

An Adult Woman Suffer from Recurrent Hypoglycemia with Suspicion of Insulinoma

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Abstract: An adult woman 37 years old, suffer from recurrent hypoglycemia with suspicion of insulinoma. Clinical diagnosed of insulinoma was made based on the chief complaint of weakness and other symptoms of hypoglycemia. The signs and symptoms improves after drinking sugar water or getting a glucose infusion. From ultrasound results there is a small hypoechoic lesion on the pancreatic corpus. Abdominal CT scan with contrast shows multiple solid masses in the tail and neck of the pancreas, supporting insulinoma. Patient refused surgery. She was treated conservatively by regulating their diet and regularly monitoring blood sugar levels.

Keywords: recurrent hypoglycemia, trias Whipple, pancreatic multiple solid mass

1. Introduction

Insulinoma (islet cell adenoma) is a neuroendocrine tumor derived from the pancreatic Langerhans island cells that produce excess insulin. Insulinoma is the most common cause of hypoglycemia associated with endogenous hyperinsulinemia. Insulinoma also produces other hormones such as ACTH, glucagon, somatostatin, gastrin and chorionic gonadotropin. Insulin produced by this tumor is secreted suddenly so that in a short time cause blood glucose levels are very fluctuating. Most of these tumors (90%) are benign and the rest (10%) are malignant.

The incidence is rare, occurring in 1-4 people per 1 million of the general population per year. In contrast to normal pancreatic beta cells, insulin secretion in insulinoma does not require glucose stimulation and does not stop even when glucose levels are normal. Insulin is produced continuously is a cause of lower blood glucose levels below normal or hypoglycemia. Physically, this tumor does not show tumor-related abnormalities. The disorder arises when the state of hypoglycemia has occurred. In case of rapidly developing insulinoma and cause symptoms of hypoglycemia belonging to neuroglikopenik such as seizures and coma (1-4).

Therefore we reported a case of suspicion of insulinoma in a 37-years-old woman who has recurrent hypoglycemia. This case report is made because insulinoma is uncommon and there are often constraints in diagnosis and therapy.

2. Case

A 37-years-old woman came with a major complaint of a weak body since 3 months. Weakness is felt worsening since a week before hospitalized. Weakness does not improve if the patient rest or sleep. Patients also complained of headache since 7 days before admission. Sometimes accompanied by blurred vision, cold sweat, nausea and vomiting. All of these complaints are reduced and disappear when the patient drinks sugar water or receives glucose infusion. Patients had a history of low blood sugar levels known since 3 months ago when treated at RS Parama Sidhi Singaraja due to weak body complaints. No history of taking medication before. History of heart disease, high blood

pressure, diabetes, kidney disease, liver disease, lung disease is denied. No family of patients has ever had a similar illness. The patient is a housewife, never consumes alcohol or smokes. On physical examination conducted on February 15, 2017, the general condition appears moderate, fully alert, blood pressure 110/70 mmHg, pulse 80 times / min regular, respiration 20 times / minute, axillary temperature 36.20C. Eye examination is not obtained anemia or jaundice. In the neck region is not obtained enlarged lymph nodes. On examination of the heart and lungs are found within the normal range, while the physical examination of abdomen did not reveal any abdominal masses, tenderness and bowel sounds are within normal limits. Upper and lower extremities are cold. No edema was obtained. Full blood examination was obtained WBC 6.30 g / dl, Hb 10.88 g / dl, Hct36,98% and PLT 359 g / dl. Laboratory Results SGOT 21,10 U / L, SGPT 23,0 U / L, BUN 5,0 mg / dl, creatinine 0,55 mg / dl, blood sugar 70 mg / dl. Bilirubin total 0.18 mg / dL, Direct bilirubin 0.10 mg / dL, indirect bilirubin 0.08 mg / dL Results of chest X-ray: heart and lung did not appear abnormalities. Plain abdominal photo also does not appear abnormalities. Abdominal ultrasound results performed at RS Parama Sidhi Singaraja: small hypoechoic lesions of the pancreas corpus, may be an insulinoma. CT head scan results: no apparent of infarct / hemorrhagic / SOL intraparenchyme of the brain.



