

Late-Diagnosed Insulinoma Revealed by Recurrent Hypoglycemia: A Case Report

Anas El Wassi¹, El Mjabber Marwa¹, Berrada Othmane^{1*}, Benjelloune Kenza Touimi¹, Amal Hajri¹, Driss Erguibi¹, Rachid Boufettal¹, Saad Rifki Jai¹

¹Department of Digestive Cancer Surgery and Liver Transplantation, Ibn Rochd University Hospital, Casablanca

DOI: <https://doi.org/10.36347/sasjm.2026.v12i09.012>

| Received: 02.07.2026 | Accepted: 07.09.2026 | Published: 16.09.2026

*Corresponding author: Othmane Berrada

Department of Digestive Cancer Surgery and Liver Transplantation, Ibn Rochd University Hospital, Casablanca

Abstract

Case Report

Insulinoma is the most common functioning neuroendocrine tumour of the pancreas, yet it remains rare, with an incidence below 5 cases per million per year. Its diagnosis is frequently delayed because of misleading, non-specific symptoms dominated by neuroglycopenic features that are often mistaken for neurological or psychiatric disorders. We report the case of a 60-year-old man with a three-year history of recurrent hypoglycaemia whose loss-of-consciousness episodes were initially interpreted as epileptic seizures and wrongly treated with antiepileptic drugs, and in whom the diagnosis of insulinoma was eventually established on documented inappropriate endogenous hyperinsulinism concomitant with hypoglycaemia, and supported by a suggestive pancreatic MRI. The patient underwent surgical enucleation of a 1.5 cm tumour of the pancreatic body; definitive histopathology confirmed a grade 2 (G2) well-differentiated neuroendocrine tumour, with immunohistochemical expression of synaptophysin and chromogranin A and a Ki-67 index of 3%. This case highlights the typical diagnostic delay of this tumour and the need to consider insulinoma in any non-diabetic adult presenting with organic hypoglycaemia.

Keywords: insulinoma; pancreatic neuroendocrine tumour; hypoglycaemia; endogenous hyperinsulinism; Whipple's triad; pancreatic enucleation.

Copyright © 2026 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Insulinoma is a tumour arising from the beta cells of the islets of Langerhans, responsible for excessive and inappropriate insulin secretion leading to hypoglycaemic episodes. It is the most common functioning neuroendocrine tumour of the pancreas, while remaining rare, with an incidence below 5 cases per million population per year [1,2]. It may occur at any age, with a peak in the fifth decade and a median age of around 50 years; it affects both sexes almost equally and is solitary and benign in approximately 90% of cases [2,3].

Its main pitfall lies in the diagnostic delay. Neuroglycopenic signs are often predominant and poorly reported by patients, so that many are given erroneous neurological or psychiatric diagnoses for several years [4]. The mean diagnostic delay is in the order of 12 to 18 months but may reach several years [5]. We report the case of a patient in whom the diagnosis was made only after a three-year course, in order to illustrate this characteristic diagnostic delay and to review the clinical,

biochemical, radiological and therapeutic features of this condition.

CASE REPORT

A 60-year-old man with no relevant past medical history presented with a three-year history of recurrent hypoglycaemic episodes, documented by blood glucose values between 0.30 and 0.50 g/L.

These episodes manifested mainly as neuroglycopenic features, namely confusion and loss of consciousness, with no reported adrenergic signs. The episodes of loss of consciousness had initially been interpreted as epileptic seizures, leading to the inappropriate initiation of antiepileptic therapy, which was continued without any improvement in symptoms. They occurred most often in the fasting state and during the day, and resolved after carbohydrate intake. There were no associated vomiting, abdominal pain or other symptoms. The whole course took place in a context of apyrexia with preserved general condition.

Citation: El Wassi, A., El Mjabber, M., Berrada, O., Benjelloune Touimi, K., Hajri, A., Erguibi, D., Boufettal, R., & Rifki Jai, S. (2026). Late-Diagnosed Insulinoma Revealed by Recurrent Hypoglycemia: A Case Report. *SAS J Med*, 12(9), 908-912. <https://doi.org/10.36347/sasjm.2026.v12i09.012>

Laboratory work-up revealed a high insulin level of 233.14 pmol/L with a concomitant capillary blood glucose of 0.37 g/L, consistent with inappropriate endogenous hyperinsulinism. C-peptide and proinsulin were not measured. The remaining work-up, performed to exclude differential diagnoses and to screen for associated multiple endocrine neoplasia type 1 (MEN1), was unremarkable: calcium, PTH, albumin, liver function tests, TSH and 8 a.m. cortisol were normal, thereby ruling out, in particular, adrenal insufficiency and associated parathyroid involvement.

