CASE REPORT

Paroxysmal ‘funny turns’ in an elderly woman – a 95-year-old with an insulinoma

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Abstract

A 95-year-old woman was admitted to hospital with a fractured neck of femur following a fall. There was no past history of note other than numerous episodes of ‘funny turns’ preceding falls some of which resulted in fractures. During her admission she had a ‘funny turn’. Immediate investigations revealed hypoglycaemia and subsequent biochemical abnormalities, most likely due to a benign endocrine tumour – an insulinoma.

Keywords: funny turns, falls, hypoglycaemia, insulinoma

Case history

A 95-year-old woman was admitted to hospital following a fall. After having a hemiarthroplasty for a right neck of femur fracture she was referred for rehabilitation. There was no past history of diabetes, ischaemic heart disease or cerebrovascular disease. Systemic examination was unremarkable. She was on no medication. Four days post admission, she became drowsy and unable to answer questions. She was obeying commands but appeared aphasic. There was no pyrexia and she was stable haemodynamically. Examination of the gastrointestinal, cardiovascular, and respiratory systems was normal. Examination of the central nervous system revealed a Glasgow coma scale of 10/15, gurgling in the throat and absent gag reflex. Pupils were equal and reacting to light. There was no facial droop, lateralising signs nor cerebellar signs. Power was decreased to 3/5 globally and plantar response was bilaterally flexor. A cerebrovascular episode was thought likely and a computerised tomography brain scan was considered, however a BM stix was requested.

The bedside BM stix revealed a blood sugar of 1 mmol/l. She was treated with an intravenous bolus of 25 g of glucose with prompt recovery and complete resolution of the abnormal neurological signs.

Subsequent discussion with the family revealed an interesting picture with previous episodes described as the patient looking vague, her legs giving way but no loss of consciousness. These symptoms were noted to come on during long car journeys and her son noted a ‘similarity’ to his wife’s insulin dependent diabetes symptoms when a meal was inadvertently delayed and so treated his mother by giving her a meal, or sweets and putting her to bed to recover from the ‘funny turn’. These episodes had been going on for about 10 years. The family testified and she denied taking insulin or any other hypoglycaemic agent, or any substance ‘over the counter’.

During hospitalisation over a four-week period she had a number of symptomatic hypoglycaemic episodes with BMs of less than 2 mmol/l requiring treatment. A 72-h fasting test had to be terminated after 6 h when she felt funny and her BM dropped below 2 mmol/l. Blood samples were sent off to assess plasma insulin and C peptide levels during this episode. Further examination did not show any clinical features of multiple endocrine tumours or mesenchymal tumors (secreting IGF-2).
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Methods

Investigations performed to confirm an insulinoma

Glucose = <2 mmol/l; plasma insulin = 11.1 micro units/ml (normal range: 6–26 micro units/ml); C-peptide level = 879 pmol/l (normal range: 120–600 pmol/l); serum cortisol = 549 nmol/l (normal range: 200–600 nmol/l); prolactin = 150 mu/l (normal range up to 400); sulphonylurea level = <2.0 ng/l; vasoactive intestinal polypeptide level ≤ 4 pmol/l (normal ≤ 30); pancreatic polypeptide = 51 pmol/l (normal ≤ 300); glucagon = 19 pmol/l (normal ≤ 50); serum gastrin = 5 pmol/l (normal ≤ 40); somatostatin level = 41 pmol/l (normal ≤ 150); neurotensin level = <10 pmol/l (normal ≤ 100).

Ultrasound of the abdomen did not reveal any abnormality. The gut hormones were requested to rule out other neuro-endocrine tumours.

Although insulin antibodies were not measured to rule out insulin auto-immune syndrome, the endocrinologists felt that insulinoma was the most likely diagnosis on the basis of this clinical picture and test results.

The diagnosis of insulinoma was confirmed on the basis of the above clinical picture and test results. It was decided to treat her medically using diazoxide and not surgery would be considered if medical therapy failed.

Discussion

Insulinomas are characterised by symptomatic hypoglycaemia from unregulated insulin release. They are the second most common functioning islet cell tumours following gastrinomas. Although they can occur at any age, they are most common during the 5th to the 7th decade; median age is 55 years [1]. Symptoms may be present for up to three decades before a diagnosis is reached [2]. Fasting hypoglycaemia, symptomatic hypoglycaemia and relief from intravenous glucose – Whipple’s triad are diagnostic of insulinoma.

