

## CASE REPORT

# Successful Preoperative Localization of a Small Pancreatic Insulinoma by Diffusion-Weighted MRI

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### ABSTRACT

**Context** Insulinoma is the most common functioning endocrine tumor of the pancreas responsible for fasting hypoglycemia resulting from autonomous insulin hypersecretion. Most insulinomas are small and difficult to localize with conventional imaging. We successfully localized a small insulinoma in our patient using diffusion-weighted magnetic resonance imaging before surgery. **Case report** We report the case of a female patient with a clinical suspicion of insulinoma. A preoperative MR with diffusion-weighted imaging was performed and localized a small nodule in the pancreatic tail. Treatment consisted of surgical enucleation. Histologic examination identified a neuroendocrine tumor compatible with an insulinoma. **Conclusion** Diffusion-weighted imaging can be useful in detecting and localizing small insulinomas, especially for those with no hypervascular pattern.

### INTRODUCTION

Pancreatic neuroendocrine tumors are rare neoplasms of the pancreas. Insulinomas represent the most common functioning neuroendocrine tumors of the pancreas. Surgery remains the only curative treatment in localized insulinomas. Therefore, preoperative imaging for exact localization is necessary for planning the surgical approach and strategy. Preoperative localization by conventional imaging modalities is generally difficult because of their small size at the time of diagnosis. Imaging findings vary according to the histopathological features and the lesions are detected with difficulty. We report a case of an insulinoma successfully localized by diffusion-weighted imaging (DWI).

### CASE REPORT

A 49-year-old woman presented to our emergency department in a hypoglycemic coma and was immediately admitted to the intensive care unit. Her

initial glucose level was 36 mg/dL (reference range: 70-110 mg/dL) associated with an increased C-peptide level. Her past history was significant for hypoglycemic attacks which had been recurring for about two years. An insulinoma had already been suspected in this patient few weeks previously; an assessment in another hospital by contrast-enhanced multidetector CT scan (Figure 1) and contrast-enhanced magnetic resonance imaging (MRI), without DWI, was inconclusive.

Once her condition was stable, a prolonged supervised fast test was carried out. Initial glucose level was 55



**Figure 1.** Arterial phase CT scan. The lesion is barely seen (arrow) and remains isoattenuating to the surrounding pancreatic parenchyma.

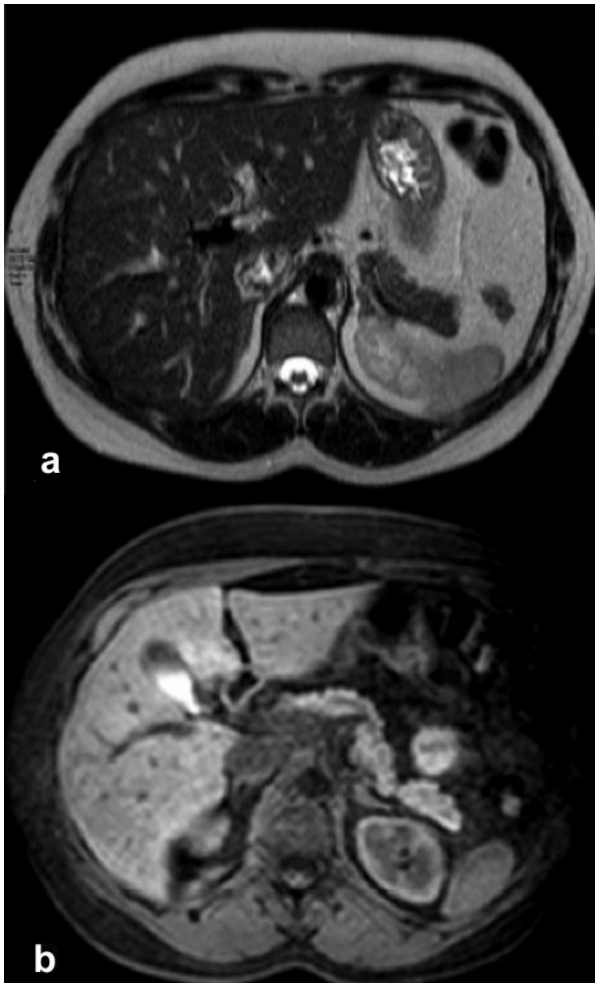
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**Key words** Diffusion Magnetic Resonance Imaging; Insulinoma; Pancreatic Neoplasms

