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A Rare Case Report - Big Insulinoma of Pancreas

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Abstract: ***Insulinomas account for 60% of islet cell tumours (ICT) and are typically hypervascular, solitary small tumours, 90% of which measure less than 2cm and 30% measuring less than 1cm in diameter. Approximately 10% are multiple, 10% are malignant and 4-7% are associated with MEN I; these tumours are usually multiple and can be malignant in up to 25%. The tumour is characterized by endogenous hypersecretion of insulin and the subsequent development of symptoms of neuroglycopenia and symptoms resulting from the catecholaminergic response, which may not always be present. Early localisation of the disease is essential to prevent lethal hypoglycaemia. We report a case of big insulinoma of size of 4 cm in a 45 year old female which was diagnosed on triple phase CT Scan abdomen and was treated with distal pancreatectomy along with splenectomy.***

Keywords: Insulinoma

1. Introduction

Pancreatic endocrine tumors are rare lesions, with a reported incidence of four cases per 1 million patient-yr. Of these lesions, insulinomas are the most common. The majority of patients diagnosed with an insulinoma are between 30 and 60 yr of age, with women accounting for 59%. Most insulinomas are sporadic in origin. In two series, 7.6% and 12% of patients with insulinoma had multiple endocrine neoplasia type I syndrome. Insulinomas are more likely to be multiple in patients with multiple endocrine neoplasia type I. Almost all insulinomas are located within the pancreas, even though aberrant cases have been described in the duodenum, ileum, lung and cervix. Patients with insulinoma have symptoms of hypoglycaemia resulting from neuroglycopenia and increased catecholamine release. Surgical excision is the treatment of choice and is curative in most cases. Diagnosis of this pathology relies on clinical features along with laboratory tests and imaging investigations to aid in localisation.

2. Case Report

A 45 years old female patient, housewife by occupation, resident of Gajipura, Todabheem, district Karauli, Rajasthan presented to emergency room with history of pain epigastrium , moderate in intensity radiating to back associated with abdominal distension, vomiting and not passing flatus and stool for the last 3 days. She was admitted in the emergency with tentative diagnosis of Intestinal Obstruction, ? Pancreatitis (which later on was found to be because of large Insulinoma in the pancreas obstructing the main pancreatic duct). In ward, when patient was kept nil by mouth because of the intestinal obstruction, she went into hypoglycaemia (Random blood sugar was 36mg/dl). Immediately 100ml of Dextrose 25% was given and random blood sugar came out to be 375 mg/dl. After sometime again she became drowsy and random blood sugar was again taken which was 40mg/dl. On further enquiring, the patient gave history of episodes of light headedness with transient loss of consciousness on skipping meals , on and off for the last 6 years, which were relieved with taking tea and sugar orally. Suspicion of insulinoma arose and on further investigating we found high insulin and c-peptide levels and low sugar levels in the blood during the period of hypoglycaemia, on keeping the patient on water only. On Investigating the patient, Serum Amylase was 701 U/L, Lipase was 2228U/L, Random Blood Sugar was 26 mg%. Other Investigations were within normal limits.

CT Scan (Fig -1, fig 2 and Fig 3) was done – which was suggestive of-:

1) Well defined heterogeneously enhancing lesion in the distal part of body of pancreas – most likely Insulinoma.
2) Acute Pancreatitis.

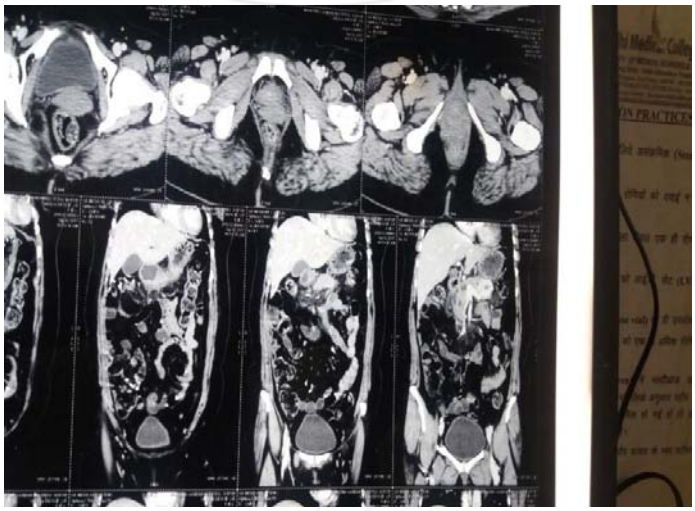

Figure 1: CT Scan showing Insulinoma in the tail of pancreas.

