Case Report

Picking up an insulinoma – The challenges ahead

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Abstract

Insulinoma is a rare pancreatic neuroendocrine tumour (PNET) with an incidence rate of 4 per million population, and the most common cause of hypoglycaemia due to endogenous hyperinsulinism. We present the story of a 61-year-old male, who was extensively evaluated at many hospitals for his symptoms of giddiness, uneasiness and recurrent black outs for the last 3 months, his symptoms disappearing with a carbohydrate rich meal or sweets. Random sugar and fasting sugar values noted were low, with elevated insulin and C-peptide levels. Diagnosis of insulinoma was confirmed by a DOTA PET scan involving the tail of the pancreas and then surgically removed. Early detection is crucial for early surgery to allay symptoms. We describe our diagnostic and treatment plan with reference to previously published reports.

Keywords: DOTA PET scan, gastrinoma, insulinoma, multiple endocrine neoplasia, pancreatic neuroendocrine tumours

Introduction

According to the symptoms, pancreatic neuroendocrine tumours (PNET) are classified as secretory and non-secretory tumours. Non-secretory tumours constitute 50% of NETs and are usually silent. Among the secretory tumours, 25% are insulinomas while 15% are gastrinomas[1] The remaining 10% are in patients with syndromes that predispose them to cancer, such as multiple endocrine neoplasia type 1, Von Hippel–Lindau disease, tuberous sclerosis complex, neurofibromatosis type 1, and glucagon cell adenomatosis.[2] Insulinoma is a functional neuroendocrine tumour that secretes insulin. The islet cell tumours are the commonest cause of hypoglycaemia due to endogenous hyperinsulinism. Many a time it is associated with other endocrine gland tumours – especially in a rare condition called multiple endocrine neoplasia type 1 (MEN1) involving the parathyroid, pancreatic and pituitary glands – the three Ps. Male to female ratio is 2:3. Median age to diagnosis is around 47 years.[1] They are usually solitary and 2 cm. After localization, surgical excision is the treatment of choice. For benign tumours, the prognosis is excellent.

Case Presentation

A 61-year-old male, with no known co-morbid conditions, was referred to our hospital, with frequent complaints of giddiness, uneasiness, sweating and experience of near black outs off and on for the last few months which improved with a carbohydrate-rich meal or sweetened foodstuff. He was extensively evaluated outside, but nothing was conclusive. The only significant finding noted was a low blood sugar determined by fingerstick method during the above episodes.

On admission, fingerstick blood sugar level detected was 40 mg/dL, and this was treated with dextrose injections. His blood sugar was monitored at regular intervals and he was advised to have chocolates, fruit juices and candies while in the hospital. Most episodes noted were usually after fasting, or after exercise

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and early in the morning. He did not have any known history of neither diabetes mellitus, hypertension, hypothyroidism, pituitary disease nor had he any significant family history of the same.

Physical examination revealed a well-nourished male with a BMI of 25.8 kg/m^2. His blood pressure noted was 124/80 mmHg, pulse rate 104/min and respiratory rate 14/min. His central nervous system, respiratory system, cardiovascular system, genitourinary system examinations were within normal limits.

Presence of low blood glucose <55 mg/dL, symptoms of hypoglycaemia and resolution of hypoglycaemic symptoms after the blood glucose level is raised, reminded us of the Whipple's triad and Insulinoma was kept as a possibility. The problem here lay in locating it.

Except low fingerstick blood sugar level (40 mg/dL), all other initial blood investigations including complete blood count, liver function tests, creatinine, electrolytes, thyroid function tests, urine routine and microscopic examination were within normal limits [detailed reports below, Table 1]. There was evidence of high serum insulin levels and connecting peptide (C peptide) levels with low blood sugar levels. Ultrasound abdomen (as a part of routine investigations) was inconclusive. Upper gastrointestinal endoscopy was suggestive of gastritis and distal esophagitis. Since nothing was conclusive, we planned for a DOTA PET scan (gallium 68 Dotatate positron emission tomography/computed tomography) and it revealed evidence of a Somatostatin receptor expressing lesion of about 2 cm involving the tail of the pancreas which was likely to be neoplastic disease of neuroendocrine aetiology. No other definitive abnormal Somatostatin receptor expressing lesion or lymph node were noted in rest of the scan [Figures 1 and 2]. Contrast enhanced computerized tomography (CECT) abdomen pancreatic protocol done subsequently reported as hyper enhancing tiny pancreatic lesion likely to be an insulinoma [Figures 3 and 4], multiple simple hepatic cysts and degenerative lumbar disc disease.

