CASE REPORT

Hypoglycaemia in a patient who is non-diabetic

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SUMMARY

A 59-year-old Caucasian man was seen in clinic following general practitioner's referral presenting with a 1-year history of hypoglycaemia. It was deemed important given his history that an insulinoma should be ruled out. The patient had an induced episode of hypoglycaemia while under medical supervision; C-peptide, insulin and insulin-like growth factor levels were measured. These results strongly suggested an insulinoma. He was subsequently referred to our local tertiary centre for surgical workup and excision of the insulinoma. This case reminds us that insulinoma, although rare, is an important differential to rule out in non-diabetic hypoglycaemia. Often the diagnosis is overlooked as their symptoms mimic many other conditions. Although there is no specific Driver and Vehicle Licensing Agency advice, we, as the healthcare provider, should be ensuring the patients inform them.

BACKGROUND

Low blood glucose levels have been recorded and documented in the literature since the early 19th century. However, not until the treatment of diabetics in the 1920s was it understood that overtreatment with excess insulin would cause low blood sugars. Similar patient populations were recognised. They had similar symptoms to those overtreated with insulin; however, they were neither diabetic nor taking insulin. They called the condition hyperinsulinism. The first cure was reported in 1929 following the surgical removal of an insulinoma.¹

Although a relatively rare condition, with an incidence rate of 0.4/100 000 person-years, it is an important condition not to be misdiagnosed as it can be easily treated once diagnosed.² Although a relatively rare condition, with an incidence rate of 0.4/100 000 person-years, it is an important condition not to be misdiagnosed as it is easily treatable once identified. A proportion of them make a wider syndrome called MEN 1 (multiple endocrine neoplasia); these are autosomal-dominant conditions that affect the endocrine glands (pituitary, parathyroid and pancreas).

CASE PRESENTATION

A 59-year-old Caucasian man was seen in clinic following general practitioner's (GP) referral. He reported a 1-year history of hypoglycaemic episodes. He had seen his GP on several occasions but never presented to the accident and emergency department. Over the year these episodes were increasing in frequency. During an episode, his blood sugar level would drop to 2.1 mg/dL; despite this, he never lost consciousness. There was no

clear cause. However, the patient did think that it was more likely to occur following a cup of coffee. There were neither neuroglycopenic symptoms (change in behaviour, mood, confusion or visual disturbance) nor any sympathoadrenergic symptoms (palpitations, tremors and diaphoresis) reported.

His medical history was unremarkable; previously he had an inguinal hernia repair. He had no history of alcohol misuse and was a non-smoker. There was no significant family history. Examination revealed a body mass index of 30. Blood pressure was 140/80 mm Hg; all other examinations were unremarkable.

It was concluded that this patient needed further work-up to rule out an insulinoma.

INVESTIGATIONS

Fasting hypoglycaemia induced:

Blood sugar 2.5 mg/dL

Serum C-peptide 649 pmol/L

Serum insulin-like growth factor 1 33.1 (normal range 7.1–21.1) nmol/L

Serum insulin 131 pmol/L

A CT of the abdomen was performed (see figure 1). This found a 1.4 cm enhancing mass arising from the head of the pancreas, with preserved pancreatic mass volume and no duct dilation. There were no liver metastases or any other significant abnormalities on the scan.

DIFFERENTIAL DIAGNOSIS

- ▶ Refractory hypoglycaemia
- ▶ Familial persistent hyperinsulinaemic hypoglycaemia of infancy
- ▶ Primary islet-cell hyperplasia (nesidioblastosis)
- ▶ Insulin misuse
- ▶ Non-insulinoma pancreatogenous hypoglycaemia syndrome
- ▶ Postgastric bypass hypoglycaemia.

TREATMENT

The patient was referred to a surgical specialist centre, Guys & St Thomas' National Health Service (NHS) Trust, for excision of the tumour.

OUTCOME AND FOLLOW-UP

Success of the surgical treatment has been defined as being free of symptoms for 6 months or longer following surgery.

DISCUSSION

The two main bodies of data regarding insulinoma have come from two case series from the Mayo Clinic. Their two datasets are from 1927 to 1986 and a later one from 1987 to 2007.

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Figure 1 An axial view of the abdomen capturing the insulinoma.

Although insulinomas are rare, it is still important to consider the possible diagnosis in any patient presenting with non-diabetic hypoglycaemia. The Mayo Clinic case series from Olmstead County from 1987 to 2007 found that 73% of patients experienced only hypoglycaemia in the fasting state, 21% experienced symptoms while fasting and postprandially. A further 6% with confirmed insulinoma reported only postprandial hypoglycaemia.²

Most patients who have an insulinoma, unlike this case, experience other symptoms. These can be split into two groups. The neuroglycopenic symptoms are normally associated with the hypoglycaemic state and are corrected once a normal blood sugar is achieved; they include altered behaviour, confusion and visual disturbance.³ The sympathoadrenergic symptoms include palpitations, sweating and tremors.⁴ These symptoms are often responsible for masking the underlying diagnosis and can lead to a delay in recognition of the underlying pathology. The same Mayo Clinic cohort found that the average time between onset of symptoms and diagnosis was 1.5 years.⁵ If suspected, the patient should be referred to a specialist centre early for testing and diagnosis. The majority of cases are curative with surgery.⁵ Once cured the patient's former quality of life can be returned.

Initial blood testing can confirm the diagnosis of an insulinoma. However, it does not locate the site of the tumour. Rather than explorative pancreatic surgery, a number of other specialist tests have been developed. Initially, a transabdominal ultrasound (US) or CT of the abdomen should be performed. In our case, CT located the tumour, and hence no further imaging was required. However, if CT or US is unable to locate any pancreatic abnormalities, then radionuclear imaging should be considered.⁶ The two techniques available are ¹¹¹In-pentetreotide imaging and fluorine-18-L-dihydroxyphenylalanine positron emission tomography.⁷ The choice of scan is dependent on which services are available locally. If these non-invasive tests are negative but the patient continues to demonstrate endogenous hyperinsulinaemic hypoglycaemia, then invasive tests should be performed. Endoscopic US has been found to be more sensitive than CT or transabdominal ultrasonography in the detection

of pancreatic insulinomas. The alternative to this is selective arterial calcium stimulation, the main advantage of which is that it is a dynamic test and has been shown to be more sensitive than endoscopic US.⁸

The Driver and Vehicle Licensing Agency (DVLA) have a specific form for patients with diabetes taking insulin called the DIAB1 medical form.⁹ However, there is no section in the form for patients who are non-diabetic who experience hypoglycaemic episodes. It is obvious that patients with an insulinoma are at a similar risk to patients who are overtreated for their diabetes and therefore had hypoglycaemic episodes, and as such should have to inform the DVLA.

Learning points

- ▶ Insulinomas are a rare condition characterised by episodes of hypoglycaemia normally associated with fasting but can occur postprandially.
- ▶ Insulinoma is often a late diagnosis, as the characteristic symptoms are often misdiagnosed. If suspected, early referral to specialist centre for testing and confirmative diagnosis is appropriate as the majority of cases are curative.
- ▶ There is currently no Driver and Vehicle Licensing Agency (DVLA) advice for drivers with an insulinoma, but only for patients with diabetes prone to hypoglycaemic episodes. We as the patients' healthcare providers should be raising awareness of the condition and advising patients to inform the DVLA.

Contributors WT wrote the main body of the manuscript. DU has helped to edit and amend various versions along the way with CP helping to amend the final version.

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