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CASE REPORT

Unusual Magnetic Resonance Image of an Insulinoma with Extensive Desmoplastic Reaction

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ABSTRACT

Context Unlike other islet-cell tumors, insulinomas are usually benign. Most insulinomas have a high signal intensity on T2-weighted images and a low signal intensity on T1-weighted images, and are hyperintense on immediate post-gadolinium images. However, in rare cases, insulinomas may be hypointense on T2-weighted images and on immediate post-gadolinium images, mimicking a ductal adenocarcinoma.

Case report We present a case of a surgically proven insulinoma which was hypointense on both T2-weighted and immediate post-gadolinium T1-weighted images, but hyperintense on late phase T1-weighted images. Histopathological examination of the surgical specimen revealed a prominent desmoplastic reaction which accounted for the low signal on T2-weighted images and the contrast enhancement pattern. Delayed contrast enhancement reflects the desmoplastic component of this tumor.

Conclusions Insulinomas with an extensive desmoplastic reaction may appear hypo-intense on T2-weighted images with minimal enhancement on immediate post-gadolinium images. Late phase fat-suppressed T1-weighted post-gadolinium images may be useful in the detection of such tumors.

INTRODUCTION

Islet-cell tumors of the pancreas are rare tumors and account for only 1-5% of all pancreatic tumors [1]. The most common islet cell tumors are insulinomas, accounting for 70-75% of the total number. The estimated prevalence is around 1 per 1,000,000 inhabitants per year [2]. They are usually small (90% are less than 2 cm) and solitary (90%). Approximately 10% are associated with MEN type-I syndrome in which multiple insulinomas may occur [1, 3]. The median age at diagnosis is about 50, except in cases of insulinomas in patients with MEN 1 in whom the median age is the mid 20s. The male:female ratio is 2:3. The majority of insulinomas are located within the pancreas, and there is an equal distribution between the head, body and tail. Ectopic insulinomas (less than 1%) may be found in nearby structures such as the stomach and the duodenum [4].

The diagnosis is made on the basis of clinical, biochemical and pathological findings.The malignant nature of these tumors sometimes cannot be judged histologically, but is determined by the presence of metastases or local invasion [1, 4]. Therefore, radiological findings may play a critical role not only in the detection, but also in the characterization of these lesions as benign or malignant [1, 4]. Sensitivity and specificity, as well as the detection of extrapancreatic extension, are generally superior with MRI as compared to other imaging modalities [1]. Typically, insulinomas are hyperintense on T2-weighted images, hypointense on T1-weighted images and hyperintense on immediate post-gadolinium images [1]. The authors report the case of a 33-year-old male with an insulinoma

associated with a prominent desmoplastic reaction.

CASE REPORT

A 33-year-old male was admitted to the Emergency Department with loss of consciousness. His blood glucose level was 36 mg/dL (reference range: 70-110 mg/dL) on admission. He was given 10% dextrose intravenously and the symptoms resolved. The patient reported that he had a 2-year history of recurrent episodes of blurred vision, confusion, vertigo and headache. The symptoms worsened 1-3 hours postprandially and were relieved by food intake. The patient was subsequently admitted to the hospital for a further work-up. Laboratory analysis showed low serum glucose levels with high serum insulin levels. On prolonged fasting, serum glucose was 31 mg/dL, the concurrent plasma insulin level was 58.6 IU/mL (reference range: 8.9-28.4 IU/mL) and the C-peptide level was 7.00 ng/mL (reference range: 1.1-5.0 ng/mL). He had no family

