Diabetic striatopathy: a rare complication of hyperglycaemia

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Br J Diabetes 2025;**25**(1):14-17
https://doi.org/10.15277/bjd.2025.472

Key words: type 2 diabetes, diabetic striatopathy, hyperglycaemia, non-ketotic hemichorea/hemiballism

Introduction

The term diabetic striatopathy was introduced into the medical literature about a decade ago.[1] This nomenclature describes a very uncommon medical syndrome characterised by hyperglycaemia, primarily in persons living with type 2 diabetes (T2DM), along with chorea, hemiballismus and basal ganglia abnormalities on CT/MRI brain imaging. Frequently reported in Asian countries, this acute-onset movement disorder is a complication of poorly controlled diabetes.[2] Understanding diabetic striatopathy is essential for accurate diagnosis and management, especially in the context of increasing diabetes prevalence, and will aid improvements in treatment approaches for affected individuals. We highlight a presentation of diabetic striatopathy to our hospital and the challenges with diagnosis and management that it posed.

Case presentation

Patient information

A 47-year-old man of Afro-Caribbean origin with known T2DM presented to the Accident and Emergency unit at our hospital in March 2023 with lethargy, new-onset confusion, polyuria and hyperglycaemia. His blood glucose levels were high at >33. 3 mmol/L) but ketones were absent (<0.1 mmol/L). Blood gas analysis showed a normal pH of 7.35 (normal range 7.32-7.43), HCO_3- 29.1 mmol/L) (normal range 20-28), lactate 2.3 mmol/L) (0.6-1.4) and acutely impaired renal function (urea 20 mmol/L, creatinine 349 umol/L, estimated glomerular filtration rate (eGFR) 17 mL/min/1.73m^2, sodium (Na+) 121 mmol/L, potassium (K+) 4.5 mmol/L).

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Clinical findings

He did not meet the criteria for hyperosmolar hyperglycaemic state, as his calculated serum osmolality was 298 mosmol/kg, which is below the 320 mosmol/kg threshold, nor for diabetic ketoacidosis and was managed with intravenous insulin and fluids. His HbA_{1c} was 18.2% (175 mmol/mol). His blood sugars remained elevated between 15-26 mmol/L.

T2DM had been diagnosed in 2014, and his past medical history included hypertension, multiple strokes (both hemorrhagic and ischaemic), gout and unprovoked deep vein thrombosis on long-term anticoagulation. He also had a history of erectile dysfunction, for which he took phosphodiesterase inhibitors pro re nata. There was no documented evidence of diabetic retinopathy screening.

His regular medications included linagliptin, empagliflozin, edoxaban, atorvastatin, ezetimibe, losartan, amlodipine, bisoprolol, sertraline, omeprazole, cyanocobalamin and allopurinol.

Six days after admission, he developed chorea of his right arm with mild dysarthria but no other abnormal neurological findings.

Diagnostic assessment

A CT scan completed on the same day ruled out an acute stroke. However, it showed an old lacunar infarct/gliosis of the right cerebellum, the head of the right caudate nucleus, the deep white matter and the gangliocapsular region; and background moderate small vessel disease. There was unilateral hyperdensity of the left lentiform nucleus, more prominent this time compared with previous images (Figure 1). The differentials considered for these hyperdense areas were mineralization or striatal lesions resulting from poorly controlled diabetes.

On discussion with the neurology team, and given the acute onset of the unilateral chorea, the history of poorly controlled diabetes and the CT scan showing a classical basal ganglia hyperdensity on the contra-lateral side, it was concluded that the right arm chorea was most likely diabetic striatopathy, as a result of his longstanding poor glycaemic control. An MRI was not completed at the time. No anti-chorea medications were started as the patient's symptoms largely resolved with the attainment of euglycaemia.

Figure 1. Brain CT images **A** and **B**, showing area of hyperdensity of the left lentiform nucleus (red arrows) (March 2023)

