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Adult-Onset Nesidioblastosis: A Challenge In Diagnosis and Management in Resource Limited Countries: A Case of Recurrent Hypoglycemia after Partial Pancreatectomy for Nesidioblastosis

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Abstract

We report a 44 year old male patient with recurrent attacks of hypoglycemia (RBS 40-50 mg/dL), neuroglycopenic symptoms, and weight loss, prompting evaluation for causes of hyperinsulinemic hypoglycemia. Initial investigations confirmed endogenous hyperinsulinemia (elevated C-peptide: 3.4 ng/mL, insulin: 18.1 μIU/mL) via prolonged fasting, suggesting insulinoma or nesidioblastosis. Imaging (Gallium Dotatate PET-CT, EUS) identified a pancreatic tail lesion, prompting distal pancreatectomy. Histopathology examination confirmed nesidioblastosis. Post-surgery, transient diabetes developed but hypoglycemia recurred at 4 months. Octreotide treatment failed and diazoxid treatment successfully resolved symptoms.

This case underscores nesidioblastosis as a critical differential diagnosis in hyperinsulinemic hypoglycemia when insulinoma is excluded, highlighting the role of diazoxide when surgery fails or is refused. Early recognition and multidisciplinary management are vital for improving outcomes in similar conditions.

Keywords: Hypoglycemia; Nesidioblastosis; Gastroenterology

Introduction

Nesidioblastosis, a rare cause of hyperinsulinemic hypoglycemia, is characterized by diffuse pancreatic β-cell dysfunction and poses significant diagnostic and therapeutic challenges, particularly in low-resource settings. While predominantly reported in neonates, adult-onset cases further complicate management due to overlapping clinical features with insulinomas and limited access to specialized diagnostic modalities [1, 2]. In resource-constrained environments, histopathological confirmation is often hindered by inadequate infrastructure, while first-line therapies like Diazoxide remain inconsistently available due to cost and supply barriers. Surgical interventions, including partial pancreatectomy, are frequently performed but carry risks of persistent or recurrent hypoglycemia, necessitating long-term pharmacological management.

Case Presentation

We report Mr. H.H.A. a 44-year-old male presented with 4-year history of watery diarrhea, patient sought medical advice 4 years ago but his condition was not diagnosed and the watery diarrhea persisted and patient lost follow up. 12 months ago, patient presented with history of significant hypoglycemic attacks of 3 months duration during which the patient experienced dizziness, blurring of vision and sweating, occurring with no predisposing factors especially when the patient was fasting, and RBS during the attacks reached 40 – 50 mg/dl. Symptoms improved on eating sweets or with glucose infusion. Patient also reports unintentional weight loss (perceived and not measured) during the last 3 months, not associated with anorexia. His past medical history was significant for hypertensive on calcium channel blocker and ARBS & HBV infection diagnosed 24 years ago and is on antiviral therapy. His family history showed no similar conditions. patient was referred to our hospital for further investigations. Clinical examination was unremarkable. He was vitally stable and had no clinical sign of insulin resistance and his BMI was 26.1 kg/m^2.

Investigations

As demonstrated in table (1) patient had normocytic normochromic anemia and dyslipidemia.He had a normal morning cortisol level which excluded adrenal insufficiency.

Table 1: Showing the results of laboratory investigations

Stool analysis "3 successive samples "	- loose consistency - Pus cells: 1-2 - R.B. Cs : 1-2 - No parasitic cysts or ova.
Urine analysis	- Pus cells: 0-1 - R.B.Cs : 0-1 - No proteins, glucose or casts.
HB.	10.6
M.C.V.	82 (76 – 100)
M.C.H.	28 (26 – 32)
TLC	5.4
Platelets	228
ESR	27
INR	0.9
ALT	19

AST	26
Total bilirubin	0.6
Alkaline phosphatase	69
Albumin	3.8
Total protein	6.8 (6.6 – 8.3)
Creatinine	1
Urea	31
Na	138
K	3.7
CaFBS	9.1 84
2HPP	130
HBA1C	5.9%
Total cholesterol	223
LDL	143
Triglycerides	166
HDL	47
HBsAg **HBV DNA PCR**	+ve 37 IU/ml (<5 IU/ml)
HCV antibody	negative
HIV antibody	negative
Faecal Calprotectin	31 (Negative: <50)
TSH	5.9 (0.27 – 4.2)
Free T3	3.3 (2 – 4.4)
Free T4	1.4 (0.9 – 1.7)
Glucagon	191 (<209)
5-HIAA	3.8 (2 – 6)
Vasoactive intestinal polypeptide	8.3 (0 – 30)

