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Insulinoma in Pregnancy

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Introduction

Insulinoma is a rare cause of hypoglycaemia.[1, 2, 3] We report a case of insulinoma in pregnancy, in which the insulin resistance of pregnancy may have been protective and reduced the severity of hypoglycaemic attacks until rapid normalisation of insulin sensitivity postpartum.

Case report

The patient, referred to as IP, is a 19-year-old nulliparous female with no significant past medical history.

First Presentation:

At 29 weeks gestation, IP had an unresponsive episode at home. Witness account was consistent with a tonic-clonic seizure and a post-ictal period characterised by extreme agitation. At the scene IP's capillary blood glucose was 2.1 mmol/L, which was corrected with the administration of buccal 40% dextrose gel and intramuscular (IM) glucagon by paramedics.

In the Accident and Emergency Department (A&E), IP's observations and physical examination were normal apart from a tachycardia of 130bpm. Routine blood tests were unremarkable. However, IP's blood glucose remained labile, with repeated episodes of hypoglycaemia, requiring an intravenous (IV) infusion of 10% dextrose over the next 4 hours. IP was admitted to the Obstetric High Dependency Unit (OHDU) for further assessment.

Endocrinology were of the opinion that IP was experiencing postprandial reactive hypoglycaemia and associated stress hyperglycaemia, which were more pronounced because of the pregnancy. C-peptide and insulin levels taken at the time of arrival in A&E were 447 pmol/L and 50 pmol/L respectively, but difficult to interpret as IP had already received treatment for hypoglycaemia. These results would be normal in a normoglycaemic patient but elevated for someone with hypoglycaemia. Urine sulphonylurea screen was negative. Overall, the hypoglycaemia was therefore viewed as unlikely to be pathological.

Neurology were also consulted and felt that IP's tonic-clonic seizure may have been spontaneous or provoked by hypoglycaemia. Magnetic resonance imaging (MRI) of the brain and an electroencephalogram (EEG) showed no abnormalities. No further investigation or treatment was recommended.

IP was discharged home after 72 hours and outpatient follow-up in neurology and diabetes clinic was arranged.

Peripartum:

IP returned to hospital in spontaneous labour at 40+1 weeks gestation. A lumbar epidural was inserted for analgesia and labour was augmented with IV infusion of syntocinon. IP developed a pyrexia (38.1°C) and tachycardia (120-140 bpm), therefore treatment for sepsis was commenced. Due to foetal occiput transverse (OT) malposition, IP was transferred to the operating theatre where a healthy baby girl was delivered with the aid of Kielland's rotational forceps, under epidural top-up. Postpartum IP was admitted to the OHDU due to ongoing pyrexia and tachycardia.

24 hours later, IP was observed by a midwife to begin "writhing" in bed for 1-2 minutes, followed by a period of drowsiness and agitation. Capillary blood glucose was 2.8 mmol/L, which was treated with IV infusion of 10% dextrose with subsequent resolution of the neuroglycopenic symptoms.

Blood tests taken just prior to treatment of the hypoglycaemia showed a glucose of 1.2 mmol/L, whilst C-peptide and insulin levels were inappropriately high at 1581 pmol/L and 126 pmol/L respectively. These results along with a raised proinsulin were highly suggestive of excessive endogenous insulin secretion in keeping with insulinoma, sulphonylurea administration or autoimmune insulin syndrome. However, urine sulphonylurea screen was negative, as was testing for insulin IgG antibodies. MRI with gadolinium was performed and confirmed a 5cm tumour at the head of the pancreas consistent with an insulinoma.

On days 2 and 3 postpartum, IP had several episodes of mild hypoglycaemia with associated confusion, often related to breast feeding. These were treated with IV infusion of 10% dextrose, as well as dietary modification.

Outcome:

IP was discharged home with dietary advice and seizure-safety guidance. She attended endocrinology clinic, where multiple endocrine neoplasia type 1 (MEN-1) was excluded.

At 8 weeks post delivery, IP underwent an elective pancreaticoduodenectomy (Whipple's procedure). Pathology of the excised specimen showed it to be a grade 1, well-differentiated, neuroendocrine tumour with reassuring features. There were no peri-operative complications but IP did develop mild pancreatic insufficiency. IP has had no further episodes of hypoglycaemia.

Discussion

Insulinoma is a rare, neuroendocrine tumour of the pancreas with an estimated incidence of 1-4 cases per million people per year. It is a functional tumour of the beta cells of the islets of Langerhans, which produce, store and secrete insulin to regulate plasma glucose concentration. Around 90% of insulinomas are benign, but can cause significant morbidity through intermittent and inappropriate secretion of insulin leading to hypoglycaemia. Insulinomas are associated with MEN-1 in 4-10% of cases.[1, 3]

Patients generally present with episodic hypoglycaemia characterised by neuroglycopenic or adrenergic symptoms (Table 1). This is often brought on by fasting or exercise, but may also occur postprandially or at random. Due to the vague and intermittent nature of these symptoms diagnosis can be elusive.[1, 2, 3] As highlighted by this case, the insulin resistance found in pregnancy may protect against hypoglycaemic episodes.

Neuroglycopenic	Adrenergic
Confusion	Diaphoresis
Abnormal behaviour	Palpitations
Personality changes	Tremor
Visual disturbances	Anxiety
Seizure	Weakness
Coma	Nausea

Table 1: Hypoglycaemic symptoms.[1, 2, 3]

Whipple's Triad:

1. Neuroglycopenic symptoms
2. Hypoglycaemia measured at the time of symptoms
3. Symptoms relieved by the administration of glucose

Figure 1: Whipple's triad of hypoglycaemia.[2]

Diagnostic Criteria:

- Neuroglycopenic symptoms
- Hypoglycaemia measured at the time of symptoms
- Symptoms relieved by the administration of glucose
- Increased serum insulin level (≥43 pmoml/L)
- Increased serum C-peptide level (≥200 pmol/L)
- Increased proinsulin level (≥5 pmol/L)
- Absence of serum/urine sulphonylureas

Figure 2: Diagnostic criteria for insulinoma.[1, 2, 3]

Diagnostic criteria for insulinoma comprise of Whipple's triad (Figure 1) and biochemical changes consistent with endogenous hyperinsulinism (Figure 2).[1, 2, 3] C-peptide (a product of proinsulin cleavage to insulin) and insulin are concomitantly released from an insulinoma, resulting in abnormally elevated serum levels during proven hypoglycaemia.

Common imaging modalities include trans-abdominal/endoscopic ultrasound, computed tomography (CT) and MRI. Most tumours are intrapancreatic, occurring with equal tendency in the head, body and tail of the pancreas.[1, 3]

The mainstay of insulinoma treatment is surgical resection, which is curative in 77%-100% of cases. Surgery can range from local excision, partial pancreatectomy to Whipple's procedure. Medical management to reduce hypoglycaemic episodes involves dietary modification, diazoxide (a direct inhibitor of insulin release) and octreotide.[1, 3]

References

1. Shin JJ, Gorden P, Libutti SK. Insulinoma: pathophysiology, localization and management. *Future Oncol*. 2010;6(2):229-237.
2. Whipple AO, Frantz VK. Adenoma of islet cells with hyperinsulinism: a review. *Ann Surg*. 1935;101:1299–1335.
3. Okabayashi T, Shima Y, Sumiyoshi T, et al. Diagnosis and management of insulinoma. *World J Gastroenterol*. 2013;19(6):829-837.