CASE REPORT

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Recurrent Severe Hypoglycemia in a 43 Year Old Extreme Obese Woman with Insulinoma: A Case Report

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ABSTRACT

Insulinomas are very rare neuroendocrine tumors (4 cases per million individuals per year) leading to insulin hypersecretion and occurring more often in women at any age. A 43-year-old extreme obese woman was referred to Dr Kariadi General Hospital with complaints history of repeated unconsciousness due to recurrent episodes of symptomatic severe hypoglycaemia (previously been hospitalized several times in regional hospitals in last six years). Physical examination: Body Mass Index Class II obesity (Asia-Pacific). Laboratory: recurrent hypoglycaemia (random blood glucose range 30-50 mg/dL), Fasting Blood Glucose 105 mg/dL (n: 80-109), 2 hours Postprandial Blood Glucose 44 mg/dL (n: 80- 140), C-peptide levels (taken during hypoglycaemia) 13.59 ng/ml (n:1.1-4.4). Abdominal Ultrasonography: grade 2 fatty liver, Fibroscan: no fibrosis or steatosis, Plain Head MSCT: no visible abnormalities, contrast abdominal magnetic resonance imaging: solid lesion in the body of pancreas (AP 1.2 x LL 1.2 x CC 1.3 cm) tends to be a picture of insulinoma. Patient underwent distal pancreatectomy with immunohistochemical results of an insulinoma. Post surgery the patient never had hypoglycaemia. We described a 43-year-old extreme obese woman with recurrent episodes of symptomatic severe hypoglycaemia. Laboratory (low random blood glucose, high C-peptide) and imaging examinations (solid lesion in the body of the pancreas on Contrast Abdominal MRI) support the diagnosis of insulinoma. Surgery is the treatment of choice for insulinomas. Patients with recurrent severe hypoglycemia, increase in C-peptide levels and solid lesion in pancreas are clinical manifestations of Insulinoma.

Keywords: Insulinoma, recurrent hypoglycemia, C-peptide

INTRODUCTION

Insulinomas are the most common, yet still rare, hormone-producing pancreatic neuroendocrine neoplasms (panNEN) with a reported incidence of 0.7 to 4 cases per million per year and the incidence is slightly higher in women than in men. More than 99% of insulinomas are located in the pancreas, where its tumor locations are evenly distributed. Most insulinomas present with the Whipple triad: (1) symptoms, signs, or both consistent with hypoglycemia; (2) a low plasma glucose measured at the time of the symptoms and signs; and (3) relief of symptoms and signs when the glucose is raised to normal.[1] We herein described an case report from Dr. Kariadi Hospital Semarang regarding recurrent severe hypoglycemia in a 43 year old extreme obese woman with insulinoma. The aim of this case report is to make us more aware and able to diagnose and carry out the management cases of insulinoma.

CASE ILLUSTRATION

A 43-year-old extreme obese woman was referred to emergency departments of Dr Kariadi Hospital from the regional hospital with complaints history of repeated unconsciousness due to recurrent episodes of symptomatic severe hypoglycemia. Patients have previously been hospitalized several times in regional hospitals due to recurrent episodes of symptomatic severe hypoglycemia (loss of consciousness) in the last six years. Patients have no history of diabetes mellitus. On Physical examinations she was fully alert. Her weight was 125 kg, and her height was 155 cm, with Body Mass Index (BMI) of 52.09 kg/ m^2 (Class II Obesity Asia-Pacific). Heart, lung and abdominal examination were normal. Laboratory tests were obtained recurrent hypoglycaemia (random blood glucose range 40-60 mg/dL), fasting blood glucose 105 mg/dL (n: 80-109), 2 hours post prandial blood glucose 44 mg/dL (n: 80-140), HbA1c 4,5% (n < 5.7), serum glutamic oxaloacetic transaminase (SGOT) 169 U/L (15-34), serum glutamic pyruvic transaminase (SGPT) 539 U/L (15-60), C-peptide levels (taken during hypoglycaemia) 13.59 ng/ml (n: 1.1-4.4). Abdominal ultrasound shows grade 2 fatty liver, no fibrosis or steatosis on fibroscan, no pancreatic mass was visible on contrast abdominal multi-slice computed tomography (MSCT), solid lesion in the body of the pancreas (size ± AP1.2 x LL1.2 x CC1.3 cm) tends to be a picture of insulinoma on contrast abdominal magnetic resonance imaging (MRI) (**Figure 1**), no visible abnormalities on Plain Head MSCT.

Preoperative management consisted of Dextrose 10% infusion 20 drops per minute, Dextrose 40% 3 flasks if blood glucose is less than 70 mg/dL, Dextrose 40% 2 flasks if blood glucose is less than 100 mg/dL, Dexamethasone injection 5 mg twice daily intravenous and giving snacks every 4 hours. Monitoring blood glucose in patients every 4 hours. During the operation a mass was found in the cauda of the pancreas, so patient underwent distal pancreatectomy (**Figure 2**) with immunohistochemical results of an insulinoma (**Figure 3)**.

