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Case Report

Insulinoma- Rare pancreatic tumor

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ABSTRACT

Insulinoma is hormone producing neuroendocrine pancreatic tumor. Insulinoma is a type of functional neuroendocrine tumor characterized by hypersecretion of insulin, causing hypoglycemia. It typically presents as a solitary benign tumor but can be associated with multiple endocrine neoplasia type 1 (MEN1). Patients with insulinoma have hypoglycemic episodes, more characteristically as fasting hypoglycemia.
46 yrs. old male having recurrent episode of Syncopal attack, sweating, excessive thrust, and weakness last 3 to 4 yrs. His blood sugar level was always below normal range at time of attack. No H/O diabetes, Hyper tension or any other chronic illness.
On detail examination and investigation, we found that his blood sugar level fall 01 hrs. After food intake and blood sugar fasting and post prandial (F=46 mg/dl & PP= 180 mg/dl) is impaired. C Peptide level, serum insulin level is high. MRI shows growth near head of pancreas.
Partial pancreatectomy done and sample send for histopathological examination which shows well differentiated pancreatic neuroendocrine tumor with no lymph node involvement and congested spleen.
The Whipple triad, named after the American surgeon Allen O. Whipple (1881-1963), is the diagnostic hallmark establishing the existence of a hypoglycemic disorder and has the following 3 features: (1) symptoms, signs, or both consistent with hypoglycemia; (2) 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 a normal level (2, 3). Insulinoma is usually diagnosed by biochemical testing. Surgical resection is the preferred treatment choice.

1. Introduction

Insulinoma is rare, low to intermediate grade subset of neuroendocrine tumors (NET) of Pancreas. Neuroendocrine tumors of the pancreas are rare and comprise 1 - 2% of clinically apparent pancreas neoplasms; much less common than exocrine tumors.[1] Most common in body or tail where there are more islets cells. Radiologically Solid or cystic well circumscribed enhancing lesion generally seen in body & tail of Pancreas. Liver is most common site for metastasis.

In insulinoma patients, the 10-year survival rate is 88% after successful surgical removal, and 87.5% of patients get cured (being free of symptoms for at least six months) after surgery.[2,3] The 10-year survival in malignant insulinomas was 29% after successful surgical removal in one study, and the 5-year survival was 24% in another.[2,4] Patients with MEN1 syndrome or malignant insulinomas have a higher rate of failing initial surgery or experiencing recurrent disease.[2]

The etiology of solitary insulinoma is not clearly understood. Normally high plasma glucose concentration would trigger the secretion of insulin from the pancreatic beta cells and vice versa. In patients with insulinoma, insulin

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still gets secreted, even when plasma glucose concentration is low. Hyperinsulinemia could result from an upregulated translation process due to a variant of insulin splice. [5]

Insulinoma is usually diagnosed by biochemical testing when there is high clinical suspicion. Surgical resection is the preferred treatment choice. Localization with imaging studies is fundamental to characterize the tumor better before surgical resection. Other treatment options are also available depending on the stage and grade of the tumor.

According to the most recent clinical practice guidelines, critical diagnostic findings are present when the confirmed fasting plasma glucose concentrations are preferably below 45 mg/dL (2.5 mmol/L) or below 55 mg/dL (3.0 mmol/L) (Hypoglycemia—depending on guidelines and cutoffs—the optimal cutoff level for blood glucose is currently still a matter of debate), plasma insulin concentrations of at least 3 μU/mL (18 pmol/L), plasma C-peptide concentrations of at least 0.6 ng/L (0.2 nmol/L), and plasma proinsulin concentrations of at least 5.0 pmol/L. [6,7]

2. Case Report

46 yrs. old male having chief complain of Giddiness, pain abdomen, flushing, palpitation, sweating and recurrent episode of loss of consciousness since 2019. Symptoms corrected after giving Dextrose saline or oral glucose. No history of fecal or urinary incontinence or post ictal headache/confusion.

No history of diplopia/headache/galactorrhea /constipation/urinary incontinence. No other significant history. On detail investigation it is found that Blood Picture shows Normocytic Normochromic Anema with relative neutrophilia. Oral Glucose tolerance test shows impaired glucose tolerance and fasting sample shows 40.99 mg/dl. Liver function test &Thyroid function test was normal.

Fasting Insulin Level is 87.76 mU\L (N=1.7-31 mU\L) which is high and C-Peptide level is 6.2 ng/mL (N=0.48-5.05 ng/mL) which is also high. Pt. Symptoms worsen day by day with early morning hypoglycemia with restless and palpitation with increase appetite. No history of loose motion, insomnia, Pancreatitis.

As we are in remote places so pt. referred to SGPGI, Lucknow for further treatment and evaluation with provisional diagnosis of Insulinoma.

On investigation in SGPGI 72 hrs. fasting test shows: Insulin: 528.9pmol/L (N= 17.8-173 pmol \L), C-Peptide: 3.04 nmol/L (N=0.37-1.47 nmol\L), S. Cortisol:232.1 nmol\L, Growth Hormone: 3.35 ng/ml, S. Prolactin: 351.0 mIU/L (N=85-319 mIU\L).

CT abdomen shows: Ill-defined hyper enhancing lesion in distal body of pancreas- likely neuroendocrine tumor of 10 mm size. Distal Pancreatectomy with splenectomy done and specimen sent for histopathological examination (HPE).

Operative finding shows: Nearly 1.5 X1.2 cm oval shaped hypoechoic intraparenchymal lesion in the proximal body of pancreas 3 mm away from pancreatic duct. Weight 60 gm, Size: 1.5X1.2 cm. Sugar level increased to 129 mg/dl after removal of tumor. Pt. respond well and recovered and on insulin therapy as sugar level high after resection of tumor.

