ISSN: 2754-4931

Journal of Gastroenterology & Hepatology Reports

SCIENTIFIC Research and Community

Case Report

Open Access

Chronic Hyperinsulinemia Masquerading as Neuropsychiatric Disease: A Case of Uncinate Process Insulinoma Managed with Pancreaticoduodenectomy

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ABSTRACT

Insulinoma is the most surgically curable cause of endogenous hyperinsulinemia, yet it carries one of the longest average diagnostic delays in clinical endocrinology. The central reason is deceptively simple: its symptoms sweating, tremor, behavioral change, loss of consciousness are not intuitively hormonal. They are intuitively psychiatric, neurological, or cardiac. Patients are investigated for epilepsy, panic disorder, and cardiac arrhythmia while their fasting insulin levels remain unmeasured. This case illustrates that pattern in its most striking form: a 33-year-old woman whose recurrent episodes of syncope and progressive weight gain were attributed to lifestyle factors for two years before a structured biochemical evaluation revealed glucose of 26 mg/dL with a simultaneously elevated insulin and C-peptide. The clinical question this case raises is not merely how this was missed but why the correct diagnostic test was never ordered, and what structural changes in clinical practice might prevent the same delay from recurring.

Case Presentation: A 33-year-old Albanian woman presented electively to Barleti University Polyclinic, Tirana, requesting a definitive diagnostic evaluation. She described a two-year history of episodic weakness, profuse diaphoresis, dizziness, and recurrent loss of consciousness, with symptoms reliably occurring in the fasting state or during prolonged physical exertion. She had gained 20 kilograms over the same period and reported persistent hunger as a constant companion between episodes.

Multiple emergency department visits had not yielded a diagnosis. Blood glucose had been recorded around 60 mg/dL on at least one occasion; she had been administered intravenous saline and counselled to eat sweets when symptoms arose. No hormonal investigation insulin, C-peptide, proinsulin had been ordered at any of these visits. No endocrinological referral had been made.

On the day of her elective presentation, fasting blood samples were drawn during a symptomatic period. The results were unambiguous: glucose **26 mg/dL**, insulin **26.3 µU/mL**, C-peptide **3.64 ng/mL**. An elevated endogenous C-peptide at that degree of hypoglycemia is definitive biochemical proof of autonomous insulin secretion, precluding exogenous administration and factitious hypoglycemia. HbA1c was 4.84%, consistent with chronic recurrent hypoglycemia rather than any form of diabetes. Cortisol was 205.6 nmol/L normal excluding adrenal insufficiency. Imaging was requested after the diagnosis was biochemically secured.

Abdominal MRI identified a 20 × 16.7 mm hypervascular nodular lesion in the uncinate process of the pancreas: T2 hyperintense, T1 hypointense, with restricted diffusion on DWI and the early intense arterial enhancement followed by delayed washout that is pathognomonic for a pancreatic neuroendocrine tumor. The main pancreatic duct was of normal caliber throughout, and no lymphadenopathy was identified.

Surgery was performed following multidisciplinary team review. Enucleation the preferred approach for small, benign-appearing insulinomas was judged technically unsafe due to the tumor's depth within the uncinate process and its anatomical proximity to both the main pancreatic duct and the superior mesenteric vessels. A pancreaticoduodenectomy (Whipple procedure) was performed. The patient was discharged on postoperative day seven with completely normalized blood glucose and no surgical complications.

Results: Fasting biochemical studies confirmed endogenous hyperinsulinemia with glucose 26 mg/dL, insulin 26.3 µU/mL, and C-peptide 3.64 ng/mL satisfying all established diagnostic criteria for insulinoma. Multimodal MRI identified a solitary 20 × 16.7 mm hypervascular lesion in the pancreatic uncinate process. A pancreaticoduodenectomy was performed based on anatomical constraints that precluded safe enucleation. Postoperative recovery was uneventful (discharge day 7), glucose normalized to physiological range, and no complications were recorded. The case represents a textbook biochemical–radiological–surgical cure of an insulinoma that had been clinically present for two years without investigation.

