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Cystic Tumors of the Pancreas: Evaluation by Ultrasonography and Computed Tomography

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Abstract. The personal series of 30 cystic tumors of the pancreas [12 serous cystic tumors (SCT) and 18 mucinous cystic tumors (MCT)] is presented. All neoplasms were evaluated with ultrasonography (US) 28 of 30 with computed tomography (CT); the tumoral histotype could be correctly defined in 73% of cases (seven of 12 SCT and 15 of 18 MCT). Percutaneous fine-needle aspiration (FNA) with diagnostic aims (preparation of cytological smears and/or biochemical assays) was performed in only 10 of 30 cases, yielding a 100% sensitivity; on the whole, the combined use of imaging modalities and FNA allowed correct characterization of the cystic tumors in 27 of 30 cases (90%). The usefulness of a precise diagnostic workup of these neoplasms is emphasized, due to their prognostic and therapeutic outcome.

Key words: Pancreas, tumors – Pancreas, cystic tumors – Pancreatic tumors, US – Pancreatic tumors, CT.

Pancreatic cystic tumors are uncommon neoplasms which can be divided into two categories with different pathologic characteristics, as well as evolution and prognosis: serous cystic tumors (SCT), always benign; and mucinous cystic tumors (MCT), often malignant and, otherwise, nearly always potentially malignant [1, 2].

SCT are often large tumors (mean diameter, 10 cm; ranging from 1–25 cm) formed by small cysts of less than 1 mm up to 20 mm in diameter. SCT are also called microcystic tumors. The cysts have a glycogen-rich serous fluid content and are lined by a single layer of cuboidal cells also rich in glycogen; they are separated by connective tissue septa, sometimes around a central, occasionally calcified, fibrous scar [1]. MCT are usually also very large (mean diameter, 10.5 cm; ranging from 2–19 cm) formed by cysts not less than 2 cm in size, uni-or multilocular, rarely connecting with the pancreatic ductal system [3]. The cysts have a thick mucinous fluid content and are lined by a single layer or multiple layers of columnar cells with a mucin-rich cytoplasm. Not uncommon are papillary projections within the cysts, very variable in number; a fibrous capsule 1–20 mm thick, eventually with focal calcifications, is constantly present [2].

Sometimes SCT may show cysts up to 8 cm in diameter [4], usually peripherally located [5] moreover, although rarely, multilocular MCT may present some cysts less than 2 cm in size [6, 7].

There are many contributions in the literature on the use of ultrasonography (US) and computed tomography (CT) for the diagnosis of these rare tumors [4–28]; however, there is one single paper discussing a large series of tumors studied with both imaging modalities within a single institution [7].

The aim of this paper is to describe the personal experience (30 cases collected between January 1981 and September 1989) stressing the possibilities and limits of both US and CT in the diagnosis of these tumors.

Materials and Methods

The personal series consists of 30 cases, 12 SCT and 18 MCT (six cystadenomas and 12 cystadenocarcinomas). SCT, ranging between 2.5 and 14 cm in diameter (median 6.1 cm), were located in the head (five cases), neck (two cases), bodytail (two cases), and tail (three cases). MCT, ranging between 3 and 15.5 cm in diameter (median 8.6 cm), were located in the head

