

# Co-Existence of Chorea-Hemiballismus and Seizure in a Stroke Patient with Diabetes Mellitus: A Case Report

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**Background.** Non-ketotic hyperglycemia chorea-hemiballismus involves irregular, involuntary movements from high blood sugar. Both hemorrhagic and ischemic strokes can cause movement disorders or seizures, complicating diagnosis since seizures may stem from either condition. The coexistence of diabetes and stroke complicates diagnosis and management due to limited literature on patients with both hemichorea and seizures.

**Case Presentation.** A 74-year-old male with poorly managed diabetes was admitted a year prior due to left sided numbness and weakness with gradual involuntary movements of left upper and lower limbs. Initially suspected of a cerebrovascular infarct, work-up and imaging showed hyperdense changes with possible hemorrhages but no distinct infarct. He was discharged on insulin, oral hypoglycemics, and an anti-cholinergic medications. HbA1c levels were maintained between 5.9% and 7.9% during follow-ups. Recently, he experienced right sided facial spasms with recurrence of involuntary movement on limbs prompting another hospital admission. Further imaging revealed hypodensities in the corpus callosum and left caudate nucleus. Electroencephalogram showed epileptiform discharges on the frontal lobe. The patient was managed as choreic-hemiballismus movement disorder with post stroke seizure, and treated with combined oral hypoglycemics and insulin, Selective serotonin re-uptake inhibitors, anti-seizure medications, and was discharged with improved involuntary movements after control of blood sugar levels during follow-up.

**Conclusion.** Nonketotic-Hyperglycemic chorea-hemiballismus is a rare and poorly understood neurologic complication of Diabetes Mellitus. Control of blood glucose combined with pharmacologic therapy to control involuntary movements remain superior in management of symptoms with good prognosis.

**Keywords.** Hemichorea, Non-ketotic hyperglycemia, Diabetic striopathy, Diabetic hemichorea, Chorea hyperglycemia basal ganglia syndrome

## Introduction

Involuntary movements from hyperglycemia are uncommon manifestations of diabetes and one of its unusual presentations is chorea. Chorea is derived from the greek word 'choreia' which literally means to dance, this consist of involuntary, continual, abrupt, rapid, brief, unsustained, irregular movements that flow randomly from one body part to another.(1)

Non-ketotic Hyperglycemia induced hemichorea can be identified by several names including "Diabetic striopathy", "Diabetic Hemichorea", or "Chorea-hyperglycemia Basal Ganglia syndrome".(2)

The estimated prevalence of this condition is 1 out of 100,000 and it is common among elderly women who

have type 2 diabetes mellitus. Majority of the reported cases are from Asia followed by Europe and America. (2)

## Case Presentation

A 74-year-old male was admitted with complaints involuntary movements on the left upper and lower extremities together with right sided facial spasms. He is known to have diabetes for 5 years and has been on poor compliance to treatment prior to the onset of neurologic symptoms. Other than diabetes, he also was diagnosed with hypertension and has been taking Angiotensin receptor blocker (irbesartan) for almost 5 years.

His present condition started 1 year prior, when he manifested with left sided numbness and weakness associated with involuntary movements of left upper and lower limbs (See Image 1.). He was admitted at a private institution as case of cerebrovascular disease infarct and worked up with a cranial computed tomography scan (Cranial CT scan) showing no evidence of infarct or

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hemorrhage except for pertinent hyperdense changes in the right caudate head and right lentiform nucleus (See Image 2.1).

A cranial Magnetic Resonance Imaging (MRI) was also done showing T1W1 hyperintensities in the right capsuloganglionic region which suggest hemorrhages. (Image 2.2)

Patient was subsequently discharged with home medications of insulin combined with oral hypoglycemic agents, and oral anti-cholinergic agent. Patient had been on regular follow up every 3 months and the patient's HbA1c levels were maintained between 5.9% to 7.9%.

Three days prior to the recent admission, the patient manifested right sided facial spasms (See image 1) which prompted subsequent consult and admission.

Upon reviewing his family history, there is a pertinence of diabetes mellitus from his maternal side however there are no other medical conditions. Review of psychosocial history shows that he was a previous smoker with 20 pack years. He previously worked as a automotive mechanic.