Conclusions: The principal lesson of this case is not anatomical it is cognitive. Insulinoma is consistently misclassified as a neuropsychiatric or cardiac condition in its early stages because clinicians encountering hypoglycemia in a non-diabetic patient rarely extend their differential diagnosis to include a functioning endocrine tumor. The diagnostic tools required to do so are inexpensive and universally available: fasting glucose, insulin, and C-peptide. The barrier is not technical it is a knowledge gap reinforced by the rarity of the condition and the tendency to treat hypoglycemia symptomatically rather than investigatively.

For clinicians in primary care and emergency medicine, the practical takeaway is direct: any non-diabetic patient presenting with unexplained hypoglycemia particularly if recurrent, fasting-predominant, or accompanied by weight gain should have insulin and C-peptide measured at the time of the event. This single step transforms a symptom into a diagnosis.

Citation: Vrenos Hodaj, Erti Ismahili, Arben Baboci, Ermira Goxha, Erald Vasili (2026) Chronic Hyperinsulinemia Masquerading as Neuropsychiatric Disease: A Case of Uncinate Process Insulinoma Managed with Pancreaticoduodenectomy. Journal of Gastroenterology & Hepatology Reports. SRC/JGHR-207.
DOI: doi.org/10.47363/JGHR/2026(7)193

For surgeons, the lesson is anatomical: the uncinate process is among the most technically demanding regions of the pancreas, and tumor location not tumor size determines whether enucleation is safe. When a lesion in this region lies in close proximity to the main pancreatic duct and the superior mesenteric vessels, pancreaticoduodenectomy is not an escalation of treatment but the anatomically correct response. Framing this choice accurately prevents both under-treatment and unnecessary patient anxiety about receiving a 'bigger operation' than expected.

Insulinoma is a curable disease. The diagnostic and surgical tools to cure it exist and are accessible. What this case demonstrates is that multidisciplinary awareness spanning emergency medicine, endocrinology, radiology, and surgery is the non-negotiable prerequisite for translating those tools into outcomes.

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Received: June 08, 2026; **Accepted:** June 12, 2026; **Published:** June 22, 2026

Keywords: Insulinoma, Pancreatic Neuroendocrine Tumor, Endogenous Hyperinsulinemia, Uncinate Process, Pancreaticoduodenectomy, Non-Diabetic Hypoglycemia, Diagnostic Delay, Multidisciplinary Management, C-Peptide, Whipple Procedure

Introduction

Insulinoma originates from the insulin-secreting beta cells of the pancreatic islets of Langerhans and constitutes the most common functional pancreatic neuroendocrine tumor (panNET), accounting for approximately 17–27% of all functioning panNETs [1]. Despite this relative prominence within the neuroendocrine spectrum, the absolute incidence remains remarkably low between 1 and 4 cases per million per year which itself contributes to diagnostic delay: most clinicians encounter fewer than two or three cases in a lifetime of practice [2].

The diagnostic challenge in insulinoma is not biochemical complexity it is clinical pattern recognition. Symptoms arise from two interconnected mechanisms: the adrenergic counter-regulatory response to hypoglycemia (producing sweating, palpitations, tremor, and hunger) and the direct neuroglycopenic effect of glucose deprivation on the central nervous system (producing cognitive slowing, behavioral change, confusion, and in severe cases, seizure or syncope). Neither symptom cluster is specific to insulinoma. Patients are frequently evaluated for epilepsy, panic disorder, transient ischaemic attack, or cardiac arrhythmia often repeatedly before the underlying metabolic etiology is identified [3]. Whipple's triad symptomatic hypoglycemia, documented low plasma glucose, and resolution with glucose correction was described in 1935 and remains the cornerstone of clinical suspicion, yet it is frequently satisfied at emergency department visits without triggering a biochemical investigation [4].

The case we describe is a contemporaneous example of this pattern. Our patient satisfied Whipple's triad at multiple emergency visits over two years. The step that was never taken simultaneous measurement of insulin and C-peptide alongside glucose would have made the diagnosis straightforwardly at any of those presentations. This paper uses her case as a framework for reviewing the biochemical, imaging, and surgical management of insulinoma, with particular emphasis on the clinical recognition failures that characterize the diagnostic gap and the anatomical reasoning that governs the surgical approach.

