Cystic Tumors Mistaken for Pancreatic Pseudocysts

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A small fraction of pancreatic cysts are neoplastic rather than inflammatory in origin. Failure to recognize the true nature of a neoplastic cyst will lead to an incorrect treatment strategy. This is a report of eight patients whose cystic neoplasms were misdiagnosed and maltreated. Five of the eight tumors proved to be malignant. Five were drained by anastomosis to a viscus and one by aspiration; drainage was recommended for the other two. Treatment by drainage led to complications (persistent painful gastric ulcer, infection in the cysts), growth of new cysts, no cures, but missed opportunities to cure cancer. Three patients with no metastases at first operation had metastatic spread to the liver, omentum, or lungs at reoperation. In three of the five cases initially treated by cystenterostomy (including one cancer), subsequent resection was possible and probably curative. One cystadenocarcinoma was watched for 3 years before apparently curative resection. Guidelines based on serum and cyst amylase levels, morphologic appearance, angiography, pancreatography, and biopsy are given for the purpose of differentiating inflammatory cysts from neoplastic cysts of the pancreas. Confusion of these entities should not occur, but errors can often be corrected.

THE MAJORITY OF CYSTIC LESIONS of the pancreas are pseudocysts, which are collections of pancreatic secretions surrounded by a fibrous wall having no epithelial lining. Pseudocysts are of inflammatory or traumatic origin, and occasionally will resolve spontaneously.[1,2] Excision is not commonly feasible, except for small pseudocysts located distally in the tail of the gland[3–5] and most are treated by drainage, either internally into the gastrointestinal tract or externally.

Fifteen per cent of pancreatic cysts are neoplastic,[6] benign, or malignant. These cysts always have an epithelial lining and never resorb spontaneously. Neoplastic cysts must be excised. Drainage is inappropriate, inadequate, and injurious.

We report a series of patients with cystadenomas and cystadenocarcinomas in whom a misdiagnosis of pseudocyst initially led to improper treatment. These cases illustrate the complications consequent to avoidable errors, and also show that subsequent salvage often remains possible even years later.

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Materials and Methods

The hospital records of the patients treated by the senior author at the Massachusetts General Hospital (MGH) from July 1, 1977 to June 30, 1986, were reviewed. During this period a total of 13 patients with pancreatic cystic neoplasms and 35 patients with pseudocysts were treated. Eight cases of cystic neoplasm mistaken for pseudocyst were discovered among these. The latter group comprises the basis for this study.

Case Reports

Case 1

A 61-year-old female discovered her own painless abdominal mass. She had a 10-pound weight loss, but denied any history of excessive alcohol, trauma, or pancreatitis. Examination showed a mobile, nontender mass in the epigastrium. Computed axial tomography (CAT) scan showed an 8-cm cystic lesion in the head of the pancreas, which was believed to be a pseudocyst (Fig. 1). During the following 4 months the cyst was watched for resolution; however, it increased in size. Her physician then recommended internal drainage of the cyst, at which time the patient referred herself to the MGH for a second opinion.

The serum amylase was normal. Endoscopic retrograde cholangiopancreatography (ERCP) showed no communication between the cyst and a bowed but otherwise normal pancreatic duct. Angiography suggested tumor vessels in the region of the cyst. At laparotomy the pancreas was normal except for a 9-cm thin-walled cyst in the head of the gland. A presumptive diagnosis of cystic neoplasm was made, and a pylorus-preserving pancreaticoduodenectomy was performed. Examination of the specimen showed multiple small loculations containing brown serous fluid. On microscopy there was a cuboidal epithelial lining of the cysts,