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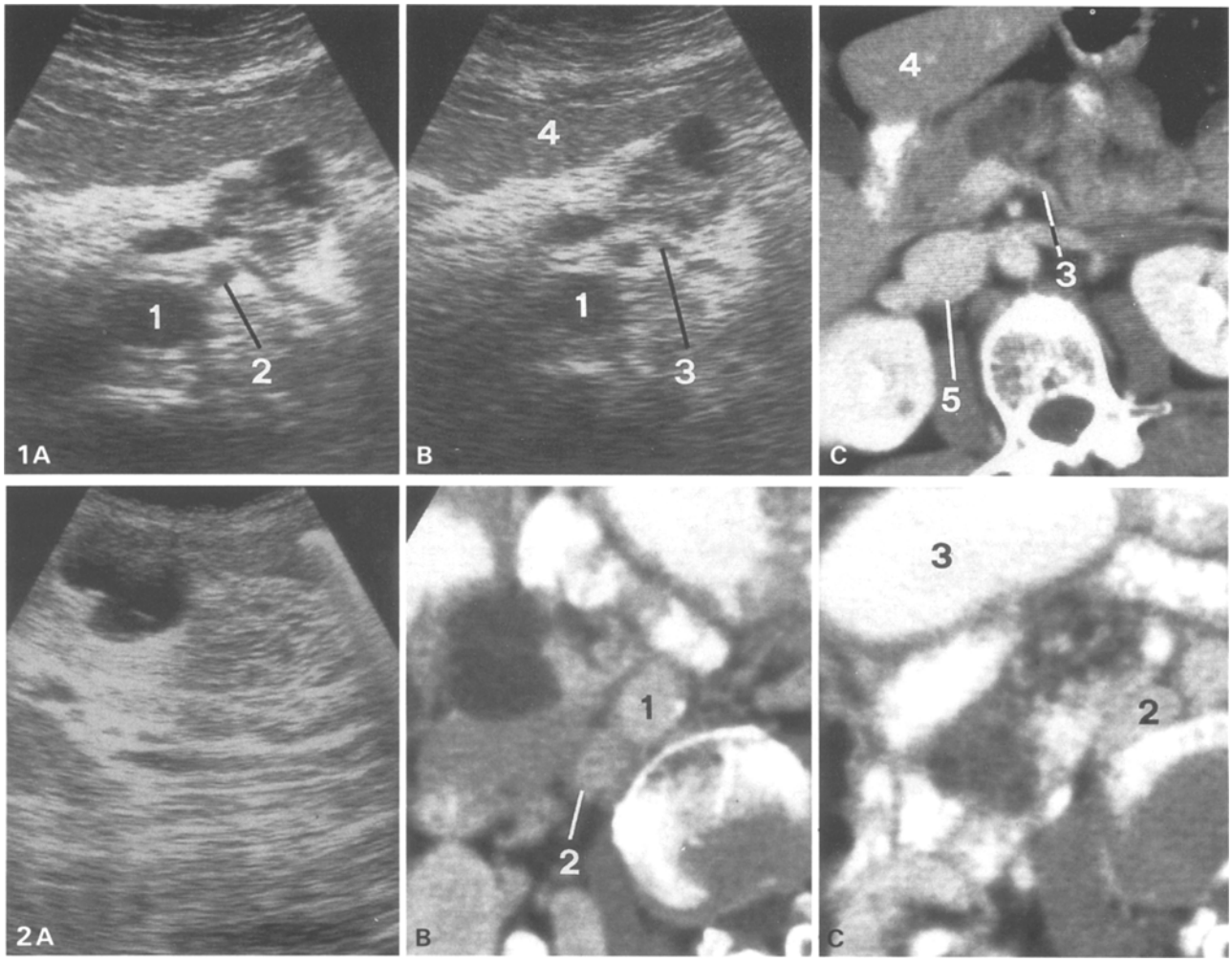

Fig. 1. SCT. **A, B** US: contiguous axial scans. Mass of the pancreatic body, in which multiple small cysts can be seen (honeycomb appearance) and in its most anterior part, a cyst slightly more than 1 cm in diameter. **C** CT. The tumor, in which multiple small low-density areas can be recognized (cystic lesions), is well separated from the adjacent parenchyma. *1*, aorta; *2*, superior mesenteric artery; *3*, splenoportal venous axis; *4*, liver; *5*, inferior vena cava.

Fig. 2. SCT. **A** US: longitudinal scan. Mass of the pancreatic head presenting, in its caudal part, multiple small cysts and, in its cranial part, a large cyst about 4 cm in diameter. **B** CT: cranial scan. The large cyst can be seen. **C** CT: caudal scan. Typical honeycomb appearance. *1*, aorta; *2*, inferior vena cava; *3*, stomach.

(five cases), body (one case), bodytail (nine cases), tail (one case) as well as two that involved nearly the whole pancreas.

All patients underwent US, 28 of 30 CT, and 10 of 30 US-guided fine-needle aspiration (FNA). Only five of 30 patients had selective abdominal angiography. One patient also had magnetic resonance imaging (MRI).

Ten of 12 patients with SCT underwent radical surgery (three pancreatoduodenal resections, two segmental resections of the pancreatic neck, and five distal pancreatectomies with splenectomy). In the remaining cases, cystojejunostomy was performed in one patient because of the tumor size and large peripheral cysts; in another case, where the tumor was located in the pancreatic head, gastroenteroanastomosis with biliary diversion was performed due to the patient's age.

Thirteen of 18 patients with MCT had radical surgery (two pancreatoduodenal resections, one segmental resection of the pancreatic body, one distal pancreatectomy without and nine with splenectomy). The remaining five patients had palliative diversion operation due to the infiltration of peripancreatic vessels and/or to the presence of distant metastases.