Etiology and Molecular Background

The great majority of insulinomas approximately 90–93% are sporadic and arise as isolated lesions Multiple insulinomas and multifocal disease occur predominantly in the setting of Multiple Endocrine Neoplasia type 1 (MEN1), a germline syndrome caused by loss-of-function mutations in the MEN1 gene on chromosome 11q13 [5]. MEN1-associated insulinomas are typically diagnosed at a younger age, are more likely to be multiple, and require a fundamentally different surgical approach than their sporadic counterparts. For this reason, genetic context should be systematically assessed at diagnosis, particularly in patients under 40 years of age or those with a personal or family history of hyperparathyroidism or pituitary disease.

At the molecular level, somatic mutations in YY1 encoding a ubiquitous transcription factor have been identified in approximately 30% of sporadic insulinomas, suggesting dysregulation of transcriptional control as a mechanism of autonomous insulin secretion [6]. KRAS mutations have also been described in a subset of cases. Perhaps more clinically significant are the genomic differences between indolent and aggressive insulinomas: the latter are characterized by ATRX and DAXX mutations, activation of the alternative lengthening of telomeres (ALT) pathway, loss of PDX1 and insulin expression, and upregulation of ARX and alpha-1-antitrypsin a molecular phenotype that reflects fundamental divergence from normal beta-cell biology [7]. These markers are increasingly being incorporated into risk stratification at the time of pathological review.

Incidence and Epidemiology

Population-based registries from the United States and Europe consistently report insulinoma incidence between 0.7 and 4 cases per million per year. There is a modest female predominance across most series. Peak presentation occurs in the fourth to sixth decade of life, though the condition can arise at any age including in the pediatric and geriatric populations, where presentation is often atypical [8]. In our patient a 33-year-old woman the demographic characteristics are consistent with published series.

Approximately 90% of insulinomas are histologically benign (WHO Grade 1 or 2 with no evidence of metastasis at the time of diagnosis). Five-year survival for localized, well-differentiated insulinoma reaches 94–100%; for metastatic disease, reported survival drops to 24–67% depending on tumor grade and the extent of hepatic involvement. The distinction between indolent and aggressive disease cannot be made on clinical or radiological grounds alone it requires formal histopathological and immunohistochemical analysis, including Ki-67 proliferation index, Chromogranin A, Synaptophysin, and, increasingly, molecular markers.

Clinical Features and the Misdiagnosis Problem

Understanding insulinoma's clinical presentation requires appreciating what it mimics rather than what it resembles in its own right. Neurogenic symptoms driven by catecholamine release in response to falling glucose include tremor, diaphoresis, tachycardia, anxiety, and hunger. Neuroglycopenic symptoms, resulting from direct glucose deprivation of cortical neurons, encompass diplopia, cognitive slowing, amnestic episodes, personality change, and, in severe cases, loss of consciousness or generalized seizure. Table 1 summarizes this distinction.

Table 1: Symptom Clusters in Insulinoma by Pathophysiological Mechanism

Neurogenic (Adrenergic / Cholinergic)	Neuroglycopenic (CNS Glucose Deprivation)
Tremor, Palpitations, Tachycardia, Anxiety Diaphoresis, Hunger, Paresthesia, Circumoral Tingling	Blurred Vision, Diplopia, Cognitive Impairment Personality Change, Amnesia, Confusion Seizure, Stupor, Loss of Consciousness

What makes this symptom profile clinically treacherous is its overlap with conditions that clinicians encounter far more frequently. Anxiety disorder explains the tremor and palpitations. Epilepsy explains the loss of consciousness. Cardiac arrhythmia explains the presyncope. The postprandial relief (or in many patients, the relief after eating that follows the episode) can even mimic postprandial hypoglycemia a condition that rarely warrants the same level of biochemical investigation [9].

