

# Insulinoma in a patient with type 2 diabetes

Insulinomas are rare pancreatic islet cell tumours occurring in four per million per year.<sup>1</sup> They are usually benign, small and solitary, although up to 16% are malignant.<sup>2</sup> While most are sporadic, multiple endocrine neoplasia type 1 is present in up to 16% of patients. The characteristic clinical manifestation of an insulinoma is fasting hypoglycaemia, although some patients also have postprandial hypoglycaemia, with neuroglycopenic symptoms which may or may not be preceded by sympathoadrenal (autonomic) symptoms.<sup>3</sup> We report a rare case of normalising blood glucose and hypoglycaemia in a patient with long-standing type 2 diabetes.

## Case report

An 82-year-old frail male patient with type 2 diabetes, dementia and stable chronic kidney disease was admitted twice to the medical admission unit over a period of six weeks with hypoglycaemia. He had been taking metformin and gliclazide but over the last few months had been having recurrent episodes of hypoglycaemia in his care home; hence both oral hypoglycaemic agents were gradually withdrawn and stopped. None of his other medications was known to cause hypoglycaemia. Glycaemic control continued to improve spontaneously, evident by a progressive decline of his HbA<sub>1c</sub>.

During his last hospital admission he was admitted being generally unwell for the last few weeks and was hypoglycaemic on admission. The patient was treated with intravenous dextrose infusions but continued to have recurrent hypoglycaemic episodes off the infusion. Electrolytes were within the reference range; eGFR was low at 53ml/min/1.73m<sup>2</sup> but had been stable over the last few months. Liver function tests showed a low albumin of 23g/L (ref range 35–50) with an elevated alkaline phosphatase level of 196U/L (ref range 30–120). HbA<sub>1c</sub> was 4.9% (30mmol/mol). Adrenal insufficiency was excluded with an adequate cortisol response to synacthen. Urine sulfonyleurea screen was negative. Inappropriately elevated insulin and C-peptide levels were demonstrated during his hypoglycaemic

Variable	Result	Reference range
Venous glucose	0.4mmol/L	2.5–11
Serum insulin	11.6mu/L	1.6–10.9
C-peptide	4.38nmol/L	0.11–0.61

**Table 1.** The patient's results during one of his hypoglycaemic episodes

episodes (see Table 1). Abdominal ultrasound showed multiple hepatic metastasis with a urinary bladder mass causing bilateral hydronephrosis. Abdominal CT scan revealed a focal pancreatic head lesion, locally advanced urinary bladder tumour. Multiple hepatic and pulmonary metastatic deposits were also documented. Unfortunately, the patient continued to deteriorate and passed away. The clinical diagnosis was metastatic insulinoma supported by strong biochemical and radiological evidence. Bladder tumour was considered to be coincidental.

## Discussion

The diagnosis of insulinoma depends on the exclusion of the more common causes of hypoglycaemia, especially in patients with pre-existing diabetes, and on the demonstration of inappropriately raised plasma insulin and C-peptide levels during a spontaneous or induced episode of hypoglycaemia (e.g. 72-hour fast). Imaging techniques are then used to localise the tumour. Accurate preoperative localisation of an insulinoma is essential.

Non-invasive procedures available include: transabdominal ultrasonography, spiral CT, 111-In-pentetreotide imaging, and fluorine-18-L-dihydroxyphenylalanine positron emission tomography.<sup>4,5</sup> In patients with endogenous hyperinsulinaemic hypoglycaemia and negative non-invasive radiologic localisation studies, endoscopic ultrasonography or a selective arterial calcium stimulation test with hepatic venous sampling can be performed to localise the tumour.<sup>6,7</sup>

Surgical removal of the insulinoma is the treatment of choice. Overall, with appropriate preoperative localisation studies plus intraoperative ultrasonography and palpation, a tumour

(or tumours) can be identified in 98% of patients with insulinomas. Medical therapy should be considered in the patient whose insulinoma was missed during pancreatic exploration, who is not a candidate for or refuses surgery, or who has unresectable metastatic disease. The therapeutic choices to prevent symptomatic hypoglycaemia include diazoxide, octreotide, lanreotide, verapamil and phenytoin.<sup>8–13</sup> The overall survival rate of patients with insulinoma does not differ from that expected in the general population. Survival, however, is significantly worse in the patients with malignant insulinomas. The cumulative incidence of recurrence is 6% at 10 years and 8% at 20 years. Insulinoma in patients with pre-existing diabetes is extremely rare; indeed, the incidence of diabetes among patients with insulinoma is much lower than that in the whole population. There are sporadic case reports of insulinoma presenting in both type 1 and 2 diabetes.<sup>14,15</sup>

In conclusion, our case report emphasises that it is important to consider insulinoma as a possible differential diagnosis while investigating patients with diabetes who are experiencing recurrent unexplained hypoglycaemia.

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## Declaration of interests

There are no conflicts of interest declared.

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References are available online at [www.practicaldiabetes.com](http://www.practicaldiabetes.com).

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