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# A Case Report of Insulinoma in a South Indian Population

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***Abstract:***
*A 45 year old female, cook by occupation presented in an irritable state with irrelevant talks for the past half an hour with additional complaints of recurrent episodes ofgiddiness, lightheadedness,sweating , tachycardia and increasing body weight for the past three years. Routine investigations of the patient revealed normal values except for a random CBG of 58mg/dl.This made us suspect the patient to be a case of hypoglycemia for evaluation.Further investigations revealed Insulin/glucose ratio =5.09 ,Insulin/C-peptide ratio=30.04 . CT abdomen revealed a 2x2.5 cm well defined hypoechoeic lesion in the head of pancreas.A final diagnosis of insulinoma was established.Surgical gastroenterologist opinion was sought ,Whipples procedure was done and the specimen was sent for analysis. Before the new diagnosis, the patient wasn't aware that her symptoms could be treated with Whipples procedure that could possibly clear the symptoms with appropriate post procedure medication andmonitoring, thus explaining how diagnostic difficulties with such underlying conditions could affect the patient's wellbeing.*

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## I. Introduction

Insulinoma is the most common type of functional pancreatic neuroendocrine tumor (NET) that manifests with hypoglycemia caused by inappropriately high insulin secretion.Their incidence is estimated to be about 4 cases per 1 million person. It more commonly presents as a solitary benign tumor, but it can sometimes be associated with multiple endocrine neoplasia type 1 (MEN1). Patients with insulinoma have hypoglycemic episodes, more characteristically as fasting hypoglycemia typically associated with neuroglycopenic symptoms such as confusion, behavior changes, difficulty with concentration, dizziness, blurred vision, paresthesias, and seizures. The presence of the Whipple triad, which consists of low blood glucose less than 2.8 mmol/L (50 mg/dl), hypoglycemic symptoms, and relief of symptoms following glucose ingestion is a hallmark of this condition. Insulinoma is usually diagnosed by biochemical testing when there is high clinical suspicion but then the diagnosis is often delayed by years because of its rarity.

## II. Case Report

A 43 year old women was brought to the emergency room in an irritable state with irrelevant talks for the past half an hour . Past history revealed that she has recurrent episodes of giddiness, lightheadedness, sweating , tachycardia which were prominent 3 to 4 hrs after meals and history of increasing wight for the past 3 years. Upon general examination she was obese .On examining Central nervous System ,the patient appeared drowsy, arousable with pain stimuli, irrelevant talks present, not following verbal commands, DTR normal with plantar flexors .CBG showed 58 mg/dl for which IV 25%dextrose was administered and she recovered.Routine investigations were done and the findings are listed below.

**Complete blood count:**

| | |
|---|---|
| Hemoglobin | 12g/dl |
| RBC | 4.92 million cells/cu.mm |
| WBC | 9100 cells/cu.mm |
| HCT | 35.8 % |
| MCV | 89 fL |
| MCHC | 33.1 g/dl |
| Platelet count | 3.5 lacs/cu.mm |

**Renal Function test:**

| | |
|---|---|
| Random blood sugar | 100 mg/dl |
| Urea | 29 mg/dl |
| Creatinine | 0.8 mg/dl |
| Sodium | 137meq/L |
| Potassium | 4 meq/L |

**Liver function test:**

| | |
|---|---|
| Serum bilirubin<br>Direct<br>Indirect | 0.6 mg/dl<br>0.2 mg/dl<br>0.4 mg/dl |
| SGOT | 21 U/L |
| SGPT | 20U/L |
| Serum ALP | 89 IU/L |
| Total protein | 7.5g/dl |
| Albumin | 4.1g/dl |
| Globulin | 3.4g/dl |