Figure 1: Abdominal ultrasonografi

The patient was diagnosed with observation of recurrent hypoglycemia with suspicion of insulinoma. Patients were given Dextrose infusion 10% 20 drops / minute. Dextrose 40% is given when blood sugar levels below 60 mg/dL. Furthermore, it is planned to perform CT scan of abdominal

with contrast , C-Peptide, fasting insulin. The patient is monitored for blood sugar every 4 hours and is monitored for signs of recurrent hypoglycemia.

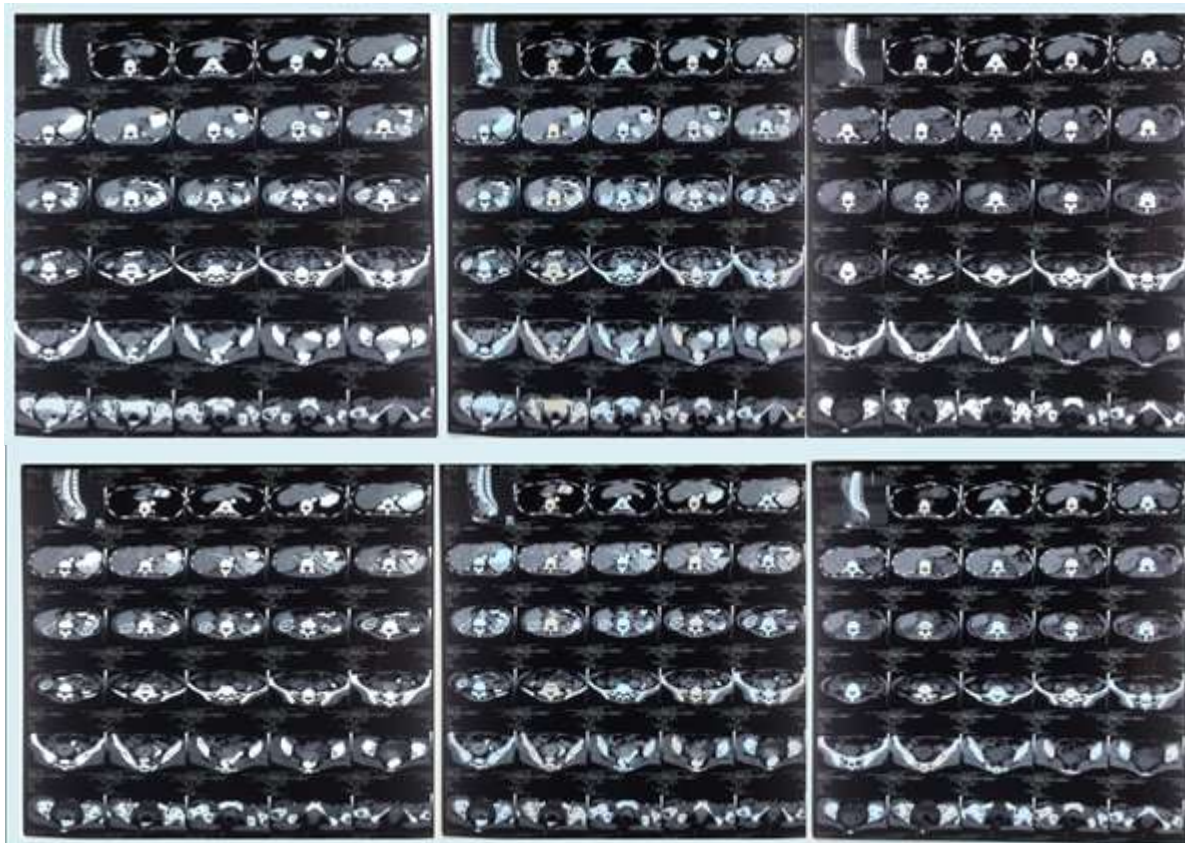


Figure 2: Abdominal CT Scan

TGL	JAM	BS	TGL	JAM	BS	TGL	JAM	BS
10/2/17	21.00	49	13/2/17	06.00	59	15/2/17	06.00	92
	21.30	340		06.30	200		12.00	71
	22.00	255		12.00	77		17.30	85
11/2/17	01.00	51		18.00	136		21.15	96
	03.00	68		22.00	114		22.00	83
	05.30	72	14/2/17	06.00	99	16/2/17	01.00	110
	08.00	169		12.00	80		04.00	53
12/2/17	06.00	76		18.00	144		06.00	131
	07.90	127		22.00	92			

