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CASE REPORT

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Enucleation of a solitary pancreatic tail insulinoma: a case report and review of the literature

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Abstract

Introduction: Insulinomas are the most common pancreatic neuroendocrine tumors. They secrete insulin and result in endogenous hyperinsulinaemic hypoglycemia. The diagnosis of insulinoma was classically based on the fulfillment of Whipple's triad; hypoglycaemia (plasma glucose <50mg/dL), neuroglycopaenic symptoms, and the prompt relief of such symptoms with the administration of glucose. Preoperative localization of the insulinoma will help to plan the type of surgery necessary, either enucleation or pancreatic resection, and also decide on the approach, either open or laparoscopic. **Case description:** A 53-year-old farmer presented with neuroglycopenia symptoms with biochemical evidence of endogenous hyperinsulinaemic hypoglycemia during the mixed meal test. Imaging evidence in the form of CT and MRI showed a benign, approximately 1cm, solitary pancreatic tail insulinoma. Intraoperative ultrasonography confirmed the findings and the patient underwent enucleation of the tumor. Histology revealed a grade 2 pancreatic neuroendocrine tumor with confirmation of an insulinoma on immunohistochemistry. **Conclusion:** Pancreatic insulinomas, a rare pancreatic tumor, the commonest of the pNET present with neuroglycopenia. Diagnosis entails biochemical confirmation of endogenous hyperinsulinaemic hypoglycemia on a 72-hour prolonged fasting test. Noninvasive imaging in the form of CT as the first line, followed by MRI is used for localization and assessment of resectability. EUS and ASVS are additional invasive imaging in diagnostic difficulty. Enucleation and intraoperative ultrasonography is the treatment of choice for small, benign, pancreatic insulinomas.

Keywords: Pancreatic insulinoma. Enucleation. Neuroendocrine tumors.

Introduction

Insulinomas, although rare, are the most common type of pancreatic neuroendocrine tumors. They represent 1-2% of all pancreatic neoplasms and occur in 1-4 people per million in the general population [1,2]. These functioning tumors of Islet cells secrete insulin and result in endogenous hyperinsulinaemic hypoglycemia [3]. Insulinomas follow the 90's rule, with 90% reported to be benign, 90% solitary, 90% intrapancreatic, and 90% <2cm in size. They are evenly distributed throughout the pancreas and extrapancreatic insulinomas causing hypoglycemia are rare [4].

Intermittent excessive secretion of insulin to the bloodstream results in a cluster of symptoms due to neuroglycopenia including confusion, fatigue, double vision, behavioral and personality changes, seizures, and even coma. Autonomic symptoms also occur after hypoglycemia-induced compensatory sympathomimetic activity and include tremors, palpitations, anxiety, and hunger [5]. Although initially thought to occur only during fasting or after exercise, such symptoms may occur during the postprandial period as well.

The diagnosis of insulinoma was classically based on the fulfillment of Whipple's triad; hypoglycaemia

(plasma glucose <50mg/dL), neuroglycopaenic symptoms, and the prompt relief of such symptoms with the administration of glucose. Biochemical diagnosis involves the measurement of plasma glucose, insulin levels, C peptide levels, and proinsulin levels during a 72hour prolonged fast [6].

Preoperative localization of the insulinoma will help to plan the type of surgery necessary, either enucleation or pancreatic resection, and also decide on the approach, either open or laparoscopic. The exact location of the tumor, its relationship to vital structures, and the presence of metastasis are best seen on computed tomography and hence it is the first-line imaging modality for insulinoma [7]. However, magnetic resonance imaging (MRI) has superior sensitivity and specificity in detecting insulinomas and extrapancreatic spread [8].

Methods

Study design

The present case report study followed the CARE rules – Case Report. Available at: https://www.care-statement.org/. Accessed on: 02/20/2024.

Ethical Approval

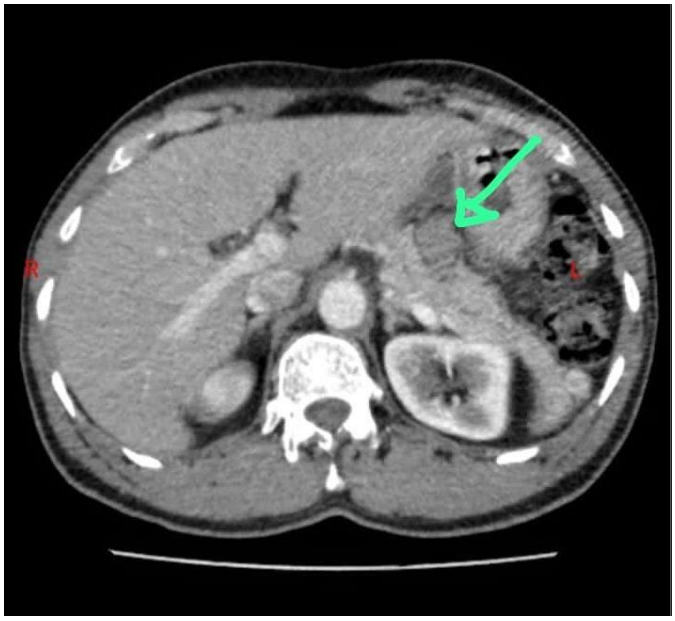
Our institution does not require ethical approval for reporting individual cases or case series.

