CASE REPORT

Reactive hypoglycaemia: a rarely considered 'stroke mimic' in non-diabetic individuals

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SUMMARY

Hypoglycaemia is a well-documented 'stroke mimic'. The literature documents numerous case reports of patients presenting with focal neurological deficits subsequently attributed to hypoglycaemia. The significant majority of these cases are found in patients with pre-existing diabetes. We present case histories of two patients with no history of diabetes presenting to secondary care with reactive hypoglycaemia causing transient symptoms that were responsible for referral as a possible transient ischaemic attack. Although uncommon, metabolic disturbances such as hypoglycaemia should be considered in all patients presenting as a suspected stroke, even if they are not known to have diabetes.

BACKGROUND

The diagnosis of an acute stroke and transient ischaemic attack (TIA) relies heavily on a thorough history from an inquisitive historian. Despite significant advancement in imaging techniques, the diagnosis remains a clinical one, particularly when considering a diagnosis of a TIAs. There are a myriad of alternative pathologies that present to the TIA clinic that may mimic such, meaning that the potential for misdiagnosis is significant unless careful attention is given to obtaining a thorough history.

'Stroke mimics' such as seizures, demyelination, space occupying lesions and metabolic disturbances including hypoglycaemia are well documented in the literature.¹⁻³ Hypoglycaemia is a common complication in patients with diabetes following adjustment of antidiabetic medications, in particular sulphonylureas or insulin, or changes in caloric intake or significant weight loss.⁴ Consequently, a medical history of diabetes mellitus and treatment with one or more hypoglycaemic agents should act as a major prompt to the consideration of hypoglycaemia as the cause for the neurological symptoms reported in a TIA clinic. However, in absence of these factors, stroke physicians might not consider the possibility of hypoglycaemia in their differential diagnosis.

We present two cases of reactive hypoglycaemia, in non-diabetic patients, of patients referred to our TIA service with symptoms of focal neurological deficit initially thought to be secondary to TIA/minor stroke. On reviewing the literature, we could find no documented cases of reactive hypoglycaemia mimicking stroke.

CASE PRESENTATION

Case 1

A 65-year-old right-handed retired engineer was referred to the rapid access TIA clinic from his general practitioner with recurrent episodes of transient slurred speech and associated sweating with no focal limb weakness. His medical history included cancer of the vocal cords for which he underwent radiotherapy 10 years previously; squamous cell lung cancer, in remission postpneumectomy and chemotherapy 7 years previously; Barrett's oesophagus; malignant large bowel polyps removed endoscopically; liver haemangiomas; asthma; postural hypotension and iron deficiency anaemia. He was not known to have diabetes and was not prescribed any hypoglycaemic agent.

He was an ex-smoker and consumed between 20 and 25 units of alcohol per week.

These symptoms had occurred intermittently over the previous 3 years with up to 12 episodes experienced over a 2-year period. An ambulatory 24-hour blood pressure (BP) monitor did not record any periods of significant hypotension, with an average BP of 126/76 mm Hg.

His carotid Doppler imaging demonstrated a 51%–70% stenosis of the left internal carotid artery with a completely occluded right internal carotid artery—thought to be secondary to his previous radiotherapy. His subsequent CT angiogram of carotid and vertebral arteries confirmed the Doppler findings and revealed an incomplete circle of Willis with congenitally absent left posterior communicating artery. MRI of the brain demonstrated only chronic small vessel changes. Due to his significant bilateral carotid stenosis and clinical suspicion of postural hypotension, initially, his symptoms were thought to be due hypoperfusion syndrome. He was commenced on fludrocortisone 100mg daily with a modest improvement in symptoms as well as being referred for carotid endarterectomy. Prior to his surgery, he developed angina with subsequent investigations revealing coronary artery disease. This was treated with a drug-eluting stent in his proximal and mid right coronary artery. He then underwent a left-sided carotid endarterectomy.

Despite successful surgery, he continued to have recurrent focal neurological symptoms. Prior to one of his hospital presentations, the attending paramedic recorded a serum glucose concentration of 2.6 mmol/L at the scene of his symptoms, which improved with oral supplementation. All subsequent laboratory blood glucose levels documented were within normal limits. On closer questioning,

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he admitted that since undergoing chemotherapy for lung cancer, he rarely felt hungry and often went without food for several hours. Furthermore, his symptoms were often preceded by periods of fasting or unusually large meals.

Given the absence of symptomatic improvement despite carotid endarterectomy and the concomitant presence of hypoglycaemia during one episode of symptoms, a diagnosis of reactive hypoglycaemia was considered. He was investigated for reactive hypoglycaemia, adrenal insufficiency and insulinoma.

Case 2

An 89-year-old man attended the accident and emergency (A&E) department in July 2016 with a transient left-sided facial droop, lasting a few minutes. On examination, there was no demonstrable focal neurology. He had a medical history of chronic kidney disease, hypertension, pulmonary fibrosis, a previous TIA in 2007, aortic and mitral regurgitation and suprapubic catheter following prostatectomy. He was not known to be diabetic and was not prescribed any hypoglycaemic agents.

Blood tests including his glucose level and lipid profile were normal. His BP was recorded at 126/63 mm Hg.

He was urgently referred to our TIA service and reviewed on the same day where his BP was recorded at 147/71 mm Hg and demonstrated no significant drop on standing. He was diagnosed with a suspected right hemispheric TIA, commenced on clopidogrel 75 mg daily and an urgent MRI brain scheduled.

A Carotid Doppler Ultrasound Scan was performed showing <30% stenosis of the carotid arteries bilaterally, and an ECG showed sinus rhythm.