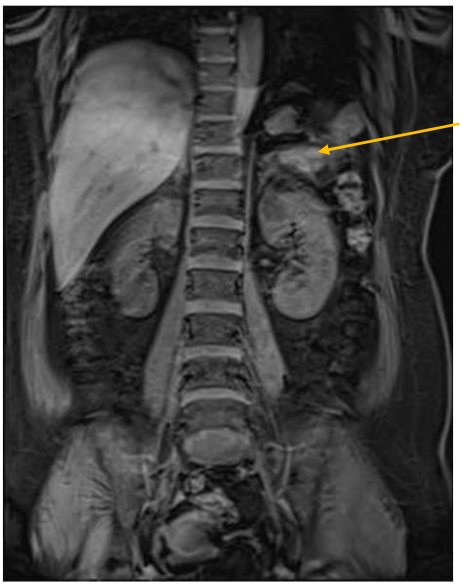

Figure 1. Contrast abdominal MRI

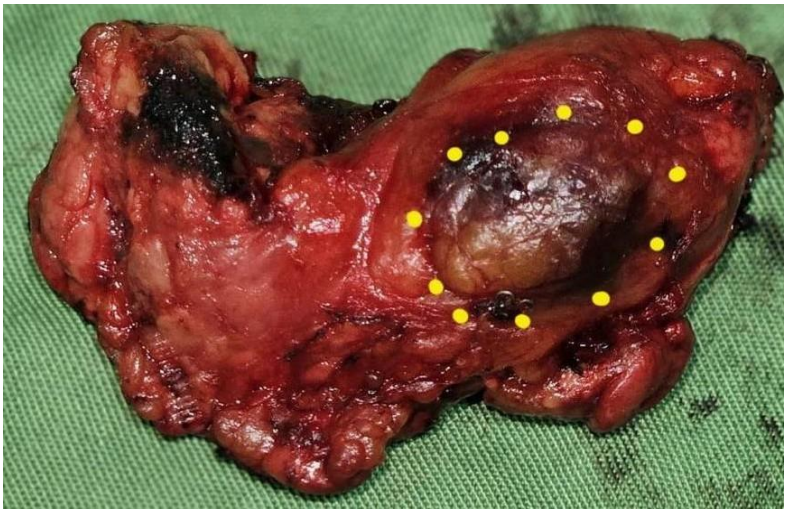

Figure 2. Distal pancreatectomy

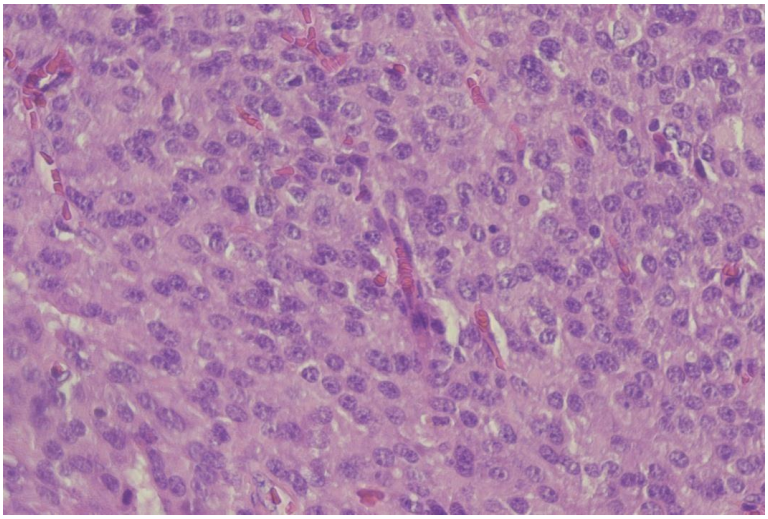

Figure 3. Immunohistochemical of an insulinoma

Patients are treated in a regular ward after distal pancreatectomy. Patient consciousness is composmentis, condition and hemodynamics were stable, and patient has a drain installed. Patient never experienced hypoglycaemia after surgey, blood glucose tests had increased. Postoperative management in regular ward consisted of Nacl 0.9% infusion 20 drops per minute, Ranitidine injection 50 mg twice daily intravenous, metformin 500 mg twice daily oral, Vitamin B12 1 tablet twice daily oral. Patient was discharging home then 6 days later. One week later the patient was checked into the clinic and blood glucose monitoring was normal.

