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Case Report

A Case Report: Persistent Recurrent Hypoglycemia in Type 2 Diabetes Mellitus Despite Withdrawal of Oral Antidiabetic Therapy: A Diagnostic Pitfall Revealing Insulinoma

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Abstract

Background: Hypoglycemia in Type 2 Diabetes Mellitus (T2DM) is typically drug-induced. Persistent hypoglycemia after discontinuation of all glucose-lowering agents is rare and suggests alternative etiologies such as insulinoma. ***Case Presentation:*** A 56-year-old female with T2DM presented with recurrent fasting hypoglycaemia despite cessation of all oral antidiabetic medications. Initial attribution to sulfonylurea uses delayed further investigation. Persistent hypoglycemia prompted endocrine evaluation revealing endogenous hyperinsulinemia. MRI identified a pancreatic tail lesion consistent with insulinoma. ***Conclusion:*** This case highlights diagnostic anchoring bias in diabetic patients and underscores the importance of evaluating persistent hypoglycemia beyond medication-related causes.

Keywords: Insulinoma; Hypoglycemia; Type 2 Diabetes Mellitus; Hyperinsulinemia hypoglycemia; Pancreatic neuroendocrine tumor; Diagnostic delay.

INTRODUCTION

Hypoglycemia is a frequent complication in patients with diabetes mellitus and is most associated with pharmacological therapy, particularly insulin and sulfonylureas. However, persistent hypoglycemia following complete withdrawal of glucose-lowering medications is unusual and mandates evaluation for endogenous causes [1,2].

Insulinoma is a rare pancreatic neuroendocrine tumor characterized by autonomous insulin secretion, leading to fasting hypoglycemia. Due to its rarity and nonspecific presentation, diagnosis is often delayed [3,4]. In patients with pre-existing T2DM, diagnostic delay is further exacerbated by attribution bias toward medication-induced hypoglycemia [5]. These neuro-endocrine tumours have an incidence of 1–4 cases per million annually, commonly presenting with the symptoms of Whipple's triad namely hypoglycemia, low plasma glucose, and resolution of symptoms with glucose administration [6]. Its uncommon to find the coexistence of insulinoma with type 2 diabetes mellitus (T2DM) due to which diagnostic delays occur resulting from overlapping clinical features and misattribution of hypoglycemia to antidiabetic therapy [5,6].

CASE PRESENTATION

A 56-year-old female with a 12-year history of T2DM presented with recurrent episodes of diaphoresis, tremors, palpitations, confusion, and near-syncope predominantly during fasting states.

Home capillary glucose readings documented values between 42–58 mg/dL during symptomatic episodes.

Past Medical History

- T2DM (12 years)
- Hypertension
- Dyslipidemia

Medications

- Metformin 1 g BID
- Gliclazide MR 60 mg OD
- Sitagliptin 100 mg OD

Clinical Course

Despite sequential withdrawal of gliclazide, sitagliptin, and metformin, hypoglycemia persisted for >2 weeks, suggesting non-iatrogenic etiology.

Examination

- BP: 128/78 mmHg
- Pulse: 82 bpm
- BMI: 27 kg/m²
- No organomegaly
- Neurological exam: normal between episodes

Laboratory Investigations

Table 1: Biochemical Profile

Test	Result	Interpretation
HbA1c	5.4%	Low-normal (suggestive of recurrent hypoglycemia)
Fasting glucose	52 mg/dL	Hypoglycemia
Insulin (during event)	Elevated	Inappropriate for hypoglycemia
C-peptide	Elevated	Endogenous insulin secretion
Sulfonylurea screen	Negative	Excludes drug-induced cause
Cortisol	Normal	Excludes adrenal insufficiency
TSH	Normal	Excludes thyroid cause
Renal & liver function	Normal	Excludes organ failure

Diagnostic Criteria

✓ Whipple's Triad confirmed
✓ Inappropriately elevated insulin
✓ Elevated C-peptide
✓ Negative sulfonylurea screen