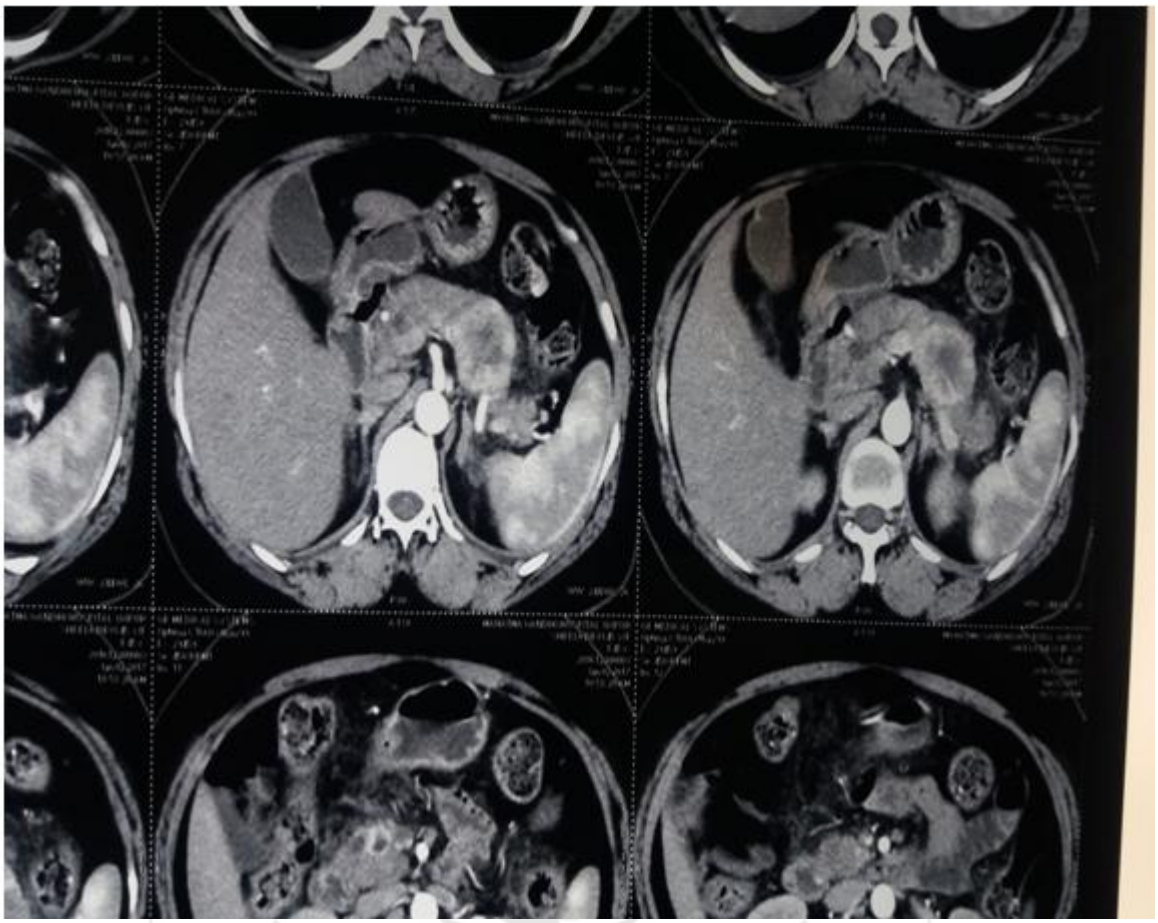

Figure 2: CT Scan showing Insulinoma in the tail of pancreas

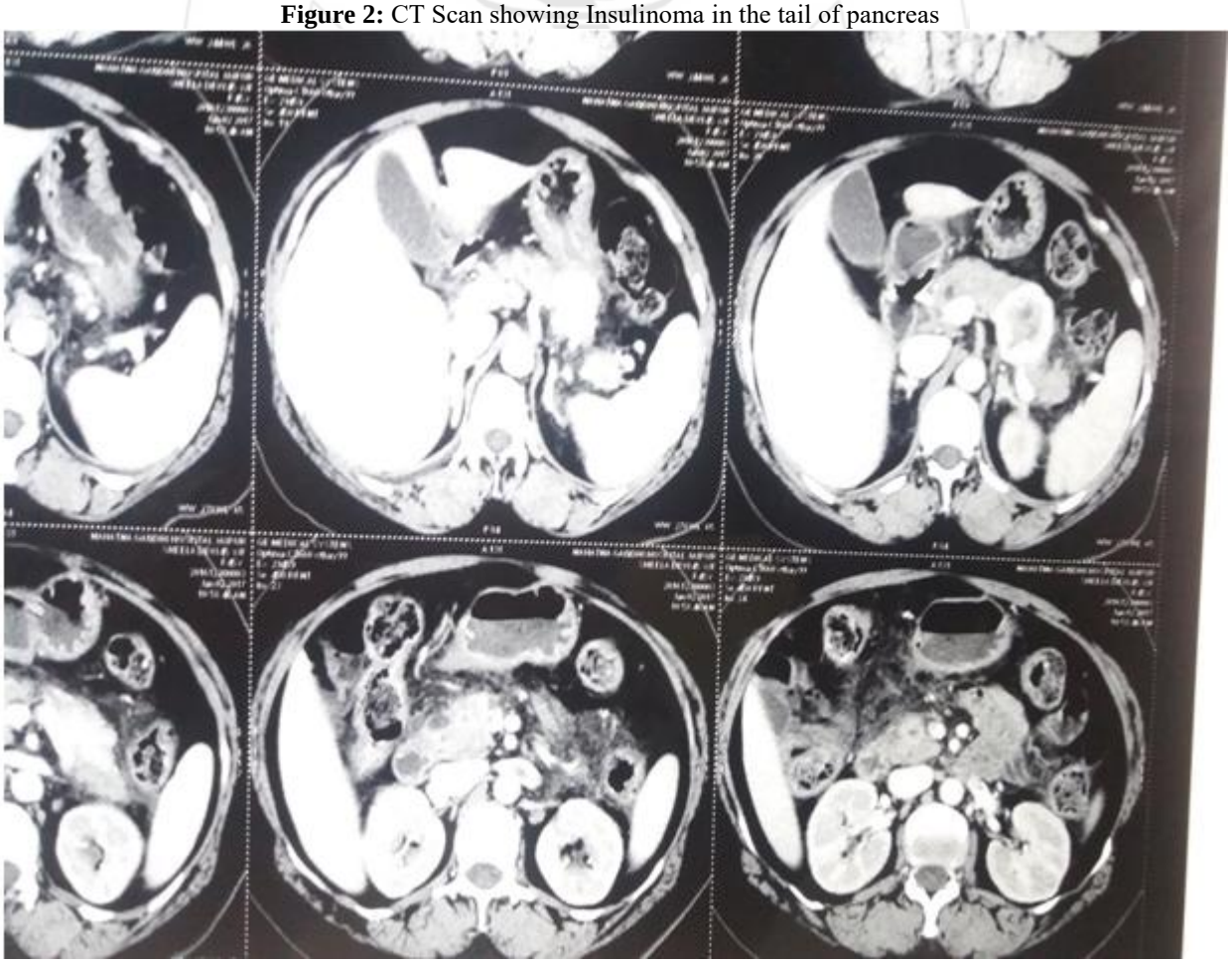

Figure 3: CT Scan showing insulinoma in the tail of pancreas.

The patient underwent distal pancreatectomy with splenectomy of the pancreatic mass 4* 3.4*3.7 cm in size(Fig 4). Intraoperative Ultrasound was also done to see for any mass lesion in the remaining part of the pancreas. But none was found.