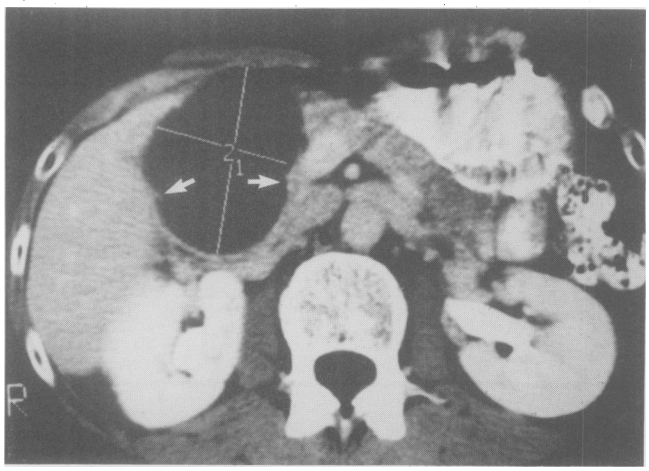


FIG. 1. CT scan showing a large cystadenoma in the head of the pancreas (case 1). There is no associated mass seen, but the internal wall is slightly irregular (arrows).

consistent with serous cystadenoma. The patient is asymptomatic 9 months later.

Case 2

A 39-year-old woman was found on routine chest x-ray to have a 10-cm ring-shaped calcification in the left upper abdomen (Fig. 2). She had no associated symptoms. There was no history of trauma or other causes of pancreatitis. Ultrasound examination showed a large cyst in the tail of the pancreas. It was assumed to be an old calcified pseudocyst, and intervention was not advised because she felt well and was assumed to be at no risk.

Three years later she still felt well but worried about the cyst. CT scan showed no change in size and no associated pancreatic mass (Fig. 3). The serum amylase level was normal. ERCP showed a normal pancreatic duct without communication to the cyst.

At laparotomy there was, in addition to the cyst, a solid mass in the body and tail of the pancreas. A distal subtotal pancreatectomy was performed. Pathologic examination showed a low-grade cystadenocarcinoma. She has been well for 4 months.

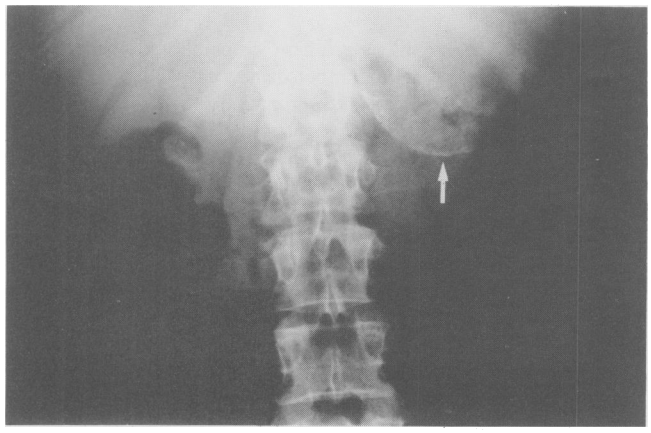


FIG. 2. Plain film of the upper abdomen (case 2). A ring-shaped calcification (arrow) is visible in the left upper quadrant (cf. Fig. 3).

Case 3

A 45-year-old woman was admitted to another hospital with a 5-year history of heartburn. There was no history of pancreatitis, abdominal trauma, or ethanol abuse. On examination, a mobile nontender mass was noted in the left upper quadrant. Barium study of the stomach suggested a retrogastric mass. Exploratory laparotomy revealed a large cyst in the body and tail of the pancreas with a normal pancreatic head. The cyst was unilocular, and had a thick wall with minimal surrounding adhesions. A cyst-gastrostomy was performed. Microscopy of the cyst wall revealed an epithelial lining.

Over the next 7 years, the patient had recurrent fevers and gastrointestinal bleeding. Follow-up ultrasound examination during her final admission showed a 12-cm, multiloculated cystic retrogastric mass. The serum amylase level was normal. At exploration the pancreas surrounding the mass was of normal consistency. A distal subtotal pancreatectomy and hemigastrectomy including the cyst-gastrostomy site was performed. Microscopy revealed mucin-producing columnar epithelium consistent with cystadenoma. There were microabscesses present in the pancreas. The patient remains well 9 years later with no sign of recurrence.

