

Case study

Pancreatic Insulinoma: A Case Report

Abstract:

Pancreatic insulinoma is a rare endocrine tumor of the pancreas characterized by excessive and inappropriate insulin secretion, leading to potentially life-threatening episodes of hypoglycemia. Despite its rarity, insulinoma remains the most common cause of organic hypoglycemia. Diagnosis relies on a diverse yet nonspecific symptomatology, necessitating meticulous patient history taking. Confirmation of the diagnosis is achieved through laboratory analyses, while computed tomography imaging typically facilitates the localization of the insulinoma, despite its small size.

In over 90% of cases, insulinoma presents as a solitary and benign tumor. Occasionally, it is associated with type I multiple endocrine neoplasia (MEN I or NEM), accounting for approximately 7 to 8% of cases. Surgical treatment generally ensures a definitive cure in the case of benign tumors. However, in the event of metastatic malignancy, the recurrence rate is approximately 60% after 3 years, with a survival rate of 1 to 4 years following repeat tumor resection.

Insulinoma remains a diagnostic challenge for healthcare practitioners. Nevertheless, thanks to an enhanced understanding of its clinical, biological, and histoprognostic characteristics, therapeutic options have advanced in recent years, notably through the development of laparoscopic surgery.

Key words: Pancreatic insulinoma – Hypoglycemia - Surgical treatment - Multiple endocrine neoplasia

INTRODUCTION :

Pancreatic insulinoma (PI) stands as a rare but clinically significant neuroendocrine tumor primarily originating within the pancreas. Despite its rarity, it remains the most prevalent form of neuroendocrine tumors affecting this organ [1]. The hallmark feature of PI is its propensity for inappropriate insulin secretion, leading to potentially life-threatening hypoglycemic episodes. The clinical importance of PI is underscored by its capacity to mimic a range of other medical conditions, necessitating vigilant diagnosis and appropriate management.

In a majority of instances, PI presents as a solitary and benign tumor, with more than 90% of cases falling into this category. Nevertheless, it is crucial to acknowledge that the relative rarity of PI should not underestimate its clinical significance. Estimated to affect between 1 and 4 individuals per million annually in Western countries, this tumor can manifest at any age. However, it most commonly surfaces within the age range of 40 to 60 years, with a slight predilection for females [2, 3].

Diagnosis of PI is typically aided by distinct biological markers, although the precise localization of the tumor may pose challenges, particularly due to its diminutive size [4]. While medical interventions can serve to mitigate symptoms related to excessive insulin secretion, surgical intervention remains the gold standard for achieving a complete cure by addressing the root cause of clinical and biological abnormalities [5]. The multifaceted nature of PI, encompassing its epidemiological, clinical, biological, and radiological facets, merits comprehensive exploration through the analysis of an illustrative case.

CASE PRESENTATION:

A 30-year-old female presented to the emergency department with recurrent seizures accompanied by signs of hypoglycemia. She reported experiencing a recurring symptomatology over the past 2 years, characterized by tremors, dizziness, and excessive sweating. Most of these episodes occurred at night and were significantly exacerbated during prolonged fasting. This symptomatology was also associated with fatigue and a noticeable but unspecified weight gain. Upon physical examination, the patient appeared to be in overall satisfactory condition but was overweight, with a body mass index (BMI) of 52.5 kg/m². Laboratory results revealed an initial blood glucose level of 0.39 g/l, a plasma insulin concentration of 70.4 μ UI/ml (2.6 - 24.9 μ UI/ml), and a peptide C level of 4.99 ng/ml (0.8 - 4.2 ng/ml).

A prolonged fasting test was conducted, confirming symptomatic hypoglycemia with hyperinsulinemia. The urine sulfonylurea test yielded negative results. Initial abdominal ultrasound did not provide conclusive findings. However, a contrast-enhanced abdominal computed tomography (CT) scan identified a millimeter-sized lesion measuring 3 mm in diameter, with an isodense appearance, located at the head of the pancreas (**Figure 1**).

An MRI could not be performed due to the patient's obesity, preventing her from fitting inside the MRI tube. Endoscopic ultrasound failed to pinpoint the pancreatic tumor's location.

