

Spontaneous hypoglycaemia in a nondiabetic man with end stage renal disease caused by repaglinide or endogenous hyperinsulinaemia: An enigma entangled

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Introduction

The commonest cause of hypoglycaemia in people with diabetes is the mismatch between insulin or oral hypoglycaemic drugs and carbohydrate intake or exercise. Hypoglycaemia in people without diabetes is usually due to reactive hyperinsulinaemia and can also result from severe illness, sepsis, malnutrition, Addison's disease, alcohol, inadvertent or factitious use of insulin or oral hypoglycaemic agents and islet cell tumours. The latter group occasionally poses a diagnostic challenge. We present a similar case where hypoglycaemia remained a mystery: an enigma entangled.

The clinical case

A 56 year old man was admitted from psychiatry ward after episode of symptomatic hypoglycaemia with capillary blood glucose of 2.5 mmol/L. His background included chronic kidney disease on thrice weekly haemodialysis, ischaemic heart disease, cerebrovascular disease, hypertension and paranoid psychosis. He was inpatient in a psychiatric ward during the episode of hypoglycaemia. He was not known to have diabetes and denied taking hypoglycaemics. His oral intake was normal and weight was stable. He had another symptomatic fasting hypoglycaemia after 22 hours of hospital admission with venous glucose of 1.5 mmol/L. Simultaneous Insulin and C-peptide levels suggested endogenous source of hyperinsulinaemia. Biochemical investigations are summarised below.

Investigation	Result	Normal limits
Venous glucose	1.5 mmol/L	
Insulin	320 mU/L	3.0–17.0
C peptide	7935 pmol/L	260–650
Sulphonyluria screen	Negative	
HbA1c	29 mmol/mol	
Chromogranin A	260 pmol/L	<60
Chromogranin B	202 pmol/L	<150
Short synacthen test	Normal	

Collateral history revealed complex psychosocial background surrounding the events. His psychiatric team confirmed that he had paranoid psychosis and believed that his family members were trying to kill him. Further information revealed that one of his close relatives had diabetes treated with metformin and repaglinide. He and his family denied drug dispensing error or mix up of tablets. His blood samples taken during hypoglycaemia were sent to the national laboratory for further drug screening to exclude inadvertent drug intake. High performance liquid chromatography (HPLC) detected his usual medications and metformin but no other oral hypoglycaemics. The laboratory also suggested that HPLC does not completely rule out presence of other drugs as some of the drugs might not have been detected due to interaction of tubes containing gel in HPLC, although the possibility of this was less likely.

Meanwhile, the medical team also suspected an insulinoma and booked CT abdomen which revealed a deformity in pancreatic head (see figures 1-4). MRI pancreas showed lobulation of pancreatic head with no foci of contrast enhancement. His case was discussed in pancreatic MDT meeting and the abnormality was thought to be an anatomical variation of pancreas rather than a tumour. The MDT recommended further investigations including endoscopic ultrasound.

Imaging



Figure 1: CT imaging of pancreas



Figure 2: CT imaging of pancreas



Figure 3: CT imaging of pancreas



Figure 4: CT imaging of pancreas

Further progress

Patient did not comply with further investigations including an inpatient supervised fast and prolonged glucose tolerance test. Therefore, he was managed conservatively during hospital stay for 6 weeks and did not have further hypoglycaemic episodes. He and his family was educated for identification and management of hypoglycaemia. He was discharged with glucometer, oral dextroglucagon and glucagon injecton as required. He and his family did not report any hypoglycaemic events during his outpatient follow up for a year.

Discussion

The cause of fasting hypoglycaemia in this case remains unknown. Hyperinsulinaemia induced by repaglinide remains a strong suspicion, supported by his psychosocial background with possibility of fowl play, family history of metformin and repaglinide intake, detection of metformin by HPLC, technical limitation of HPLC to detect some drugs and the fact that he did not have further hypoglycaemia for a year. Endogenous hyperinsulinaemia due to insulinoma could not be entirely excluded due to patient non-compliance for further investigations, although it seems less likely due to above mentioned reasons.

Learning points

Chronic kidney disease poses a challenge in investigations for hypoglycaemia. Renal failure is a cause of hypoglycaemia and can falsely elevate chromogranin and C-peptide levels as they are excreted renally. Therefore, one should exercise caution when interpreting these results.

Hypoglycaemia due to sulphonylureas and repaglinide should always be considered in hypoglycaemia with high insulin and non suppressed C-peptide levels. Repaglinide is a prandial insulin secretagogue, and is primarily excreted in bile but clearance is reduced in advanced renal impairment (eGFR less than 30 mL/min). Therefore, prolonged monitoring of blood glucose is required in patients with suspected repaglinide intake. If sulphonyluria (and repaglinide) screen is negative, the endogenous source of hyperinsulinaemia should be sought. Surreptitious intake of insulin leads to hypoglycaemia with high insulin and suppressed C-peptide levels.

Irrespective of the cause of hypoglycaemia, patients should be counselled to identify symptoms of hypoglycaemia, measure capillary blood sugar and promptly treat hypoglycaemia. Long term follow up is essential. Hypoglycaemia may also have personal implications, e.g., driving and occupation.

References

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