Case Report

A 53-year-old otherwise fit and healthy Sri Lankan farmer, from a rural farming community presented with recurrent episodes of postprandial symptomatic hypoglycaemia for 1 year, with worsening symptoms over 6 months. Symptoms included episodic dizziness, sweating, and hunger in the postprandial period, typically 2 hours after a meal. Symptoms were relieved with meals and consequently frequency of meals was increased to 10 per day with increased appetite. It was not associated with early morning symptoms, major hypoglycaemic episodes, weight gain, or loss. He was unable to continue farming owing to the severity of his symptoms. His body weight was 52,0 kg and his body mass index was 20kg/m^2, not pale, and had no features of micronutrient deficiencies. The rest of the general and systemic examination was normal. His thyroid, renal, and liver profiles, 9 am cortisol and serum calcium levels, FSH, LH, and serum testosterone levels were all normal.

Fasting plasma glucose was 65mg/dL. Plasma glucose 4 hours after the extended oral glucose tolerance test was 35mg/dL. He developed symptomatic hypoglycemia 90 minutes into the mixed meal test. Plasma glucose was 19mg/dL, insulin levels 23.1 mIU/L (>3), C peptide levels 4.41 ng/mL (0.6), and Insulin/ C peptide ratio <1. Serum pro-insulin levels were not available. These biochemical findings confirmed endogenous hyperinsulinaemic hypoglycemia. Abdominal ultrasonography was normal. Contrast-enhanced computed tomography (CECT) scan of the chest and abdomen revealed a 10x9mm lesion in the pancreatic tail with arterial phase enhancement without features of metastasis suggestive of a solitary benign insulinoma. Magnetic resonance imaging (MRI) of the pancreas was also suggestive of the same. Figure 1 shows an axial cut of the CECT abdomen demonstrating solitary pancreatic tail insulinoma.

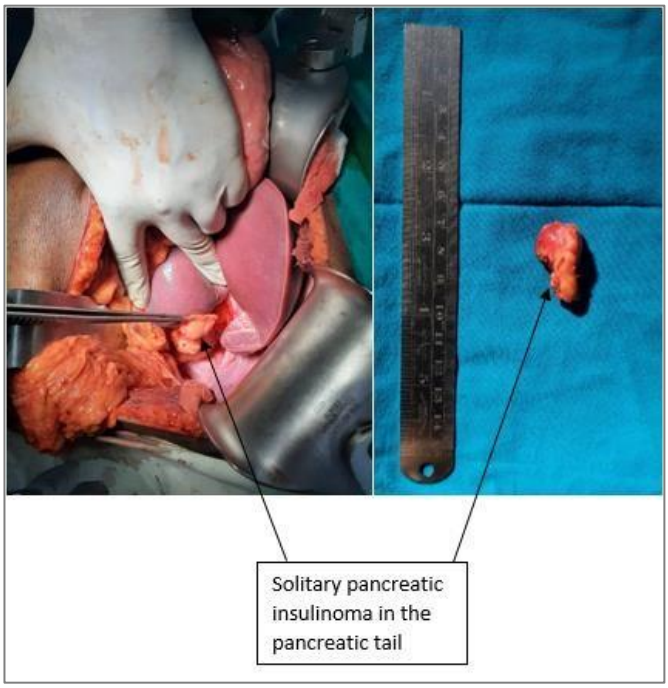
Figure 1. Axial cut of CECT abdomen demonstrating solitary pancreatic tail insulinoma.



Source: Own Authorship.

The patient underwent enucleation of the solitary pancreatic tail insulinoma through an extended left subcostal incision under general anesthesia by the gastrointestinal surgeon. Intraoperative manual palpation and ultrasonography of the pancreas did not reveal further occult lesions. The postoperative period was complicated by left lung lower zone collapse, pancreatic fistula, and perisplenic collection, all of which were managed conservatively. The patient was discharged on post-op day 20. He has had no further hypoglycaemic episodes on follow-up at 1 2,3 and 6 months. Figure 2 shows intraoperative and specimen images of the insulinoma.

Figure 2. Intraoperative and specimen images of the insulinoma.



Source: Own Authorship.

Histology revealed a 5x10x11mm grade 2 pancreatic neuroendocrine tumour, which stained positive for synaptophysin and Chromogranin A on immunohistochemical analysis with R0 resection margins. The Ki67 proliferation index was 5.8%.