**Thyroid function test:**

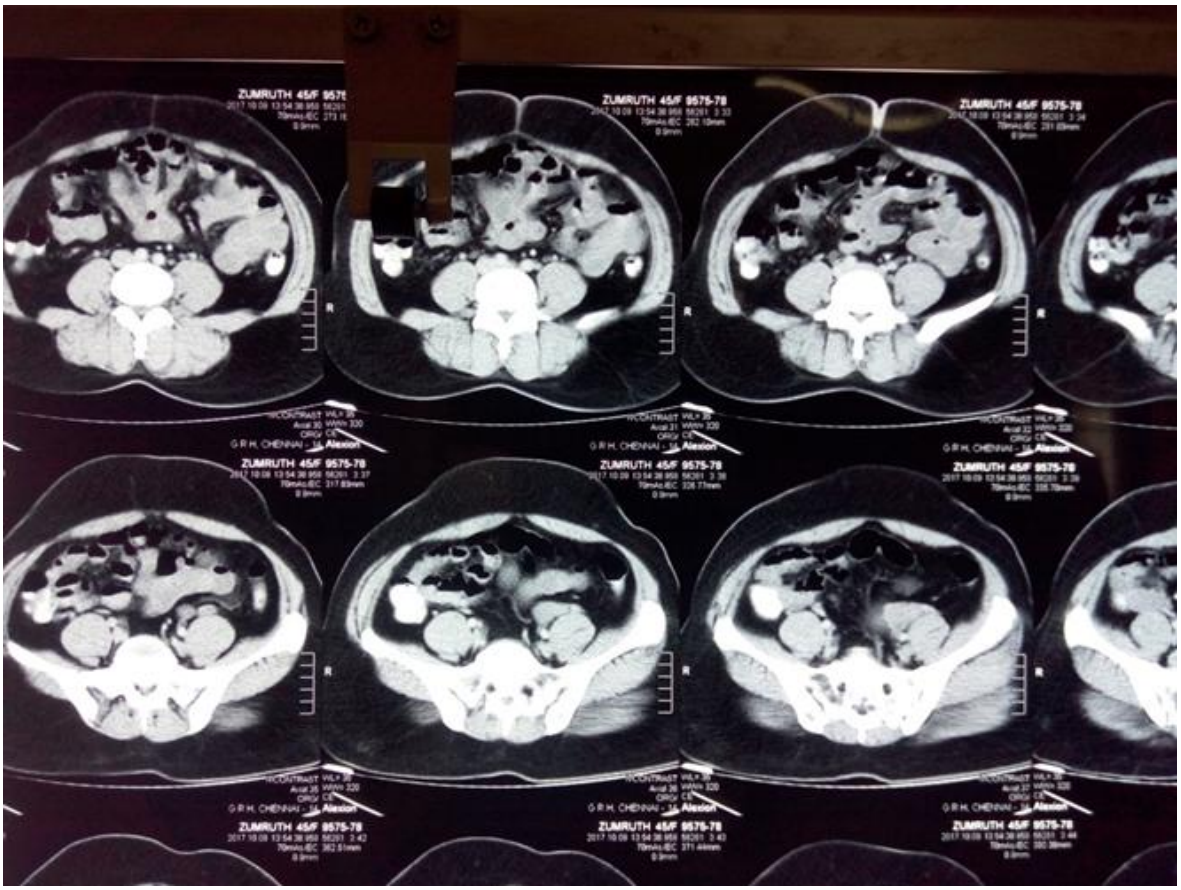
| | |
|---|---|
| Free T3 | 120 ng/dl |
| Free T4 | 1.3 ng/dl |
| TSH | 0.4 mIU/L |

**Other Investigations:**

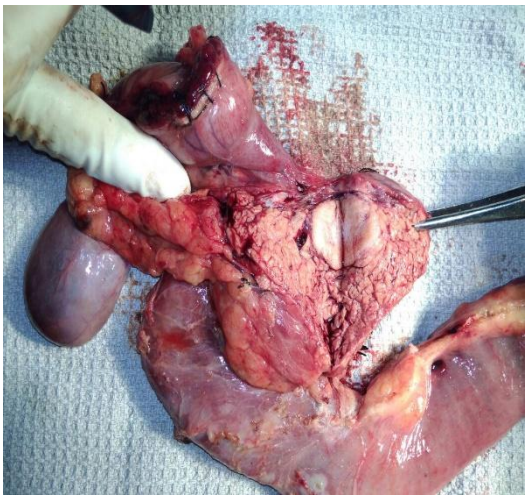
| | Baseline-7 AM | Fasting -11AM | Fasting -3 PM |
|---|---|---|---|
| CBG(mg/ml) | 108 | 64 | 52 |
| Insulin(m IU/ml) | 25 | 265 | 286 |
| C peptide(ng/ml) | 11.6 | 8.82 | 9.23 |

| | |
|---|---|
| Insulin/Glucose ratio | 5.09 |
| Insulin/C peptide ratio | 30.04 |
| Serum Calcium | 9.6 mg/dl |
| Chest X-Ray | Normal |
| USG abdomen and pelvis | 2cm x 2.5 cm mass; well definedhypoechoeic lesion in head of pancreas |
| CECT Abdomen | 2cm x 2.1 cm enhancing massin the head of pancreas |