Weight gain, as seen prominently in our patient, is a particularly underappreciated clinical feature. The chronic hyperinsulinemia that defines insulinoma inhibits lipolysis, promotes lipogenesis, and stimulates appetite through direct hypothalamic effects. The result is progressive weight accumulation in a setting where the patient is simultaneously motivated to eat frequently both by genuine hunger and by the learned behaviour that eating resolves the episodes. In retrospect, the combination of episodic neuroglycopenic symptoms with progressive weight gain and fasting predominance is a recognizable clinical fingerprint. Prospectively, in an emergency setting, it rarely triggers a hormonal workup.

Pathophysiology

Normal glucose homeostasis depends on the tight reciprocal regulation of insulin secretion and hepatic glucose output. As blood glucose falls, pancreatic beta cells reduce insulin release, allowing hepatic glycogenolysis and gluconeogenesis to maintain euglycemia. Insulinoma cells have lost this feedback entirely: they secrete insulin in an autonomous, glucose-independent fashion, continuously driving glucose into peripheral tissues while simultaneously suppressing hepatic glucose production [10]. The resulting state of chronic hyperinsulinemia creates a metabolic environment that is profoundly abnormal at the cellular level long before clinical symptoms become apparent.

The counter-regulatory response activation of the sympathoadrenal axis, cortisol and glucagon release is preserved in most patients, at least early in the disease course. This is what produces the neurogenic symptoms that often dominate the early clinical picture and why adrenergic symptoms frequently precede the more dangerous neuroglycopenic ones. Over time, however, with recurrent hypoglycemia, the threshold for adrenergic counter-regulation rises and symptomatic awareness may diminish a phenomenon analogous to hypoglycemia unawareness in insulin-treated diabetes. This progression makes early diagnosis not merely convenient but genuinely important for patient safety.

Diagnosis

Biochemical Framework

The biochemical diagnosis of insulinoma rests on demonstrating inappropriate endogenous insulin secretion in the context of documented hypoglycemia. The established thresholds endorsed by the Endocrine Society and the European Neuroendocrine Tumor Society (ENETS) require simultaneous documentation of: fasting plasma glucose < 55 mg/dL, insulin ≥ 3 μU/mL, C-peptide ≥ 0.6 ng/mL, proinsulin ≥ 5 pmol/L, beta-hydroxybutyrate ≤ 2.7 mmol/L, and a negative oral hypoglycaemic agent screen [11]. These criteria serve two purposes: confirming endogenous hyperinsulinemia and excluding exogenous insulin administration and sulfonylurea-induced hypoglycemia.

C-peptide measurement is particularly critical. Because C-peptide is co-secreted with insulin from beta cells but is absent from commercial insulin preparations, a normal or elevated C-peptide during hypoglycemia confirms that the source of insulin is endogenous — directly ruling out factitious hypoglycemia, which represents a clinically important diagnostic pitfall. In our patient, C-peptide of 3.64 ng/mL at a glucose of 26 mg/dL provides this confirmation unambiguously.

When spontaneous symptomatic hypoglycemia is not captured incidentally as in our patient, where it was the 72-hour supervised fasting test remains the diagnostic gold standard. Published series demonstrate that 99% of patients with insulinoma will develop biochemically confirmed hypoglycemia during this protocol, with 75% developing it within 24 hours.

Imaging Localization

Imaging should follow, not precede, biochemical diagnosis. A biochemically unconfirmed lesion on imaging carries an unacceptably high risk of misattribution pancreatic incidentalomas are common, and not every hyper vascular nodule is an insulinoma. Once the biochemistry is confirmed, localization imaging serves a surgical rather than diagnostic purpose.

Contrast-enhanced CT is typically the first-line modality, with reported sensitivity of 54–80% for insulinoma detection. MRI with gadolinium enhancement particularly when pancreatic-specific sequences (T2 fat-saturated, DWI, dynamic arterial phase) are employed achieves sensitivity up to 85% and is increasingly preferred as the primary localization tool at specialized centers [12]. Endoscopic ultrasound (EUS) offers the highest sensitivity (81%) and specificity (90%) among non-invasive modalities and provides uniquely valuable information about the tumor's spatial relationship to the main pancreatic duct information that directly determines surgical feasibility of enucleation. Table 2 summarizes the comparative performance of available modalities.

