CASE REPORT

A Wolf in Sheep’s Clothing:
A Non-Functioning Islet Cell Tumor of the Pancreas
Masquerading as a Microcystic (Serous Cystic) Adenoma

Henning Gerke1,5, Michaell F Byrne1, Huiwen Bill Xie2, Erik K Paulson3, Douglas S Tyler4, John Baillie1, Paul S Jowell1

1Division of Gastroenterology, Department of Medicine; 2Department of Pathology; 3Department of Radiology; 4Department of Surgery, Duke University Medical Center. Durham, NC, USA. 5I Medical Department, Johannes Gutenberg University. Mainz, Germany

ABSTRACT

Context The endosonographic appearance of a microcystic “honeycomb” lesion of the pancreas usually indicates a serous cystic adenoma.

Case report We report a case of a non-functioning islet cell tumor that has the typical microcystic “honeycomb” appearance of a serous cystic adenoma. The implications for endoscopic ultrasound diagnosis and management of cystic pancreatic lesions are discussed.

Conclusion Islet cell tumors are a rare differential diagnosis of microcystic pancreatic lesions. If fine needle aspiration remains non-diagnostic preoperative distinction from serous cystic adenomas may be impossible.

INTRODUCTION

When cystic lesions of the pancreas are encountered, it is important to distinguish those with malignant potential such as mucinous cystic adenomas and neuroendocrine tumors from serous cystadenomas (microcystic adenomas), in which malignant degeneration is rare. Resection in pancreatic microcystic adenomas is not always mandatory, especially in asymptomatic patients [1, 2]. Endoscopic ultrasound (EUS) is increasingly used to characterize these lesions; however, there is significant overlap in the endosonographic features of benign and malignant or potentially-malignant cystic pancreatic lesions [3]. Therefore, accurate preoperative diagnosis based on radiological or endosonographic criteria is difficult or impossible unless the lesion has a typical microcystic “honeycomb” appearance that is characteristic of a serous cystadenoma (SCA) [1, 4, 5, 6, 7], leaving little doubt about the diagnosis. We present a case of a nonfunctioning islet cell tumor whose endosonographic appearances mimicked those of an SCA.

CASE REPORT

A 62-year-old Caucasian man was diagnosed with a rectal cancer (T1 M0 N0) during investigation of heme positive stool. The staging abdominal computed tomography (CT scan) revealed a 4x4.5 cm multicystic lesion located in the pancreatic body. He had no history of pancreatitis or diabetes. He denied significant alcohol intake, abdominal pain,
weight loss or steatorrhea. The family history was negative for pancreatic disease or malignancy. Routine laboratory studies including complete blood count, liver function tests, and serum lipase and amylase were within normal limits.

The patient was referred to Duke University Medical Center (DUMC) for further evaluation of his pancreatic lesion by endoscopic ultrasound (EUS), which was performed using a linear echoendoscope (Pentax EG-3630U, Orangeburg, NY, USA). The pancreatic lesion had a microcystic “honeycomb” appearance (Figure 1) suggestive of an SCA. EUS-guided fine needle aspiration of the lesion was performed using a 22 gauge needle. Cytology was non-diagnostic; it showed a hypocellular aspirate comprised of debris and rare degenerative cells without evidence of malignancy. Analysis of cystic fluid showed a normal amylase of 42 IU/L (reference values: 30-110 IU/L). Other cyst fluid markers were not obtained.

The patient underwent an uncomplicated transanal excision of his rectal cancer. A follow-up CT scan did not show any change in size of the multicystic pancreatic mass (Figure 2) and this was subsequently removed by a distal pancreatectomy and splenectomy. The tumor was well circumscribed and encapsulated with a maximum dimension of 6 cm. Histology of the tumor showed a prominent microcystic pattern admixed with solid areas (Figure 3a). Tumor nuclei were round or ovoid, with a fairly distinctive, finely stippled chromatin pattern and an inconspicuous nucleolus (Figure 3b). No atypical features such as pleomorphism, necrosis or increased mitotic activity were identified. Immunohistochemical studies showed that the tumor cells were positive for chromogranin and synaptophysin (Figures 3c and 3d). The pathologic diagnosis was islet cell tumor.

Preoperative hormone levels had not been measured and an octreotide scan had not been performed. The patient did not have symptoms consistent with a clinical syndrome of a functioning neuroendocrine tumor, nor did he have evidence of multiple neuroendocrine syndrome (MEN) type 1. He did well postoperatively, and on a follow-up CT 26 months later there was no evidence of local recurrence or distant metastasis.