→ Consistent with endogenous hyperinsulinemic hypoglycemia

Imaging

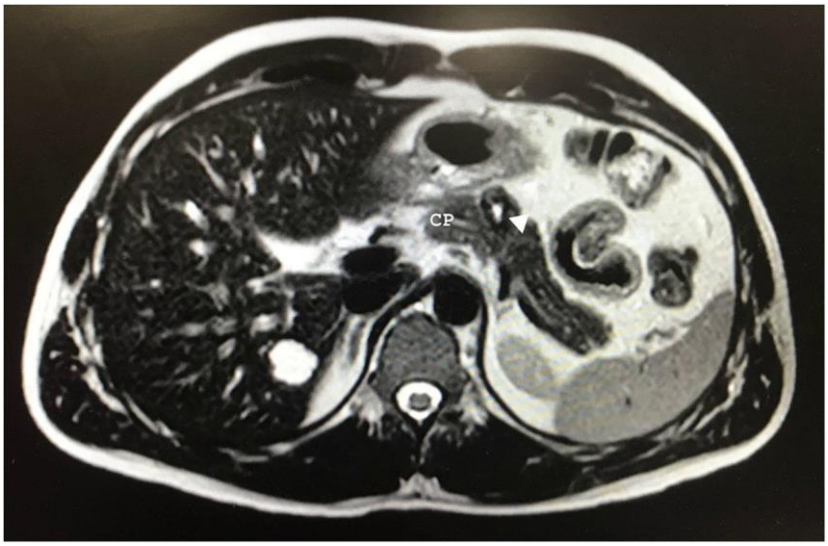

Figure 1: MRI Abdomen (Pancreas)