HPE examination shows Partial Pancreatectomy and splenectomy: Well - differentiated Pancreatic Neuroendocrine tumor (Grade I) with No Peripancreatic Lymph node involvement and congested spleen.

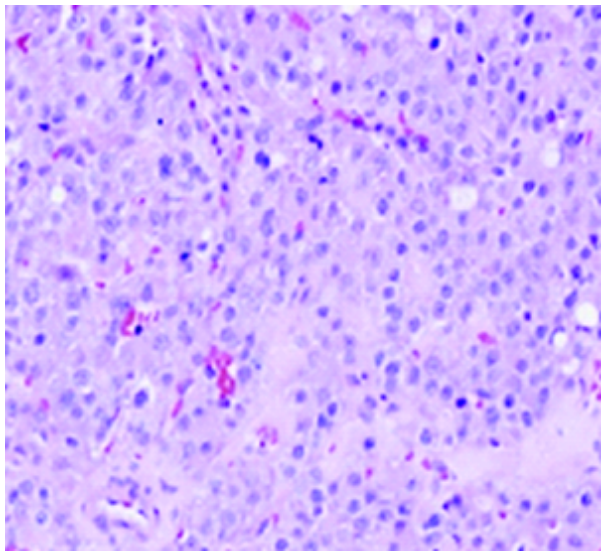

Figure 1: · Monotonous cells demonstrating round nuclei with salt and pepper-like chromatin.(40X)

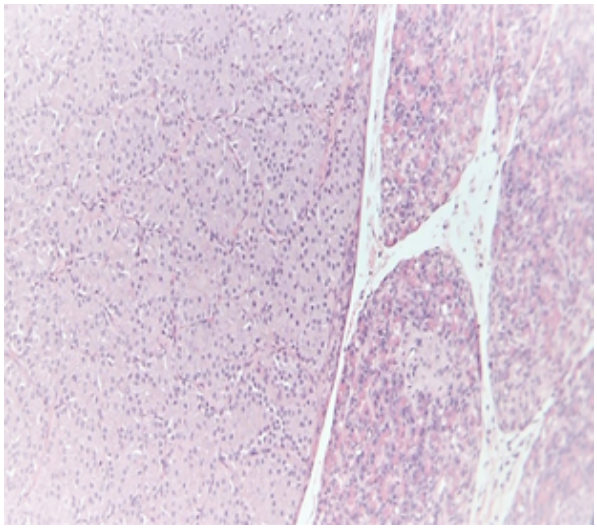

Figure 2: Trabecular, nested, gyriform or solid architecture.(10X)

Table 1: Symptoms of insulinoma and frequency

Neuroglycopenic symptoms	Adrenergic symptoms
Confusion (80%)	Diaphoresis (69%)
Visual disturbances (59%)	Tremors (24%)
Amnesia or coma (47%)	Palpitations (12%)
Abnormal behavior (36%)	Hyperphagia/weight gain (50%)
Seizures (17%)	

Note: Data are from multiple studies. [8–10]

3. Discussion

Our current understanding of insulinomas began with the discovery of pancreatic islet cells by Paul Langerhans in 1869. [8,11,12] In 1922, the extraction of insulin, or "isletin", from a dog's pancreas by Banting and Best led the way to several studies that examined the physiologic significance of the hormone. [8] The following year, in 1923, patients with blood sugars below 70 mg per 100 cc whose symptoms improved by feeding. [8]

Two important steps in diagnosis of Insulinoma. First is biochemical test followed by radiological evaluation like CT, MRI, PET scan & Glucagon-like peptide-1 receptor (GLP-1) imaging for localization of Tumor. Post operative confirmation done by Histopathological examination & IHC Confirmation.

Histology examination and immunostaining for chromogranin A, synaptophysin, and insulin should be done to support the diagnosis of insulinoma. [2] A Ki67 index should also be obtained for grading, especially when a patient demonstrates an aggressive clinical course. [2]

In 1935, Whipple and Frantz published a manuscript summarizing the historic advances that defined insulinomas, along with their own observations. This paper, represented the first published account of the diagnostic "Whipple's Triad": (1) symptoms of hypoglycemia provoked by fasting; (2) circulating glucose level less than 50 mg/dL at the time symptoms presented; and (3) the relief of symptoms with the administration of glucose. [8]

Unfortunately, only 53% of patients are diagnosed within 5 years of experiencing their first symptom. [9,13] Spontaneous hypoglycemia from insulinoma can cause neuroglycopenic symptoms. Insulinomas typically present with neurologic symptoms of confusion, dizziness, and behavioral changes. [9,10,14] In severe cases, patients can present with seizures and coma. [9,10,14] Glucose levels below 55 mg/dL produces a surge in catecholamine levels that subsequently cause palpitations, trembling, diaphoresis, and tachycardia. [9,12] All these symptoms are relieved or prevented when the patient consumes glucose rich food, as described by Whipple and Frantz (Table 1). [8]

4. Conclusion

Diagnosing insulinoma precisely requires keen clinical observation and laboratory tests. It is rare neuroendocrine tumor. The 48-hour test can be used to accurately diagnose insulinoma in the majority of insulinoma patients, with very few having to complete the full 72-hour test. Preoperative CT scan is helpful in ruling out metastasis. Following the diagnosis of insulinoma, the definitive treatment of the tumor is surgery. In the cases of missing insulinomas, SACS (Selective Arterial Calcium Stimulation) is a helpful tool to identify the anatomic region of the lesion in the pancreas. Newer drugs like sunitinib and everolimus, have had encouraging results in progression-free survival.

5. Source of Funding

None.

6. Conflict of Interest

None.

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