DISCUSSION

Pseudocysts constitute 80-90% and cystic neoplasms 10-15% of all cystic lesions seen in the pancreas. Most cystic neoplasms are mucinous cystadenomas and SCAs. Rare pancreatic tumors such as islet cell tumors can have a cystic appearance [8]. SCAs are distinguished from other cystic pancreatic

Figure 1. Transgastric EUS using a linear echoendoscope showing a microcystic lesion in the pancreatic body.

Figure 2. CT scan performed with intravenous and oral contrast shows a thin walled cystic mass extending anterior from the body of the pancreas. The internal septations are not seen on this scan.
neoplasms by their benign behavior; serous cystadenocarcinomas have been reported [9, 10, 11, 12] but they are rare. Consequently, the malignant potential of SCAs is considered low and resection may not be warranted in asymptomatic patients [1]. Therefore, it is important to obtain an accurate preoperative diagnosis if this neoplasm is suspected. Despite advances in cross-sectional imaging, it remains difficult to distinguish one type of cystic lesion from another [13, 14, 15, 16, 17]. Due to its superior spatial resolution, EUS is an excellent tool for characterizing cystic lesions of the pancreas [4]. However, the EUS features of neoplastic and non-neoplastic cystic pancreatic lesions and those with and without malignant potential overlap and interobserver agreement is poor [3]. An exception to this diagnostic dilemma is the classical microcystic lesion that characterizes a SCA. It consists of a multicystic mass that sometimes contains a central scar with a characteristic “sunburst” type calcification seen on CT scanning [18, 19, 20]. The innumerable cysts are usually smaller than 2 cm and give the lesions its typical “Swiss cheese” or “honeycomb” appearance. The sensitivity of this morphologic finding in SCA is compromised by the fact that the classical honeycomb pattern occurs in only 20-50% of cases [21, 22, 23]. The term “microcystic adenoma” which has been used synonymously with SCA has been criticized because oligocystic lesions are common and...
macrocystic variants have been described [1, 13, 21, 24, 25, 26, 27, 28, 29, 30]. This explains why the correct preoperative diagnosis of SCA was obtained in as few as 20-40% of cases in some series [13, 15, 24]. However, if present, the classical features of the “honeycomb lesion” are usually considered conclusive for diagnosis. The presented case makes us question whether this is unequivocally true, if even typical SCAs may be indistinguishable from other neoplasms such as an islet tumor.

Islet cell tumors are rare neoplasms that can present as cystic pancreatic masses [8, 18, 22, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43]. They constitute 0.7% to 3.4% of cystic pancreatic neoplasms [8, 35, 44, 45, 46]. Buetow et al. [42] found cystic changes in 42 out of 124 islet cell tumors; cysts were more common in nonfunctioning than in functioning islet cell tumors. In a series by Ligneau et al. [41], 7 out of 13 cystic islet cell tumors were characterized as microcystic. Histology of these tumors suggests that vesicular arrangement of tumor cells is responsible for the microcystic appearance. Two of the microcystic islet cell tumors described in the series by Ligneau et al. [41] were preoperatively diagnosed as serous adenomas.

We conclude that islet cell tumors should be considered in the differential diagnosis of the pancreatic “honeycomb lesion”. Even the radiological appearance of sunburst type calcification has been described in an insulinoma [47], indicating that this radiological appearance is also less specific for an SCA than previously thought. In contrast to the far more common SCAs, islet cell tumors are frequently malignant and hence warrant resection. Fine needle aspiration (FNA) can provide additional information to allow these tumors to be distinguished from each other. However, the cytology is often non-diagnostic as in the case presented here. On rare occasions when cyst fluid is demonstrated to contain high levels of insulin, a functioning insulinomas is the likely diagnosis, but there is no difference between islet cell tumors and SCAs with respect to other cyst fluid markers [44]. Cyst insulin levels have not been investigated in nonfunctioning islet cell tumors [8]. The small size of the cysts makes aspiration of sufficient amounts of cyst fluid for analysis difficult. If the diagnosis remains in doubt and the patient is a good surgical candidate, resection is indicated. In patients with increased surgical risk or those with cysts in the pancreatic head that would require a Whipple’s procedure, watchful waiting may be acceptable, acknowledging the minimal risk of malignant transformation of an SCA and the small risk that a potentially malignant islet cell tumor has been missed.

Received April 3rd, 2004 - Accepted April 14th, 2004

Keywords Diagnostic Imaging; Endosonography; Insulinoma; Pancreatic Neoplasms

Abbreviations SCA: serous cystadenoma

Correspondence
Henning Gerke
I Medical Department
Johannes-Gutenberg University
Langenbeckstr. 1
55131 Mainz
Germany
Phone: +49-6131.177.275
Fax: +49-6131.175.595
E-mail address: henninggerke@web.de

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