Insulinoma: A commonly misdiagnosed pancreatic tumour

S Shah, A Patel, J Prajapati, A Modi, R Arora, P Sharma

Citation

S Shah, A Patel, J Prajapati, A Modi, R Arora, P Sharma. *Insulinoma: A commonly misdiagnosed pancreatic tumour*. The Internet Journal of Gastroenterology. 2009 Volume 9 Number 1.

Abstract

Insulinomas are rare tumors of the neuroendocrine variety. Importantly, insulinomas are seldom malignant; if metastatic disease is not found at the time of initial diagnosis, it is unlikely to develop in the future (albeit rare metachronous metastases and local recurrence at the surgical site have been reported). Symptoms due to excessive insulin secretion can mimic psychoses and misdiagnosis is common. We report the case of a twenty five year old man who was treated for four years as a case of psychosis. It was only when one of the physicians got a fasting blood sugar level done that the diagnosis of insulinoma was suspected. He had a three centimeter tumour in the uncinate process which was enucleated and the patient was cured. Thus, accurate diagnosis is essential for this potentially curable condition.

INTRODUCTION

Insulinomas are rare tumors of the neuroendocrine variety. Most insulinomas are found to be solitary benign pancreatic nodules, with only 2% to 10% of patients having multiple tumors. In these patients, MEN 1 should be suspected. Excessive secretion of insulin by the tumor leads to neuroglycopenic and/or sympathoadrenal symptoms induced by hypoglycemia.and should lead to a strong suspicion of insulinoma. These symptoms may be confused with psychosis leading to misdiagnosis.

After biochemical confirmation of insulinoma, imaging and localization is typically obtained by CT scan. If undetected and the clinical suspicion is still high, then arteriography, ultrasonography (transabdominal, endoscopic, and intraoperative), or 111-In-penteotreotide or octreotide scintigraphy may be pursued.

Surgery is the treatment of choice which cures the patient

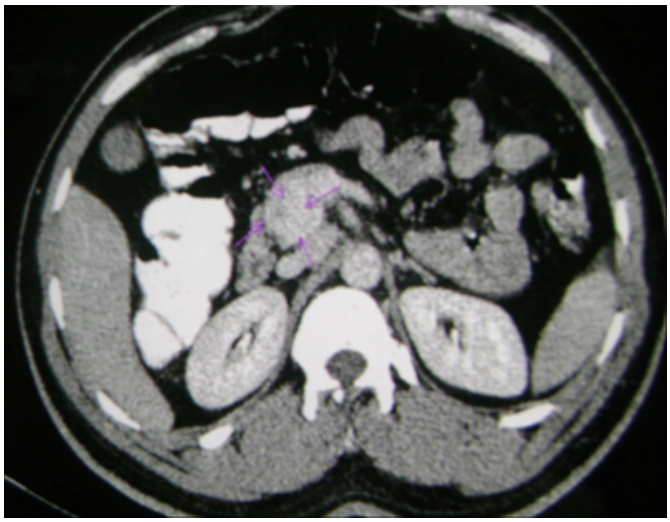
CASE SUMMARY

A 25yr old male presented with episodes of loss of consciousness in early morning hours and altered behaviour for four years. When no neurologic disorder could be found, he was started on antipsychotic medication. He also had an increase in appetite over this period and a weight gain of twenty kgs. The symptoms were relieved relieved on taking food. One of the physicians he consulted advised a fasting blood glucose level and it was found to be 42 mg%. Two subsequent fasting sugar levels were below 50mg%. The fasting serum insulin levels [44.2 µu/ml (normal: 6-27µu/ml)] and C peptide levels [3.5ng/ml (normal 0.9-4ng/ml)] were elevated. The patient was referred to us with this biochemical picture.

A contrast enhanced CT scan of the abdomen showed a 32mm x 27mm well defined lesion in the uncinate process of pancreas showing significant enhancement on pancreatic parenchymal phase of contrast.

Figure 1

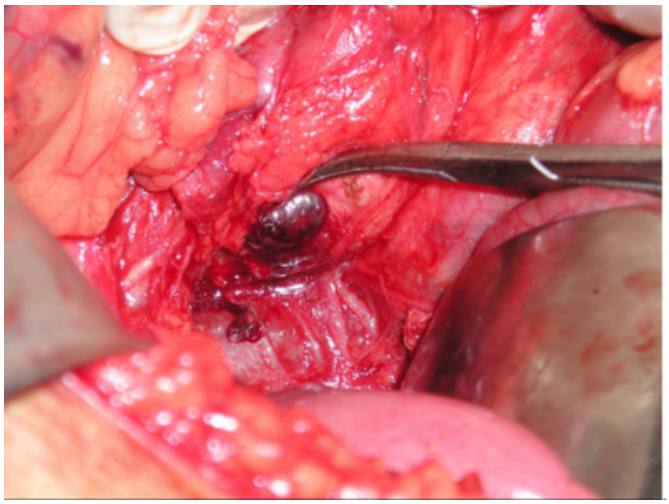
Figure: C T scan showing the tumour



We took up the patient for surgery with the intent of enucleating the tumor. The pancreas was mobilized revealing a 3cm diameter mass on the posterior surface of the uncinate process.