**CECT Abdomen picture:**



This enhancing lesion in the head of pancreas in CECT Abdomen with other features in this patient with decreased CBG with increased Insulin/glucose ratio and increased Insulin/C-peptide ratio suggest that the patient had symptoms of hypoglycemia due to Insulinoma.
After obtaining the SGE opinion, the patient underwent WHIPPLES procedure and the resected specimen was sent for analysis.



## III. Discussion

Insulinomasare the most common cause of hypoglycemia related to endogenous hyperinsulinism that can occur sporadically or in conjunction with MEN-1 syndrome which is an autosomal dominant disorder associated with mutations in the *MEN1* gene mapped to chromosome 11q13[1].Insulinomas occur in 1-4 people per million in the general population and represent 1%-2% of all pancreatic neoplasms[2].Insulinomas can occur at any age and have an equal gender distribution.As many as 90% of insulinomas have been reported to be

benign, 90% are solitary, > 90% occur at intrapancreatic sites, and 90% are < 2 cm in diameter[3].The etiology and pathogenesis is not clearly known.The episodic nature of the hypoglycemic attack is due to the intermittent secretion of insulin by the tumor[2].Patients may go many years before seeking medical attention as they do not always present with the classical sympathoadrenergic symptoms associated with hypoglycemia. Instead, they may present with an undiagnosed seizure disorder, unintended weight gain, or nonspecific symptoms such as confusion or abdominal pain [3].The classical diagnosis of insulinoma depends on satisfying the criteria of Whipple's triad, which remains the cornerstone of the screening process: hypoglycemia (plasma glucose < 50 mg/dL); neuroglycopenic symptoms; and prompt relief of symptoms following theadministration of glucose. Although the median delay between symptom onset and diagnosis is approximately 18 to 35 months [3,4], some individuals are not diagnosed for decades.Insulinomas classically cause fasting hypoglycemia, but are also known to lead to postprandial hypoglycemia. In one review, 21% of individuals with insulinomas experienced both fasting and postprandial hypoglycemia, whereas only 6% experienced postprandial hypoglycemia exclusively [5].

The gold standard for biochemical diagnosis of insulinomaremains measurement of plasma glucose(<50mg/dl), insulin(5 m IU/L), C-peptide(0.6 ng/ml) and proinsulin(20 pmol/L) during a 72-h fast[6].A number of non-invasive techniques are available for the localization of a suspected insulinoma, including transabdominal ultrasonography, CT and/or MRI of CT is accepted as the first-line investigation for visualizaton. Invasive modalities, such as Endoscopic Ultrasound(EUS) and Angiography and Arterial stimulation( ASVS) have been shown to be highly accurate in the preoperative localization of insulinomas and have frequently been shown to be superior to non-invasive localization techniques. Manual palpation of the pancreas by an experienced surgeon and ultrasonography are both sensitive methods for the intraoperative detection of the site of insulinomas[7]. The sensitivity of these two methods is clinically acceptable and has been reported as 75%-95% and 80%-100%, respectively[8]

Once an insulinoma is diagnosed biochemically and localized preoperatively, surgery is the next step. Surgical resection of insulinoma is the gold standard of care and provides the only means for curative treatment of the disease.[9,10,11] Patients with the biochemical diagnosis of insulinoma achieve surgical cure ranging from 77% to 100%.[9,12] The surgical approach can be open {93.4%) or laparoscopic (6.8%).[11]. Surgical complications include pancreatic fistula(most common), pseudocyst, intra-abdominal abscess, pancreatitis, hemorrhage, and diabetes[9].

Medical therapy is reserved for patients who are awaiting surgery or patients with malignant insulinoma with unresectable metastasis comprising approximately 4.4% of the patient population[11].The initial drug of choice for patients with insulinoma is diazoxide, a nondiuretic benzothiadiazine derivative. Somatostatin analogs octreotide and lanreotide have also provided another class of agents that are useful in the symptomatic management of insulinoma in patients with receptors for the drug.In addition ,newly approved agents such as sunitinib and everolimus, have had encouraging results in progression-free survival.[13,14].

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