Results

Serous Cystic Tumors

Eight of the 12 SCT showed a honeycomb appearance both at US and CT, due to the presence of small contiguous cysts (Fig. 1 A–C); in three cases, both modalities showed the presence of cysts around a central solid connective tissue area with a calcification; in two cases, the tumor, with a honeycomb appearance, had large cysts more than

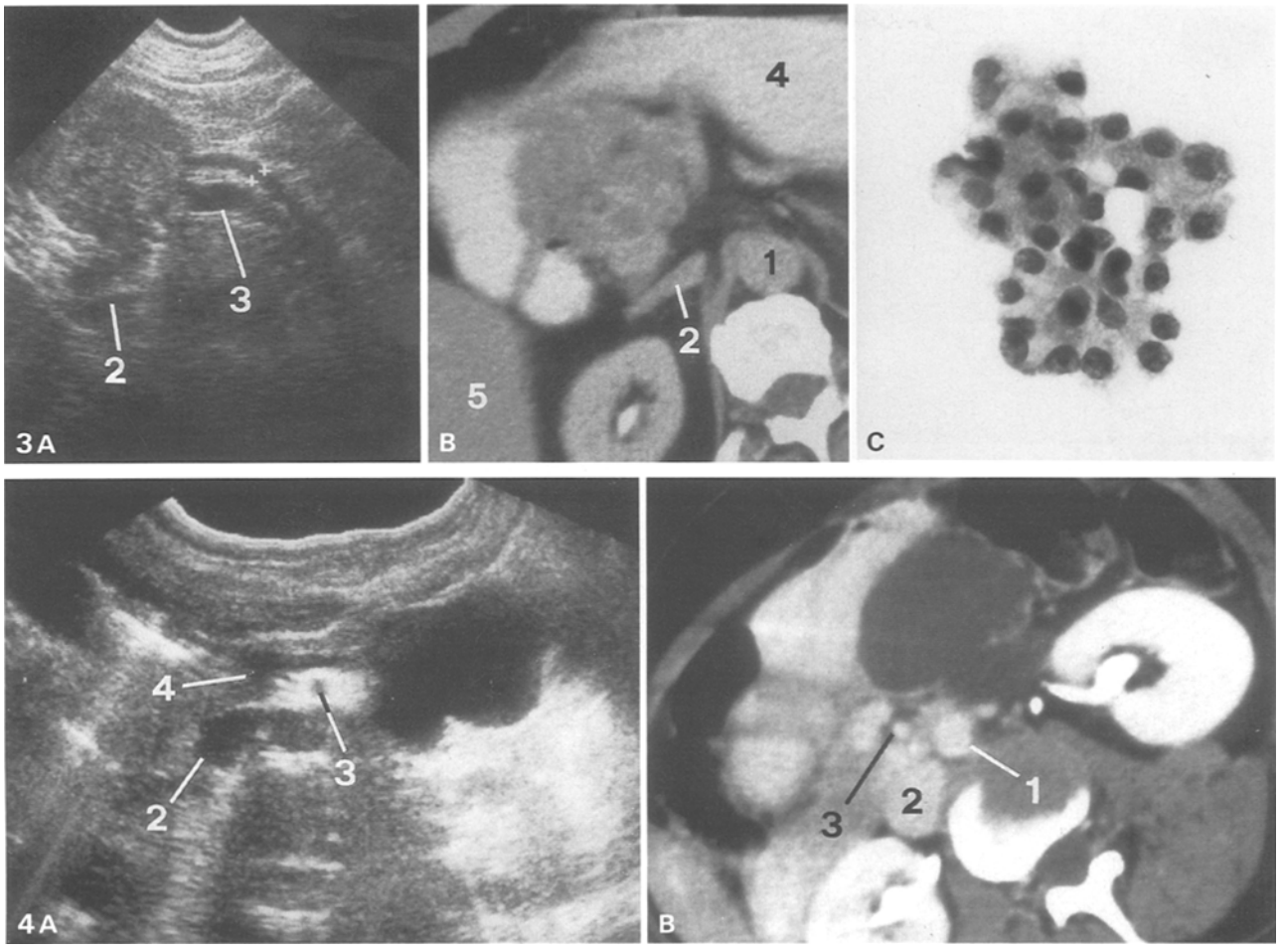

Fig. 3. SCT. **A** US: axial scan. Hypoechoic mass of the pancreatic head, with diffuse echostructural inhomogeneities. Slight dilation of the pancreatic duct (between calipers). **B** CT. Mass in the pancreatic head with solid inhomogeneous density. **C** Cytological smear (FNA). Clusters of serous cells with acinar pattern, characterized by scanty granular cytoplasm and monomorphic nuclei (Hematoxylin & eosin, original magnification, ×400). *1*, aorta; *2*, inferior vena cava; *3*, splenoportal venous axis; *4*, stomach; *5*, liver.

Fig. 4. SCT. **A** US: axial scan. Echo-free mass of the pancreatic bodytail, with posterior enhancement. **B** CT. The fluid density of the mass is confirmed, a thin fibrous septum can be seen within. *1*, aorta; *2*, inferior vena cava; *3*, superior mesenteric artery; *4*, splenoportal venous axis.