Symptoms of hypoglycaemia include confusion, slurred speech, irritability, sweating, trembling, pallor and palpitations [3]. The interval from onset of symptoms to diagnosis can range between one month to thirty years [1]. In 10% of cases the tumours are multiple and in 10% they are malignant with spread to the local lymph nodes and the liver. They are frequently associated with multiple endocrine tumours (MEN-1). Extrapancreatic insulinomas are rare and usually arise in extrapancreatic tissue.

Diagnosis

This is made by demonstrating fasting hypoglycaemia with raised or normal insulin levels (inappropriate in the presence of hypoglycaemia). Normally C-peptide (pro-insulin or insulin precursor) levels are similar to insulin levels, and are therefore decreased in hypoglycaemia but raised in insulinoma.

Since insulinomas result in an impaired ability to process the pro-insulin molecule, there is an increase in the pro-insulin/insulin ratio. A ratio of >20% is suggestive of insulinoma. An elevated cortisol level helps to rule out hypoglycaemia due to suppression of the hypothalamic–pituitary–adrenal axis.

Differential diagnosis

An elevated or normal fasting plasma insulin level with normal or elevated C-peptide in the presence of hypoglycaemia points to a diagnosis of insulinoma. The normal insulin level in this condition is inappropriate for the degree of hypoglycaemia. Fasting hypoglycaemia and elevated C-peptide levels are reported in the insulin autoimmune syndrome [4]. This condition is characterised by high titres of insulin antibodies (in patients who have never been exposed to insulin). The presence of high titres of insulin antibodies excludes the possibility of insulinoma and the presence of high C-peptide levels excludes factitious hypoglycaemia [4]. Drugs containing a sulphydryl group such as methimazole may play a part in the insulin autoimmune syndrome [4].

Alimentary tract hypoglycaemia (pseudoinsulinoma) is a condition recognised after gastric surgery. It is also accompanied by hypoglycaemia and inappropriate insulin levels and insulin/glucose ratio. Recognition of this condition after gastric surgery may prevent unwarranted exploration for insulinoma [5]. Exogenous administration of insulin can be excluded by demonstration of depressed levels of C-peptide with elevated levels of insulin. Normal or elevated levels of C-peptide are not consistent with exogenous administration of insulin.

Elevated levels of sulphonylureas in hypoglycaemia can document factitious hypoglycaemia due to these agents. Normal insulin/glucose ratio excludes hypoglycaemia due to liver failure and tumours secreting insulin like growth factors, fibrosarcoma, mesothelioma and haemangioendothelioma. A ratio of >0.3 is significantly abnormal and the diagnosis of insulinoma should be considered [6].

Treatment

Definitive treatment is surgical resection based on the location of the tumour by the use of CT contrast, MRI scanning, abdominal ultrasound, endoscopic ultrasound [7] and selective angiography [8] with selective sampling for insulin levels.

Abdominal ultrasound will localise about 33% [9] of the tumours. CT contrast can locate 44% of such tumours and selective arteriography can diagnose 50% of
tumours and is suggestive in another 25% [9]. Transhepatic portal venous sampling is the most accurate [10] but can have a false negative rate of 15%. Tumours not localised by any of these measures can variably be palpated at surgery [7]. Post-operative mortality can be between 3.7 and 12% [9]. Surgery consists of enucleation or pancreatic resection. Pancreatic fistulas may develop especially after enucleation [7]. Post-operative morbidity may occur in up to 1/3rd of operated patients [9].

In the older more frail patient medical treatment is usually advised, using diazoxide as the first line of therapy [11]. It causes a rise in blood sugar by decreasing pancreatic insulin production. Thiazides usually enhance the action of diazoxide. Success with diazoxide therapy is reported to be 70% [11]. The calcium channel blocker verapamil has been successfully used in a 94-year-old woman who refused surgery [12].

**Conclusion**

This is the oldest woman so far reported in the literature presenting with an insulinoma induced spontaneous hypoglycaemia. Her insulin and C-peptide levels are inappropriately raised in response to hypoglycaemia. There is no question of self-medication with hypoglycaemic drugs. Because of her general frailty she was not subjected to invasive investigations to localise an insulin-secreting tumour. She responded very well to diazoxide therapy with no recurrence of her symptomatology.

**Key points**

- ‘Funny turns’ and falls in older people can be due to hypoglycaemic episodes.
- Insulinomas are most common in older people.
- Medical therapy can be effective in relieving symptoms of hypoglycaemia in such tumours.

**References**


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