Three days later, he was attended with identical symptoms and a similar clinical presentation. He was again referred to the TIA clinic with suspected crescendo TIAs. On revisiting the history of the presentation, it was apparent that his symptoms began shortly after eating large daily meals. Furthermore, he reported also having had six similar episodes previously, occurring on a weekly basis.

INVESTIGATIONS

Case 1

An extended glucose tolerance test (eGTT) showed a normal glucose profile for the first 2 hours but a drop to 3.0 mmol/L at 150 min before improving to 3.5 mmol/L at 3 hours (figure 1). A prolonged 72-hour fasting glucose test revealed a drop in

serum glucose to 2.2. Insulin and insulin C-peptide levels were both within normal limits at <3 pmol/L and 261 pmol/L respectively—thus excluding exogenous insulin and insulinoma. Serum 9am cortisol was also unremarkable at 171 nmol/L, excluding Addison's disease.

Case 2

MRI of the brain showed no acute infarction or major haemorrhage but evidence of multiple previous microhaemorrhages possibly suggestive of cerebral amyloid angiopathy. However, given the temporal relationship of his symptoms occurring after consuming large meals, these MRI findings were not thought to have been relevant to the man's symptoms.

An eGTT was organised (figure 1), confirming a diagnosis of reactive hypoglycaemia.

DIFFERENTIAL DIAGNOSIS

Reactive hypoglycaemia, adrenal insufficiency and insulinoma.

TREATMENT

Case 1

The patient was diagnosed with reactive hypoglycaemia for which he was referred to a dietitian and commenced on a low-Glycaemic Index diet and advised to take frequent meals. Consideration was given to a trial of acarbose should his symptoms remain problematic.

Case 2

Advice was given with regard to eating more frequent and smaller portioned meals at specific times.

OUTCOME AND FOLLOW-UP

Case 1

At the time of submission, the patient has only one further episode which occurred after missing his midday meal and was terminated by the administration of sugary drinks by their partner.

Case 2

At the time of submission, no further episodes of transient neurological deficit had occurred after the aforementioned dietary changes.

DISCUSSION

While the need to consider hypoglycaemia as a potential alternative explanation to stroke in patients presenting with acute neurological deficit is well documented in the setting of patients known to have diabetes, a literature review searching for 'TIA', 'hemiplegia' and 'hemiparesis' with 'hypoglycaemia' did not reveal any previous case publications of reactive hypoglycaemia mimicking stroke.

A medical history of diabetes mellitus and use of medications prone to causing hypoglycaemia frequently acts as a prompt when assessing patients in the TIA clinic to consider the possibility of fluctuations in blood glucose concentration as a cause for the symptoms reported. These cases demonstrate the importance of considering hypoglycaemia as a cause even in 'non-diabetic patients'.

Postprandial hypotension is an important differential diagnosis for consideration in both cases. We could not find any documentation of hypotension on either case's arrival to the A&E department, or drop in postural BP when assessed in our

Extended Glucose Tolerance Test (Two Cases)

Figure 1 A graph showing the results of extended glucose tolerance testing for cases 1 and 2.

clinic. Although BP was not recorded during eGTT; given the hypoglycaemia demonstrated on each eGTT, reactive hypoglycaemia was thought to be a much more probable cause for their symptoms.

The differential diagnoses for non-diabetic patients presenting with hypoglycaemia include reactive hypoglycaemia, alcohol, Addison's disease, liver failure, severe sepsis and insulinoma.⁵

Reactive hypoglycaemia (also referred to as postprandial hypoglycaemia) may be considered in the presence of a triad of symptoms known as Whipple's triad⁶:

1. Symptoms consistent with hypoglycaemia.
2. Low plasma glucose concentration.
3. Resolution of symptoms when the plasma glucose concentration is corrected.

In such patients temporal relationship of consumption of a meal with high Glycaemic Index prior to onset of symptoms is common. The aetiology is thought to be due to hyperinsulinism in response to high-carbohydrate loads. Furthermore, susceptible patients commonly have a degree of insulin resistance causing a rapid, abrupt rise in insulin secretion postprandially resulting in a precipitous drop in serum glucose.⁷

The signs and symptoms of hypoglycaemia are multiple and range from subtle deficits in concentration and confusion to coma.⁴ Case 1 in this series presented with constitutional symptoms as well as more focal neurological signs and demonstrates the importance of enquiring about such symptoms as part of a thorough history. In patients with multiple vascular risk factors, it can be easy to rush to a diagnosis of TIA and in doing so, overlook alternative possibilities such as hypoglycaemia.

The neurological deficit seen in cases such as these are easily reversible with correction of plasma glucose concentration. Mistakenly attributing a focal neurological deficit to acute ischaemia exposes the patient to unnecessary emotional distress at the diagnosis and potential physical harm due to the burden of antiplatelet and antilipid medication and major carotid surgery as well as impact of unnecessary driving restrictions or inflated health and travel insurance premiums.

Learning points

- ▶ A thorough history including chronology and temporal relationships of symptoms and presentations is paramount in the correct diagnosis of stroke in order to exclude reversible alternative diagnoses.
- ▶ Reactive hypoglycaemia is a rare but important cause of stroke mimic.

Contributors The case series was compiled by KC after initial discussions with DE regarding differential diagnoses for the presentations described. WW: wrote initial paper including abstract, background, case 1 and discussion. BH: wrote case 2, obtained patient consent and created graphical form of extended glucose tolerance test results. DE: diagnostic work-up, analysis and evaluation of glucose tolerance test results and reviewed final manuscript. KC: reviewed and edited manuscript.

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