Table 2: Comparative Performance of Imaging Modalities in Insulinoma Localization

Modality	Sensitivity	Specificity	Clinical Notes
CT (contrast-enhanced)	54–80%	75%	Most common first-line study; widely available
MRI (gadolinium)	54–85%	65–80%	~85% with dedicated pancreatic sequences; preferred at specialized centers
EUS	81%	90%	Best tool for duct proximity assessment; operator-dependent
ASVS	93%	86%	Arterial stimulation venous sampling; reserved for occult disease
GLP-1R PET	87%	94%	Preferred in indolent/localized disease; emerging as gold standard
SSTR PET/CT	39–53%	14–50%	Preferred in aggressive or metastatic disease; low sensitivity for benign insulinoma

Treatment

Surgery with curative intent remains the treatment of choice for localized insulinoma and is recommended in all patients fit for operation [13]. The specific surgical approach is determined primarily by the tumor's anatomical relationship to the main pancreatic duct (MPD) and adjacent vascular structures — not by tumor size alone.

For the majority of insulinomas those that are small (typically < 2 cm), superficially located, and situated at least 2–3 mm from the MPD enucleation is the preferred operation. It preserves functional pancreatic parenchyma, avoids the long-term risk of exocrine insufficiency and diabetes mellitus, and can be performed laparoscopically or with robotic assistance in experienced centers. Enucleation does, however, carry meaningful complication rates: postoperative pancreatic fistula (POPF) is reported in up to 46–50% of deep-seated enucleations in proximity to the MPD, reflecting the difficulty of achieving a clean dissection plane in this anatomical setting [14,15].

When enucleation is not safely feasible, anatomical resection is indicated based on tumor location. For lesions of the pancreatic body or tail, distal pancreatectomy with or without splenectomy is the standard approach. For tumors of the pancreatic head or uncinate process, pancreaticoduodenectomy (the Whipple procedure) is the appropriate operation. It is important to frame this choice correctly in clinical communication: a Whipple procedure for a benign uncinate insulinoma is not an overtreatment it is the anatomically correct resection when enucleation cannot be performed safely.

Medical management primarily with diazoxide (which inhibits insulin secretion via K-ATP channel activation) or long-acting somatostatin analogues is reserved for patients who are surgically unfit, who decline operation, or in whom surgery is being deferred. Response rates are partial and variable, and neither approach is curative.

Case Presentation

Clinical History and Emergency Department Course

Our patient was a 33-year-old Albanian woman with no prior diagnosis of diabetes, seizure disorder, or cardiac disease. She presented to Barleti University Polyclinic, Tirana, seeking a definitive evaluation after two years of episodic symptoms. Episodes were characterized by weakness, profuse sweating, dizziness, and on several occasions complete loss of consciousness. They occurred reliably in the fasting state — on waking, during prolonged exercise, and in the hours before meals and resolved promptly with food intake. Between episodes she described constant hunger and a progressive weight gain of approximately 20 kilograms.

She had attended multiple emergency departments across the city during this period. On the occasions documented in her records, blood glucose ranged around 60 mg/dL at the time of presentation; she was administered intravenous saline, instructed to eat sweets when feeling weak, and discharged without further investigation. Insulin and C-peptide were never measured. The working impression at those visits appeared to be benign reactive hypoglycemia a clinical decision that was not investigated further.

Her elective presentation to our service was initiated by her own persistence. She arrived requesting an explanation for symptoms that she recognized were occurring with increasing frequency and at progressively lower glucose levels.