Subsequently, an abdominal MRI conducted at another facility equipped with an appropriate machine revealed a lesion located at the junction of the pancreatic head and uncinate process, measuring 14 mm along its longest axis. This lesion exhibited irregular contours with hypointensity in T1-weighted images and slight hyperintensity in T2-weighted images. Following gadolinium injection, the lesion demonstrated enhancement patterns similar to pancreatic parenchyma. The body and tail of the pancreas appeared normal (**Figure 2**).

Additional investigations, including pituitary MRI and cervical ultrasound, showed no abnormalities. Furthermore, other hormonal parameters, such as serum cortisol, parathormone, ACTH, and thyroid function, were within normal ranges, ruling out multiple endocrine neoplasia.

During open surgical exploration, complete mobilization of the pancreas was performed. Bimanual palpation of the gland identified a nodule at the pancreatic head, unrelated to the biliary ducts.

Consequently, enucleation of the nodule was carried out, revealing an encapsulated pancreatic mass measuring 20x15 mm (**Figure 3**).

Histological analysis exhibited positive staining for synaptophysin and CD56, with a Ki67 marker estimated at 10% and 2 mitoses in 10 high-power fields. The anatomopathological diagnosis confirmed a well-differentiated neuroendocrine tumor (Grade 2, according to the 2010 WHO classification) of the pancreas, with functional and biological behavior consistent with pancreatic insulinoma.

Immediately post-surgery, blood glucose levels returned to the normal range. The patient was discharged without hypoglycemic symptoms after 5 days. Currently, with over 2 years of follow-up, the patient demonstrates a favorable clinical course.

DISCUSSION :

Insulinoma represents the most common form of pancreatic neuroendocrine tumors, with an estimated incidence of 1 to 4 cases per million people per year [6]. While it can occur at any age, it is most frequently diagnosed between the ages of 40 and 60, with a slight female predominance [7-8].

Fasting hypoglycemia in patients with insulinoma is a result of unregulated insulin production by tumor cells. This secretion escapes the normal mechanisms of glucose homeostasis regulation, leading to inappropriate plasma insulin concentrations. The abnormal absence of insulin secretion suppression in response to decreased blood glucose levels is particularly indicative of insulinoma [11].

The diagnosis of insulinoma relies on a symptomatology that is often characteristic but not specific, necessitating a thorough medical history. The classic Whipple triad, which combines neuroglycopenic symptoms, blood glucose levels < 0.5 g/l, and rapid symptom resolution following sugar ingestion, is rarely present at the outset and signifies the organic nature of hypoglycemia [12].

Morphological examinations are commonly employed as a first-line approach, although the detection of small pancreatic tumors measuring less than 1.5 mm can be challenging [7]. Abdominal ultrasound and abdominal CT have lower sensitivity than MRI for detecting small tumors, with a sensitivity ranging from 85 to 95% [13-14]. In magnetic resonance imaging (MRI), insulinoma typically appears as hypointense lesions in T1-weighted images, exhibit high enhancement intensity after gadolinium injection, and show slight hyperintensity in T2-weighted images [15-16].

The malignancy of insulinoma is defined based on criteria such as the presence of metastases, invasiveness, tumor size, mitotic count, and proliferation index. Some consider the presence of metastases as the sole criterion for malignancy. Malignant insulinomas account for 5 to 10% of cases [17].

Immunohistochemistry is commonly used to identify normal or pathological neuroendocrine cells and characterize their secretions. General neuroendocrine markers like Neuron Specific Enolase (NSE) and synaptophysin are often essential in confirming the diagnosis of neuroendocrine tumors [4].

While medical treatment may be considered in some cases, surgery remains the treatment of choice for pancreatic insulinoma. During surgical exploration, a meticulous examination of the pancreatic gland is

essential for locating the tumor. Bimanual palpation and intraoperative ultrasound can assist in precisely localizing the lesion [18]. In a study involving 29 patients suspected of having insulinoma, surgical exploration allowed for precise localization of lesions in 79.3% of cases, with no false positives [3].

The enucleation technique is often preferred, but it may not be feasible in cases of large tumor sizes or complex anatomical relationships. In such cases, pancreatic resection may be necessary, with options such as distal pancreatectomy or pancreaticoduodenectomy (Whipple procedure) [19].