Image 1. Video clips of involuntary movements and Facial spasms (Scan QR code)

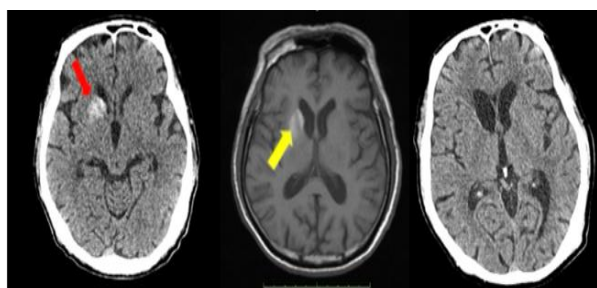


Image 2.1. Hyperdense changes (red arrow) on cranial CT scan

Image 2.2. T1 Hyperintensities in the right capsuloganglionic region (yellow arrow) weighted MRI

Image 2.3. Repeat Cranial CT scan (Recent admission)

Upon assessment, neurologic exam showed normal cranial nerve assessment. Motor strength however was slightly decreased on the left side with only a grade of 4 out of 5 on MRC (modified research council) grading. Involuntary uncoordinated "snake and dance" like movements on left upper and lower extremities (see image 1). Laboratory tests showed normal blood chemistry however HbA1c levels were elevated at 13.2%

with a random blood sugar of 439g/dL. The patient was admitted as a case of a suspected post stroke seizure versus cerebrovascular infarct with poorly controlled Diabetes Mellitus. Repeat cranial CT scan showed subcentimeter low density changes in the genu of the corpus callosum and body of the left caudate nucleus with no evidence of hemorrhages (See image 2.3).

An electroencephalogram (EEG) was performed which showed single epileptiform discharges originating from the right frontal region. (see image 3)

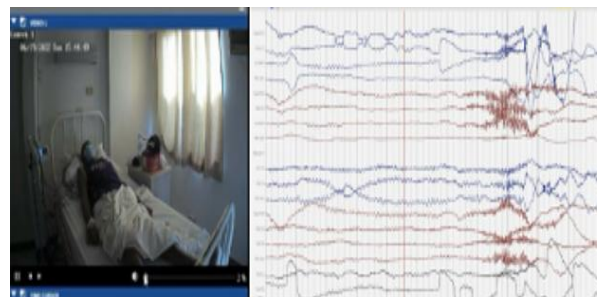


Image 3. Partially recorded video clip of patient's Electroencephalogram (EEG) (Scan QR Code)



The patient was treated for hyperglycemia induced choreic-hemiballismus movement disorder with post stroke seizure disorder. Blood sugar levels were controlled within target levels of less than 130mg/dL (pre feeding) and less than 180 mg/dL (post prandial) using long and intermediate acting insulin and intravenous hydration with saline. Oral anti-convulsant (Levetiracetam 500 mg tablet, twice a day and Tegretol 200 mg tablet, once daily) and a serotonin re-uptake inhibitor (sertraline 25 mg tablet, once daily) were also given to control spasms. Other maintenance medications were also continued from the previous follow-up such as cilostazol 100 mg tablet, once daily; Irbesartan 150 mg tablet once daily, and atorvastatin 40 mg tablet, once daily. Over time, symptoms of involuntary movements improved. He was discharged on the 4<sup>th</sup> Hospital Day, with adequate control of blood sugar within target levels. Long-acting insulin (glargine) and a DPP4-inhibitor combined with biguanide (Sitagliptin + metformin 50/1000 mg tablet, twice daily) were continued at home. Upon follow-up the patient, his blood sugar was controlled within target range of 140-180g/dL, pre and post prandially, with decreased involuntary movements and facial twitching and improved activities of daily living. Overall, he was satisfied with the results of the treatment outcome.

## Discussion

Nonketotic-Hyperglycemic chorea-hemiballismus is a rare condition is associated with both or either one of the two following conditions: (1) chorea/ballism and (2) striatal hyperdensity on computed tomography scan or hyperintensity on T1-weighted Magnetic resonance imaging. (2)

The pathogenesis for developing this involuntary movements involves several theories. One theory which could explain this is the *metabolic disorder theory*, wherein the state of state of hyperglycemia induces the anaerobic metabolism and the tricarboxylic acid cycle becomes suppressed, therefore the principal energy source is the gamma-aminobutyric acid (GABA) which becomes depleted leading to neurotransmitter imbalance, eventually leading to dance-like extrapyramidal symptoms. Another theory involved is the *ischemic injury or ion deposition theory*, wherein the ischemic injury leads to proliferation of astrocytes and the expression of zinc friendly metalloproteins and deposition of magnesium leading to the findings of hyperdensities on T1-weighted imaging findings on MRI. The *hemorrhagic theory* on the other hand states that the hematoma is limited to the lenticular nucleus and putamen nucleus, which does not compress the internal capsule and peripheral structures, nor does it cause edema and space occupying consequences. The *dopaminergic and estrogenic theory* on the contrary explains to us that hyperglycemia may directly lead to changes in dopaminergic activity in the striatum of predisposed patients with dopamine receptors up-regulated and metabolism decreased while estrogen antagonizes the function of dopamine in the substantia nigra striatum system, which leads to the activation of dopamine receptor in the striatum system. Overall this leads to activation of the direct loop in the basal nucleus neural loop and weaken the inhibitory effect of the indirect loop as shown in the figure below. (figure 4)