Case 4

A 71-year-old woman had 1 year of epigastric pain, nausea and vomiting, diarrhea, and a 25-pound weight loss. There was no history of pancreatitis, abdominal trauma, or ethanol abuse. On abdominal examination there was no tenderness or mass. Serum amylase and blood tests of liver function were normal, but a CT scan demonstrated a 6-cm single cyst of the pancreas. At exploratory laparotomy, the entire pancreas was indurated and fibrotic. The cyst in the head of the gland had a smooth translucent wall and contained clear mucoid fluid. A cyst-gastrostomy was performed. Biopsy of the cyst wall revealed columnar, mucin-producing epithelium with no evidence of malignancy.

The patient was well for 6 months, but then noted recurrence of epigastric pain and became jaundiced. CT demonstrated a cyst in the head of the pancreas. Gastroscopic examination showed a persistent patent communication between the stomach and the cyst cavity. At laparotomy the common bile duct measured 3 cm in diameter and a choledochoduodenostomy was performed. The pancreatic cyst was left intact.

The patient continued to have epigastric pain and weight loss and was referred to the MGH 8 months later. A presumptive diagnosis of cystic neoplasm was made from the evidence cited and the persistence of the lesion by CT scan. Angiography showed tumor vessels in the pancreatic head and encasement of the gastroduodenal artery. At operation, a multiloculated cystic tumor of the pancreatic head was resected by pancreaticoduodenectomy, including the site of the cyst-gastrostomy (Whipple's operation) (Fig. 4). Microscopy showed a well-differentiated mucinous cystadenocarcinoma, with malignant cells present at one resection margin.

The patient remains symptomatically well 2.5 years later, although she has been unable to gain weight. Follow-up CT scans have shown no recurrence thus far.

Case 5

A 51-year-old female presented with a several-month history of epigastric and right upper quadrant pain associated with a 50-pound weight loss. There was no history of pancreatitis, trauma, or ethanol abuse. Cholecystography showed cholelithiasis, for which she had cholecystectomy. Her pain continued after operation.

Two months later a CT scan showed a 15-cm multicystic mass in the region of the pancreatic tail with two 3-cm cysts in the pancreatic head. ERCP showed no communication between the cysts and the pancreatic duct. At re-exploration the entire pancreas was firm and there were mul-

tiple small cysts in the head. The cysts, which were believed to be too small to be drained internally, were emptied by needle aspiration. The cystic mass in the region of the tail of the pancreas was found to be of renal origin and was partially resected. Cytologic examination of the aspirated pancreatic cyst fluid revealed atypical epithelial cell clusters.

Four months after the second operation, the patient was readmitted for jaundice. CT scan showed a combined cystic and solid mass in the pancreatic head and a dilated common bile duct. Reassured that she had recurrent pseudocysts that did not require immediate remedy, the patient deferred further treatment for personal reasons. Eight months later, she referred herself to the MGH for continuing pain and jaundice. The serum bilirubin level was elevated at 4 mg/dL, but the serum amylase level was normal. Endoscopy showed extrinsic duodenal compression in the periampullary region, and results of endoscopic biopsy of the duodenal wall revealed moderately differentiated adenocarcinoma. At laparotomy, three quarters of the pancreas was replaced by a large multiloculated cystic mass, and the liver was found to harbor several metastatic lesions. Results of biopsy of one of these showed poorly differentiated mucin-producing adenocarcinoma. A choledochoduodenostomy resolved her jaundice, but her condition deteriorated progressively. She died 8 months after the third operation.

