CASE REPORT

Insulinoma presenting with cardiac arrest and cardiomyopathy

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SUMMARY

A 33-year-old woman presented with ventricular fibrillation cardiac arrest and was found to have a blood glucose of 1.83 mmol/L. Cardiac catheterisation revealed a dilated left ventricle with an ejection fraction (EF) of 26% and angiographically normal coronary arteries. Continuous dextrose infusion was required to treat hypoglycaemia, which prompted consideration of insulinoma as a possible cause for her cardiomyopathy. Whipple's triad was demonstrated; a 72 h fast provided biochemical evidence of insulinoma, and imaging localised a tumour in her pancreas. The tumour was resected and pathology confirmed insulinoma; pancreaticoduodenectomy cured her hypoglycaemia. No alternate cause of cardiomyopathy was found and 4 months after surgery her EF improved to 41%. High insulin levels can close cardiac K_{ATP} channels associated with dilated cardiomyopathy; the catecholamine surge from hypoglycaemia may also contribute to ventricular remodelling. Hypoglycaemia can cause QT segment prolongation, and may have precipitated fibrillation in this patient's arrhythmia-prone myocardium.

BACKGROUND

Insulinomas are rare islet cell tumours (incidence 0.4/100 000 person-years). Most patients with an insulinoma describe episodic neuroglycopenic symptoms (such as confusion, visual changes and altered behaviour) or sympathoadrenal symptoms (such as palpitations, sweating and tremors). Cardiomyopathy is not a typical complication of insulinoma, although it has been reported in other diseases that cause hypoglycaemia.^{1 2} In a large series of patients with insulinoma, the median age at presentation was 47 years and the duration of symptoms at diagnosis was less than 1.5 years.³ When evaluating a patient for insulinoma, Whipple's triad (symptoms of hypoglycaemia, low blood glucose (BG) during the symptoms and relief of symptoms with normalisation of BG) establishes hypoglycaemia as the cause of the patient's symptoms. Insulinoma is diagnosed biochemically by demonstrating inappropriately high insulin levels during a period of hypoglycaemia. Ultimately, surgical pathology confirms the diagnosis. We showcase our patient's unusual presentation and propose cardiomyopathy as a rare complication of insulinoma.

CASE PRESENTATION

A 33-year-old woman suffered a ventricular fibrillation (VF) arrest while exercising. Following immediate bystander cardiopulmonary resuscitation (CPR), medics noted a low BG of 1.83 mmol/L. On her

arrival to the hospital, cardiac catheterisation was promptly performed to investigate a possible ischaemic cause of the VF arrest. Coronary arteries were angiographically normal, but left ventriculography revealed global hypokinesis with ejection fraction (EF) 26%. After medical stabilisation, an implantable cardioverter defibrillator (ICD) was placed and the patient was transferred to a tertiary care hospital for evaluation of hypoglycaemia. After transfer, an echocardiography confirmed dilated cardiomyopathy with an EF of 23% (figure 1). The ECG did not show any ischaemic changes or repolarisation abnormalities that might predispose to cardiac arrest. She was extubated and fortunately did not have evident neurological injury. Further history was obtained; she denied a family history of cardiomyopathy or sudden cardiac death, denied use of recreational drugs and denied recent viral illnesses. Her early hospital course was notable for persistent hypoglycaemia requiring continuous dextrose infusion, raising suspicion for insulinoma. She subsequently described a 10-year history of episodic palpitations, light-headedness, shakiness and sweats that occurred after fasting, strenuous activity and 'sugary' foods. She also described subtle and progressive dyspnoea on exertion that began approximately 2 years prior to the arrest. Three episodes involving neuroglycopenic and sympathoadrenal symptoms were observed during her hospital stay, including one that was intentionally provoked by a 72 h fast (summarised in table 1).

INVESTIGATIONS

HIV serology, iron studies, protein electrophoresis and thyroid studies were normal. Cardiac MRI was

Figure 1 Apical four-chamber view of heart on echocardiography shortly after ventricular fibrillation arrest, demonstrating dilated cardiomyopathy.