**Abbreviations** ADC: apparent diffusion coefficient; DWI: diffusion-weighted imaging; PNET: pancreatic neuroendocrine tumor

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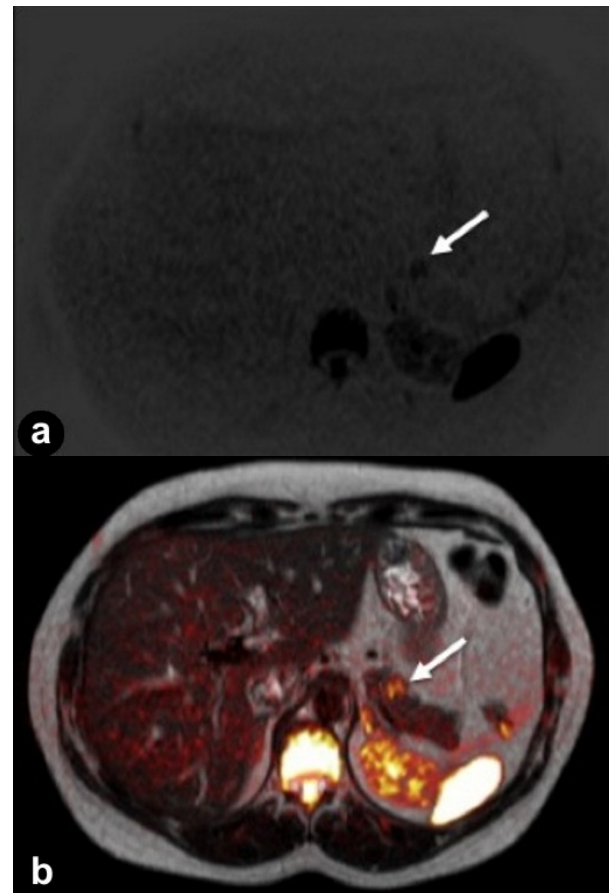
**Figure 2.** Axial T2-weighted spin-echo image (a.) and axial T1-weighted spin-echo image with fat suppression (b.) at the level of the pancreatic tail did not show any lesion.

mg/dL, plasma insulin level was 7.3  $\mu$ IU/mL (reference range: 5-25  $\mu$ IU/mL) and C-peptide level was 6.7 ng/mL (reference range: 1.6-3.6 ng/mL). At the sixth hour of the test, hypoglycemic symptoms occurred. Simultaneously, blood samples showed an increase in plasma insulin (8.5  $\mu$ IU/mL) and C-peptide (7.6 ng/mL) levels in the presence of marked hypoglycemia (44 mg/dL). Those data were suggestive of an insulinoma. She was then examined for multiple endocrine neoplasias. MRI of the hypophysis, hypophysis hormonal analysis and intact parathormone levels were normal. An octreotide scintigraphy (OctreoScan<sup>®</sup>, Mallinckrodt, Petten, The Netherlands) was also performed and was not conclusive. Finally, endoscopic US scanning detected a hypoechoic 14 mm nodular lesion at the pancreatic tail. It was homogenous and well shaped, compatible with a neuroendocrine tumor. Fine needle aspiration was performed at the same time and the pathology was compatible with a pancreatic neuroendocrine tumor. Based on the clinical, biochemical and histological features, the lesion was diagnosed as an insulinoma.

