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CASE REPORT

Malignant Insulinoma Arising from Intrasplenic Heterotopic Pancreas

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ABSTRACT

Context Heterotopic pancreas is defined as ectopic pancreatic tissue without vascular or anatomic continuity with the normal pancreas. The spleen is a rare site of origin. This case report describes a patient with a malignant insulinoma which originated from an intrasplenic heterotopic pancreas. **Case report** A 46-year-old man with three previous episodes of neuroglucopenic and adrenergic symptoms was referred to our hospital. A fasting test was performed and discontinued due to hypoglycemic symptoms. Preoperative studies failed to demonstrate any pancreatic lesions. However, a heterogeneous encapsulated tumor in the spleen was found on MRI. During surgery, only the splenic tumor was found, with neither vascular nor anatomical connections to the normal pancreas. Pathology reported a malignant insulinoma. Insulin and proinsulin were documented by immunohistochemistry. After one year of follow up, the patient is free of symptoms and no recurrent disease has been documented. **Discussion** Only seven cases of splenic heterotopic pancreas have been reported, six with cystic mucinous neoplasms. In addition, only one case of a malignant insulinoma arising from heterotopic pancreas has previously been described. This is the second case reported of an insulinoma arising from heterotopic pancreas and the first to originate from intrasplenic heterotopia.

INTRODUCTION

Pancreatic neuroendocrine neoplasms are rare tumors with an annual incidence of 2-5 cases per million [1]. Insulinoma represents approximately 33 to 40% of all resected pancreatic neuroendocrine neoplasms and is the most frequent among the functional group. However, recently, it has been demonstrated that it is no longer the most frequent resected pancreatic neuroendocrine neoplasm, non-functional tumors being the most frequent [2, 3].

Most insulinomas are benign with only 5.8 to 8% demonstrating malignant behavior [4, 5]. Heterotopic pancreas incidence in reported autopsy series ranges from 0.55 to 13.7% [6]. They arise from the upper gastrointestinal tract (duodenum and stomach), jejunum, liver, colon and lymph nodes. The spleen is a very rare site of origin [7, 8].

This case report describes a patient with a malignant insulinoma originating from an intrasplenic heterotopic pancreas.

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Key words Insulinoma; Pancreas; Spleen

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CASE REPORT

We report the case of a 46-year-old man who was referred to our hospital for further evaluation after three episodes of neuroglucopenic and adrenergic symptoms. These episodes were characterized by dizziness, blurred vision, headache and confusion, improving after ingestion of simple carbohydrates. In addition, a low serum glucose level was documented in the last episode (less than 50 mg/dL; reference range: 65-103 mg/dL).

A fasting test was performed and discontinued at 9.5 hours due to hypoglycemic symptoms with a serum glucose level of 38 mg/dL, insulin 53 µU/mL (reference range: 0-25 µU/mL), proinsulin greater than 200 pmol/L (reference range: 0-23.2 pmol/L) and C-peptide 4.4 ng/mL (reference range: 0.80-3.90 ng/mL).

A CT scan, EUS, MRI and 185MBq SC-^{99m}Tc scintigraphy failed to demonstrate any pancreatic lesion. However, a heterogeneous encapsulated tumor in the inferior splenic pole was found at MRI (Figure 1).

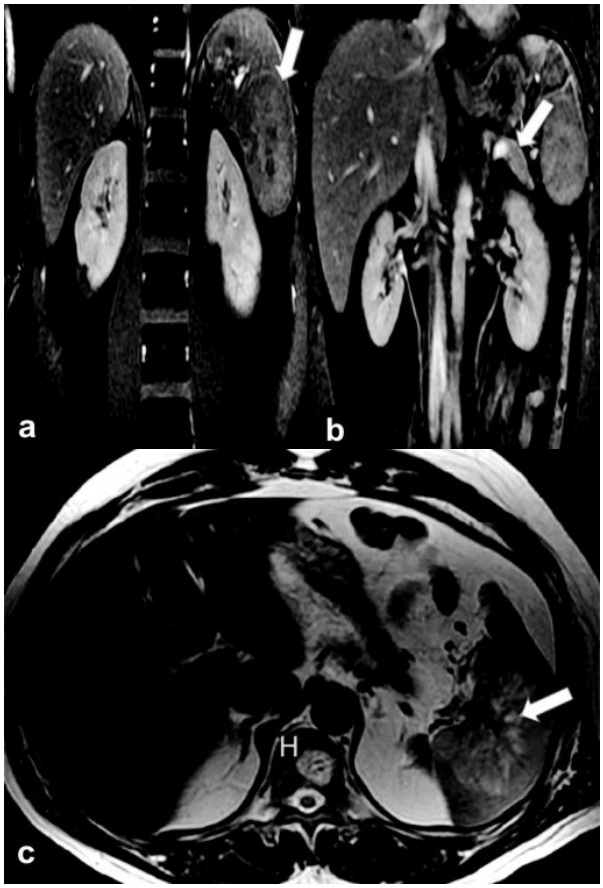

Figure 1. -Intrasplenic insulinoma. FATSAT T1-MRI sequence with gadolinium. Intrasplenic lesion (**a.** arrow). Distal pancreatic tail without neoplasic infiltration (**b.** arrow). Axial MRI intrasplenic lesion (**c.** arrow).