The case was then handed over to the team of surgeons. An elective distal pancreatectomy was done under general anaesthesia [Figures 5 and 6] and the specimen was sent for histopathology. Microscopic examination of the specimen reported findings consistent with insulinoma and negative for malignancy [Figure 7]. Immunohistochemistry using site directed antibodies against insulin, proinsulin, and chromogranin A, also confirmed a well differentiated G1 neuroendocrine tumour. Post-operative recovery was uneventful and blood sugar monitoring was done at four hourly intervals. Interestingly his random blood sugar was always above 100 mg/dL and he did not have any symptoms of hypoglycaemia, and thus dextrose injections were not required. After stabilization, he was finally discharged on the tenth post-operative day.

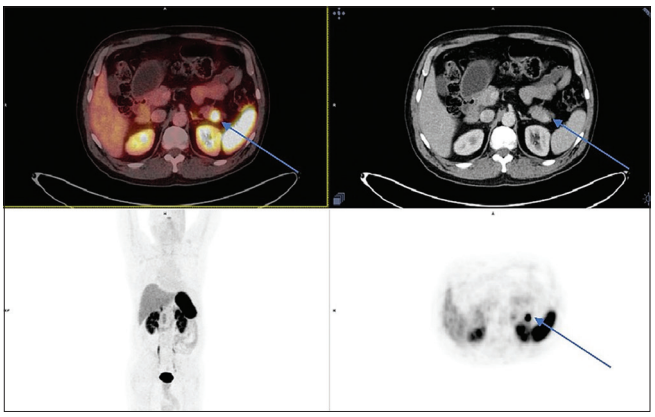

Figure 1: DOTA scan showing suspected insulinoma-cross sectional

Table 1: Investigations

Test	Day 1 [ward]	Day 3 [ward]	Day 7 [post op]	Normal value
INR	0.96	1.1		<1.1
CRP	0.08 mg/dL			0.08-0.79 mg/dL
Creatinine	1.01 mg/dL	1.02 mg/dL	0.83 mg/dL	0.74-1.35 mg/dL
Haemoglobin	15 gm/dl	11 gm/dL	14 gm/dL	11.5-16.5 gm/dL
TLC	6900/cu mm	10400 per cu mm	6800/cu mm	4000-11000/cu mm
Platelets	179000/cu mm	195000 per cu mm	225000/cu mm	150000-410000/cu mm
Serum protein	7.0 gm/dL	5.4 gm/dL		6.6-8.3 gm/dL
Serum albumin	4.30 gm/dL	3.26 gm/dL		3.5-5.2 gm/dL
Serum sodium	140 mEq/L	139 mEq/L	140 mEq/L	136-146 mEq/L
Serum potassium	3.9 mEq/L	3.8 mEq/L	3.9 mEq/L	3.5-5.5 mEq/L
Random blood sugar	40 mg/dL			80-130 mg/dL
Serum cortisol fasting		2.39 U/mL		5-25 U/mL
CA19.9		37.20 U/mL		0-37 U/mL
AFP		1.19 ng/mL		10-20 ng/mL
CEA		3.54 ng/mL		0-2.5 ng/mL
Insulin (fasting)		31 mIU/L	12 mIU/L	<25 mIU/L
Insulin (2 hours post prandial)		170 mIU/L	40 mIU/L	16-166 mIU/L
C-Peptide		2.0 ng/mL		0.5-1.2 ng/mL
Plasma Glucose fasting	44 mg/dL	60 mg/dL	84 mg/dL	70-100 mg/dL
Plasma Glucose post prandial	70 mg/dL	92 mg/dL	110 mg/dL	100-140 mg/dL