Prolonged Fasting Test: -

- C-Peptide: 3.4 ng/mL
- Insulin: 18.1 μIU/mL
- Insulin/C-Peptide ratio: <1

According to the results of the prolonged fasting test, if the C-Peptide > 0.6 ng/mL, Insulin > 3 μIU/mL, Insulin/C-Peptide ratio < 1, These findings are consistent with increased endogenous insulin secretion e.g. Insulinoma versus Nesidioblastosis for confirmation with imaging modalities.

Imaging

Abdominal Ultrasound: Showed that the Liver is of average size, of bright echo pattern. A small 1.3 x 1.1cm solid hypoechoic focal lesion is seen in segment IV, having central intralesional vascular doppler signals. This focal lesions was biopsied and histopathological examination revealed chronic hepatitis of mild activity, bridging fibrosis with no evidence of malignancy

Triphasic CT and CT enterography: Unremarkable study (Figure 1)

Esophagogastroduodenoscopy (EGD): Mild antral gastritis

Colonoscopy: Normal, however multiple biopsies were taken from the normal looking ileum mucosa and histopathological examination revealed mild chronic ileitis with preserved villi.

Enteroscopy: was done to evaluate for small bowel causes of diarrhea and revealed that the mucosa of the terminal ileum showed scattered erosions and histopathological examination demonstrated mild chronic ileitis with preserved villi, no evidence of granuloma, dysplasia or malignancy in all sections examined.

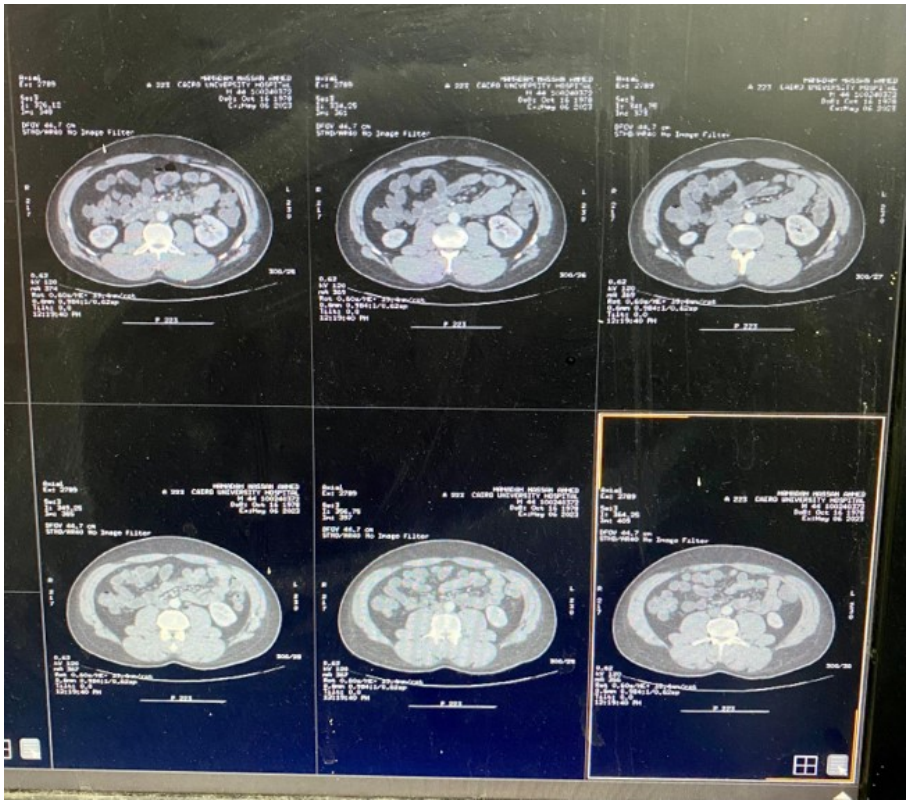

Figure 1: Triphasic CT scan of the abdomen was unremarkable

Gallium Dotatate PET-CT:

As seen in figure (2&3) an enhancing DOTATATE avid nodule is seen between the pancreatic tail and the splenic hilum measuring 20mm and achieving 20 SUV-max, it is directly related to the inferior anterior surface of the pancreatic tail with no definite clear separation in between. The rest of the pancreas is clear and devoid of any enhancing or DOTATATE avid lesions. Figure is suggestive of an exophytic insulinoma versus a splenule.