Biochemical Evaluation

Table 3: Fasting Biochemical Results During Symptomatic Episode

Parameter	Result	Reference Range
Fasting Blood Glucose	26 mg/dL ↓↓	70–100 mg/dL
HbA1c	4.84%	4.0–5.6%
Fasting Insulin	26.3 µU/mL ↑↑	< 3 µU/mL during hypoglycemia
C-Peptide	3.64 ng/mL ↑↑	0.6–2.0 ng/mL
Cortisol	205.6 nmol/L	150–600 nmol/L (normal)

The biochemical picture was unambiguous (Table 3). A fasting glucose of 26 mg/dL with a simultaneously measured insulin of 26.3 µU/mL and C-peptide of 3.64 ng/mL satisfies all established diagnostic thresholds for endogenous hyperinsulinemia. The elevated C-peptide definitively excludes exogenous insulin as the cause. HbA1c of 4.84% reflects chronic recurrent hypoglycemia rather than diabetes. Normal cortisol excluded adrenal insufficiency as a contributing diagnosis. The multidisciplinary team confirmed the biochemical diagnosis of insulinoma and proceeded directly to localization imaging.

Multimodal Imaging and Localization

Abdominal MRI was performed using a comprehensive multisequence protocol: T1- and T2-weighted imaging, T2 fat-saturated sequences, T1 VIBE without contrast, diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) mapping, post-contrast dynamic sequences with arterial, portal venous and delayed phases, subtraction imaging, and Cholangio-MRI. General abdominal survey findings were unremarkable, with a single simple cyst (6.5 mm) in hepatic segment VII representing an incidental finding of no clinical significance. Biliary, portal, splenic, adrenal, and renal structures were normal.

Within the pancreas, a well-defined nodular lesion measuring 20 × 16.7 mm was identified within the uncinate process, with an exophytic growth pattern. Signal characteristics were fully consistent with a hypervascular neuroendocrine tumor: T2 hyperintense, T1 hypointense, restricted diffusion on DWI, and early intense arterial enhancement with washout on delayed sequences. These MRI characteristics are the expected and pathognomonic radiological fingerprint of insulinoma. The main pancreatic duct was of normal caliber throughout its course, and no regional lymphadenopathy was identified.

Radiological Impression
A 20 × 16.7 mm lesion in the uncinate process of the pancreas with MRI signal characteristics fully consistent with a hypervascular pancreatic neuroendocrine tumor, in the appropriate clinical and biochemical context for insulinoma.

Surgical Decision-Making and Operative Management
Following multidisciplinary team review of the biochemical and imaging data, the patient was referred for surgical assessment. The initial surgical consideration as is standard for a well-defined, apparently benign insulinoma measuring less than 2 cm was enucleation. Current ENETS and North American Neuroendocrine Tumor Society (NANETS) guidelines favour enucleation for small insulinomas when the tumor is superficial and located more than 2–3 mm from the main pancreatic duct.

In this case, enucleation was judged to be technically unsafe. The uncinate process occupies one of the most anatomically complex regions of the abdomen, bordered anteriorly by the superior mesenteric vein and artery, medially by the portal vein, and posteriorly by the aorta and inferior vena cava. A 20 mm lesion seated deeply within this process, in the immediate vicinity of the main pancreatic duct, presents a dissection challenge that existing published data quantify concisely: deep uncinate tumors in proximity to the MPD carry postoperative pancreatic fistula rates exceeding 46–50% with enucleation, a complication rate that equals or exceeds that of formal resection while offering none of the margin security of a Whipple procedure.

After intraoperative assessment confirmed that a safe enucleation plane could not be guaranteed, a pancreaticoduodenectomy was performed by the surgical team. The operative procedure was completed without intraoperative complications. The postoperative course was uneventful; the patient was discharged on day seven with blood glucose fully normalized to the physiological range, with no evidence of endocrine or exocrine insufficiency at discharge.

Discussion
The diagnostic trajectory in this case two years of emergency attendances, a glucose of 26 mg/dL, and no insulin measurement is not unusual. Published series consistently report mean diagnostic delays of two to five years from symptom onset to confirmed diagnosis of insulinoma, and the mechanism of delay is almost always the same: clinicians treating symptomatic hypoglycemia without investigating its cause [16]. This is not a resource problem; measuring fasting insulin and C-peptide is neither expensive nor technically demanding. It is a clinical recognition problem rooted in the low prior probability of insulinoma and the high phenotypic overlap with conditions that are seen far more commonly.