2 cm in diameter at its periphery (Fig. 2A–C). CT with intravenous contrast allowed a better assessment of the vascularized connective bands between the cysts, as well as a better separation from the adjacent unaffected parenchyma.

Two of 12 SCT appeared solid (hypoechoic at US, hypodense at CT: Fig. 3A and B); nevertheless, both presented in their periphery some small areas with fluid content, misdiagnosed as necrosis. In the two remaining SCT, both modalities showed one large cystic lesion, 3.5 and 6 cm in diameter (Fig. 4A and B); one of these lesions also had a thin septum.

The overall information yielded by US was similar to that yielded by CT. Of the eight SCT with a honeycomb appearance, only seven could be properly characterized on the basis of the US and CT patterns. In the remaining case, which also presented two large peripheral cysts, the imaging modalities were dubious and the correct diagnosis was obtained by US-guided FNA due to the presence, on the cytological smear, of cells without atypias and a high-glycogen content. The two solid-appearing tumors were considered by both US and CT to be ductal adenocarcinomas; US-guided FNA (performed in one case) properly characterized the lesion (Fig. 3C).

The remaining two neoplasms presented as a cystic lesion more than 2 cm in diameter; the diagnosis of pseudocyst was unlikely, due to the lack

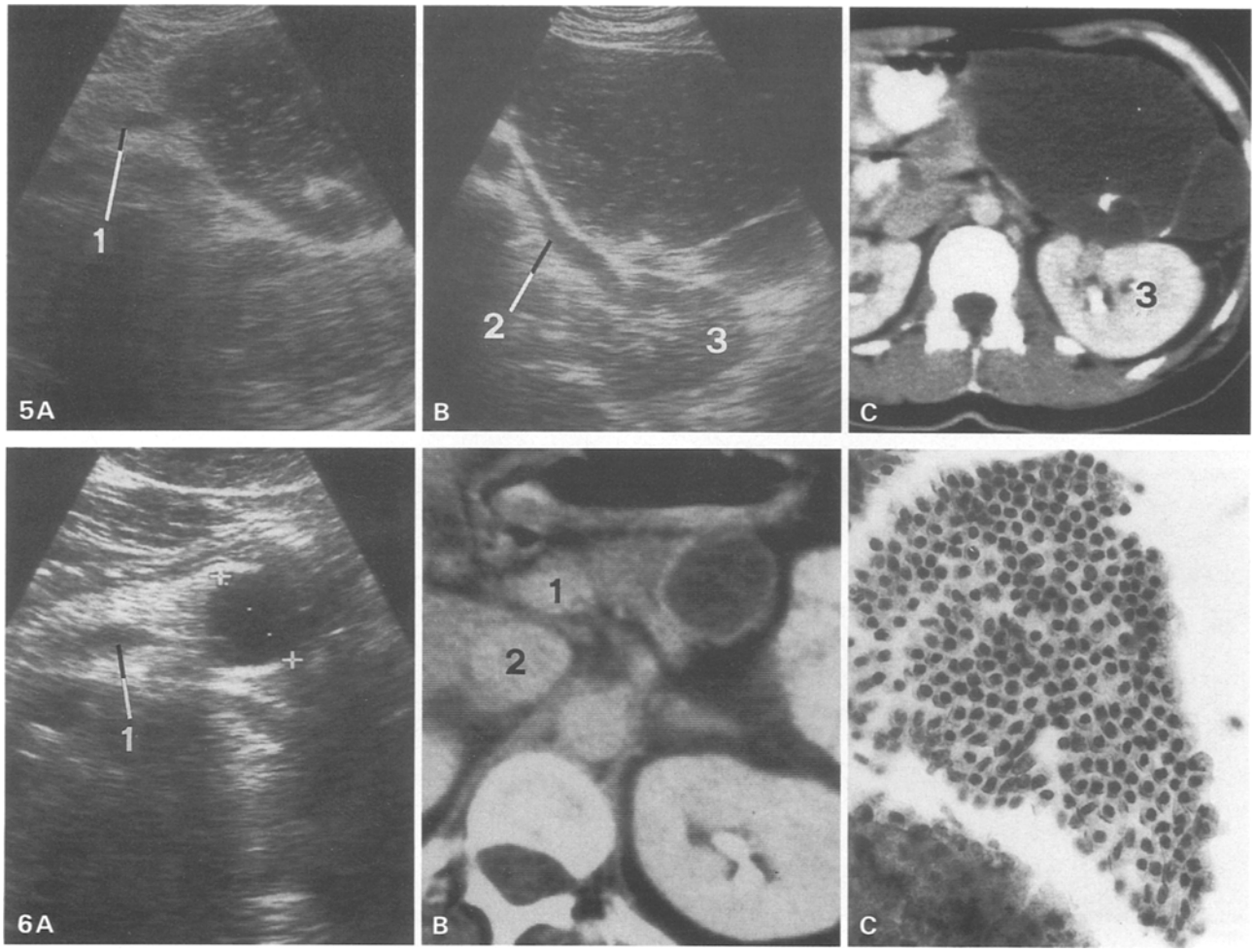