Abdominal MRI showed a pancreas of normal size, with preserved contours and homogeneous signal, harbouring at the level of the body a focal (nodular) signal abnormality, isointense on T1 and T2, hyperintense on diffusion-weighted sequences, with intense and homogeneous enhancement after contrast injection — similar to aortic enhancement on the arterial phase — measuring 15 × 15.7 mm on an axial slice. Overall, the MRI appearance was suggestive of a pancreatic neuroendocrine tumour consistent with an insulinoma.

As regards management, the patient received dexamethasone 1 mg/day as a hyperglycaemic agent during the five days preceding surgery. After pre-anesthetic assessment, he underwent surgical management. Exploration, after colo-epiploic detachment and separation of the transverse mesocolon from the anterior aspect of the pancreas, confirmed a 1.5 cm mobile nodule arising from the upper part of the pancreatic body. Enucleation of the nodule was performed, complemented by drainage of the lesser sac with a Salem sump tube. Frozen-section examination concluded to an organoid tumour. Definitive histopathological examination confirmed a well-differentiated neuroendocrine tumour; immunohistochemistry demonstrated expression of synaptophysin and chromogranin A, with a Ki-67 proliferation index of 3%, corresponding to a grade 2 (G2) well-differentiated pancreatic neuroendocrine tumour (insulinoma) according to the WHO classification. Postoperatively, blood glucose normalised and the hypoglycaemic episodes resolved.



Figure 1: Axial abdominal MRI showing a focal nodular lesion of the pancreatic body with intense, homogeneous enhancement on the arterial phase, consistent with a hypervascular neuroendocrine tumour (insulinoma)



Figure 2: Intraoperative view after colo-epiploic detachment and exposure of the anterior aspect of the pancreas; the nodule of the pancreatic body is identified



Figure 3: Intraoperative view of the pancreatic bed after enucleation of the nodule



Figure 4: Gross surgical specimen: the enucleated nodule

DISCUSSION

Insulinoma is a functioning neuroendocrine tumour that arises from the beta cells of the islets of Langerhans and is the leading cause of endogenous hyperinsulinaemic hypoglycaemia. It is the most common functioning pancreatic neuroendocrine tumour but remains rare, with an incidence of about 1 to 4 cases per million person-years [1,2]. It is solitary, benign and smaller than 2 cm in roughly 90% of cases, is distributed fairly evenly throughout the pancreas, and occurs in the

setting of multiple endocrine neoplasia type 1 in 5 to 10% of cases [8].

This case illustrates the two classic pitfalls of insulinoma: its misleading clinical presentation and the resulting diagnostic delay.

Clinically, hypoglycaemic symptoms usually combine adrenergic signs (sweating, palpitations, tremor) and neuroglycopenic signs (impaired consciousness, confusion, visual disturbances, even

coma), typically occurring in the fasting state and away from meals^{1,4}. In our patient, the picture was dominated exclusively by neuroglycopenic manifestations (confusion, loss of consciousness), with no adrenergic signs — a common situation that wrongly suggests a neurological or psychiatric cause and largely accounts for the diagnostic delay, here of three years. Indeed, the episodes of loss of consciousness had initially been labelled as epileptic seizures and treated with antiepileptic drugs without success, a characteristic illustration of the diagnostic wandering associated with this tumour; it is the lack of improvement under treatment that should prompt reconsideration of the diagnosis and a search for organic hypoglycaemia. Although the median age at onset is about 50 years, presentation in a patient over 60 is less usual, which adds to the interest of this observation [3].

Diagnosis first relies on documenting organic hypoglycaemia. Whipple's triad combines the occurrence of symptoms during fasting, their concomitance with hypoglycaemia, and their relief by carbohydrate intake [6]. Confirmation is then biochemical: during hypoglycaemia (blood glucose ≤ 0.55 g/L), an insulin level ≥ 3 mIU/L, C-peptide ≥ 0.6 ng/mL and proinsulin ≥ 5 pmol/L establish inappropriate insulin secretion [6]. In our patient, the combination of a markedly elevated insulin level of 233.14 pmol/L with a concomitant capillary glucose of 0.37 g/L met the criterion for inappropriate endogenous hyperinsulinism. C-peptide and proinsulin could not be measured in our setting; this measurement is nonetheless recommended, as it distinguishes an insulinoma (elevated C-peptide) from surreptitious exogenous insulin use (suppressed C-peptide), and represents a limitation of our observation [6].

When hypoglycaemia is not spontaneously documented, the supervised 72-hour fast remains the reference test, with almost all patients with an insulinoma becoming symptomatic within a 48-hour fast [6,7]. The work-up also allowed exclusion of the main differential diagnoses of organic hypoglycaemia (adrenal insufficiency, malnutrition, neoplastic context) and screening for MEN1, given that insulinoma occurs in this setting in 5 to 10% of cases, where it is then frequently multiple [8].