In order to precisely localize the tumor and to assess the local spread before surgery MRI was repeated

using DWI. The examination was performed on a 1.5-T scanner (Achieva, Philips, Best, The Netherlands). DWI was obtained using a single-shot echo-planar imaging technique in the axial plane under free breathing with a body coil. We used two b factors: 0 and 1,000 s/mm<sup>2</sup> and the apparent diffusion coefficient (ADC) was calculated. Fusion images, between T2-weighted sequences and diffusion-weighted images, were employed. No contrast material was injected since it had not been conclusive on the first MRI examination. No lesion could be seen on T2-weighted sequences (Figure 2a) and on T1-weighted fat suppressed images (Figure 2b). The lesion was only visible on DWI (Figure 3a) and on fused images (Figure 3b) as a 14 mm diameter nodular structure with high signal intensity. Furthermore, the apparent diffusion coefficient in that area was reduced as compared to the normal pancreatic parenchyma.

At surgery, the tumor was found at the localization defined by the MRI and enucleation was performed. Macroscopic features revealed a well-circumscribed soft mass of 16 mm in diameter (Figure 4). Microscopically, we observed a well-delimited but not encapsulated mass composed of uniform cells arranged in nests or in a trabecular pattern. Mitotic activity was low with less than 1 mitotic figure per 10 HPF and a Ki67 index <2%. Stromal hyalinization and fibrosis



**Figure 3.** Axial diffusion-weighted imaging (DWI) (a.) and fused image (b.) clearly show the tumor (arrows) with marked high signal intensity in the pancreatic tail.

were present but no amyloid deposition was observed (Figure 5a). Immunohistochemically, the tumor cells expressed neuroendocrine markers: chromogranin, synaptophysin and CD56 (Figure 5b). Postoperatively, plasma glucose and insulin concentrations remained within the normal range and the symptoms of hypoglycemia were completely resolved.

## DISCUSSION

Pancreatic neuroendocrine tumors (PNETs) are rare neoplasms of the pancreas originating from the islets of Langerhans or totipotential stem cells called nesidioblasts. PNETs are usually classified into functioning (causing classical endocrine syndrome) and non-functioning tumors. Insulinomas arise from islet beta cells and are the most common functioning neuroendocrine tumors of the pancreas responsible for typical hypoglycemic symptoms. More than 90% of insulinomas are benign, intra-pancreatic solitary tumors [1]. The detection of insulinomas is difficult because of the small size of the tumors (55-70% of insulinomas are less than 1.5 cm) [2]. For detection purposes, a combination of endoscopic ultrasonography with thin slice CT scan is generally used.

Because surgery remains the only curative treatment, accurate localization of the tumor is necessary. A variety of non-invasive imaging modalities have been used for preoperative localization, including CT, ultrasonography (US) and MRI. The latest studies have demonstrated that MRI is superior for identifying small pancreatic insulinomas when compared with other imaging techniques [3, 4]. Using the conventional sequences, small insulinomas usually have a low signal on T1-weighted sequences (especially on T1-weighted fat-suppressed sequences) and a high signal on T2-weighted sequences [4]. Some insulinomas containing abundant fibrous tissue may show low signal intensity on both T1- and T2-weighted images [5]. Insulinomas typically show strong enhancement in the arterial phase and prolonged enhancement relative to the normal pancreas in the delayed phase [6]. However, the timing

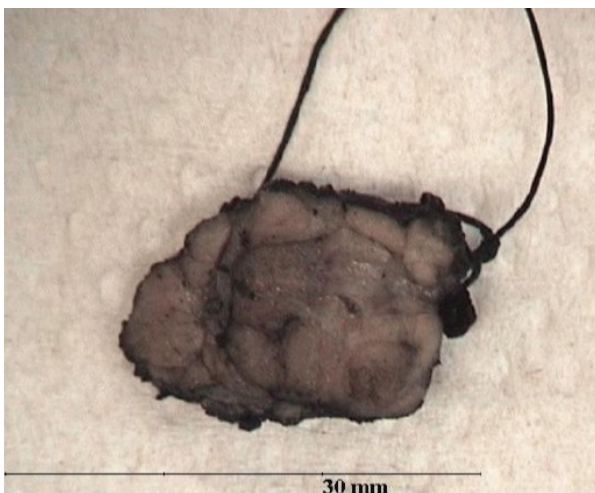


Figure 4. Macroscopy of the enucleated nodule.

