Abdominal Imaging

Published online: 28 May 2008

Abdom Imaging (2008) 33:571–574
DOI: 10.1007/s00261-007-9278-1

Peritumoral steatosis associated with insulinomas: appearance at imaging

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Abstract

We report three patients with insulinoma tumors and distinct peritumoral steatosis, well demonstrated with several imaging modalities. This unique appearance can aid in pre-operative diagnosis and guide biopsy.

Key words: Insulinoma—Steatosis—MRI—CT—Ultrasound

Insulinomas are a rare type of pancreatic islet cell neoplasm with estimated incidence of four cases per 1 million person-years [1]. Clinical symptoms of hypoglycemia related to endogenous insulin production are the hallmark of insulinoma. Such symptoms include fatigue, weakness, tremulousness, and hunger; such symptoms become worse with fasting [2]. The diagnosis of insulinoma should principally be based on clinical and biochemical findings. Imaging methods are then used to localize the tumor and provide anatomic information for subsequent surgical resection.

On CT imaging, insulinomas are typically circumscribed nodules, which become hyperdense in the early phases of intravenous contrast enhancement, although 20% may only be seen in retrospect [3]. Similarly, on MR imaging, islet cell neoplasms usually enhance early after gadolinium administration although the overall imaging appearance can be variable, particularly depending on tumor size [4]. On ultrasound imaging, insulinomas typically appear as solitary, small, hypoechoic solid masses, both by transabdominal and intraoperative imaging.

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Approximately 90% of insulinomas are histologically benign, with the remainder most commonly metastasizing to lymph nodes or the liver [1, 5, 6]. When present hepatic islet cell metastases are usually hyperenhancing [7].

In this report, we demonstrate an interesting imaging observation seen with both primary and metastatic insulinomas. Specifically, we observed gross fat surrounding both primary pancreatic insulinoma and hepatic insulinoma metastases using ultrasound, CT, and MR imaging.

Case reports

Case 1 (Fig. 1)

A 57–year-old female presented with 10 months of neuroglycopenic symptoms, described by the patient as "getting goofy", including amnestic episodes of confusion, staggering, and unresponsiveness. She was found to be profoundly hypoglycemic during these episodes and, after 7 months of symptoms, underwent a contrast-enhanced CT, which showed a 1.1 cm enhancing mass in the body of the pancreas with adjacent gross fat in the pancreatic parenchyma. With the assistance of intraoperative ultrasound, a distal pancreatectomy was performed with pathology showing insulinoma with adjacent steatosis in the pancreas. Her blood sugars normalized post-operatively.

Case 2 (Fig. 2)

A 74-year-old male with recent diagnosis of prostate cancer presented with presumptive diagnosis of hepatocellular carcinoma after staging CT with intravenous contrast showed incidental enhancing masses in the liver. Interestingly, over the 2 weeks prior to presentation, he