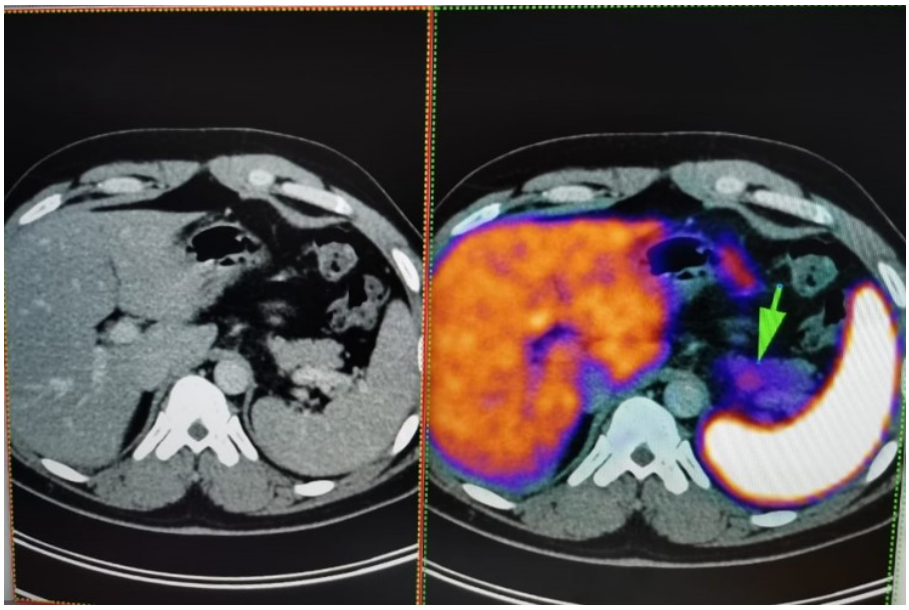

Figure 2: Gallium Dotatate PET-CT showing avid nodule in the distal pancreatic region separable from the spleen

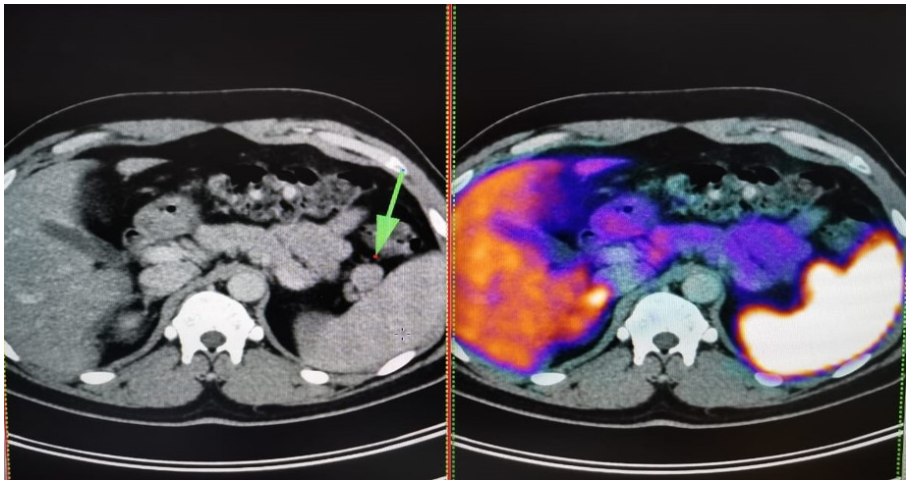

Figure 3: shows the splenule obeying the same uptake as rest of the spleen

EUS:

There is a solid well-defined hypoechoic mass lesion at the pancreatic tail 22x20mm (Figure 4), hard in elastography and separable from the spleen. Whole pancreatic parenchyma showing lobulation, stranding and honeycomb appearance, EUS features suggestive of chronic pancreatitis.