After negative screening tests for multiple endocrine neoplasia (MEN-1), surgery was performed. During the procedure, a well-encapsulated tumor in the inferior splenic pole and hilum was found. There were neither anatomical nor vascular connections to the normal pancreas.

Following the splenectomy, further intra-operative exploration of the entire pancreas was performed without finding any additional tumors.

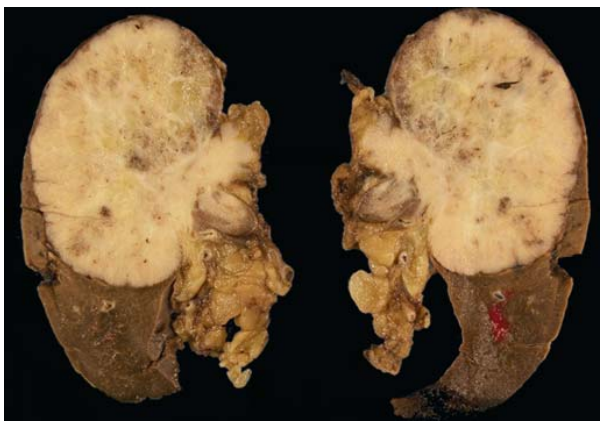

Figure 2. Macroscopic aspect of a intrasplenic neuroendocrine carcinoma with hilum invasion.

Macroscopic examination revealed a 7.6x4.4 cm white-colored nodular heterogeneous tumor with abundant adipose tissue in the splenic hilum where five lymph nodes were resected (Figure 2).

From the microscopic standpoint, perineural and vascular invasion were present in addition to three metastatic lymph nodes. His mitotic rate was 4 per 10 HRF and positive immunohistochemistry for insulin and proinsulin were documented. In this regard, the histological diagnosis was consistent with a malignant, moderately differentiated insulinoma arising from intrasplenic heterotopic pancreas (Figure 3).

The patient tolerated the surgical procedure without complications. After one year of follow-up, he is free of symptoms and no recurrent disease has been documented in follow-up laboratory and imaging tests (CT scan, MRI and scintigraphy).

DISCUSSION

Heterotopic pancreas is defined as aberrant pancreatic tissue without vascular or anatomic continuity with the normal pancreas [8]. The splenic location of heterotopic pancreas has an incidence of 0.4 to 1% suggested by autopsy studies [6, 9]. They are usually small and subcapsular.

Up to now, seven cases of splenic heterotopic pancreas have been reported, six with cystic mucinous neoplasms present within them [7, 8, 10].

Hennings J *et al*. described the case of a 3 cm malignant insulinoma arising from heterotopic pancreas adjacent to the ligament of Treitz and separated from the pancreas. Following tumor resection, the patient recovered well and has been symptom-free [11].

There was controversy in our case that the insulinoma may have originated from the normal pancreatic tail and invaded the splenic hilum and inferior pole, as was the case of Wang H *et al*., who reported a malignant non-functional endocrine neoplasm originating from the pancreatic tail with invasion to the spleen. During

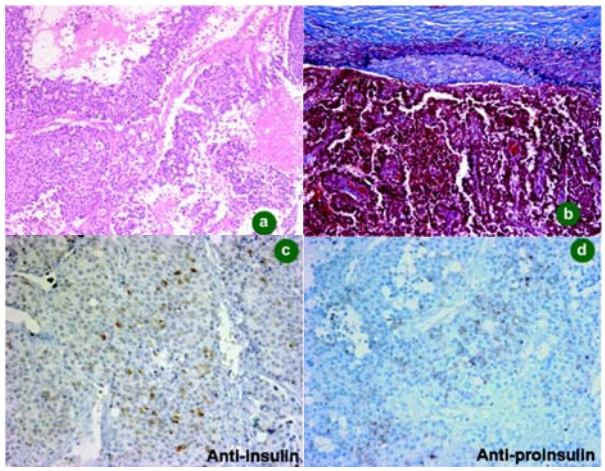

Figure 3. A moderately differentiated neuroendocrine carcinoma with *en masse* necrosis and atypical mitoses (**a.**). Tumor venous invasion is documented with Masson-Verhoeff´s stains (**b.**), and insulin (**c.**) and proinsulin (**d.**) synthesis with immunohistochemistry.

resection, they found the pancreatic tail scarcely connected to the splenic blood vessels and penetrating into the red substance of the spleen. A distal pancreatectomy with splenectomy was performed in this case and, after two years of follow-up, the patient is free from recurrence and metastasis [12].

On the contrary, in our case, the tumor was surrounded by splenic tissue and, in concordance with the case reported by Hennings *et al*., separated from the normal pancreas without vascular or anatomic continuity. To our knowledge, this is the second case reported of an insulinoma arising from heterotopic pancreas and the first originating from intrasplenic heterotopia.

Even though splenic heterotopic pancreas and malignant insulinoma are rare entities they must be kept in mind by specialized surgical teams interested in pancreatic neoplasm management. This also points out the importance of surgical treatment and intra-operative exploration in the context of a hormonal syndrome, despite failure to find any pancreatic lesion in preoperative imaging studies.

Conflict of interest The authors have no potential conflicts of interest

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