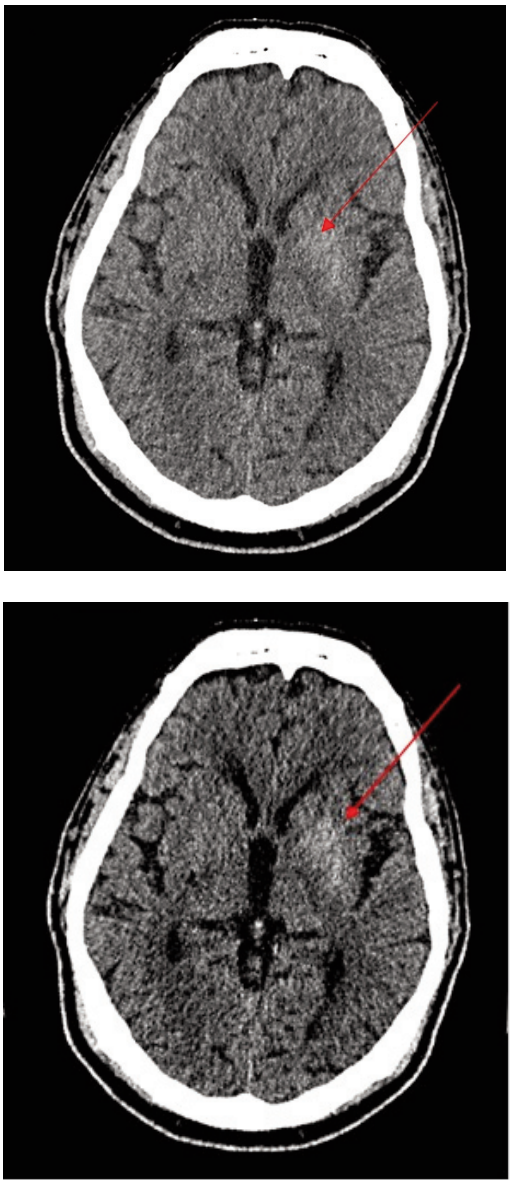
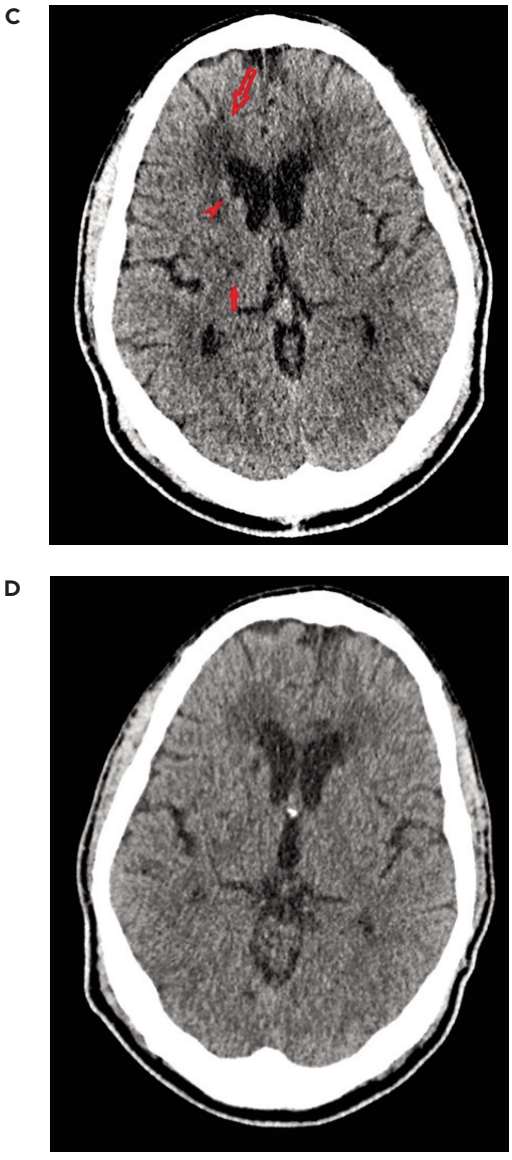


Figure 2. Brain CT images. **C**: April 2023, axial section depicts head of caudate nucleus infarcts (red arrow head), lacunar infarcts of the gangliocapsular region (red arrow) and moderate burden of small vessel disease (red open arrow). **D**: April 2023, unenhanced axial section demonstrates resolved hyperdensity of the left striatum



After eight days in hospital, he was discharged to continue insulin therapy, with Humulin I 20 units twice a day in addition to his regular oral diabetes medications.

Clinical course

One month later, he reported to the ambulatory unit of the hospital with worsening involuntary chorea of the right upper limb. Abnormal movements initially involved the right arm, later spreading to involve the shoulder. The chorea was constant, fluctuated in intensity and worsened during periods of increased anxiety. Neurological examination showed a slight pronator drift, mildly increased tone and slight hyper-reflexia on the right arm. He had bilateral extensor plantar reflexes with unimpaired gait. Power was difficult to assess because of the chorea. His random blood glucose on arrival was 5.1 mmol/L.

Therapeutic intervention

An MRI brain scan could not be completed due to patient agitation while in the scanner. A head CT scan was completed with no acute intracranial finding, i.e. intracranial haemorrhage, acute infarct or mass lesions. It did, however, show head of caudate nucleus infarcts, lacunar infarcts of the gangliocapsular region and moderate burden of small vessel disease (Figure 2).

After assessment by the neurology team, he was started on tetrabenazine 25 mg three times daily with marked improvement of the involuntary movement.