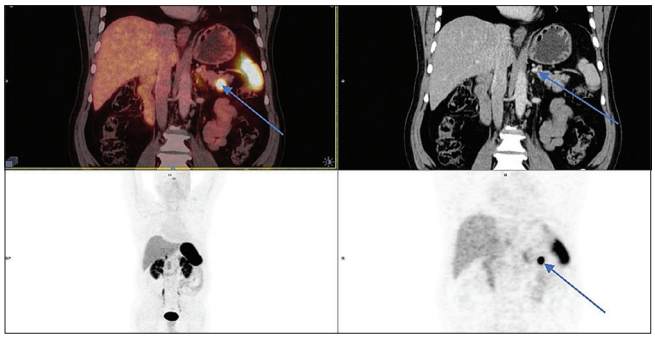

Figure 2: DOTA scan showing suspected Insulinoma – sagittal section

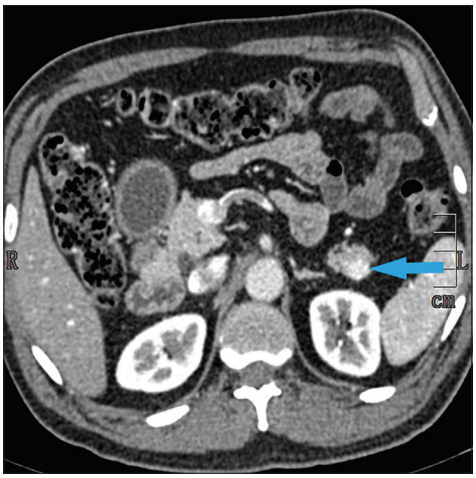

Figure 4: CECT abdomen in the portal venous phase showing the lesion in the pancreatic tail

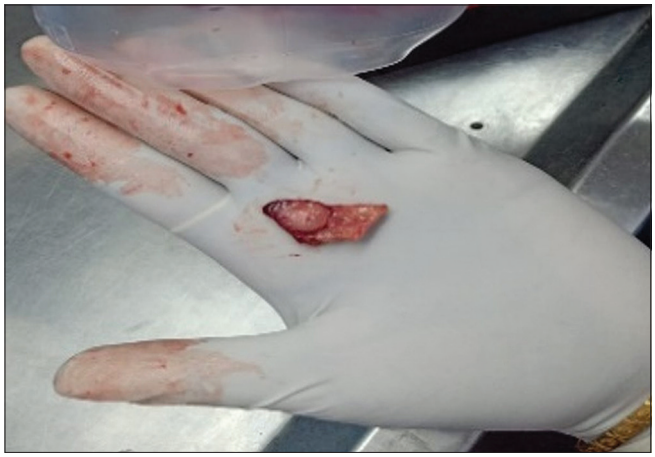

Figure 6: Resected specimen

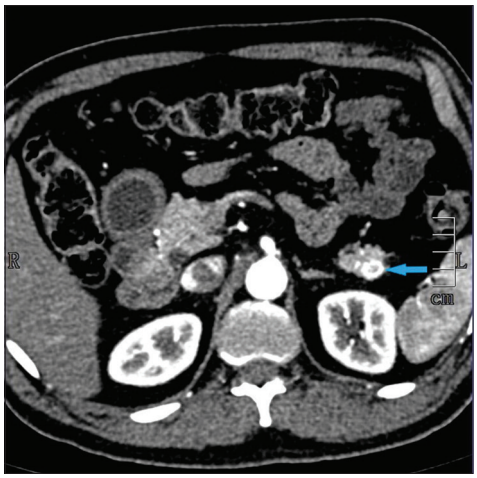

Figure 3: CECT scan of abdomen in the arterial phase showing hyper-attenuating lesion in the tail of the pancreas – insulinoma