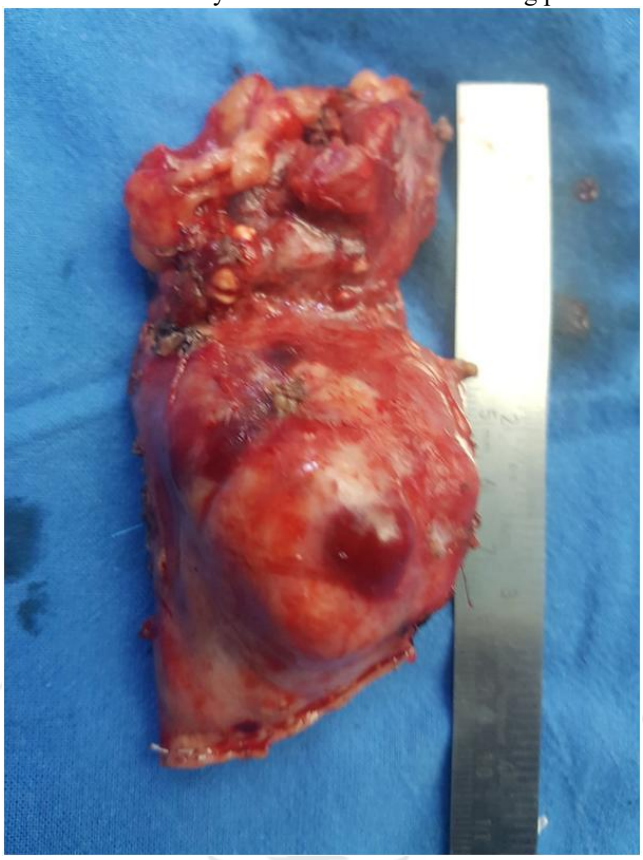

Figure 4: Distal Pancreatectomy containing the Insulinoma with proximal cut margin with the stapler.

Immediately after removal of the mass, her glucose level increased to 245 mg/dl and even went upto 600 to 700 mg/dl by the evening of the operation. Post-operatively glucose levels were consistently higher and she experienced no further hypoglycaemic episodes infact she has to be taken on insulin to control the sugar levels. Histopathological evaluation was consistent with endocrine neoplasm-insulinoma of pancreas. The patient was discharged in good health with proper glucose level on 8th post operative day.

3. Discussion

Hypoglycaemia is a common medical emergency. Among hospitalised patients, it is most common in those with diabetes, but also occurs in patients with renal insufficiency, liver disease, malnutrition, congestive heart failure, sepsis or cancer. Diabetes on treatment with insulin is an important cause of hypoglycaemia among ambulatory groups. Factitious use of insulin or sulphonylurea drugs is probably the most common cause of hypoglycaemia among patients who do not have diabetes. Occasionally, hypoglycaemia can be induced by endocrine tumours, including pancreatic tumours that secrete insulin and non-islet-cell tumours that secrete insulin-like growth factors like hepatoma, adrenocortical tumors and carcinoids. Symptoms of hypoglycaemia include both neurogenic symptoms from adrenergic as well as cholinergic stimulation and neuroglycopenic symptoms as a direct result of a decrease in brain substrate. Signs and symptoms of hypoglycaemia are diaphoresis, warmth, hunger, weakness, tingling sensations, paraesthesia, difficulty in thinking, confusion, shaking, tremulousness, tiredness, drowsiness, palpitations, tachycardia, faintness, dizziness, nervousness, anxiety, difficulty in speaking, blurred vision, stupor or coma. The diagnosis of insulinoma is suggested by endogenous hyperinsulinaema in the presence of hypoglycaemia and reversal of the symptoms by administration of glucose (Whipple's triad). Insulinomas are uncommon- the yearly incidence is estimated to be 1 in 2,50,000. Insulinomas account for 60% of islet cell tumours (ICT) and are typically hypervascular, solitary small tumours, 90% of which measure less than 2cm and 30% measuring less than 1cm in diameter. Approximately 10% are multiple, 10% are malignant and 4-7% are associated with MEN I; these tumours are usually multiple and can be malignant in up to 25%. Almost all insulinomas are located within the pancreas, even though aberrant cases have been described in the duodenum, ileum, lung and cervix. The tumour is characterized by hypersecretion of insulin and the subsequent development of symptoms of neuroglycopenia and symptoms resulting from the catecholaminergic response, which may not always be present.

In patients with insulinoma, there is continued secretion of insulin despite a lower glucose level. Insulin is synthesised as a single-chain precursor proinsulin – which is cleaved into a C-peptide and insulin, both of which are secreted in equimolar concentrations. Diagnostic criteria for insulinoma include a serum insulin concentration of more than 6 microU/ ml, a detectable concentration of serum C peptide, and a high proinsulin concentration, concomitant with symptoms of hypoglycaemia and blood glucose

concentration of less than 45 mg per deciliter during fasting. Hypoglycaemia induced by sulphonylurea may have an identical presentation like an insulinoma; a negative screening for sulphonylurea is required to confirm the diagnosis. Our patient was fitting into all the above mentioned criteria.

Once a clinical and biochemical diagnosis is established, the imaging modalities are used for localisation of tumour. Recently, several prospective studies have investigated the relative utility of currently available techniques, and helped to establish a diagnostic work-up on evidence-based information. Because of its high sensitivity and its ability to obtain whole body images, scintigraphy with 111 In-octreotide is considered the initial imaging procedure of choice for gastroenteropancreatic tumours (including carcinoids and ICT). However, specifically in insulinomas scintigraphy with 111In-octreotide has been shown to be less sensitive than other islet cell tumours(ICT), probably due to the lack of somatostatin receptors type 2.