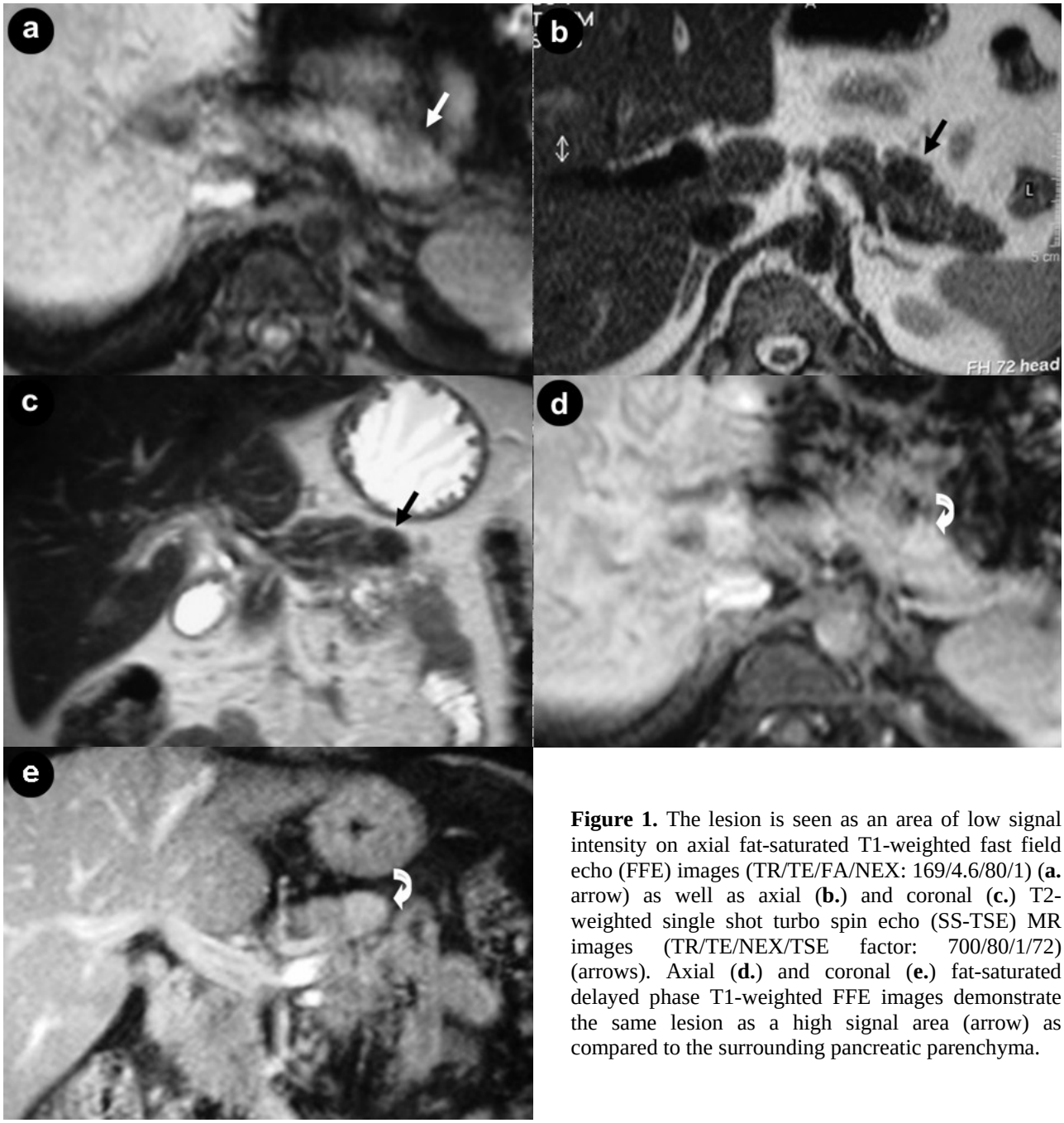

Figure 1. The lesion is seen as an area of low signal intensity on axial fat-saturated T1-weighted fast field echo (FFE) images (TR/TE/FA/NEX: 169/4.6/80/1) (**a.** arrow) as well as axial (**b.**) and coronal (**c.**) T2-weighted single shot turbo spin echo (SS-TSE) MR images (TR/TE/NEX/TSE factor: 700/80/1/72) (arrows). Axial (**d.**) and coronal (**e.**) fat-saturated delayed phase T1-weighted FFE images demonstrate the same lesion as a high signal area (arrow) as compared to the surrounding pancreatic parenchyma.

