Original Research Paper

Volume - 12 | Issue - 10 | October - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Internal Medicine

HOW NOVEL NUCLEAR IMAGING AIDED THE DIAGNOSIS IN A CASE OF RECURRENT HYPOGLYCEMIA- A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT Insulinomas are a type of rare neuroendocrine tumor most frequently found in the pancreas. Adults without diabetes most frequently develop hyperinsulinemic hypoglycemia from them, and the majority are benign. According to the so-called "rule of 10," 10% of insulinomas are ectopic, 10% are multiple, 10% are malignant, and 10% are linked to MEN1. We present a case of insulinoma, which was undetectable with conventional investigations.

KEYWORDS : Insulinoma, Recurrent hypoglycaemia, Nuclear imaging, Gallium DOTATOC

INTRODUCTION:

Insulinomas affect 1-4 individuals per million in the general population and are the most frequent cause of hypoglycemia associated with endogenous hyperinsulinism. Tremor, diaphoresis, and palpitations are typical autonomic symptoms of insulinoma, whereas neuroglycopenic symptoms include disorientation, visual problems, behavioral changes, seizure, and coma. Standard endocrine testing, particularly the extended fasting test, is used to diagnose suspected patients. When an insulinoma has been diagnosed, non-invasive imaging techniques like computed tomography and magnetic resonance imaging are utilized to identify the exact location of Insulinoma. Insulinomas are usually benign, small (less than 2 cm), and occasionally challenging to localize using conventional imaging techniques. In challenging circumstances where biochemical and conventional imaging are unable to pinpoint the lesion, 68-Gallium DOTATATE and 68-Gallium DOTATOC scans can help with the diagnosis[1–3]

CASE REPORT:

Mrs. S, a 51-year-old lady from Dhaka, Bangladesh, with a known history of systemic hypertension, presented with a history of frequent lowering of blood sugars, necessitating the intake of food every 2 hours and a gain of around 10 kgs of weight in the last 1.5 years. She underwent multiple biochemical and imaging testing in her hometown, but the diagnosis was still elusive. She was worried about her frequent hypoglycemic episodes and visited our hospital for further care.

On examination, her general physical exam, vital signs, and systemic examination were within normal limits. Her basic investigations are given in Table 1. Fasting sugar was noted to be 42mg/dl. We went ahead and did Fasting insulin and C-Peptide levels, which were well within normal limits (22.0 µlU/ml and 3.3 ng/mL respectively).

A 640 slice Contrast Enhanced CT abdomen was done and it was notable for no significant abnormalities. An endocrinologist's inputs were obtained and the case was discussed in detail with the endocrine team. It was decided to go ahead with a 68Gallium DOTATOC PET scan to look for any neuroendocrine tumor like Insulinoma.

68Gallium DOTATOC PET scan was notable for **abnormal Ga-68 DOTATOC avid somatostatin receptor-expressing ill-defined arterially enhancing lesion (measuring approximately 1.6 x 1.5 cm) in the distal body of the pancreas.** Imaging features were suggestive of primary pancreatic neuroendocrine tumor-likely **insulinoma** (Figure 1).

Surgical removal of the tumor was done by performing distal pancreatectomy and the histology of the lesion was comprised of monomorphic cells with polygonal shaped, enlarged nuclei with speckled chromatin, small nucleoli, and moderate amphophilic cytoplasm, arrange as cords, nests, and trabeculae with an acinar pattern at foci, features suggestive of neuroendocrine tumor, likely insulinoma (Figure-2). Immunohistochemistry confirmed the presence of Insulinoma.

Post-surgery, her hypoglycemic symptoms improved and her blood sugars were gradually normalized. She was doing well during her first follow-up.

DISCUSSION:

Neuroendocrine tumors are uncommon tumors that exhibit significant heterogenecity. The natural history, biological behavior, response to therapy, and prognosis of neuroendocrine neoplasms vary widely.[4]Hypoglycemia brought on by very high insulin secretion is a symptom of insulinoma, a form of functional neuroendocrine tumor (NET). Although it often manifests as a single benign tumor, multiple endocrine neoplasia type 1 (MEN1) can occasionally be linked to it.[5]

The annual incidence ranges between 1 to 3 per million. The condition presents a challenge in terms of clinical manifestation, diagnostic testing, surgical treatment selection, and pathological classification.(6) When examining an insulinoma, there are two essential steps. When there is a strong clinical suspicion, the first step is to use biochemical testing to confirm the diagnosis. The next step is to localize the tumor. (5,7)

The gold-standard test for identifying an insulinoma is a 72-hour fasting test. Plasma glucose levels below 55 mg/dL, insulin levels above 3 microUnits/mL, C-peptide levels above 0.6 ng/mL, and a concurrently negative sulfonylurea level all point to hyperinsulinemia as the cause of the hypoglycemia.(5)

Given that insulinomas are often solitary and have a diameter of less than two centimeters, localizing the lesion may be difficult. According to studies, MRI imaging has a sensitivity of between 55 to 90% for detecting insulinomas, as opposed to a reported 75% for CT imaging. Although it has been observed that EUS has high specificity (85–95%), insulinomas are frequently seen in areas of the pancreas, making it more challenging to visualize them.[7] Selective arterial calcium stimulation testing with hepatic venous sampling or endoscopic ultrasonography can be used to locate the tumor in individuals with an established insulinoma and unsatisfactory outcomes from noninvasive radiologic localization tests. These procedures require competent professionals because they are invasive.[2]