CONCLUSION

Pancreatic insulinoma, although rare, represents a neuroendocrine tumor that is often benign but likely to be life-threatening due to the hypoglycemic events it causes. While confirmation of the diagnosis is relatively easy, precise localization of the tumor can be difficult. Currently, endoscopic ultrasound is considered the gold standard for the localization of insulinomas. Treatment relies primarily on surgery, which has benefited from advances in laparoscopic surgery in recent years.

Ethical approval

This [case reports](#) didn't require review by Ethics committee Ibn Sina University Hospital, Rabat, Morocco

Consent

Written [informed consent](#) was obtained from the patient for publication of this case report and accompanying images.

REFERENCES

1. Vaidakis D, Karoubalis J, Pappa T, et al. Pancreatic insulinoma: current issues and trends. *Hepatobiliary Pancreat Dis Int.* 2010;9(3):234–241.
2. Cryer PE, Axelrod L, Grossman AB, et al. Evaluation and management of adult hypoglycemic disorders: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2009;94:709–728.
3. Quinkler M, Strelow F, Pirlich M, et al. Assessment of suspected insulinoma by 48-hour fasting test: a retrospective monocentric study of 23 cases. *Horm Metab Res.* 2007;39:507–510.
4. Van Bon AC, Benhadi N, Endert E. Evaluation of endocrine tests: the prolonged fasting test for insulinoma. *Neth J Med.* 2009;67:274–278.
5. Agin A, Charrie A, Chikh K. Fast test: clinical practice and interpretation. *Ann Endocrinol.* 2013;74:174–184.

6. Azimuddin K, Chamberlain RS. The surgical management of pancreatic neuroendocrine tumors. *Surg Clin North Am.* 2001;81:5125.
7. Apodaca-Torrez FR, Triviño T, Lobo EJ, et al. Pancreatic insulinomas: diagnosis and treatment. *Arq Gastroenterol.* 2003;40(2).
8. Gouya H, Vignaux O, Augui J, et al. Endoscopic sonography and a combined protocol for preoperative evaluation of pancreatic insulinomas. *AJR Am J Roentgenol.* 2003;181:987–992.
9. Calender A. Génétique des tumeurs neuroendocrines. *Rev Prat.* 2002;52:256–261.
10. Marx S, Spiegel AM, Skarulis MC, et al. Multiple endocrine neoplasia type 1: clinical and genetic topics. *Ann Intern Med.* 1998;129:484.
11. Mitrakou A, Ryan C, Veneman T, et al. Hierarchy of glycemic thresholds for counterregulatory hormone secretion, symptoms, and cerebral dysfunction. *Am J Physiol.* 1991;260:E67–E74.
12. Suzuki K, Miyamoto M, Miyamoto T. Insulinoma with early morning abnormal behavior. *Intern Med.* 2007;46:405–408.
13. Therasse E, Taillefer R. Imaging of endocrine tumors of the pancreas. *Ann Endocrinol.* 1995;56:509–510.
14. Owen NJ, Sohaieb SAA, Peppercorn PD, et al. MRI of pancreatic neuroendocrine tumors. *BJR.* 2002;74:968–973.
15. Gualdi GF, Casciani E, Poletti E. Imaging of neuroendocrine tumors. *Clin Ter.* 2001;152(2):107–121.
16. Iihara M, Kanbe M, Okamoto T, et al. Laparoscopic ultrasonography for resection of insulinomas. *Surgery.* 2001;130:1086–1091.
17. Reubi JC, Waser B. Concomitant expression of several peptide receptors in neuroendocrine tumors: molecular basis for in vivo multi-receptor tumor targeting. *Eur J Nucl Med Mol Imaging.* 2003;30:781–793.
18. Service FJ, Dale AJ, Elveback LR, Jiang NS. Insulinoma: clinical and diagnostic features of 60 consecutive cases. *Mayo Clin Proc.* 1976;51:417–429.
19. Placzkowski KA, Vella A, Thompson GB, et al. Secular trends in the presentation and management of functioning insulinoma at the Mayo Clinic, 1987–2007. *J Clin Endocrinol Metab.* 2009;94:1069–1073.

FIGURES



Figure 1 : Abdominal CT scan showing a well-defined nodule in the pancreatic uncus.