Tumour localisation should be undertaken only once the biochemical diagnosis is established. It is often difficult, as the tumour is usually small (90% are smaller than 2 cm and 30% smaller than 1 cm) [1]. Endoscopic ultrasound, whose sensitivity exceeds 90%, and cross-sectional imaging (CT, MRI) are complementary, and a multimodal approach is recommended [1,9]. On MRI, an insulinoma typically appears as a nodule that is hyperintense on T2 and on diffusion-weighted imaging, with intense arterial enhancement reflecting its hypervascular nature — an appearance found in our

patient, whose body nodule showed enhancement comparable to that of the aorta on the arterial phase.

Treatment of insulinoma is surgical and is the only curative option, with a cure rate of around 90% [1,10]. Enucleation is the technique of choice for benign, solitary and superficial tumours, as in our case, and can be performed by open or laparoscopic approach [1,11]. Preparation with a hyperglycaemic agent — here dexamethasone — aims to prevent perioperative hypoglycaemia. Endoscopic ultrasound-guided radiofrequency ablation represents a minimally invasive alternative under evaluation for selected small insulinomas [12]. The definitive diagnosis remains histopathological, complemented by immunohistochemistry: positivity of neuroendocrine markers (chromogranin A, synaptophysin, CD56) confirms a well-differentiated neuroendocrine tumour, and the Ki-67 proliferation index allows grading according to the WHO classification [8]. In our case, definitive immunohistochemistry showed expression of synaptophysin and chromogranin A with a Ki-67 proliferation index of 3%, confirming a well-differentiated neuroendocrine tumour of grade 2 (G2); although most insulinomas are grade 1 tumours, this G2 grade warrants careful postoperative surveillance.

CONCLUSION

Insulinoma is a rare but curable cause of organic hypoglycaemia in the non-diabetic adult. Its diagnosis is too often delayed, as illustrated by this case of a 60-year-old patient symptomatic for three years, owing to misleading neuroglycopenic symptoms. In any non-diabetic patient with documented fasting hypoglycaemia, insulinoma should be systematically considered; the approach combines confirmation of inappropriate endogenous hyperinsulinism, localisation by multimodal imaging, and surgical treatment, which most often achieves complete cure.

REFERENCES

1. Giannis D, Moris D, Karachaliou GS, Tsilimigras DI, Karaolanis G, Papalampros A, *et al.*, Insulinomas: from diagnosis to treatment. A review of the literature. J BUON. 2020;25(3):1302–14.
2. Hofland J, Falconi M, Christ E, Castaño JP, Faggiano A, Lamarca A, *et al.*, European Neuroendocrine Tumor Society 2023 guidance paper for functioning pancreatic neuroendocrine tumour syndromes. J Neuroendocrinol. 2023;35(8):e13318.
3. Sada A, Yamashita TS, Glasgow AE, Habermann EB, Thompson GB, Lyden ML, *et al.*, Comparison of benign and malignant insulinoma. Am J Surg. 2021;221(2):437–47.
4. Nashidengo PR, Quayson FW, Abebrese JT, Negumbo L, Enssle C, Kidaaga F. Varied presentations of pancreatic insulinoma: a case

- report. Pan Afr Med J. 2022 May 25;42:69. doi: 10.11604/pamj.2022.42.69.34839. PMID: 35949463; PMCID: PMC9338700.
5. Câmara LG, *et al.*, High-grade insulinoma detected in a patient with a 5-year history of severe hypoglycaemias. Pan Afr Med J. 2017;27:142. [adapt to the exact reference]
 6. Cryer PE, Axelrod L, Grossman AB, Heller SR, Montori VM, Seaquist ER, *et al.*, Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2009;94(3):709–28.
 7. Vezzosi D, Bennet A, Fauvel J, Caron P. Insulin, C-peptide and proinsulin for the biochemical diagnosis of hypoglycaemia related to endogenous hyperinsulinism. Eur J Endocrinol. 2007;157(1):75–83. [or the chosen 72-hour fast reference]
 8. Marini F, Giusti F, Brandi ML. Genetic disorders and insulinoma/glucagonoma. Endocr Relat Cancer. 2024;31(5):e230337.
 9. Christ E, Antwi K, Fani M, Wild D. Innovative imaging of insulinoma: the end of sampling? A review. Endocr Relat Cancer. 2020;27(4):R79–92.
 10. Mehrabi A, Fischer L, Hafezi M, Dirlewanger A, Grenacher L, Diener MK, *et al.*, A systematic review of localization, surgical treatment options, and outcome of insulinoma. Pancreas. 2014;43(5):675–86.
 11. Tamburrino D, Partelli S, Renzi C, Crippa S, Muffatti F, Perali C, *et al.*, Systematic review and meta-analysis on laparoscopic pancreatic resections for neuroendocrine neoplasms. Expert Rev Gastroenterol Hepatol. 2017;11(1):65–73.
 12. de Nucci G, Imperatore N, Mandelli ED, di Nuovo F, Mancino MG, *et al.*, Endoscopic ultrasound-guided radiofrequency ablation versus surgical resection for treatment of pancreatic insulinoma. Clin Gastroenterol Hepatol. 2023;21(11):2834–43.