Patient was referred to general surgery and underwent laparoscopic distal pancreatectomy, intra-operative frozen section revealed normal pancreatic tissue so the operation was turned to open pancreatectomy with removal of the tail, body up to neck of the pancreas.

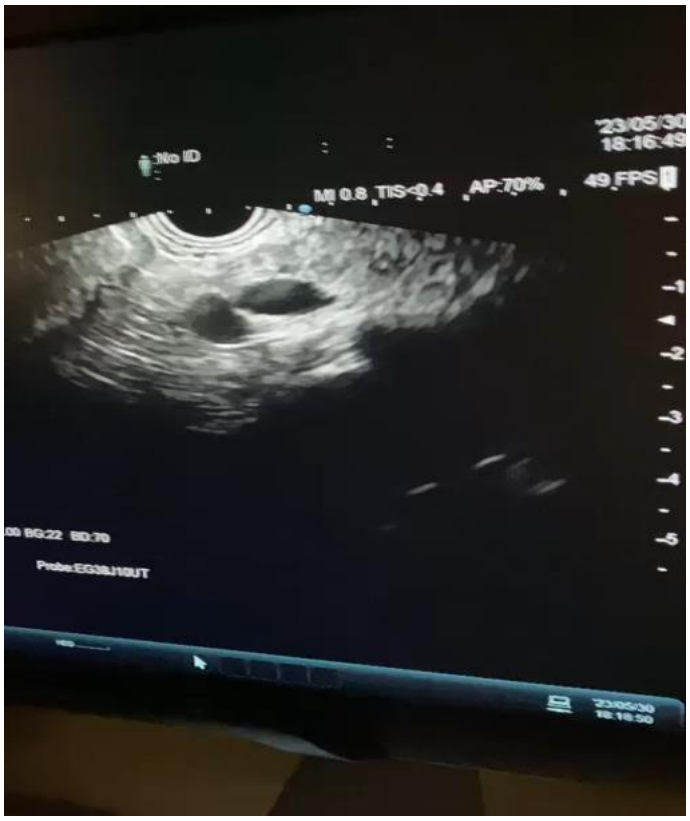

Figure 4: EUS figure showing solid mass lesion at the pancreatic tail

Histopathology Examination of the Surgical Specimen

Normal exocrine pancreatic component as well as focal nodular hyperplasia of islet cell clusters with hypertrophied insulin secreting cells with giant nuclei and ductulo-insular complexes formation.

Diagnosis: Figure compatible with Nesidioblastosis.

Post-Operative Follow Up

The diarrhea improved after the surgery. The patient developed hyperglycemia, diagnosed as diabetic, and insulin was prescribed, and his RBS readings were controlled for 4 months on treatment.

After 4 months, he started to develop recurrent hypoglycemic attacks, omitting the use of insulin and the diarrhea recurred. Then he was re admitted for further evaluation. Prolonged fasting test was re done which showed the same result consistent with endogenous hyperinsulinemia.

Treatment

Upon revising the related literature due to local unavailability of Diazoxide, multiple case reports discussed the success of somatostatin analogue in treating adult onset nesidioblastosis. Octreotide was therefore started by a dose of 100 mg S.C. every 8 hours together with diet modification.Yet the trial failed at controlling the hypoglycemic attacks.Due to failure of octreotide and the local unavailability of diazoxide this raised the option of surgery, a multidisciplinary meeting was held to discuss the possibility of re-operation and the available surgical options.Dynamic MRI abdomen was done to delineate any localized lesions within the pancreas which revealed no sizable pancreatic lesions. This raises the possibility of total pancreatectomy as the only feasible surgical procedure. Yet the operation carried a high mortality rate. And upon consulting the patient, he refused

the surgical procedure.

Therefore, trials were done to provide the Diazoxide as our last resort.A Diazoxide was imported and he was started on the least advised dose of 5mg/kg/day PO divided q8-12hrs initially. Patients' symptoms improved with resolution of hypoglycemic episodes.