history of diabetes. Physical examination was unremarkable. An MRI of the abdomen was performed with a 1.5 tesla MR scanner (Gyroscan Intera; Philips Medical Systems, Eindhoven, The Netherlands) using a four element phased-array body coil. This system has a maximal gradient strength of 30 mT/m and a slew rate of 150 mT/m/msec. Routine precontrast MRI with a slice thickness of 6.5 mm and intersection gap of 1 mm yielded no evidence of disease. However, thin section precontrast MR imaging with a slice thickness of 3 mm, and an intersection gap of 0.3 mm demonstrated a mass lesion having a diameter of 12 mm in the junction of the pancreatic body and tail. The lesion was hypointense on axial T1-weighted breath-hold spoiled gradient echo (fast field echo: FFE) images with fat suppression (repetition time/echo time/flip angle/number of excitations, TR/TE/FA/NEX factor: 169/4.6/80/1) and T2-weighted single shot turbo spin echo (SS-TSE) (TR/TE/NEX/TSE factor: 700/80/1/72) images (Figure 1abc). After i.v. gadolinium (Magnevist, Schering, Germany) injection, the mass was hypointense relative to the surrounding pancreatic tissue during the arterial phase but hyperintense on the late phase (5^{th} minute) images (Figure 1de). MR imaging consisted of a multisection acquisition and an acquisition matrix of 128x256 pixels. Based on the clinical, laboratory and MRI findings, the lesion was diagnosed as an insulinoma and resected surgically. At surgery, a 1.5 cm solid tumor and a few peripancreatic lymph nodes of 0.4 cm diameter were enucleated. There was peripancreatic invasion. Therefore, the disease was classified as a malignant well-differentiated neuroendocrine tumor (according to the WHO classification) with an extensive desmoplastic reaction (Figure 2) ("desmoplastic reaction" refers to the abundant growth of fibrous or connective tissue) [5]. There was no microscopic vascular or perineural invasion. Congo red staining for amyloidosis was negative. The mitosis rate was 1 per 40 high-power fields. Immunohistochemical studies for chromogranin and cytokeratine-18 were positive, indicating a neuroendocrine tumor. After surgery, the patient had both clinical and biochemical remission for a 2 year period.

DISCUSSION

Once the diagnosis of insulinoma is made based on clinical and biochemical findings, imaging studies are necessary in order to look for evidence of malignant features as well as to define the surgical approach [1]. Numerous radiological modalities can be utilized for the detection of these tumors with varing success; however, non-invasive methods must be used initially [6]. Dynamic contrast-enhanced CT (especially biphasic CT) and MRI (especially precontrast fat-saturated T1- and T2-weighted and dynamic post-gadolinium T1-weighted images) are common noninvasive radiological methods used in the evaluation of these tumors. Since most insulinomas are hypervascular and small at presentation, thin-section CT and MRI techniques, and dynamic post-contrast examination should be used [1, 7]. Typically, insulinomas are seen as sharply defined, round or oval masses within the pancreas. They are hyperintense on MRI and hyperdense on CT in relation to normal pancreatic tissue during the arterial and capillary phases of the contrast bolus, which accounts for the hypervascular nature of these tumors [7, 8].

On pre-contrast CT images, insulinomas are usually isodense to normal pancreatic tissue; as a result, they are not usually seen unless

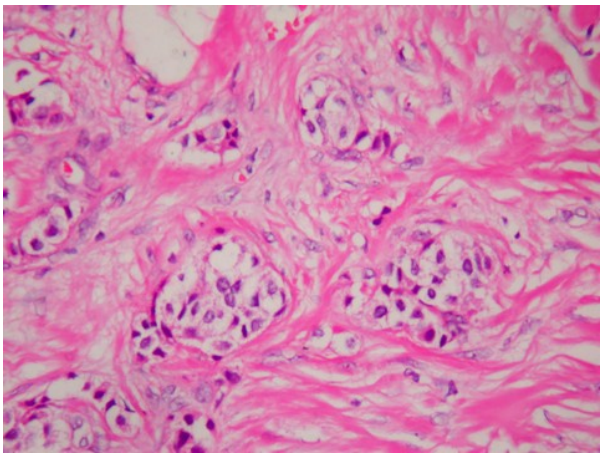

Figure 2. Microscopic section shows extensive collagen fibers within the lesion (H&E x40).

they alter the contour of the pancreas [1]. However, a few cases of hyperdense insulinomas which were cystic or calcified have been described on pre-contrast CT [6]. Kurosaki *et al*. [9] reported a case with a hyperdense insulinoma in which the presence of psammoma bodies was observed. Calcification, which may occur in approximately 20% of pancreatic endocrine tumors, is more common in malignant than in benign neoplasms [1, 7].