Figure 2

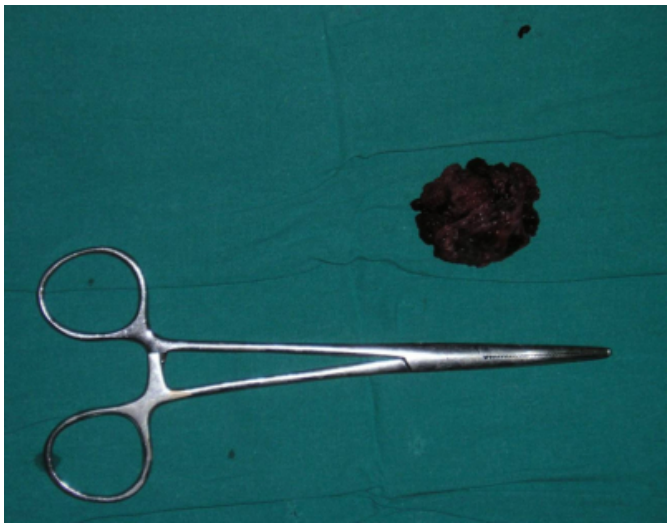
Figure 2: the tumour in the uncinate process



The mass was enucleated. (Figure 3: The resected specimen). There was no fear of damaging the pancreatic duct at this site. During the surgery the patient was given 5%glucose infusion. The blood sugar level was 90mg% 2 hours after the surgery without a glucose drip and remained within normal limits thereafter. The postoperative period was uneventful. The patient lost the excess weight he had gained over the next two months. He is disease free and asymptomatic after 18 months of surgery.

Figure 3

Figure 3: The resected specimen



DISCUSSION

Islet cells of the pancreas are scattered all over the gland, hence insulinomas can arise from any part of the pancreas as seen arising from the uncinate in the above case. Importantly, insulinomas are seldom malignant; if metastatic disease is not found at the time of initial diagnosis, it is unlikely to develop in the future (albeit rare metachronous metastases and local recurrence at the surgical site have been reported) (4). This contrasts sharply with the natural history and patterns of recurrence of other neuroendocrine neoplasms/carcinomas of the pancreas, which probably all have the biologic ability to metastasize if left untreated.(4). It is unknown whether this unique feature of insulinomas results from their different underlying tumor biology or occurs simply because, owing to their profound symptom complex, these tumors are virtually always surgically excised early, when they are small. (4).

Despite the profound symptom complex, misdiagnosis of insulinoma is common and to make a diagnosis of insulinoma, the clinician must consider it. (2,3,5). Insulinoma should be suspected in all patients who present with neurological (recurrent seizures, especially when multiple and without response to anticonvulsive drugs) and psychiatric symptoms with a fluctuating course .(2) They can present with neuroglycopenic or adrenergic symptoms or both.(6) Uncontrolled secretion of insulin results in hypoglycemia, manifested by neuroglycopenic symptoms such as blurred vision, confusion, and abnormal behavior, which may progress to loss of consciousness and seizure. In response to hypoglycemia, the body releases catecholamines, which elicit perspiration, anxiety, palpitations, and hunger (4) other symptoms include visual changes, unusual behavior, palpitations, diaphoresis, and tremulousness (2).

The diagnosis of insulinoma syndrome is established by supervised fasting of the patient, to include a laboratory work-up and observation. Serum levels of plasma glucose, C-peptide, proinsulin, insulin, and sulfonylurea are measured at intervals of 6 to 8 hours and at the point when symptoms develop. Patients with insulinoma have an insulin level greater than 3 mcIU/mL (usually greater than 6 mcIU/mL) when blood glucose is less than 40 to 45 mg/dL with an insulin-to-glucose ratio of 0.3 or more, reflecting the inappropriate secretion of insulin at the time of hypoglycemia.(1,4). Factitious hypoglycemia should be suspected in patients who have access to insulin or antidiabetic secretagogue drugs through work or relatives (10).

Once the biochemical diagnosis is established, localization studies performed as part of the preoperative evaluation include upper endoscopy with EUS of the pancreas and duodenum and multidetector CT. For the very rare patient in whom tumor localization is not successful, it is best to

proceed with a regionalization study to determine whether the tumor is located to the right or left of the mesenteric vessels with selective arterial calcium stimulation and hepatic vein sampling. (4, 7) Intraoperative ultrasound (IOUS) can be used to localize the lesion during surgery.

The definitive management is surgical removal. It is important to remove the tumor with the capsule completely, as local recurrence can occur. If enucleation is not possible, segmental resection of the pancreas, distal pancreatectomy, or pancreaticoduodenectomy may be necessary. (4)

Medications such as diazoxide and somatostatin can be used for patients who are not surgical candidates or who otherwise have inoperable tumours. Aggressive therapy targeting the tumor is needed to debulk the disease that is present. (2) As malignant insulinomas can often be indolent in terms of tumor growth, surgical resection, hepatic artery chemoembolization, and RFA can be considered whenever possible. (4) Streptozocin-based chemotherapy should also be considered.

The case here was treated as a case of psychosis for four years before the right diagnosis was made. Curative resection was possible even after this long delay in diagnosis given the benign nature of the disease. Thus accurate timely diagnosis is essential.

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