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Table 1 Tests performed during two unprovoked symptomatic hypoglycaemic events and a 72 h fast in a 33-year-old woman with cardiomyopathy

Test (SI units)	Episode #1	Episode #2	72 h Fast	Typical findings for insulinoma
Whipple's triad demonstrated	Yes	Yes	No	Yes
Glucose (mmol/L)	2.2	2.5	3	<3
Insulin (pmol/L)	83.3	118.1	49.3	≥20.8
C-peptide (nmol/L)	—	0.7	0.5	≥0.06
Proinsulin (pmol/L)	—	—	8.2	≥5
β-Hydroxybutyrate (mmol/L)	—	—	0.33	≤2.7
Sulfonylurea panel	—	—	Negative	Negative

not performed due to the recent ICD placement. A 72 h fast was initiated and stopped at 21 h when the patient developed hypoglycaemic symptoms with glucose metre showing BG of 2.38 mmol/L. Laboratory test performed at this time showed inappropriately elevated insulin, C-peptide and proinsulin levels and no serum ketones, suggesting excessive endogenous insulin (table 1). CT revealed a 0.9×1.9×1.7 cm mass in the head of the pancreas consistent with neuroendocrine tumour (figures 2 and 3).

TREATMENT

Despite a dextrose infusion, symptomatic hypoglycaemia persisted. While awaiting surgery, inpatient trials of octreotide and diazoxide resulted in labile BG. She underwent a pancreaticoduodenectomy and histopathology confirmed an insulinoma in the head of the pancreas. She was placed on an ACE inhibitor (lisinopril), β-blocker (carvedilol) and amiodarone for her cardiomyopathy and risk of arrhythmia.

OUTCOME AND FOLLOW-UP

Her BG normalised postoperatively. An echocardiogram at 4 months showed an improved EF of 41% with a slight reduction in left ventricle diastolic dimension (6.6 cm–6.2 cm).

DISCUSSION

Unique features of our patient's presentation with insulinoma include her relatively young age, extended duration of symptoms before diagnosis, cardiac arrest and cardiomyopathy. Our patient described symptoms for almost 10 years, which

Figure 2 CT of the abdomen (axial view) showing insulinoma. **Figure 3** CT of the abdomen (coronal view) of insulinoma.

highlights the risk of delayed diagnosis in this rare disease, and suggests that uncommon sequelae may only develop after protracted exposure to the endocrine and metabolic effects of insulinoma. To our knowledge, this is the first report of a patient with insulinoma presenting with cardiomyopathy and VF arrest. While the pathophysiological connection is not definitively established in this case, we hypothesise that the insulinoma caused her cardiomyopathy, based on reports linking cardiomyopathy to hypoglycaemia and hyperinsulinaemia in other disease states. In diabetic cardiomyopathy, chronic hyperinsulinaemia likely mediates hypertrophy through multiple cell signalling pathways.⁴ For example, hyperinsulinaemia increases cellular ATP levels through elevated glucose metabolism, which subsequently closes cardiac K_{ATP} channels that have been linked to idiopathic dilated cardiomyopathy.^{1 5} Case reports of hypoglycaemia secondary to anorexia nervosa causing Takotsubo cardiomyopathy implicate catecholamine excess as another possible mechanism.² Though this morphology was not seen in our patient, we postulate that episodic catecholamine excess also contributed to her cardiomyopathy. We cannot exclude the possibility that this patient's VF triggered diffuse and irreversible myocardial injury. However, the patient's prompt return of circulation after CPR limits the likelihood that the arrest itself precipitated permanent myocardial injury. Furthermore, her symptoms of chronic exertional dyspnoea suggest long-standing undiagnosed heart failure. Our patient's insulinoma likely contributed to her VF arrest through multiple mechanisms. Her dilated cardiomyopathy created a substrate for arrhythmogenesis and either QTc prolongation associated with hypoglycaemia² or catecholamine excess may have precipitated the VF. The gradual improvement in her EF may reflect resolution of hypoglycaemic injury and accompanying heart failure management.

Learning points

- ▶ Patients with insulinoma may present with rare complications such as dilated cardiomyopathy or cardiac arrest.
- ▶ Medical management is unpredictable for temporising glycaemic control in insulinoma, but surgery is usually curative.
- ▶ Cardiomyopathy associated with insulinoma may not present with Takotsubo morphology as is seen in other hypoglycaemic conditions.

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Competing interests None.

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