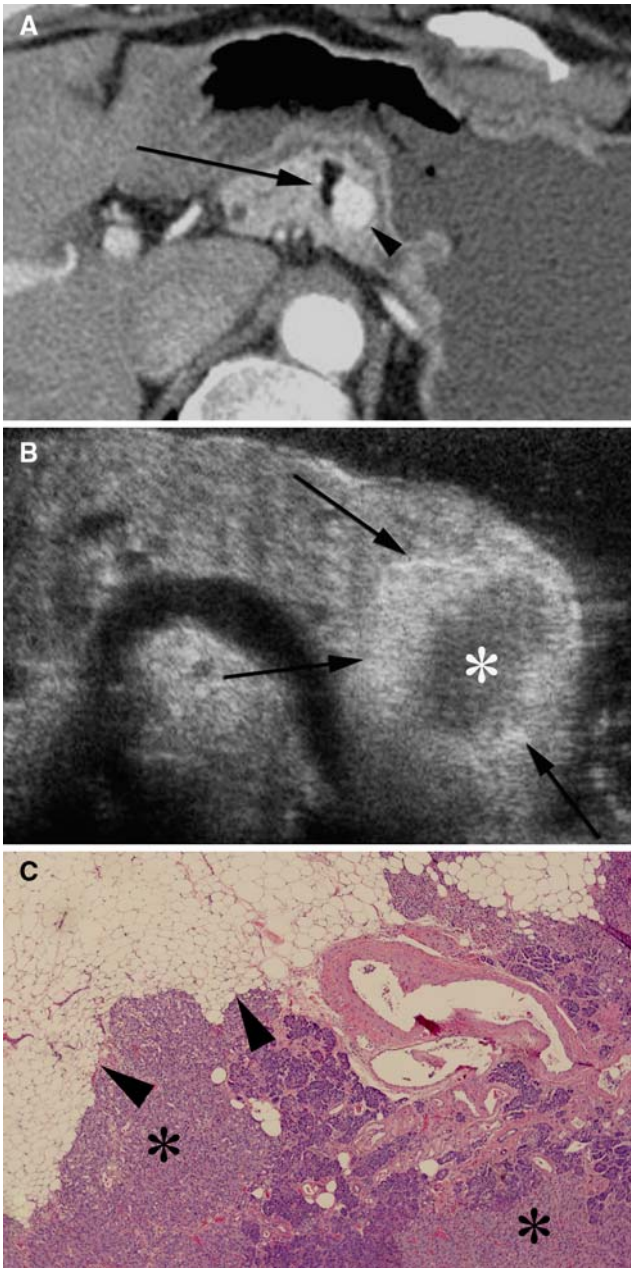

Fig. 1. 57-year-old female with pancreatic insulinoma. (**A**) Axial contrast-enhanced CT during pancreatic-phase enhancement shows a 1.1 cm enhancing mass in the body of the pancreas with gross fat along its right lateral margin (*arrow*). (**B**) Intra-operative ultrasound image shows the hypoechoic insulinoma in the body of the pancreas (*asterisk*) and surrounding hyperechoic fatty change in the pancreatic parenchyma (*arrows*). (**C**) Photomicrograph of H&E specimen showing insulinoma (*asterisks*) with adjacent fatty pancreas (*arrowheads*).

reported spells of confusion and diaphoresis, relieved with food intake. A subsequent MRI showed these liver tumors as well as an infiltrating 4 cm mass in the tail of the pancreas (Fig. 2). Chemical shift MR imaging showed hepatic peritumoral signal drop-out on the out of phase images, consistent with hepatic steatosis. Ultrasound-guided biopsy was performed, showing hepatic insulinoma metastases. He was taken to surgery where a distal pancreatectomy and splenectomy was performed for an infiltrating insulinoma, and the hepatic tumors were resected or treated with radiofrequency ablation.

Case 3 (Fig. 3)

A 58-year-old male, status-post distal pancreatectomy for symptomatic insulinoma 3 years prior, presented with recurrence of hypoglycemic symptoms including altered vision and diminished concentration. Contrast-enhanced CT showed four small intensely enhancing liver masses with surrounding hepatic fat. Initial attempt at ultrasound-guided liver biopsy showed only hepatic steatosis. Repeat ultrasound-guided biopsy directed to the discrete hypoechoic element confirmed metastatic insulinoma with adjacent hepatic fatty changes. The patient then underwent both surgical resection and intraoperative RFA of a total of ten hepatic metastases.

Comment

The finding of localized fat surrounding hepatic insulinoma tumors is likely due to the known effect of insulin to increase the synthesis and accumulation of triglyceride in hepatocytes [8]. This is supported by our imaging studies, which showed localized fat surrounding the hepatic tumors in our two patients with hepatic metastases, with sparing of more distant liver parenchyma. We can only hypothesize a similar mechanism in the pancreas, although some have suggested that peritumoral ischemia or duct obstruction can cause fatty changes in the pancreas [9].