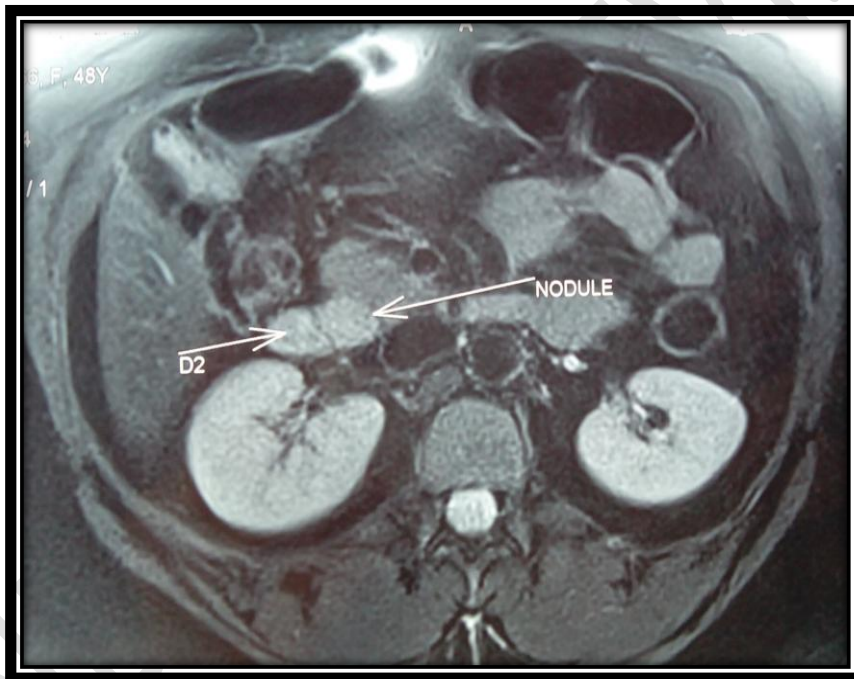


Figure 2 : MRI image of a nodule in the head of the pancreas located at the junction of the head and the uncinus process of the pancreas, causing a bulge in the lower part of D2, without dilation of the Wirsung duct or bile ducts.

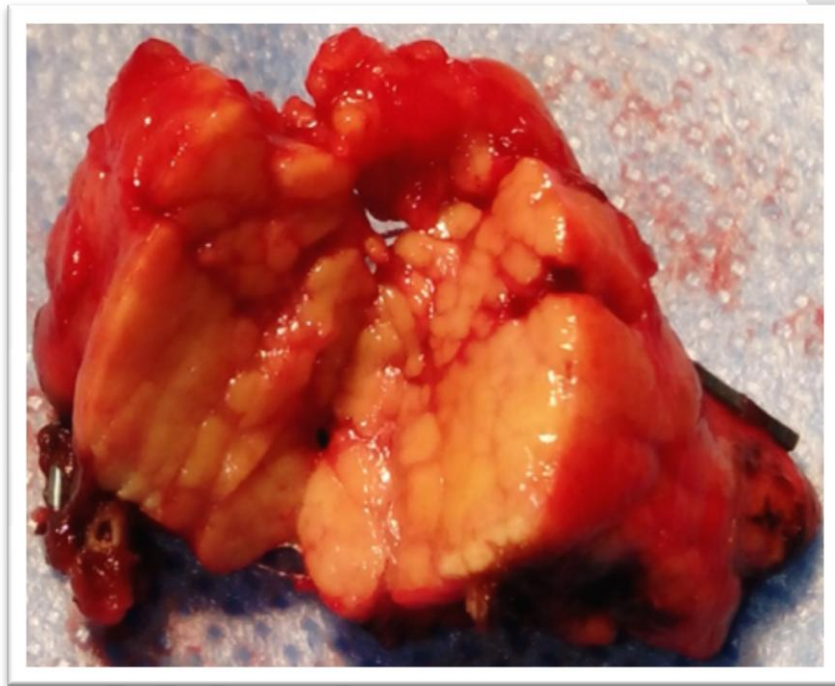


Figure 3: Surgical specimen of tumor resection of the uncinata process of the pancreas nodule.