Not Just an Accident: A Case of Insulinoma

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Introduction

- Insulinomas are a rare cause of recurrent hypoglycemia in non-diabetic patients, occurring in 1-3 people per million a year.
- The diagnosis can often be missed or delayed due to the rarity of the condition and the complex diagnostic workup.
- This case report is to detail the rare tumor found in a patient with no previous history of hypoglycemic symptoms. We also outline a diagnostic approach to evaluating hypoglycemia in non-diabetic patients.

Case Presentation

- A previously healthy 37-year-old woman was admitted following a motor vehicle accident likely due to a hypoglycemic seizure, with initial glucose of 32mg/dL.
- During her hospitalization, she had recurrent episodes of fasting and postprandial hypoglycemia (32-70mg/dL) with established Whipple's triad. She required continuous dextrose 10% solution infusions to maintain normoglycemia. She denied any pre-existing glycopenic symptoms prior to admission.
- Insulin autoantibodies and sulfonylurea screen tests were undetectable. Thyroid labs were normal. She had a low random cortisol and prophylactic doses of steroids were initiated while further testing was underway. Steroids were later stopped and repeat cortisol testing off steroids and cosyntropin stimulations test were normal.
- A 72-hr fasting test was consistent with diagnosis of insulinoma (see below). Abdominal magnetic resonance imaging (MRI) revealed a 1.3 cm mass at the tail of the pancreas (see figure 1).
- She underwent laparoscopic distal pancreatectomy and pathologic evaluation of the tumor was consistent with a well-differentiated neuroendocrine tumor (see figure 2). The patient had a good response to surgery with no recurrence of hypoglycemia and was safely discharged home.
- The patient also had an incidental finding of a pituitary microadenoma which raised concerns about the presence of multiple endocrine neoplasia type 1 (MEN1) syndrome. However, she had no biochemical evidence of parathyroid or pituitary disease. Genetic testing was negative for MEN1 syndrome.

	Patient's labs	Expected Diagnostic Values in Insulinoma
Glucose (mg/dL)	46	<55
C-Peptide (nmol/L)	1.35	>0.2
Beta hydroxybuterate (mmol/L)	0.086	<2.7
Insulin (microU/mL)	13.2	>3
Proinsulin (pmol/L)	193.9	>5
Insulin ab	Negative	Negative
Sulfonylurea	Negative	Negative

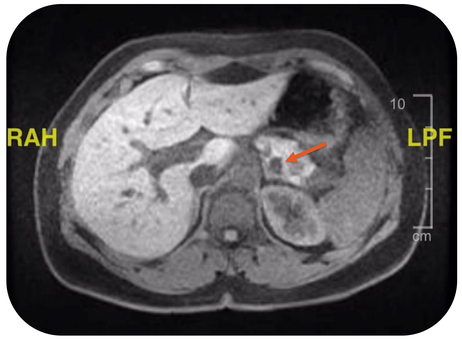


Figure 1: Abdominal MRI T1 pre-contrast imaging demonstrating 13 mm focal area of lower signal intensity

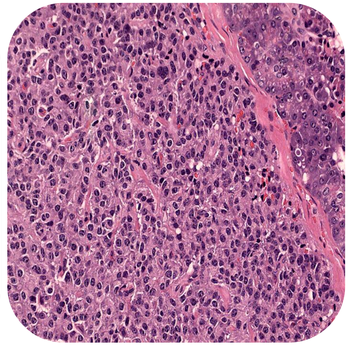
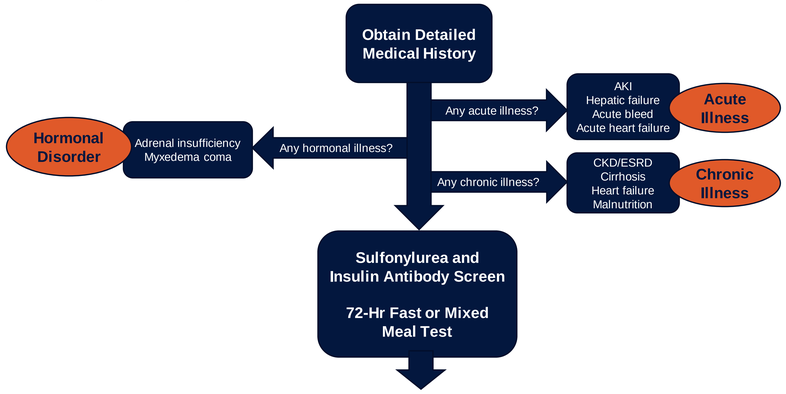


Figure 2: Histopathology of resected mass shows the insulinoma cells.



Labs under hypoglycemic conditions (Glucose <55mg/dL)						
	Insulinoma	NIPHS	Sulfonylurea	Exogenous Insulin	Insulin Autoimmune syndrome	Non-insulin Mediated
C-peptide	High	High	High	Low	High	Low
Proinsulin	High	High	High	Low	High	Low
Insulin	High	High	High	High	High	Low
BHB	Low	Low	Low	Low	Low	Low
Sulfonylurea Screen	Negative	Negative	Positive	Negative	Negative	Negative
Insulin antibodies	Negative	Negative	Negative	Negative	Positive	Negative

Figure 3: Algorithm for evaluation of recurrent hypoglycemia in non-diabetic patients

Discussion

- Insulinomas are commonly present in patients that are middle aged, female, and with a higher BMI.
- Classically, insulinomas are said to follow the "rule of 10" stating that 10% are multiple, 10% are malignant, 10% are associated with MEN1, and 10% are ectopic.
- Approximately 30% arise in each the body, tail, and head of the pancreas.
- The diagnosis is based on findings of inappropriate elevation in endogenous insulin production (high insulin, C-peptide, and proinsulin, and low BHB) during a 72-hour fast. Notably, while a 72-hour fast protocol is diagnostic for insulinoma, our patient experienced hypoglycemia if dextrose 10% solution was held for more than 30 minutes, indicating severity of insulin excess.
- Once biochemical diagnosis is established, tumors are localized through invasive or non-invasive procedures, including transabdominal US, abdominal CT, MRI, endoscopic US, transhepatic portal venous sampling, selective arterial calcium stimulation with hepatic venous sampling, and PET scan. However, most are first identified by CT or MRI.
- According to a 60-year longitudinal study, most patients with insulinoma reported neuroglycopenic symptoms within nearly 1.5 years preceding the diagnosis. Interestingly, our patient denied any significant symptoms prior to her motor vehicle accident.
- In the preoperative period and in patients with unresectable or metastatic tumors, medical management with diazoxide and octreotide can be considered for recurrent hypoglycemia.

Conclusion

- Even though patient tend to experience progressive episodes of hypoglycemia leading to the diagnosis of Insulinoma, an initial severe episode can have tragic consequence, there fore thorough evaluation of hypoglycemia in both inpatient and outpatient setting is crucial.

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