DISCUSSION

Hypoglycemia is a common presentation in the primary care setting and accounts for about 16 of every 1000 visits to the emergency department. In patients without diabetes, it is important to rule out common precipitating factors such as medications (e.g., indomethacin or antibiotics), alcohol, caloric restriction and systemic illness. In the absence of an obvious

cause, further investigation for causes of endogenous hyperinsulinemia is warranted.[2] Insulinoma is the most common pancreatic F-NET, deriving from β-pancreatic islet cells that secrete insulin, and is associated with hypoglycemic neuroglycopenic and sympathetic-overstimulation symptoms. Insulinomas are most commonly benign, well-differentiated NETs, whereas malignant neoplasms account for approximately 5-10% of all cases. Insulinomas may occur at any age, mainly during the 5th decade of life, and have a slight female predominance. Insulinomas present with signs and symptoms early in their course and thus during diagnosis their size ranges between 0.5 cm and 2 cm. The diagnostic hallmark of insulinoma, the so- called “Whipple’s triad” or “triad of insulinoma”, was first described by Allen Whipple and Virginia Kneeland Frantz in the 1930s and consists of symptoms caused by hypoglycaemia, low blood glucose level during the episodes, symptoms relief upon blood glucose level normalization through glucose administration.[3] Patients with insulinomas suffer from recurrent episodes of hypoglycemia. The most frequent symptoms are neuroglycopenic (altered mental status, abnormal behavior, visual disturbances). Autonomic, adrenergic, and cholinergic symptoms are less frequent. The diagnosis of insulinomas can be challenging as patients are first examined in neurologic and psychiatric departments due to neuroglycopenic symptoms. Symptoms occur mainly in the fasting state, but up to 20% of patients also described postprandial symptoms.[4] In this case, the patient had a history of hospitalized several times in regional hospitals due to recurrent episodes of symptomatic severe hypoglycaemia (loss of consciousness and seizure) since 2018. Weight gain is found in only 25% - 42% of patients and monthly changes in body weight are significantly correlated with the tumor size and serum insulin concentration. Weight gain in insulinoma can be attributed to overeating to treat the hypoglycemia symptoms.[5]

Laboratory investigations for the cause of hypoglycemia, including endogenous insulin overproduction, should be ordered. Initial investigations at the time of a hypoglycemic episode include levels of serum glucose, C-peptide, insulin and β-hydroxybutyrate. Insulin is generated in the pancreas when its precursor, proinsulin, is cleaved into insulin and C-peptide. In patients with insulinoma, endogenous insulin overproduction occurs independent of serum glucose level, resulting in elevated insulin and C-peptide levels, which precipitates hypoglycaemia.[2] Patients with insulinoma characteristically develop symptoms while fasting (73%- 80%) but 6% of patients report symptoms only in the postprandial state, and 21% of patients report symptoms in both the postprandial and fasting states. Although fasting hypoglycemia has been considered the main trait of insulinoma, postprandial hypoglycemia has also been occasionally reported as the predominant feature.[5] Laboratory examination in this case found recurrent hypoglycaemia (random blood glucose range 40-60 mg/dL), fasting blood glucose 105 mg/dL (n: 80-109), 2 hours post prandial blood glucose 44 mg/dL (n: 80-140), C-peptide levels (taken during hypoglycaemia) 13.59 ng/ml (n: 1.1-4.4).Computerized tomography is currently considered the first-line imaging diagnostic test in the insulinoma visualization procedure. In this case, Contrast Abdominal MSCT was not found pancreatic mass but from Contrast Abdominal MRI found solid lesion in the body of the pancreas (size ± AP1.2 x LL1.2 x CC1.3 cm) tends to be a picture of insulinoma. MRI is a highly sensitive localization technique for seemingly occult, indolent, localized insulinomas and has become increasingly popular. Contrast Abdominal MRI is emerging as an appropriate, safe, non-invasive alternative with high sensitivity

in the localization of insulinomas.[3]

Patient management consisted of Dextrose 10% infusion 20 drops per minute, Dextrose 40% 3 flasks if blood glucose is less than 70 mg/dL, Dextrose 40% 2 flasks if blood glucose is less than 100 mg/dL, Dexamethasone injection 5 mg twice daily intravenous and giving snacks every 4 hours. Monitoring blood glucose in patients every 4 hours. Regular meals or snacks rich in slow carbohydrates, also ante noctem, are generally recommended. The inclusion of a bedtime or late-night meal is sufficient in most patients, but nocturnal tube feeding might be required to avoid nocturnal hypoglycemia in severely symptomatic patients. IV glucose administered via a central IV indwelling catheter might be needed for the control of severe recurrent hypoglycemia. Glucocorticoids are sometimes used to control the hypoglycaemia. A continuous glucose monitoring system can support patients in recognizing hypoglycemic events and prevent serious complications, especially during the night.[1]

The definitive treatment of insulinoma is surgical resection. Most insulinomas are benign and confer excellent prognosis after tumour resection, with disease-specific survival of 98% at 1 year, 92% at 5 years and 90% at 10 years.[2] The type of surgical treatment depends on the localization and size of the tumor. Enucleation is indicated in smaller tumors without contact with the main pancreatic duct. The other possibility is a left- side pancreatectomy, with or without splenectomy. A central resection of the pancreas can be performed in some specific case.[4] In this case, patient underwent distal pancreatectomy with immunohistochemical results of an insulinoma.

CONCLUSION

We described a 43-year-old extreme obese woman who had suffered from recurrent episodes of symptomatic severe hypoglycaemia. Laboratory (low random blood glucose, high C-peptide levels) and imaging examinations (solid lesion in the body of the pancreas on Contrast Abdominal MRI) with immunohistochemical results support the diagnosis of insulinoma. Surgery is the treatment of choice for insulinomas.

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