Discussion

George Laidlaw was the first to use the term Nesidioblastosis in 1938 to describe the neo-formation of Langerhans islet cells from the pancreatic ductal epithelium [1-2]. later in 1971, Yakovac used the same term to refer to pathology of the endocrine pancreas, when he described 12 children with persistent hyper-insulinaemic hypoglycaemia. Nowadays, Nesidioblastosis term is used to describe alterations in the endocrine pancreas characterized by the aberrant proliferation of the pancreatic islet cells that affects the pancreas in a diffuse way, originating from the duct epithelium and resulting in persistent hyper-insulinaemic hypoglycaemia without insulinoma [3].

In adults, most of the hyperinsulinaemic hypoglycemia cases are caused by isolated insulinomas, the nesidioblastosis being responsible for only 0.5-5% of the cases. It is not clinically or biochemically feasible to differentiate insulinoma from Nesidioblastosis, thus it is important to put both conditions in the differential diagnosis [3].

Majority of patients present with typical hypoglycemic symptoms of Whipple's triad , adrenergic symptoms, e.g. Sweating, anxiety,palpitations, hunger sensation, tremors and neuroglycopenia symptoms e.g. Cognitive dysfunction, clouded vision, memory loss, and loss of consciousness [2].Some patients present with mainly postprandial hypoglycemic symptoms due to persistent hyperinsulinemia [24-].The ideal test to assess the existence of hypoglycemia is the 72 hours fasting test, which is ideal for determining the role of insulin in the presence of hypoglycemia [3].

This test demonstrated endogenous hyperinsulinemia in our patient, which led to the implementation of imaging studies to pinpoint the lesion. After a PET CT and EUS were conducted because computed axial tomography failed to reveal the existence of a lesion, an image indicating a pancreatic tail lesion was found. Clinically, however, the patient had the Whipple triad: elevated serum insulin levels, hypoglycemia symptoms, and low blood glucose that improved after intravenous glucose injection. The patient's clinical suspicion of having an insulinoma was raised by this. The procedure for the lesion's excision was initiated due to the potential for an insulinoma to be present [5, 6, 7].

For nesidioblastosis, surgical resection is thought to be the best course of action. Its expansion is still debatable, though [8, 9]. The majority of surgeons perform distal pancreatectomy, as was the case with our patient. However, some surgeons have performed 90–95% pancreatectomy; however, some authors claim that a subtotal pancreatectomy is linked to insulin-dependent diabetes and exocrine pancreatic dysfunction in 40% of cases; after 60% of the pancreas is removed, 8% of patients will develop insulin-dependent diabetes mellitus, but these patients also have higher rates of hypoglycemia recurrence. Drugs like diazoxide, octreotide, or verapamil can be administered if surgery is unsuccessful or not recommended.Diazoxide is a non-diuretic benzothiadiazine derivative that activates ATP-sensitive potassium channels. It is commonly used in the treatment of hyperinsulinemic hypoglycemia due to its ability to inhibit insulin release. Secondary diabetes mellitus was the outcome of the distal pancreatectomy performed on our patient. Hypoglycemia, however, recurred 4 months later]5–7–10[.

The pancreas appears normal on macroscopic examination in the histological investigation; nevertheless, the results vary across individuals and are minimally altered up to the third portion of cases. Because of this, it is challenging to distinguish them from a typical pancreas [9, 11]. Other observations in nesidioblastosis patients include overexpression of insulin-like growth factor type 2, type 1 insulin-like growth factor receptor, transforming growth factor 3, and vascular ectasia similar to peliosis. This

helps much with diagnosis. In our instance, we discovered hyperplasia of the Langerhans islets without a tumor, hyperplasia of the ductal epithelium, ruling out the macroscopic and microscopic diagnosis of insulinoma, and irregularly shaped, larger, and more numerous islets. All the above, allowed us to conclude that the diagnosis was diffuse nesidioblastosis in adult [2, 7, 9].

Conclusion

Since nesidioblastosis can cause up to 4% of persistent hyperinsulinaemic hypoglycemia, it is a disease with a challenging diagnosis that should be taken into consideration in all cases when an insulinoma cannot be found. The prognosis of the condition is greatly dependent on early detection and diagnosis.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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