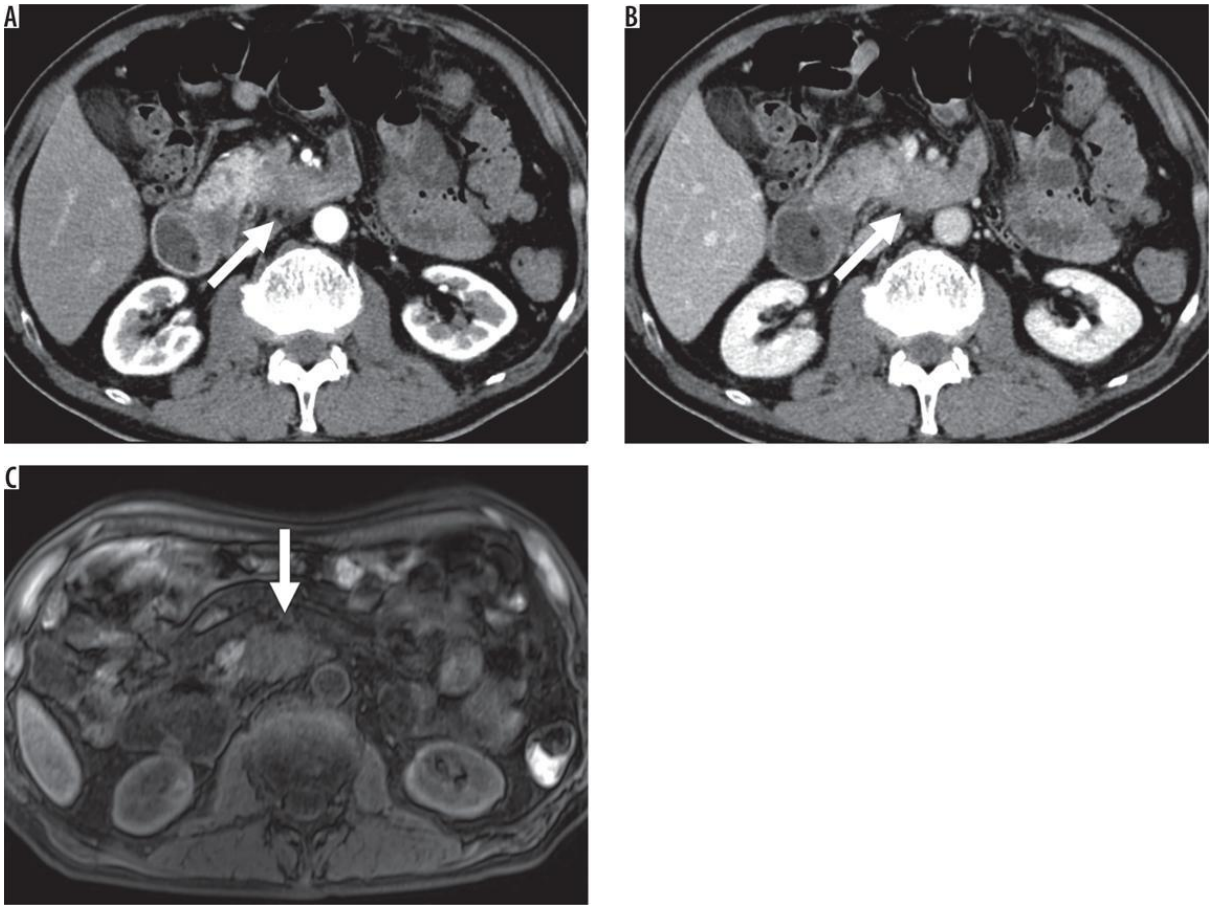

Figure 2: Contrast-enhanced MRI of the abdomen demonstrating a 1.4 cm arterially enhancing lesion in the tail of the pancreas (arrow), consistent with a pancreatic neuroendocrine tumor (insulinoma)

Timeline

Table 2: Clinical Timeline of Events

Timepoint	Event
Month 0	Stable T2DM on oral therapy
Month 10	Onset of mild hypoglycemia
Month 11	Gliclazide discontinued
Month 11.5	Persistent hypoglycemia
Month 12	Sitagliptin + metformin stopped
Month 12–12.5	Recurrent severe hypoglycemia
Month 12.5	Endocrine referral
Month 13	72-hour fast confirms hyperinsulinism
Month 13	MRI identifies pancreatic lesion
Month 14	Surgical resection
Follow-up	Complete resolution

Management

- IV dextrose during acute episodes
- Frequent carbohydrate intake
- Continuous glucose monitoring
- Laparoscopic distal pancreatectomy

Histopathology confirmed well-differentiated pancreatic neuroendocrine tumor (insulinoma).

DISCUSSION

This case illustrates a classic diagnostic pitfall: anchoring bias in patients with known diabetes mellitus, where hypoglycemia is prematurely attributed to pharmacotherapy.

Key Diagnostic Challenges: Misattribution to sulfonylurea therapy, Delay in endocrine referral, Under-recognition of fasting hypoglycemia pattern.

Pathophysiology Insight: Insulinoma causes autonomous insulin secretion independent of glucose levels, leading to neuroglycopenic symptoms during fasting states.

Why this case is important:

- T2DM masked classical insulinoma presentation
- Hypoglycemia persisted despite complete medication withdrawal
- Demonstrates coexistence of insulin resistance and insulin excess

Clinical Pearl: Persistent hypoglycemia after stopping all antidiabetic agents should never be assumed iatrogenic.

Learning Points:

- Always confirm Whipple's triad before attributing hypoglycemia to drugs
- Elevated insulin + C-peptide excludes exogenous insulin use
- Persistent hypoglycemia requires endocrine evaluation
- MRI/EUS should be used early in suspected insulinoma
- Cognitive bias is a major cause of diagnostic delay

CONCLUSION

Insulinoma should be considered in diabetic patients with persistent hypoglycemia despite discontinuation of antidiabetic therapy. Early recognition prevents neurological morbidity and enables curative surgical treatment.

Patient Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. The patient understands that anonymized clinical information and imaging will be published.

Ethics Statement

This study was conducted in accordance with institutional ethical guidelines. Formal IRB approval was not required for a single case report according to local regulations.

Conflicts of Interest: The authors declare no conflicts of interest.

Funding: No funding was received for this study.

Data Availability

All relevant data are included within the manuscript. Additional anonymized data available upon reasonable request.

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