syndrome (3.4%).[15] Like in our case, majority had no neuro-imaging changes and most of the patients (76.3%) recovered completely.[15] However, in another review of 53 cases describing patients seen with Chorea associated with hyperglycemia, all cases had a high signal intensity noted in the putamen on the T1-weighted brain MRI study.[17] The MRI-intensities resolved and correlated with the clinical improvement in chorea.[17] In our index case, brain MRI was not done due to financial constraints. Oh and colleagues[17] further noted that the mean serum glucose level measured after the onset of chorea was 481.5 mg/dl (ranging from 169 to 1264), HbA1c level was 14.4% (ranging from 9.9 to 19.2), and the serum osmolarity was 305.9 mmol/kg (ranging from 291 to 335)[17] compared to 400mg/dl, 14.5% and 343 mosm/l respectively, as seen in our index patient.

Dong and colleagues[18] documented a case of acute hyperglycemia-induced hemichoreo-ballism co-existing with stroke. Ryan and colleagues[16] in 2018 documented unilateral MRI basal ganglia T1 hyperintensities in patients with hyperglycemia-induced chorea mimicking stroke.[16] This could lead to costly imaging studies, placing less emphasis on a more readily available and cheap bedside blood glucose screening.[9] Even though complications of diabetes mellitus can result in stroke or seizure disorder, hyperglycaemia should be considered as a differential diagnosis in patients presenting with hemichoreo-dystonia upon initial clinical assessment.[18] Further imaging studies can then be requested after blood glucose has been optimized, especially if neurologic symptoms persist. Besides the abnormal involuntary movements, our index patient had no other focal neurological findings and the brain CT scan obtained showed no acute vascular anomalies. Imaging studies and necropsies of patients have helped map areas of the brain associated with particular movement disorders.[19] Based on such data, chorea seems to result from hypofunction of the indirect pathway from the putamen to the internal globus pallidus, and dystonia correlates more strongly with hyperfunction of the direct relative to the indirect pathway between the putamen and internal globus pallidus, both resulting in inappropriate disinhibition of thalamic projections to the premotor and motor cortex.[19] Even though our patient had hyperdense lesions within both globus pallidi suggestive of calcifications, this is not likely to have played a role in the clinical features. Chorea has been also been associated with lesions in the striatal nucleus, resulting in disinhibition of the external globus pallidus.[14] Dystonia has been correlated with lesions of the contralateral putamen, external globus pallidus,

posterior and posterior lateral thalamus, red nucleus, or subthalamic nucleus, or a combination of these structures. The result is decreased activity in the pathways from the medial pallidus to the ventral anterior and ventrolateral thalamus, and from the substantia nigra reticulata to the brainstem, leading to cortical disinhibition.[14]

Other possible mechanisms of hyperglycemia-induced movement disorders include reversible cerebral vascular insufficiency,[20] hyperglycemic or hyperosmolar insult leading to putaminal dysfunction,[21] interruption of striatal GABA-ergic transmission,[22] autoimmune-mediated inflammatory process. Our patient had a high serum osmolality and could have had hyperosmolar insult leading to putaminal dysfunction. Besides, lesions of the subthalamo-internal pallidal pathway have also been known to result in chorea.[23] Neurotransmitter abnormalities such as striatal cholinergic interneuron activity and dopaminergic hyperactivity in the nigrostriatal pathway have also been documented.[23]

Recent case reports have also highlighted resolution of symptoms with anti-psychotics, insulin therapy as well as clonazepam.[22,16,24] Our patient got better with use of insulin therapy and levetiracetam for presumed seizure. Levetiracetam was however soon tapered off and clinical improvement was sustained on antihyperglycemic agents. The strength of this study is that it is the first report of focal choreo-dystonia accompanying the diagnosis of DM in this environment with resolution following attainment of euglycemia with insulin. The limitation of our study was that a brain MRI was not done due to financial constraints.

CONCLUSION

Hyperglycemia was the underlying cause of the hemichorea-dystonia in our patient. The rapid resolution with attainment of euglycemic state and the otherwise normal brain imaging made other possibilities less likely. Doctors in resource-constrained settings should be aware of such rare presentations to avoid misdiagnosis as stroke or seizures and to provide prompt and goal-oriented management with a view to reducing attendant morbidity and health-care cost.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Disclosure

The authors have no multiplicity of interests to disclose.