Figure 3: Blood glucose monitoring before admission to hospital and at the time hospitalized

On the second day the CT scan was performed with contrast showing the results: multiple solid masses in the tail and neck of the pancreas, supporting insulinoma. On the 4th day laboratory tests were performed with the following results: Alkaline phosphatase 53 U / L (42-98 U / L), Albumin 4.3 g / dL (3.4-4.8 g / dL), Amylase 36.2 U / L (25-120 U / L), Lipase 43,2 U / L (13-60 U / L), CEA 1.43 ng / ml (no smoking ≤3,8 ng / ml, smoking ≤ 5, 5 ng / ml), CA 19-9 18.53 U / mL (≤ 27 U / mL), C-Peptide 1.6 ng / mL (0.9-7.1 ng / mL), plasma insulin at 59 , 6 uIU / mL. The patient was

consulted to the Digestive Surgery division. Diagnosis from Digestive Surgery was Pancreatic tumor suspected insulinoma. Patient was planned for enucleation surgery.

During the treatment, blood sugar levels was in stable range from 70-100 mg / dl with 10% Dextrose infusion and drinking sugar-containing beverages. After receiving an explanation from the Digestive Surgery division on consideration of the surgical action of the enucleation, the

patient and her family ultimately decided not to undergo surgery.

Because patient refused surgery, patient was conservatively treated and advised to periodically monitor blood sugar independently and drink sugars containing water. After 10 days, patients are allowed to stay on ambulatory care.

3. Discussion

Insulinoma is a functional endocrine neoplasm of the pancreas that produces large amounts of insulin and causes hypoglycemia. Insulinoma can occur at any age and distribution equally in both men and women. Approximately 10% of insulinoma is multiple. A total of 50% of multiple insulinomas are multiple endocrine neoplasms type 1. The etiology and pathophysiology were unclear, thought to involve the role of genetic disorders (1,5).

Clinical symptoms

Insulinoma is the most common cause of hypoglycemia due to endogenous hyperinsulinemia. Episodes of hypoglycemia attacks are associated with intermittent insulin secretion by the tumor. Symptoms of hypoglycemia vary widely and are distinguished for autonomic symptoms of diaphoresis, tremors, palpitations. While neuroglycopenic symptoms include confusion, impaired vision, changes in behavior, personal changes, seizures and coma (6,7,8).

Diagnosis of insulinoma is suspected based on clinical conditions that meet the Trias Whipple criteria: (1) hypoglycemia (blood glucose <60 mg / dl (2) autonomic or neuroglycopenic symptoms (3) symptoms of hypoglycemia improved after glucose administration, insulin, C-peptide, Pro insulin during fasting 72 hours. In insulinoma patients increased levels of insulin, C-peptide and pro insulin (5,9)

Table 1: Diagnosis of insulinoma

Classical diagnosis
Hypoglycemia (plasma glucose < 50 mg/dL)
Neuroglycopenic symptoms
Prompt relief of symptoms following the administration of glucose
Present consensus
At the time of hypoglycemia during a 72-h fasting test:
5 mIU/L (36 pmol/L) insulin threshold
0.6 ng/mL (0.2 nmol/L) C-peptide threshold
Insulin/C-peptide ratio < 1.0
20 pmol/L proinsulin cut-off level
Absence of sulfonylurea (metabolites) in the plasma or urine

Shah et al reported a case of insulinoma in a 25-year-old man, for 4 years experienced a change of behavior every morning and was initially diagnosed with psychosis (10). A similar case was also reported by Suzuki et al in a 65-year-old man who had delirium at night, a change of behavior each morning and seizure. Prior diagnosis of insulinoma this patient is treated by the neurological part as epilepsy and get anti-epilepsy drugs. Diagnosis can occur when symptoms appear unacceptable as symptoms of hypoglycemia (11).