There have been sporadic case reports, which also describe this observation. Hoshiba et al. described wedge-shaped fat peripheral to a non-functioning hepatic islet cell metastasis, which subsequently stained positive for insulin following resection [10]. Sumiyoshi et al. also described the ultrasound and MR appearance of focal fat surrounding hepatic insulinoma metastases in a symptomatic 44-year-old woman [11]. Her symptoms related to hypoglycemia resolved following angiographic embolization. Chemical shift MR imaging has also been used to show a rim of hepatic steatosis surrounding an insulinoma metastasis [12]. Eriguchi et al. reported focal fatty replacement of the body and tail of the pancreas associated with a pancreatic insulinoma in a woman with a 3-month history of hypoglycemic symptoms [9]. In addition to demonstrating peritumoral steatosis surrounding a hepatic insulinoma metastasis, Fregeville et al. showed a steatosis-deficient zone surrounding a hepatic glucagonoma metastasis [13]. This relative fat-deficient zone was thought to be due to increased hepatocyte lipolysis related to local effect of glucagon.

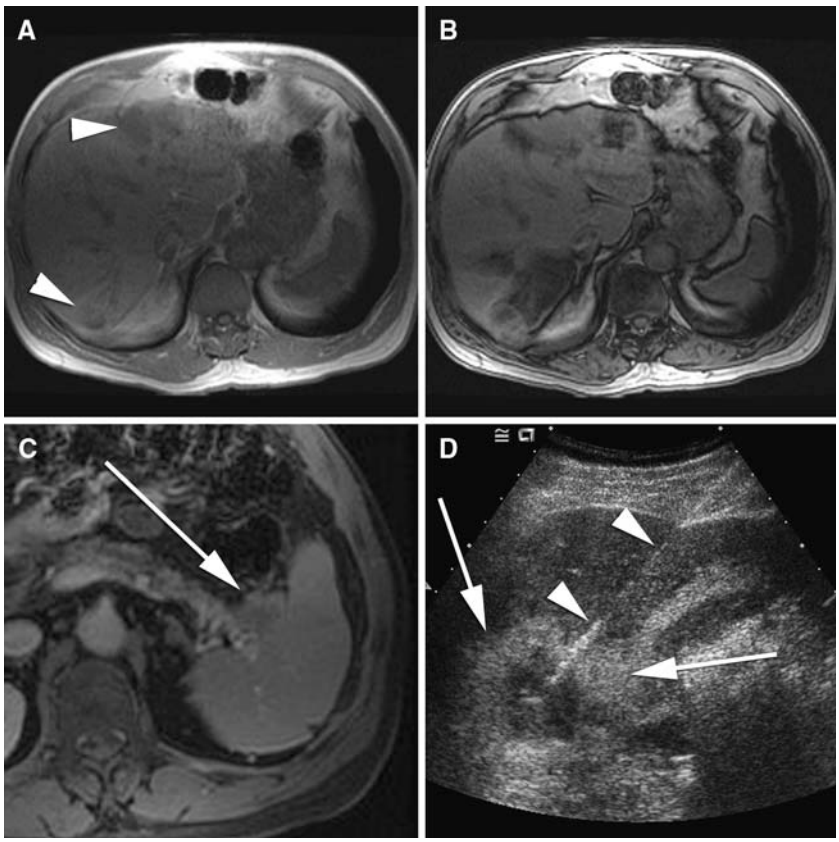

Fig. 2. 74-year-old male with metastatic insulinoma. (**A**) Axial in-phase MRI image (TR 150, TE 4.4) shows subtle hypointense masses in the liver (*arrowheads*). (**B**) Axial out-of-phase MRI image (TR 150, TE 2.2) shows considerable signal drop-out adjacent the liver masses, consistent with steatosis. (**C**) Axial post-gadolinium enhanced MRI image shows infiltrating 4 cm mass in the tail of the pancreas (*arrow*), invading into spleen. (**D**) Longitudinal ultrasound image showing biopsy needle (*arrowheads*) traversing hyperechoic steatosis (*arrows*) with tip in hypoechoic insulinoma metastasis.