The vast majority of studies often use 68Ga-DOTATOC, 68Ga-DOTANOC, and 68Ga-DOTATATE to show the potential of PET technology. Particularly, compared to somatostatin (SST) receptor scintigraphy, PET offers a greater resolution and better pharmacokinetics, with promising findings for identifying tumors that express the SST receptor and providing prognostic information.[8]

A study by Poeppel et al concluded that both 68Ga-DOTATOC and 68Ga-DOTATATE have a similar diagnostic value for finding NET

lesions, while 68Ga-DOTATOC may have a potential advantage. The 68Ga-DOTATATE's 10-fold greater affinity for binding SST_2 did not turn out to be clinically significant. SUV_{max} values with 68GaDOTATOC were typically greater than those with 68Ga-DOTATATE. [3] A study by Pallavi et al concluded that the precise localisation of an insulinoma with a DOTA-exendin-4 Ga-68 PET/CT scan is very sensitive, allowing for more effective surgical exploration.[9]

Since 640 slice CECT of the abdomen was non-contributory, we went ahead and did non-invasive 68Ga-DOTATOC imaging, which yielded satisfactory results in terms of localizing the tumor. These tests can be done with good sensitivity and specificity while localizing the lesions non-invasively.

For local disease, surgical resection is advised, but it should also be taken into account for advanced disease. Surgery can be used to treat isolated sporadic insulinomas. Diverse surgical techniques have been described by surgeons. Enucleation of the insulinoma and partial distal pancreatectomy is the most frequent of these procedures. After successful surgical removal of an insulinoma, the 10-year survival rate is 88%, and 87.5% of patients are cured (symptom-free for at least six months) after surgery.[5]

CONCLUSION:

The preoperative localization of insulinomas is frequently difficult and necessitates a variety of diagnostic techniques. However, according to various studies, the majority of tumors could be localized using standard non-invasive imaging techniques including CT, US, and MRI. Despite being invasive, EUS appears to be more successful in the hands of skilled practitioners than other imaging techniques. Nuclear imaging methods like 68-Gallium DOTATATE, 68-Gallium DOTATOC, and Ga-68 DOTA-exendin-4 PET/CT scan may be beneficial in the case of non-visible tumors.

Declarations:
Funding: No funding sources
Conflict of Interest: None
Ethical approval: Not required.

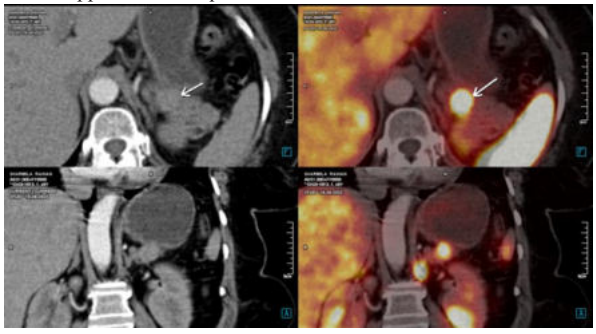

Figure 1: Ill-defined arterially enhancing lesion is seen in distal body of pancreas showing abnormal increased Ga68 DOTATOC uptake, measuring approximately 1.6 x 1.5 cm (SUVmax- 42.2)

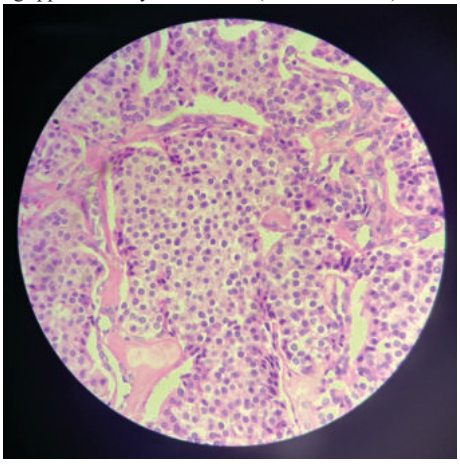

Figure 2: HPE showing monomorphic cells with polygonal shaped, enlarged nuclei with speckled chromatin, small nucleoli, and moderate amphophilic cytoplasm, arrange as cords, nests, and trabeculae with an acinar pattern at foci.

Table 1: Basic Investigations Of The Patient On Admission.

Test Parameters	Patient's data	Normal Range
Complete blood count:		
Haemoglobin	11.4 (g/dL)	11.5-16.5 (grams/deciliter)
Total White blood cell count	7.3 * 10^3 /mm^3	4-11 * 10^3 /mm^3
Neutrophils	60%	40-80%
Lymphocytes	34%	20-40%
Monocytes	5%	02-10%
Platelet count	270 *10^3 /mm^3	150-450 10^3 /mm^3
ESR	16	0-20 mm/hr
Liver Function tests:		
Total Bilirubin	0.6 mg/dL	0.0-1.3 mg/dL
Direct bilirubin	0.4 mg/dL	0.0-0.5 mg/dL
Indirect Bilirubin	0.2 mg/dL	0.0-1.2 mg/dL
SGOT/ AST	26 U/L	<31 U/L
SGPT/ ALT	21 U/L	<34 U/L
Alkaline Phosphatase	66 U/L	<98
Gamma Glutamyl Transpeptidase (GGTP)	38 U/L	<140 U/L
Renal Function Tests		
Urea	23 mg/dl	13-43 mg/dl
Creatinine	0.6 mg/dl	0.6 - 1.1 mg/dl
Random Blood Sugar	44 mg/dl	<140 mg/dl
INSULIN(FASTING) - SERUM	22.0 µlU/ml	2 - 25 µlU/ml
C-PEPTIDE(FASTING) SERUM:	3.3 ng/mL	0.8 - 3.5 ng/mL

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