The neuropsychiatric reframing of insulinoma symptoms is particularly well-documented. In one series, 70% of patients had received an alternative psychiatric or neurological diagnosis before insulinoma was identified. The predominance of neuroglycopenic symptoms behavioral change, memory impairment, confusion, loss of consciousness in the clinical picture can lead to neurological investigation (EEG, MRI brain) while the relevant investigation (fasting hormonal panel) is never performed. Our patient's presentation combined both neurogenic symptoms (diaphoresis, dizziness) and neuroglycopenic symptoms (loss of consciousness) with the characteristic weight gain that accompanies chronic hyperinsulinemia a pattern that, in retrospect, is difficult to explain by any condition other than an insulin-secreting tumor.

The imaging findings in this case demonstrate the diagnostic elegance of dedicated pancreatic MRI in the appropriate clinical context. The T2 hyperintensity, T1 hypointensity, restricted diffusion, and avid arterial enhancement with delayed washout constitute a radiological signature that is both characteristic of pancreatic neuroendocrine tumors and difficult to attribute to any benign alternative. The value of performing a complete multisequence protocol rather than a standard abdominal survey cannot be overstated: insulinomas less than 2 cm in diameter are frequently missed on non-dedicated imaging, and the uncinate process in particular is a region that requires targeted attention given its anatomical complexity and propensity for producing imaging artifacts on less rigorous protocols. The surgical decision merits detailed discussion because it illustrates a principle that is not always intuitive to non-surgical clinicians: in pancreatic neuroendocrine tumor surgery, the correct operation is determined by anatomy, not by tumor size or perceived severity. A 33-year-old woman with a 2 cm benign tumor might reasonably expect a minor operation. The uncinate location of this lesion, however, placed it within a surgical field defined by the superior mesenteric vessels and the main pancreatic duct constraints that made the most parenchyma-sparing approach (enucleation) the most dangerous one. A pancreaticoduodenectomy in this context is not an overtreatment; it is the intervention that provides the combination of safe resection and clear margins that the anatomy requires. Postoperative pancreatic fistula the principal morbidity concern with enucleation of deep-seated tumors is avoided by accepting the larger but anatomically appropriate operation. The normalization of glucose on the seventh postoperative day, without any pharmacological hypoglycaemia management, confirms complete resection of the insulin-secreting lesion. This is the expected outcome when R0 resection is achieved and no multifocal disease is present and it represents the clearest possible clinical endpoint for curative intent surgery.

Conclusion
This case of uncinate process insulinoma, diagnosed after a two-year symptomatic delay and cured by pancreaticoduodenectomy, illustrates two distinct clinical lessons that are relevant to practitioners across multiple specialties.

For Clinicians in Emergency Medicine and Primary Care
unexplained hypoglycemia in a non-diabetic patient particularly when recurrent, fasting-predominant, and accompanied by weight gain demands a hormonal investigation before it demands a clinical reassurance. The measurement of simultaneous fasting glucose, insulin, and C-peptide is the single diagnostic step that separates insulinoma from benign functional hypoglycemia. It requires no specialist, no imaging, and no significant cost. It was not performed in this case at any of multiple emergency visits over two years.

For Surgeons and Radiologists

The uncinate process presents specific technical constraints that can render enucleation hazardous regardless of tumor dimensions. When the MRI demonstrates a lesion deeply embedded within the uncinate process in proximity to the main pancreatic duct and superior mesenteric vasculature, the operative planning must account for these anatomical facts. Pancreaticoduodenectomy, in this setting, is the guideline-concordant choice and carries acceptable morbidity when performed at experienced centers. Insulinoma is one of the most biochemically tractable and surgically curable endocrine tumors in clinical medicine. What this case asks of the medical community is not technical sophistication it is clinical vigilance at the point of first contact.

Acknowledgements

The authors wish to thank Dr. Dritan Cela, Chief of Surgery, University Trauma Hospital, Tirana, for performing the pancreaticoduodenectomy and for his detailed communication of the surgical rationale, operative findings, and postoperative management to the multidisciplinary team.

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