Fig. 5. MCT (cystadenoma). **A, B** US: contiguous axial scans. Large mass of the pancreatic bodytail characterized by evenly scattered echos (typical of the mucinous content). A large calcification (**A**) and a thin hyperechogenic septum (**B**) can be seen. **C** CT. The mass has a density of 20–30 HU, in its caudal part the thin connectival septum (also shown by US) and two calcifications (the smallest one not seen with US) are recognized. *1*, splenoportal venous axis; *2*, left renal vein; *3*, kidney.

Fig. 6. MCT (cystadenoma). **A** US: axial scan. Echo-free mass of the pancreatic body, slightly more than 3 cm in diameter. **B** CT. The mass has fluid density. CT allows good evaluation of the connective tissue wall, notably thin on the lateral side. **C** Cytological smear (FNA). Clusters of round epithelial cells with well-defined mucinous cytoplasm, with monomorphic nuclei with chromatin even overall (Hematoxylin & eosin, magnification, × 250). *1*, splenoportal venous axis; *2*, inferior vena cava.

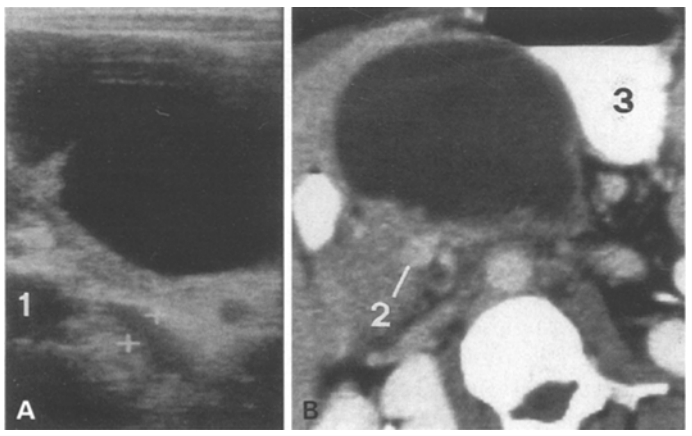

Fig. 7. MCT (cystadenocarcinoma). **A** US: axial scan. Large echo-free mass of the pancreatic bodytail, with an endocystic papillary projection on the posteromedial wall. **B** CT. The posterior wall of the cystic lesion is irregular, with solid endoluminal papillary projections. *1*, aorta; *2*, splenoportal venous axis; *3*, stomach.