Follow-up and outcome

Although the chorea had improved by the time of discharge, it was still present after five days in hospital. Tetrabenazine was increased to 150 mg daily in divided doses on outpatient review.

Discussion

Diabetic striatopathy, also known as hyperglycaemic non-ketotic hemichorea/hemiballism or diabetic hemichorea/hemiballism,[3,4] is an uncommon neurological complication of uncontrolled diabetes that remains poorly understood.[2] With a prevalence of <1 in 100,000,[5] the unifying triad of this presentation is hyperglycaemia, chorea or hemiballismus, and classical basal ganglia abnormalities on neuroimaging.[1] It has been described predominantly in elderly Asian females with poorly controlled T2DM, presenting acutely or sub-acutely and often in the absence of ketone bodies, but there are increasing reports across the globe in different populations.[6] It is a heterogenous disorder. Most reported cases are unilateral,[7] as in our case, but they are occasionally bilateral,[8] often occurring at the height of the glucose rise. Occasionally, the hyperkinetic movements occur after the initial hyperglycaemic episode.[9-11]

The molecular pathogenesis is thought to be multi-factorial, with several underlying mechanisms. Possible mechanisms put forward include neurological dysfunction from vasculopathy or metabolic changes. Hyperglycaemia-induced hyperviscosity and dehydration may lead to cerebrovascular insufficiency.[11,12] The impaired circulation leads to neurovascular uncoupling, as is seen in diabetic microangiopathy.[13] This has been supported by striatal cytotoxicity histology findings of gliosis, neuronal loss and reactive astrocytosis with abundant gemistocytes.[1] Another proposed hypothesis is the use of Gamma-Aminobutyric Acid (GABA) as an alternative energy source during the hyperglycaemic crisis because cerebral metabolism shifts to the anaerobic pathway of glucose metabolism. GABA depletion leads to thalamic disinhibition and hyperkinesia.[7,14] These theories, however, do not completely explain the unilateral onset in some cases for this is a systemic disorder. Again, there are reports of the chorea persisting or appearing after the correction of hyperglycaemia, as in our case. Further studies are needed to explain this fully.

While ischaemic and haemorrhagic strokes can cause chorea,[15,16] prior CT imaging obtained during the evaluation of our patient's strokes did not demonstrate the prominent area of hyperdensity in the left lentiform nucleus that was reported on the current admission. The repeat CT scan findings on his last visit were unchanged from the initial hospitalisation. Chorea can sometimes persist or manifest later in patients with diabetic striatopathy,[17] often reversing with normalization of glucose levels. It is possible that the chorea was triggered by the correction of the hyperglycaemia, much akin to the worsening of diabetic retinopathy with intensive glycaemic control.

The exact cause for this neuroimaging finding remains to be elucidated. Mechanisms proposed include mineralization,[18] although this is unlikely given that often the choreiform movements significantly reverse or improve with anti-chorea medication (tetrabenazine in our case) and correction of hyperglycaemia. Our case was typical, with the chorea occurring at the height of the patient's hyperglycaemia. There are reports of paradoxical cases, in which the chorea occurred after the correction of the hyperglycaemia.[10,11,17] Petechial haemorrhages have also been proposed,[19] and although possible in our case especially as he was on long-term anticoagulation with edoxaban, the haemorrhages were not evident on repeat CT scan. The two other proposed reasons are myelin destruction,[20] as occurs in neuronal injury, and gemistocyte accumulation due to neuronal infarction,[18] accounting for the T1 hyperintensity noted on MRI. MRI scans provide better yield in striatal abnormalities.[21] Unfortunately, our patient could not undergo an MRI scan due to safety concerns.

Diabetic striatopathy has an excellent prognosis. It often resolves completely following correction of hyperglycaemia,[22] with or without anti-chorea medications. Radiological resolution lags clinical improvement.[7]

Key messages

- Clinicians should have an awareness of diabetic striatopathy as a rare but significant complication of diabetes.
- Neuroimaging is crucial in diagnosing diabetic striatopathy in patients with unilateral chorea and hyperglycaemia.
- Early involvement of multiple relevant specialists; including a neurologist, radiologist and diabetologist, is key to prompt diagnosis and management of diabetic striatopathy.

Conclusion

We have presented a distinctive case of diabetic striatopathy in which chorea in association with a left lentiform nucleus hyperdense area on CT imaging initially resolved with correction of the acute hyperglycaemia. It subsequently worsened during the period of euglycaemia but responded well to anti-chorea medications. The rapid changes in the glucose milieu may have unmasked a quiescent striatal lesion from the longstanding poor glycaemic control. Complete resolution had not occurred at the time of discharge, indicating that symptoms may sometimes linger.

Conflict of interest None to declare.
Funding None.

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