On MRI, precontrast T1- and T2-weighted fat suppressed images as well as immediate post-gadolinium spoiled gradient echo images have been found useful [1, 7]. Mori *et al*. [10] indicated that short tau inversion recovery (STIR) imaging can be used, even though it has some limitations. The normal pancreatic parenchyma and most other pancreatic tumors contain a higher concentration of aqueous protein and hydrogen protons than islet-cell tumors. Thus, relative to the pancreatic parenchyma, the majority of insulinomas are of higher signal intensity on T2-weighted spin echo (SE) images and of lower signal intensity on T1-weighted SE images [1, 7]. However, in a few cases, insulinomas are hypointense on T2-weighted images. In these rare cases, the insulinomas may be desmoplastic or fibrotic; as a result, they are hypointense on T2-weighted [11, 12] and STIR [10] images, with minimal enhancement on early post-gadolinium images. Such tumors may mimic ductal adenocarcinomas. Contrast enhancement on immediate post-gadolinium images and hyperintensity on T2-weighted images distinguish these endocrine tumors from ductal adenocarcinomas of the pancreas [1, 7]. The hypointensity on the T2-weighted images of our case was explained by the presence of a prominent desmoplastic reaction with abundant fibrous tissue in the tumor. High collagen content is known to shorten T2 relaxation time [10]. Recent studies demonstrated that, if insulinomas are too small [10, 13], cystic or calcified [6], they may be hypovascular. The lesion in our case was not small, cystic or calcified; however it was hypovascular as shown by the immediate post-gadolinium images. Iglesias *et al*. [13] reported a hypovascular insulinoma in which amyloid deposits were observed. They attributed the hypovascularity of the lesion to the presence of abundant amyloid deposits and a relatively smaller vascular volume. The lesion in our case did not stain positive for amyloid with Congo red. However, similar to their case, the prominent desmoplastic reaction with a small number of vessels could explain the hypovascular appearance of our case. The marked vascular blush on delayed images may be due to the presence of a desmoplastic composition of this tumor. Lesions with prominent fibrous tissue content (such as cholangiocarcinoma) are known to exhibit prolonged enhancement on delayed phase images. Therefore, post-gadolinium delayed phase fat-saturated T1-weighted images are useful for the detection of these tumors [12].

C-peptide (above 6.1 ng/mL) and insulin levels, large size (above 2.6 cm), the presence of central necrosis, invasion of the retroperitoneal structures, and discrete nodular calcification are suggestive of malignancy in functioning tumors. The liver and the lymph nodes are the most common sites for metastatic dissemination. As in the primary tumor, liver and regional lymph node metastases tend to be hypervascular. Therefore, they are easier to detect during the arterial phase [1, 14].

Non-functioning tumors are usually larger than functioning tumors at presentation. Therefore, cystic degeneration, central necrosis and hemorrhage are more common when compared to their functioning counterparts. They demonstrate enhancement patterns similar to functioning tumors. The imaging features which may aid in the differentiation of nonfunctioning endocrine tumors from pancreatic ductal adeno-carcinomas include: the presence of calcification, lack of vascular encasement and lack of ductal encasement. Also, central necrosis and cystic degeneration are less common with non-functioning endocrine tumors [1, 7].

On transabdominal ultrasonography, the reported success rates for the detection of

insulinomas range from 9 to 63% [6]. The lesions usually appear well-demarcated, round or oval, and hypoechoic [2, 6, 7]. Intraoperative ultrasonography combined with palpation and endoscopic ultrasonography is reported to identify more than 90% and 82% of tumors, respectively [2]. Recently, endoscopic ultrasound-guided fine-needle aspiration biopsy was utilized in a case of an insulinoma [4].

Successful selective arteriographic localization rates vary between 63 and 90% for insulinomas. Typically, insulinomas are hypervascular and exhibit a homogeneous dense blush during the capillary phase [6, 7]. Arteriography, combined with both calcium injections to stimulate insulin release from the neoplastic tissue and simultaneous measurements of insulin level, is currently considered to be obsolete as a routine investigation [4, 6]. It is associated with a high complication rate (10%), but may be employed when all other imaging procedures fail and surgical exploration findings are negative [4].

In conclusion; insulinomas may be desmoplastic or fibrotic in rare cases. As a result, they may appear hypointense on T2-weighted images with minimal enhancement on immediate post-gadolinium images. Fat-suppressed T1-weighted post-gadolinium delayed phase images may be useful for the detection of such tumors.

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Abbreviations FA: flip angle; FFE: fast field echo; NEX: number of excitations; SE: spin echo; SS-TSE single shot turbo spin echo; STIR short tau inversion recovery; TE: echo time; TR: repetition time

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