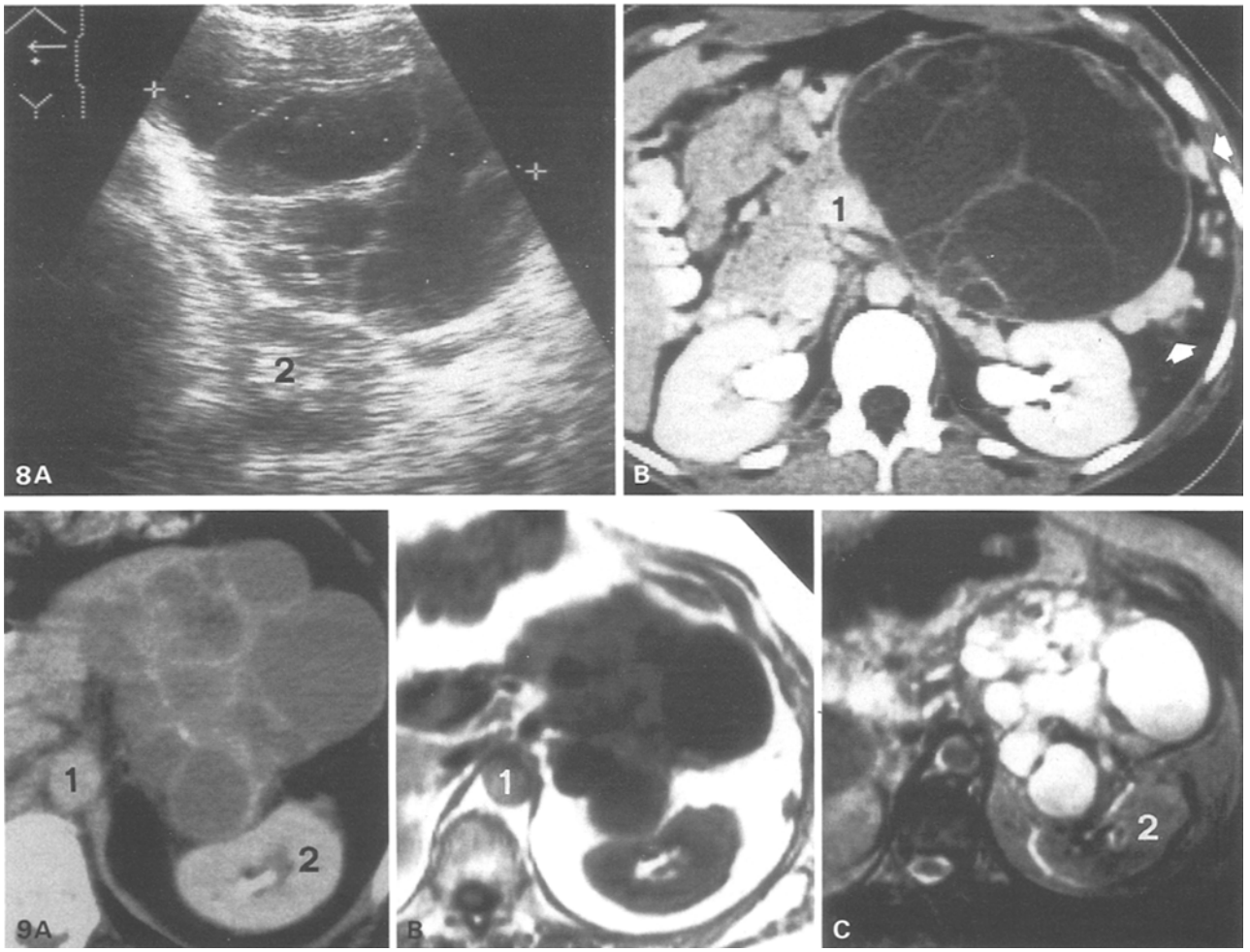

Fig. 8. MCT (cystadenoma). **A** US: axial scan. Large multiseptated mass of the pancreatic bodytail, with cysts of different sizes. **B** CT. The pattern is superimposable to the US one. The smaller cystic lesions (less than 2 cm in diameter) are well demonstrated in the posterior part of the tumor. Moreover, the thin tumoral connective tissue wall, as well as the collateral vessels (*arrows*) induced by the occlusion of the splenic vein are clearly shown. *1*, splenoportal venous axis; *2*, kidney.

Fig. 9. MCT (cystadenocarcinoma). **A** CT. Large multiseptated mass of the pancreatic tail, with some small calcifications. Solid papillary projections mainly located in the medial part of the tumor. **B, C** MRI. The mass is characterized by low intensity on the T_1-weighted image (**B**); on the T_2-weighted image (**C**), multiple high-intensity compartments, separated by low-intensity septa, seen as "dark lines." The calcifications shown by CT cannot be recognized. *1*, aorta; *2*, kidney.

of clinical data of pancreatitis, whereas a MCT was suspected. In one case, 30 ml of serous fluid were aspirated under US guidance; by means of centrifugation it was then possible to prepare a few cytologic specimens and to define the lesion as a SCT.

Thus, a correct preoperative diagnosis was achieved in 10 of 12 SCT on the basis of the information provided by the imaging modalities and US-guided FNA.

Mucinos Cystic Tumors

The great majority of MCT consisted of single or multiple cystic lesions of more than 2 cm in diameter (Figs. 5–7). Only two multicystic masses contained (along with cysts more than 2 cm in size) some cysts less than 2 cm in diameter (Figs. 8 and 9). In 14 of 18 MCT, both US and CT showed more or less notable septa (Figs. 5, 8, and 9A) and solid papillary projections of various sizes in nine of 18 (Figs. 7 and 9A). In four of 18 cases, US revealed the presence of fine echos (due to the mucinous fluid content), either evenly scattered within the mass (Fig. 5A and B) or located in its most dependent part, whereas in two of these latter cases CT demonstrated a content with a density value of 20–30 HU, slightly superior to that of

fluid (Fig. 5C). CT, moreover, identified in four of 18 tumors the presence of calcifications either parietal or within the mass (Figs. 5C and 9A), whereas US provided the same result in only two of four cases (Fig. 5A). Only CT was able to properly assess the wall thickness, being between 2 and 8 mm (Figs. 6B and 8B). The information of the two imaging modalities was similar; in fact, the additional data provided by either US or CT did not affect the final diagnosis. The US and CT features, in association with the clinical and history-related data (no previous bouts of acute pancreatitis, clinical and laboratory data negative for chronic pancreatitis), achieved a correct diagnosis of MCT in 15 of 18 cases. It was impossible to differentiate between cystadenoma and cystadenocarcinoma with the exception of four patients in whom there were signs pointing to the malignant nature of the neoplasm (infiltration of peripancreatic vessels and liver metastases). The diagnosis of MCT was confirmed in five of 14 patients by US-guided FNA; in three cases, the cytological smear showed mucin-rich columnar cells and in the remaining two, the aspirated fluid had a high content of carbohydrate antigen (CA) 19-9, carcinoembryonic antigen (CEA), and lactic dehydrogenase (LDH), and a low content of amylase.