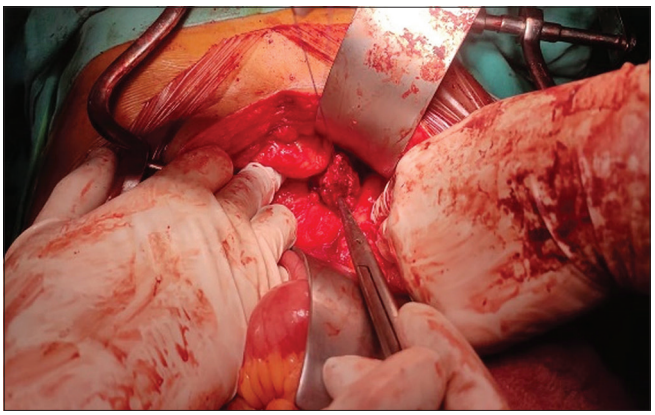

Figure 5: Intraoperative

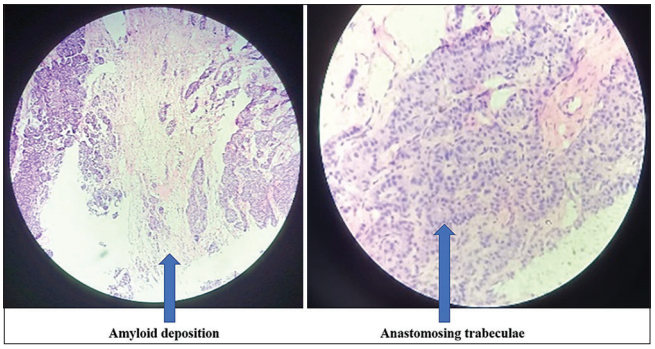

Figure 7: Histological images suggestive of insulinoma

Discussion

Insulinomas are usually benign and solitary. Incidence is one to four per million.[3] they can be found most commonly in the islet cells of Langerhans in the pancreas, but a minority do metastasise. Hypoglycaemia produced by these insulin secreting tumours may present as weakness, dizziness, confusion, visual disturbances, anxiety, sweating, palpitations and tremors [neuroglycopenic symptoms]. In our case, dizziness was the primary symptom which was witnessed mainly during fasting and after stress or exercise. Insulinoma is suggested by the Whipple's triad with symptoms of hypoglycaemia induced by fasting or exercise, plasma glucose level <55 mg/dL and reversal of symptoms after administration of glucose. The triad seemed to be prominent in our case.

The diagnosis of insulinoma is made biochemically with low blood sugar, high insulin levels and C peptide levels and thereafter confirmed with radiological imaging.

Diagnosis to localize the lesion can be done with trans abdominal ultrasound, CECT abdomen, magnetic resonance imaging (MRI) abdomen, endoscopic ultrasound, and intra-operative ultrasound. Reported sensitivity of trans abdominal ultrasound to diagnose insulinomas is 0–40%, for computed tomography (CT) abdomen is 30–60%, for MRI abdomen is 40–90%, endoscopic ultrasound is 93%, intra-operative ultrasound is 86% and helical CT scan has a sensitivity of 94%.[4]

In our case, trans abdominal ultrasound failed to detect the insulinoma and we went in for a CECT abdomen and DOTA scan, to localize the mass in the tail of the pancreas.

Most insulinomas can be cured surgically. Resection options include median pancreatectomy, pancreaticoduodenectomy, distal pancreatectomy (with or without splenectomy), depending on the site.[5] Tumour location should be confirmed intraoperatively by intra-operative ultrasound. In our case, distal pancreatectomy was done after intraoperative confirmation of the mass bimanually.

However, determination of localization remains challenging because of the small size of these tumours. Whereas the conventional imaging methods such as ultrasonography, CT, and MRT have proven to display low sensitivity, selective arterial calcium stimulation test and endoscopic ultrasound are invasive and operator dependent.[6] Ga-68 DOTA-Exendin-4 PET/CT scan is highly sensitive for identification and exact localization of insulinoma which can guide better surgical exploration.[5]

Conclusion

We conclude that diagnosing insulinomas may take a longer time in cases where we lack suspicion and newer diagnostic modalities, such as DOTA scan should be made use of as it is less invasive and has more sensitivity in diagnosing these tumours. In primary care settings, monitoring of glucose levels in fasting, post-prandial and post exercise states can go a long way in picking up these tumours.

Consent

Informed consent taken from patient for publication of the case details.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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