REFERENCES

1. **Hall V,** Thomsen RW, Henriksen O, Lohse N. Diabetes in Sub Saharan Africa 1999-2011: Epidemiology and public health implications. a systematic review. BMC Public Health. 2011 Jul 14;11(1):564.
2. **Uloko AE,** Musa BM, Ramalan MA, *et al.* Prevalence and Risk Factors for Diabetes Mellitus in Nigeria: A Systematic Review and Meta-Analysis. Diabetes Therapy. 2018 Jun; 9(3):1307.
3. **Sahay BK,** Sahay RK. Neurological emergencies - diabetes management. Neurol India. 2001 Jun;49 Suppl 1:S31-36.
4. **Jagota P,** Bhidayasiri R, Lang AE. Movement disorders in patients with diabetes mellitus. J Neurol Sci. 2012 Mar 15;314(1–2):5–11.
5. **Sanger TD,** Chen D, Fehlings DL, *et al.* Definition and classification of hyperkinetic movements in childhood. Mov Disord. 2010 Aug 15; 25(11): 1538 – 1549.
6. **Kaeley N,** Prasad H, Joseph N, Ghosh Hazra A. A Case of Chorea: A Rare and Unusual Complication of Hyperglycemia. Cureus. 2021 Oct. 13(10): e18730.
7. **Bizet J,** Cooper CJ, Quansah R, *et al.* Chorea, Hyperglycemia, Basal Ganglia Syndrome (C-H-BG) in an uncontrolled diabetic patient with normal glucose levels on presentation. Am J Case Rep. 2014;15:143–146.
8. **Bedwell SF.** Some observations on hemiballismus Neurology. 1960 Jun;10:619–622.
9. **Ruhangisa F,** Stephen H, Senkondo J, *et al.* Acute hemichorea in a newly diagnosed type II diabetes patient: a diagnostic challenge in resource-limited setting: a case report. BMC Res Notes. 2016 Aug 22;9(1):413.
10. **D'Angelo R,** Rinaldi R, Pinardi F, Guarino M. Acute chorea-dystonia heralding diabetes mellitus. BMJ Case Rep. 2013 Sep 2;2013:bcr2013009221.
11. **Kumi D,** Deenadayalan V, Ramirez M, *et al.* ODP261 Non-Ketotic hyperosmolar hyperglycemia induced hemichorea-dystonia syndrome, without radiologic striatopathy. J Endocr Soc. 2022 Nov 1;6(Supplement_1):A340–341.
12. **Wang W,** Tang X, Feng H, *et al.* Clinical manifestation of non-ketotic hyperglycemia chorea: A case report and literature review. Medicine. 2020 May 29;99(22):e19801.
13. **Striano P,** Caranci F, Pappatà S, *et al.* Hemidystonia in Uncontrolled Type 2 Diabetes Mellitus. Arch Neurol. 2011 May 9;68(5):674–674.
14. **Janavs JL,** Aminoff MJ. Dystonia and chorea in acquired systemic disorders. Journal of Neurology, Neurosurgery & Psychiatry. 1998 Oct 1;65(4):436–445.

15. **Dubey S,** Chatterjee S, Ghosh R, *et al.* Acute onset movement disorders in diabetes mellitus: A clinical series of 59 patients. Eur J Neurol. 2022 Aug;29(8):2241–2248.
16. **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.
17. **Oh SH,** Lee KY, Im JH, Lee MS. 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.
18. **Dong M,** E JY, Zhang L, *et al.* Non-ketotic Hyperglycemia Chorea-Ballismus and Intracerebral Hemorrhage: A Case Report and Literature Review. Front Neurosci. 2021;15:690761.
19. **Young AB,** Penney JB. Neurochemical anatomy of movement disorders. Neurol Clin. 1984 Aug; 2 (3):417–433.
20. **Chang KH,** Tsou JC, Chen ST, *et al.* Temporal features of magnetic resonance imaging and spectroscopy in non-ketotic hyperglycemic chorea-ballism patients. Eur J Neurol. 2010 Apr;17(4):589–593.
21. **Wintermark M,** Fischbein NJ, Mukherjee P, *et al.* Unilateral putaminal CT, MR, and diffusion abnormalities secondary to nonketotic hyperglycemia in the setting of acute neurologic symptoms mimicking stroke. AJNR Am J Neuroradiol. 2004 Jul;25(6):975–976.
22. **Jin Z,** Jin Y, Kumar-Mendu S, *et al.* Insulin reduces neuronal excitability by turning on GABA(A) channels that generate tonic current. PLoS One. 2011 Jan 14;6(1):e16188.
23. **Lanciego JL,** Luquin N, Obeso JA. Functional Neuroanatomy of the Basal Ganglia. Cold Spring Harb Perspect Med. 2012 Dec;2(12):a009621.
24. **Abdelghany M,** Massoud S. Nonketotic hyperglycemic chorea. Case Rep Neurol Med. 2014; 2014:128037.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.