In this case the patient experiences both autonomic and neuroglycopenic symptoms of hypoglycemia. These

symptoms occur repeatedly and complaints disappear after administration of glucose infusion or drinking sugar water. C-peptide levels of 1.6 ng / mL are still within normal limits. Insulin levels as 59.6 uIU / mL, The likelihood of normal results is due to the patient is not fasted 72 hours. Given that the patient has recurrent hypoglycemia, it is not possible to have a blood test under fasting conditions

Non invasive imaging

Some noninvasive techniques are available to determine the location of insulinoma, including ultrasound, CT scan and or MRI. Ultrasound sensitivity in determining the location of the tumor is only about 9% - 64%. While CT Scan sensitivity reported 33% - 64% and MRI sensitivity 40% - 90%. The sensitivity and specificity of MRI is generally superior to CT Scan including in detecting extrapancreatic metastases. In CT Scan typically the insulinoma appears hypervascular and exhibits a high degree of relief compared to normal pancreatic parenchyma at the time of contrast. If there is calcification, it is more commonly found in malignant tumors than benign tumors. CT scans are currently accepted as the first-line support for visualization of insulinoma (5,12).

In this case the ultrasound results of small hypoechoic lesions of the pancreas corpus, may be an insulinoma. CT Scan results in multiple solid masses in tail and neck pancreas, supporting insulinoma.

Invasive diagnostic modalities

Invasive diagnostic modalities are now an option in western countries, especially in patients who will undergo surgery because of higher accuracy in determining the location of preoperative insulinoma are EUS (endoscopic ultrasound) and ASVS (*angiography and arterial stimulation venous sampling*) (5).

Management

Most patients with benign insulinomas can be treated surgically. Once the insulinoma is identified surgically indicated on a localized tumor. Choice of procedure depends on tumor characteristics such as type, size and location. Atypical resection includes enucleation, partial pancreatectomy, middle pancreatectomy has the advantage of maintaining as many parenchymes as possible to reduce the risk of subsequent exocrine insufficiency. Radical resection is considered in multiple lesions, not well capsulated (5,13,14).

However, consideration of the risk of morbidity and mortality in surgery is particularly important for patients at high risk for surgery. Non-surgical treatment options include ablation with alcohol and chemoembolization, RFA (radio frequency ablation) (5).

Medical therapy to normalize blood sugar is very important in the preoperative period. Similarly, in non surgical patients such as non-resectable malignant insulinoma, multiple insulinoma, presence of surgical contraindications or in patients who resist surgery. Several strategies were

performed to control hypoglycemic episodes and improve quality of life (1,5,15,16) :

- 1) Continuous glucose monitoring effectively prevents episode hypoglycemia by alerting patients to decreased levels of glucose prior to neuroglycopenic symptoms. One example is the STG-22 which is a closed-loop glycemic control system consisting of glucose sensors to detect and monitor glucose levels and pumps to drain a certain amount of glucose or insulin as needed. The insulin and glucose pumps are regulated by the computer based on the targeted blood sugar levels prior to system initiation.
- 2) Dining arrangements. Proper meal timing can overcome or prevent hypoglycemia. In principle, shortening the

distance between two feeding schedules. It is advisable to use relatively longer absorbed carbohydrates (bread, potatoes, rice) preventing stimulate the secretion of insulin immediately.

- 3) Diaxozide 150 - 450 mg / day to inhibit insulin secretion and stimulate the process of glycogenolysis.
- 4) Corticosteroids can help stabilize blood glucose levels, for example using prednisone 1 mg / kg body weight.
- 5) Long acting somatostatin analogues such as ocreotide (sandostatin) can play a role in reducing insulin production.
- 6) Streptozotocin or chemotherapy or a combination of both for Langerhans carcinoma.