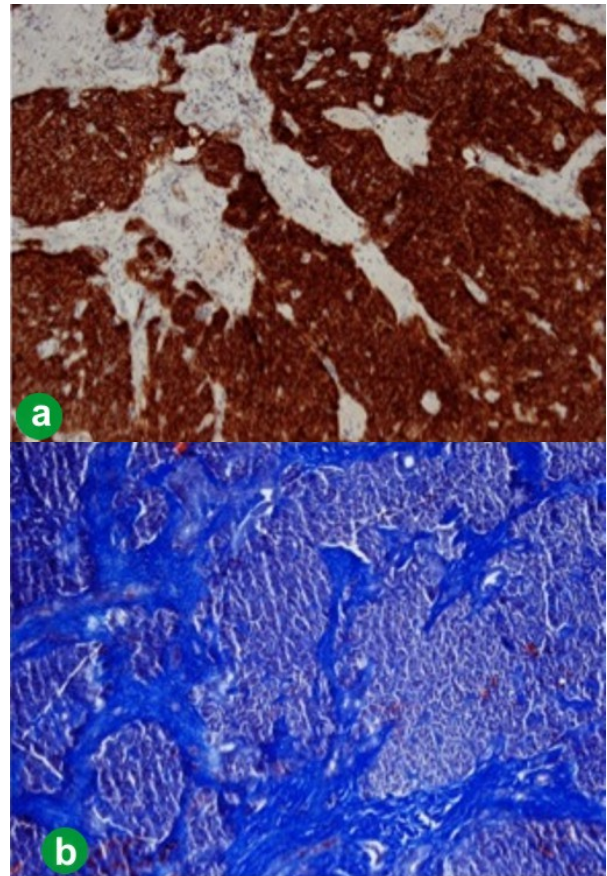


Figure 5. Microscopic section of the tumor. **a.** Immunohistochemical coloring with anti-CD56 antibodies showing the presence of neuroendocrine tumor cells. **b.** Blue stain, Masson trichrome, showing dense fibrous strands.

and the degree of enhancement can be highly variable, and enhancement of the lesion can be hard to demonstrate [5, 6]. It has also been reported that fibrosis in pancreatic tumors may reduce blood flow by compressing the arterial supply [7]. In our case, the lack of tumor enhancement could be related to the presence of dense fibrosis.

Recently, there has been a dramatic technical improvement in MRI assessment of pancreatic disease using DWI [8]. DWI is an MRI technique which detects changes in the molecular diffusion of water in biologic tissues. The degree of water motion can be quantified by calculating the ADC. Restricted water diffusion translates into a decreased signal on the ADC maps and will appear with high signal intensity on diffusion-weighted images. DWI has been used for years in brain MRI; however, it has only recently been extended to abdominal imaging. Abdominal DWI sequences are nowadays available on the latest scanners. Recent reports have suggested that high b-value DWI may be helpful in the detection and characterization of pancreatic tumors [9, 10]. It has been reported that reduced ADC is observed in most malignant lesions related to the histopathological features of the tumor [11]. In our case, the increased cellularity and dense fibrosis of the insulinoma might

be responsible for the lower ADC value as compared to that of a normal pancreas.

Our findings suggested that DWI may be a promising tool for detecting and localizing small insulinomas especially those with no hypervascular pattern because they can be detected only with great difficulty at CT. In order to confirm the interest of using DWI as shown by the present case report, we would recommend a clinical trial comparing CT, MR with DWI and endoscopy ultrasound in the detection and localization of insulinomas.

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**Conflict of interest** The authors have no potential conflicts of interest

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