On the contrary, in three of 18 cases a pseudocyst was suspected, since these patients had a history of previous bouts of acute pancreatitis; US-guided FNA, performed in two of three cases, solved the diagnostic problem, in one by means of a cytological smear, in the other due to high CEA and LDH and low amylase content.

The preoperative diagnosis was correct in 17 of 18 MCT by the information provided by the imaging modalities and by US-guided FNA.

Discussion

Pancreatic cystic tumors are a fairly rare occurrence, comprising about 6% of all nonfunctioning pancreatic neoplasms (according to their incidence in the personal series of 658 pancreatic tumors collected between January 1970 and September 1989). They are 10%–15% of all pancreatic cystic lesions [23, 29].

Serous Cystic Tumors

The very variable US and CT pattern, as described above, is fully justified by the pathologic features of the tumor. Often, both imaging modalities are capable of demonstrating these the pathognomonic honeycomb appearance provided by the many small size cysts [5]. Moreover, it has to be emphasized that the connective tissue septa between the cysts, as well as the calcifications sometimes present within the central scar, are more easily detected by CT [4, 23]. Dynamic CT, after intravenous injection of large amounts of contrast material, allows in fact to demonstrate the stromal vascularization, similar to angiography [6]. Larger cysts can sometimes also be detected at the periphery of these microcystic tumors [4]; however, there are usually no problems of differential diagnosis [7].

Nevertheless, in some occurrences the cysts are submacroscopic in size, thus beyond the resolution power of both US and CT [6] and therefore achieve a solid-appearing pattern, undistinguishable from other pancreatic tumors, notably ductal adenocarcinoma [23, 30–32]. Moreover, whenever the neoplasm presents a fairly homogeneous enhancement after intravenous injection of contrast material, the differential diagnosis vs. a nonfunctioning islet cell tumor is difficult [6].

Rarely, SCT consist mainly of cysts of more than 2 cm in diameter: in such cases their features are superimposable to the other cystic lesions of the pancreas (notably pseudocysts and MCT) [6, 21, 22, 27]. The problem related to the differential diagnosis of pancreatic cystic lesions will be discussed in detail in the paragraph on MCT. US and CT can almost always properly diagnose a SCT, in the case of honeycomb pattern. Conversely, the solid-appearing lesions or lesions characterized by large cysts can be correctly defined by US-guided FNA, with cytological smears showing the presence of glycogen-rich columnar cells [33]. Among the lesions with large cysts, the differentiation between pseudocysts and cystic neoplasms can be obtained also by the assessment of the amylase content of the aspirated fluid [34]; the levels of CEA, LDH, and CA 19-9 are moreover sufficient to distinguish SCT from malignant but not benign MCT. Finally, SCT can be associated with von Hippel-Lindau disease [2, 7]: this clinical piece of information may be useful for a correct diagnosis.

Mucinos Cystic Tumors

In MCT, US and CT patterns are strictly related to pathologic features. US and CT show the presence of uni- or multilocular cystic masses. Both modalities, in our personal experience, were equally reliable in the evaluation of the septa separating the cystic cavities (in the multilocular lesions), as well as of the endocystic papillary projec-

tions. However, some authors [4, 8] consider US to provide more precise information. As to the assessment of the tumor wall thickness and calcifications, CT proved superior in accordance to the literature [4]. The imaging modalities allow a diagnosis of malignancy only if extrapancreatic spread is present (infiltration of peripancreatic vessels, lymph nodal, and/or liver metastases) [7, 28]. As to the differential diagnosis, there are several cystic lesions of the pancreas which can be difficult to distinguish from MCT: notably, one has to consider pseudocysts, duodenal duplications, as well as several other pancreatic tumors besides the rare SCT, characterized by large cysts (discussed above).

Pseudocysts – especially the atypical ones containing blood clots or necrotic debris, those with uneven thickening of their wall, as well as the multiseptate ones [35] – can be difficult to discriminate from MCT. A differential diagnosis can often be achieved, not on the basis of imaging, but of clinical data; previous bouts of acute pancreatitis or clinical and laboratory data typical of chronic pancreatitis point to a pseudocyst, whereas the absence of these factors justifies the suspicion of MCT. Nevertheless, patients with MCT can have a clinical history of pancreatitis; in our experience this was present in 17% of cases, in fair accordance to the data reported by Johnson [7].