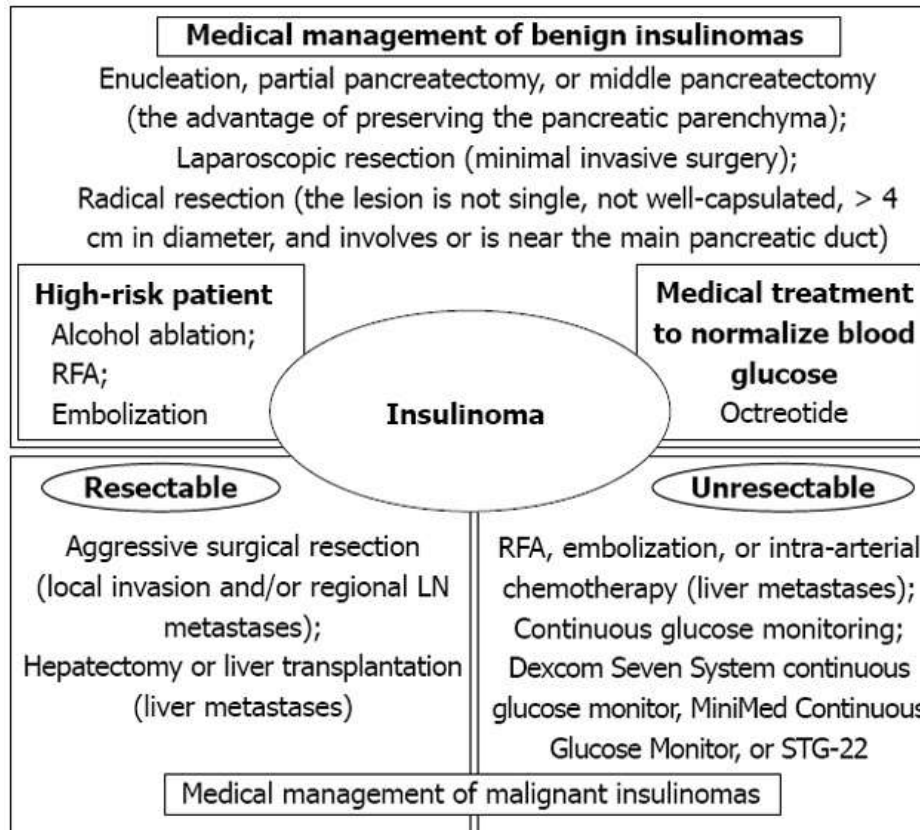


Figure 4: Management of insulinoma

In patients who have unresectable or uncontrollable malignant insulinomas of the pancreas, several strategies need to be considered to both control hypoglycemic episodes and improve quality of life, including administration of octreotide and continuous glucose monitoring. RFA: Radiofrequency ablation; LN: Lymph node.

In this case the patient may have multiple insulinomas and is planned for surgical enucleation. Patient refuses to perform surgery. Patients are given education to monitor blood sugar levels regularly. Conservative therapy by regulating the diet is still effective to prevent episodes of hypoglycemia so that patients do not have to undergo hospitalization anymore. Until now the patient did not get any other medications.

4.Summary

We reported a case of a woman, 37 years with suspicion of insulinoma. The diagnosis is made by Trias Whipple in which the patient has recurrent hypoglycemia and improves after drinking sugar water or getting a glucose infusion. From ultrasound results there is a small hypoechoic lesion on the pancreatic corpus, it may be an insulinoma. Abdominal CT scan with contrast shows multiple solid masses in the tail and neck of the pancreas, supporting insulinoma. Patient refuses surgery. She was treated conservatively by regulating their diet and regularly monitoring blood sugar levels.

Insulinoma is a rare neuroendocrine tumor and requires multiple endocrine tests and imaging tests to confirm the diagnosis. Surgical treatment is the best treatment option. In

the case of insulinoma that can not be operated, conservative therapy with medical becomes the next choice.

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