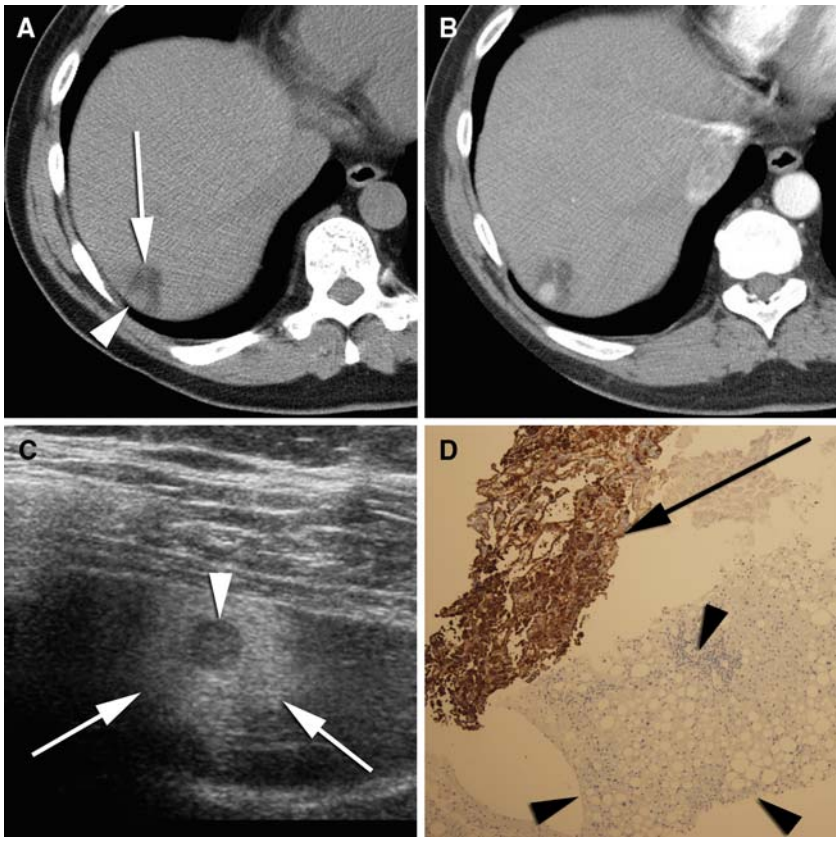

Fig. 3. 8-year-old male with recurrent insulinoma. (**A**) Axial noncontrast CT image shows subtle isodense nodule in segment 7 of the liver (*arrowhead*) with adjacent focal steatosis (*arrow*). (**B**) Axial contrast-enhanced CT image during the arterial phase shows enhancement of the liver nodule, typical of islet cell hepatic metastases. (**C**) Longitudinal ultrasound image of metastasis inferiorly in the right lobe of the liver shows focal hyperechoic fatty change (*arrows*) surrounding well defined hypoechoic metastasis (*arrowhead*). (**D**) Photomicrograph of biopsy specimen showing positive immunohistochemical insulin staining of tumor (*arrow*) with adjacent fatty liver (*arrowhead*).

Our experience with three patients further reinforces this unique observation related to insulin-producing islet cell tumors. Hepatic fatty changes resulting from insulin exposure are not unique to these neoplasms. Hepatic subcapsular steatosis has been described in 7 of 39 (18%) of patients who received intraperitoneal insulin with their peritoneal dialysate [14]. This fatty change was diagnosed based on CT imaging.

We have not seen peritumoral fat surrounding extensive hepatic islet cell metastases when such tumors stain positive for insulin. We presume this is related to the degree of insulin production proportional to tumor burden. In other words, the tumors producing a high concentration of insulin will cause sufficient adjacent fatty changes to be visible by imaging, and cause the characteristic hypoglycemic syndrome at a relatively low degree of tumor burden. Obviously, one could not survive with bulky, characteristic insulinomas metastases due to profound hypoglycemia.

In conclusion, we have demonstrated gross fatty changes surrounding insulinoma tumors in the pancreas and liver using ultrasound, CT, and MRI. This finding is important in that it suggests the diagnosis of metastatic insulinoma in the setting of hypervascular hepatic metastases, and directs image-guided biopsy towards the tumor nodule and away from adjacent focal fatty liver, and thus avoids false-negative biopsy results.

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