Endoscopic ultrasound (EUS) allows the positioning of a high frequency (7.5-10 MHz) transducer in close proximity to the pancreas. Using this approach lesions as small as 5 mm as well as tumours located in the bowel can be detected with a sensitivity of 93% and a specificity of 95% respectively in localization of intra-pancreatic lesions. EUS detected all tumours visualized by any other conventional technique questioning the necessity for other imaging modalities. Intra operative ultrasound (IOUS) also allows direct examination of the pancreas using high resolution 7.5-10 MHz transducers. The combination of IOUS and surgical palpation has led to 97% cure rates in patients with benign insulinomas. In addition, besides facilitating surgical resection, IOUS can help define the appropriate plane of resection by identifying multiple small tumours, in patients with MEN I. The majority of islet cell tumours (ICT) are isodense on unenhanced CT and will not be seen without intravenous contrast enhancement. Dual-face helical CT scan allows multiphase imaging during a single bolus of contrast administration, and can achieve sensitivities in the range 82-92%. A comparative study showed that the sensitivity of T1-weighted MR imaging is equivalent to delayed Portal Venous Phase (PVP) dynamic CT. Due to the relative rarity of islet cell tumours, it remains difficult to define the best imaging technique, although MRI is probably the investigation of choice in defining hepatic metastases. MRI is considered the most sensitive technique for demonstrating liver and bone metastases in patients with gastroenteropancreatic (GEP) tumours and is recommended for precise monitoring of response to therapy. In cases of small insulinomas not detected with the previously mentioned imaging modalities, invasive procedures may still be necessary to achieve pre-operative localization. Sensitivities ranging between 77 and 100% have been described for trans-hepatic portal venous sampling (TPVS), but this technique is associated with considerable morbidity. Selective arterial calcium stimulation and hepatic venous sampling (ASVS) using calcium as the insulin secretagogue is a powerful tool for the preoperative localization of occult insulinomas and can also help distinguish the rare forms of noninsulinoma- pancreatogenous-hyperinsulinemia (NIPHS). In a recent series of 11 patients a sensitivity of 100% was obtained with this technique, which may also identify rare extra-pancreatic insulin-secreting Neuroendocrine Tumours (NETs), mainly of the liver. Positron emission tomography (PET) using 11C-5-hydroxytryptamine (HTP), due to selective uptake in tumour tissue compared to surrounding tissue, produces very good tumour visibility and it can be used for the examination of both the thorax and abdomen. However, lack of general availability and high cost limits its use. Intra-operative nuclear imaging can be used to help define the exact location of a biochemically proven GEP and aid in its complete resection. Conventional imaging studies such as ultrasonography, CT, and MRI fail to reveal the majority of insulinomas. However they have a role in the evaluation of malignant insulinomas and in the detection of metastases. Portal vein sampling and intra-arterial stimulation of insulin secretion with calcium makes it possible to detect almost all insulinomas but they are invasive and complicated techniques. IOUS alone identifies approximately 95% of tumours but necessitates experience for the surgeon or assistance by a radiologist. Laparoscopic ultrasound as an integral part of laparoscopic procedure has also been suggested in the management of these patients.

However inability to localize the tumour during laparoscopic approach and conversion rate has been reported as high as 30% in a recent multicentre study. Preoperative endoscopic ultrasound with fine needle tattooing(FNT) combined with intraoperative ultrasound can localize the 100% of insulinomas. The technique was first advocated by Gress et al. It needs experienced endoscopist and surgeon familiar with pancreatic surgery. The overall sensitivity and accuracy of EUS is over 90% for insulinomas. CT and MRI scan are useful in the assessment of malignancy and identification of adjacent lesions. Laparoscopic enucleation is safe and effective. If the lesion seen on CT is well defined, it can be removed laparoscopically. Endoscopic ultrasonography is useful for identifying lesions in patients whose CT scans are nondiagnostic. Some previous studies have shown that pancreatic fistulas were common, but they resolved spontaneously and produced little morbidity. Laparoscopic enucleation resulted in a short hospitalization and rapid recovery for most patients. Our patient underwent Open Distal Pancreatectomy alongwith Splenectomy , had no post operative complications and she was discharged from the hospital on 8rd post operative day.

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