Discussion

Despite being rare, insulinomas are the most common type of functional pancreatic neuroendocrine tumors. They occur in all age groups (mean-51 years) with a slight female preponderance [3]. Of insulinomas, 90% are benign, solitary, intrapancreatic, and <2cm in size, while 10% are multiple, and may occur as part of a multiple endocrine neoplasia syndrome (MEN 1 syndrome) and extrapancreatic [9].

Insulinomas can present with subtle non-specific symptoms and hence diagnosis can be difficult, delayed, and even misdiagnosed as cardiac, neurological, and psychiatric disease. It is typically diagnosed less than one and a half years after the onset of symptoms [9]. The gold standard to diagnose an insulinoma is the supervised 72-hour prolonged fasting test. The present consensus is that the presence of inappropriately high levels of insulin (5mIU/L), high C peptide levels (0.6ng/mL), insulin/C peptide ratio <1, and the absence of sulfonylureas in serum or urine, at the time of detection of hypoglycemia in a 72 hour prolonged fasting test is diagnostic [10,11].

Preoperative localization of insulinomas helps to plan an optimized therapeutic strategy that is safe, and timely, with minimized surgical morbidity and mortality. Noninvasive imaging in the form of ultrasonography, CT, and MRI are used for localization. Of these helical CT has enabled the detection of 94% of insulinomas, its size and location, and defined its anatomical relationship to nearby vital structures and the presence or absence of metastatic disease indicating malignant disease and is therefore the most suitable first-line imaging modality [7]. The sensitivity of MRI to detect insulinomas varies between 40-90% and is suitable as a second-line modality.

Endoscopic ultrasound too has a high sensitivity of 94%. It can detect lesions up to 5mm, better delineates the relationship to bile ducts and nearby structures, and allows the added benefit of obtaining a fine needle aspirate. It is most sensitive for tumors in the head of the pancreas and least for tail lesions and is operator-dependent [1,7,12].

Bimanual palpation of the pancreas combined with intraoperative ultrasound is >95% sensitive but requires complete mobilization of the pancreas. Arterial stimulation venous sampling can be used for atypical insulinomas with near 100% sensitivity. Surgery is the treatment of choice for all localized tumors. The type of surgery required will vary depending on the size, location, and relationship to vital structures. Small, encapsulated tumors in the body and tail can be simply enucleated. Atypical resections, distal and middle pancreatectomies can be performed for larger tumors, close to the pancreatic duct [13,14]. The laparoscopic approach with the utilization of laparoscopic ultrasonography is increasingly being used with good results in selected patients [15].

Medical management is employed in the preoperative to prevent the development of hypoglycemia. It is also reserved for those with unresectable malignant insulinomas, multiple insulinomas, and those who do not consent to surgery. Short and long-acting octreotide, a somatostatin analog, prevents insulin secretion and hence normalizes blood glucose and has an antiproliferative and moderate antitumor effect on pancreatic neuroendocrine tumors [16-18].

Pancreatic neuroendocrine tumors are classified into 3 grades depending on the tumor size, mitotic index, Ki67 proliferation index, and the presence of angioinvasion and perineural invasion. Grade 1 – well-differentiated endocrine tumors, limited to the pancreas with benign behavior; Grade 2 – well-differentiated endocrine carcinomas with low-grade malignant behavior and extrapancreatic invasion and Grade 3 – poorly differentiated with high-grade malignant behavior [5].

Our case report included a patient with symptoms of hypoglycemia and fulfillment of Whipple's triad with biochemical evidence of endogenous hyperinsulinaemic hypoglycemia during the mixed meal test. Imaging

evidence in the form of CT and MRI showed a benign, approximately 1cm, solitary pancreatic tail insulinoma. Intraoperative ultrasonography confirmed the findings and the patient underwent enucleation of the tumor. Histology revealed a grade 2 pancreatic neuroendocrine tumor with confirmation of an insulinoma on immunohistochemistry.

Conclusion

Pancreatic insulinomas, a rare pancreatic tumor, the commonest of the pNET present with neuroglycopaenia. Diagnosis entails biochemical confirmation of endogenous hyperinsulinaemic hypoglycemia on a 72-hour prolonged fasting test. Noninvasive imaging in the form of CT as the first line, followed by MRI is used for localization and assessment of resectability. EUS and ASVS are additional invasive imaging in diagnostic difficulty. Encucleation and intraoperative ultrasonography is the treatment of choice for small, benign, pancreatic insulinomas.

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Ethical Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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Data sharing statement

No additional data are available.

Conflict of interest

The Author(s) declare(s) that there is no conflict of interest.

Similarity check

It was applied by Ithenticate®.

Peer Review Process

It was applied.

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