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Case report

A Case of 'Camouflaged Insulinoma & Diazoxide Quandary

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Abstract

Insulinomas are rare cause of neuroendocrine tumour which secretes insulin leading to hyperinsulinism. Diagnosis requires biochemical evaluation followed by tumour localization.

We report a case of an adult women, who, had multiple admissions with dizziness, funny turns and double vision for at least 2 years and seen by the multiple medical specialties before the diagnosis of Insulinoma was made.

Endoscopic Ultrasound finally localized the tumour despite negative results on multiple non-invasive imaging modalities. Prior to the localization of tumour, she was treated with dietary modifications followed by Diazoxide, which, she had to abandon due to refractory fluid overload as a result of it. A trial of SC Octreotide was started with excellent results whilst waiting for surgery. She underwent laparoscopic distal pancreatectomy on 22/02/2019.

***Keywords*: Insulinoma, Octreotide, hypoglycemia, multiple endocrine neoplasia, pancreas.**

Background

Insulinomas are rare pancreatic islet cell tumours with incidence of 1 per 250,000(Up-to-date). It usually presents with recurrent fasting hypoglycemia; however, exclusive post prandial hypoglycemic presentation can be seen in about 6% [1]. Clinical features include neuroglycopenic symptoms such as confusion, visual change and or unusual behaviour, with or without sympathoadrenal symptoms like palpitations, sweating and tremulousness [2].

Most insulinomas are solitary and benign. Multiple insulinomas are rare and tend to be associated with Multiple Endocrine Neoplasia 1(MEN1).

The biochemical diagnosis of Insulinoma is established by inappropriately high serum insulin concentrations during a supervised 72 hour fasting induced hypoglycemia or spontaneous episode of hypoglycemia. Once it is done, an effort to localise tumour should be made with various imaging modalities.

The median duration of symptoms before diagnosis was less than 1.5 years [3].

The treatment of choice for Insulinomas are surgical removal, however, medical therapy should be considered to control symptomatic hypoglycemia in patients who refuses or who is not a candidate for surgery and in patients with unresectable metastatic diseases [4].

Case presentation

A 74 years old lady with background of hypertension and asthma had multiple admissions with funny turns, dizziness and double vision for at least 2 years. She was seen by various medical specialties including cardiology, stroke medicine and rheumatology before she was noticed to have a capillary glucose of 1.2mmol/L. Whipple's triad was demonstrated during evaluation. Supervised fasting confirmed biochemical evidence of endogenous hyperinsulinaemia with inappropriately high level of serum Insulin & C-peptide during hypoglycaemia and a negative Sulphonylurea screen.

Investigations

Biochemistry during 72 hour supervised fast revealed Plasma Glucose of 1.9mmol, elevated plasma Insulin of 7.6 mU/L, raised C-Peptide of 746 pmol/L. Sulfonylurea screen was negative. It confirmed biochemical evidence of Insulinoma.

CT and MRI pancreas done in 2015 & 2018 respectively, didn't show any pancreatic lesion or malignancy.

Ocreoscan NM scan with SPECT done in July 2018, reported as no evidence of Octreotide avid lesion. Finally, in September 2018, endoscopic ultrasound showed 1.5cm mass with classic appearance of insulinoma, seen tucked between splenic vein

and artery. It appeared to be wrapped around a non-dilated pancreatic duct. Fig 1

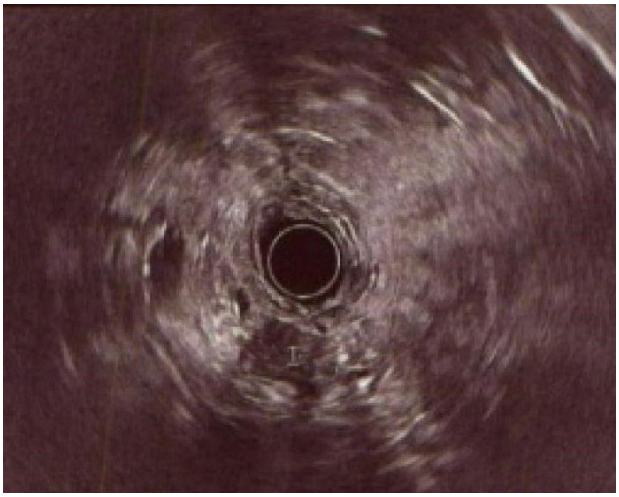

Figure 1

Treatment

Although patient was successfully managed initially with dietary modification, symptoms progressed and Diazoxide was started with excellent results. She unfortunately developed severe peripheral oedema and weight gain necessitating reduction in dose of Diazoxide. As a result, she developed persistent hypoglycaemia. Despite lowering the dose of Diazoxide, she developed clinical features of heart failure (BNP>2400, Echo - Preserved ejection fraction) and eventually she decided to stop Diazoxide because of debilitating symptomatic fluid overload. This is when we localized the tumour with EUS. At this point, she was setting alarm every hour during night to check for (& treat) hypoglycaemia. The fluid overload resolved and BNP normalized after stopping Diazoxide.

She was then started on a trial of SC Octreotide despite negative Octreotide scan, which had a dramatic effect on her symptoms and blood sugar control. She has not had a single hypo since been on Octreotide for the last 3 months whilst awaiting surgery. She successfully underwent distal laparoscopic pancreatectomy on 22/02/2019. She was asymptomatic at one month follow up following the surgery.

Outcome and follow up

Cure following surgical removal of insulinoma and she was asymptomatic after 1 month clinic follow up.

Discussion

The current case reports support that the diagnosis of Insulinoma can be challenging and has taken at least 2 years as in this case. In few cases, patients were symptomatic for decades prior to the established diagnosis [3].

The combination of transabdominal Ultrasound and triple phase spiral CT of the pancreas has a detection rate of about 70% in patients with insulinomas [1]. The sensitivity of endoscopic ultrasound stands at about 75% in localization of insulinomas which have been failed to do so in the combination scans as stated above [1].

Octreotide Scan can miss up to 40 percent of insulinomas as these tumours don't express a sufficient number of subtype 2 somatostatin receptors [5]. This case demonstrates that despite negative Octreotide scan, subcutaneous Octreotide injection can be helpful in patients with Insulinomas.

Although Diazoxide can be used for control of symptomatic hypoglycaemia in Insulinoma, it can lead to or precipitate heart failure secondary to excessive fluid retention due to antidiuretic properties [6].

Learning points

1. Although endogenous Insulin over secretion is rare, it should be considered in the differential diagnosis of patients presenting with symptoms suggesting hypoglycemia.
2. Capillary glucose should be tested in ALL unwell patients or with symptoms suggestive of hypoglycaemia
3. Glucose should be assayed by ALL blood gas analyzers (in retrospect, our hospital blood gas machine did not check for Glucose which potentially contributed to the delay in diagnosis)
4. Diazoxide can cause refractory (reversible) heart failure
5. Octreotide can still be effective in managing hypoglycaemia with Insulinoma despite negative Octreoscan

Ethics approval and consent to participate

Not applicable

List of abbreviations

SC: Subcutaneous
BNP: Brain natriuretic peptide
CT: Computed tomography
EUS: Endoscopic ultrasound
MRI:Magnetic resonance Imaging
MEN: Multiple endocrine neoplasia

Data Availability

Not applicable

Conflict of interest

All the authors declare that there is no conflict of interest for the publication of this paper.

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Authors' contributions

Dr Sonam Tshering: Contributed to writing the case history.
Dr Saquib Navid Siddiqui: Contributed in editing the paper.
Dr Irfan Khan: Overall supervisor for this paper

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