Duodenal duplications (uncommon in the adult) are located on the mesenteric side of the second part of the duodenum and often have a cystic appearance by both US and CT. The differential diagnosis is possible only when some septa can be recognized pointing to the plicae of the epithelial lining of the duodenum. The history of bouts of relapsing pancreatitis (not uncommon in duodenal duplications) must also be considered for a correct diagnosis [36].

With regard to pancreatic neoplasms, the differential diagnosis is fairly easy in cases of necrotic solid tumors (adenocarcinomas [37] and metastases [38]): the areas of necrosis are usually uneven and scattered within the tumoral mass. The distinction between some nonfunctioning islet cell tumors with cystic appearance (a very rare occurrence [27, 39, 40]) and some papillary tumors is more difficult to make; regarding the latter, it is useful to remember that these tumors are typical of young women [41].

In cases in which neither US nor CT provide a definite diagnosis, the use of US-guided FNA is suggested. The detection, on the cytologic smear, of mucin-rich cells with abundant mucinous material in the background is peculiar of MCT [33, 42]. Although the presence of cellular atypias points to a cystadenocarcinoma [14], the absence of this latter datum does not rule out malignancy since the histologic assessment of the operative specimens has demonstrated the possible coexistence, within the same tumor, of areas of epithelial lining without atypias, along with other areas with signs of malignancy [2]. Nevertheless, after diagnosing a MCT, the preoperative evaluation of its benign or malignant nature has no clinical interest, since all these neoplasms must be considered potentially malignant [2]. Whenever US-guided FNA does not yield material for a cytologic smear, the diagnosis of MCT (at least of cystadenocarcinoma) can be made by detecting, in the aspirated fluid, a high content of LDH (pointing to necrosis), CEA, as well as CA 19-9. Our experience in three cases is in accordance with the literature [9, 43–45]. Recently, Yanagisawa [46] proposed to subdivide MCT into two forms: megacystic tumors (the usual ones, object of this paper) and ductectatic tumors. The latter are extremely rare space-occupying lesions 2.5–3.0 cm in diameter, usually located in the uncinate process. They consist of small communicating cysts (1–2 cm in diameter), surrounded by a thin connective tissue capsule: their appearance is that of a circumscribed dilation of a side branch of the main pancreatic duct. Histologically, the epithelial lining is the same as in the megacystic form. The US and CT pattern, described by Itai [47] in five cases, is that of multilocular cystic masses. To be stressed is the role played by ERCP (or by percutaneous US-guided pancreatography if ERCP is technically not possible) which shows the communication between the mass and the pancreatic ductal system: its opacification is usually inhomogeneous because of the presence of filling defects due to mucoid substance within the cystic lesions.

Conclusion

The correct characterization of cystic tumors has great clinical importance because of its therapeutic and prognostic outcome. In fact, SCT are benign tumors with no recurrence after resection; however, the lack of local invasiveness justifies avoiding surgery in some circumstances (aged patients with no symptoms or with high operative risk), as clinical and US follow-up are often sufficient. MCT, without signs of infiltration of the adjacent vascular structures or distant metastases, require radical surgery. These tumors, whenever radical resection is possible, have a much better prognosis than ductal adenocarcinoma of the pancreas. A

recent review of a MCT series (21 cases collected between 1970 and 1989) showed, in fact, a survival at 5 years from radical surgery of 100% in patients with histologic diagnosis (on the operative specimen) of cystadenoma, and of 38% in cases of cystadenocarcinoma.

US and CT allow a correct diagnostic workup in a fair number of both SCT and MCT (73% in our experience) when relating the information provided by the imaging modalities with the clinical data. These results can be further improved resorting to US-guided FNA, integrating cytology with the biochemical assays: the data collected so far, both in our experience and in the literature, nevertheless must be verified further, especially with regard to the possibility of differentiating (on the basis of the biochemical assays alone) the rare SCT with large cysts from benign MCT, as well as the widely necrotic ductal adenocarcinomas from cystadenocarcinomas with important solid papillary projections.

US and CT, along with FNA, have greatly limited the use of angiography [4, 48, 49]: the latter now plays a minor role both in diagnosis and preoperative workup. The MRI results are presently superimposable to those by the other noninvasive modalities (Fig. 9B and C). Hopefully, in the future, faster scanning techniques will allow an improved spatial resolution. Moreover, the chemical shift imaging techniques could possibly differentiate between serous and mucinous fluid content [50], thus reaching a precise diagnosis in those cases with dubious US and CT features.

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