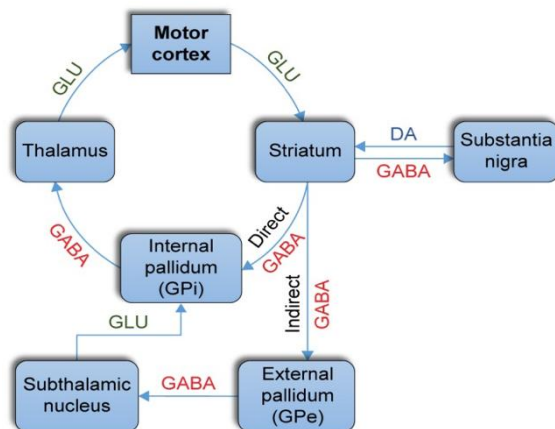


**Figure 4. Diagram of Basal Ganglia motor circuitry unit** including the Direct and indirect pathway.

Abbreviation: Dopamine (DA), Glutamate (GLU), Gamma-amino butyric acid (GABA), Globus pallidum externa (GPe), Globus pallidum interna (GPI)

Source: Nakawah, M. O., & Lai, E. C. (2016). Post-stroke dyskinesias. *Neuropsychiatric disease and treatment*, 12, 2885-2893. <https://doi.org/10.2147/NDT.S118347>

Another postulated theory is *autoimmune inflammatory response theory*. This theory postulates that increased titer of anti-glutamic acid decarboxylase (GAD) in the striatum which leads to GAD-mediated autoimmune injury.

Lastly, the *Neurodegenerative theory* explains that the glycometabolism impairs demyelination of nerve fibers and that waller degeneration of white matter results from the high oncotic pressures from hyperglycemia leading to axonal dehydration which is evident on CT and MRI. (3)

Reported cases show pathologic findings of astrocytosis abundance of gemistocytes (swollen reactive astrocytes). Also findings of hemorrhage with erythrocyte extravasation, focal microhemorrhages, extravascular hemosiderin deposits, and hemosiderin-contained macrophages with confluent infarction, lumen narrowing of arterial wall with fibrosis, punctuate calcification and calcium deposits in biopsies of cases reported. (2)

A large majority of patients presenting with chorea include have arms and legs arm-leg involvement (58.6% of cases reported), followed by arm-leg-face (22.1% of cases) and isolated arm (13.1% of cases). Bilateral involvement is sometimes noted (9.7% of cases reported). (2)

The diagnosis is confirmed by imaging findings of hyperdensities (on the contralateral side of involvement) on CT scan. Similar findings are also noted on T1W magnetic resonance imaging while T2W manifests as well delineated lesions which do not follow vascular distribution and resemble typical ischemia. These lesions are commonly found in the putamen, caudate nucleus and globus pallidus. The sensitivity of MRI is 95% while CT scan is 78%. (2) Most of cases reported also present with elevated blood glucose of upto 20-70 mmol/L (360-1300 mg/100 ml) with blood osmolality of 303-340 mosm/L and HbA1c levels of > 8%. (4)

There is no acceptable gold standard treatment for diabetic striopathy, however literature indicates that treatment primarily involves control of blood glucose levels and proper hydration to correct metabolic problems. Pharmacologic control of involuntary movements are achieved by giving antipsychotics, GABA-receptor agonists, selective serotonin reuptake inhibitors or dopamine-depleting agents. (5). The standard management of seizures is giving anti-convulsant or anti-epileptic drugs. Most patients have good prognosis with majority having resolution of symptoms with good control of blood glucose.

For cases complicated with acute ischemic stroke, Antiplatelet therapy or reperfusion therapy may appear to be beneficial, but the safety of its use needs to be fully assessed due to the possible presence of microvascular hemorrhage. (6)

Resolution of imaging findings can be seen upto 60 days on CT scan and 180 days on MRI. (2). Overall recurrence rates can be upto 18% of reported cases. (2)

## Conclusion

Nonketotic-Hyperglycemic hemichorea remain as uncommon and poorly understood neurologic complication of Diabetes Mellitus. Patients with this condition have good prognosis if managed accordingly.

Control of blood glucose combined with pharmacologic therapy remains superior in management of symptoms.

Limitations in reported cases hinder our understanding of the pathogenesis of this condition.

This case provides insight and a good presentation of improved therapeutic outcomes after adequate control of sugar corresponding to improvement in involuntary movements however, assumptions of clinical outcomes for similar cases still cannot be concluded due to the brief follow up of this case which needs to be followed through.

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