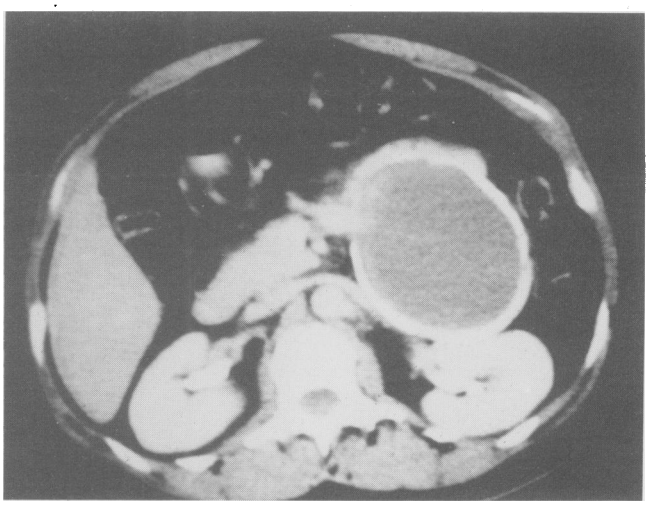


FIG. 3. Contrast-enhanced CT scan (case 2) showing a large single cystic adenocarcinoma with calcified wall. There is no associated mass seen.

Case 6

A 45-year-old woman was admitted with a several-month history of vague right upper quadrant pain and an 8-pound weight loss. There was no history of pancreatitis, ethanol abuse, or trauma. Physical examination was unremarkable. Ultrasound examination demonstrated cholelithiasis and showed an apparently normal pancreas. At laparotomy there was a smooth, thin-walled, cystic, moveable mass in the body of the pancreas. The rest of the pancreas appeared normal. A Roux-en-Y cyst-jejunostomy was performed for what was believed to be a pseudocyst. Histologic examination of the cyst wall showed only fibrosis without an epithelial lining.

Subsequently the patient was well for 2 years until she developed nausea and a 5-pound weight loss. A CT scan now showed a 3-cm multilocated mass in the region of the pancreatic tail. The patient refused surgery at this time, and 6 months later a CT scan showed the mass to have grown to 5 cm. The serum amylase level was normal. Three years after the original diagnosis, re-exploration showed a multiloculated cyst containing clear serous fluid, located in the pancreatic tail at the site of the earlier cyst-jejunostomy. The rest of the pancreas was still normal. A distal pancreatectomy was performed along with removal of the jejunal loop. Histologic study revealed mucin-secretining columnar epithelium consistent with a benign cystadenoma. She is well 6 months after her second operation.

Case 7

A 59-year-old woman with epigastric pain radiating to the back was found by CT scan to have a single large cyst in the body and tail of the pancreas (Fig. 5A). There were no gallstones seen and no history of pancreatitis, alcohol abuse, or trauma. An ERCP showed a normal pancreatic duct without communication to the cyst. A cyst-gastrostomy was performed for the presumed pseudocyst.

Six months later, she became jaundiced. ERCP now showed a long stricture of the common bile duct within the pancreas, and CT scan showed multiple cysts in the head, body, and tail of the pancreas (Fig. 5B). Angiographic examination suggested encasement of the splenic artery at its origin (Fig. 6).

At re-exploration, several small cystic tumors were found on the omentum, and results of biopsy showed a cuboidal epithelial lining. There was a mass infiltrating the base of the mesentery. Results of biopsy of the pancreatic head showed cystadenocarcinoma. She was treated with palliative biliary-enteric bypass.

Case 8

A 73-year-old man was admitted with complaints of mild epigastric pain. There was no history of pancreatitis or its antecedents. CT scan revealed a large cystic mass in the lesser sac believed to arise from the pancreas. At laparotomy, the large cyst with its thin wall, believed to be a pseudocyst, was unroofed and drained externally by marsupialization. Several liters of serous, brown fluid were drained from the cysts. Microscopy of the cyst wall showed only fibrosis. The amylase content of the cyst fluid was at normal serum levels and cytologic examination of the fluid did not reveal tumor cells.

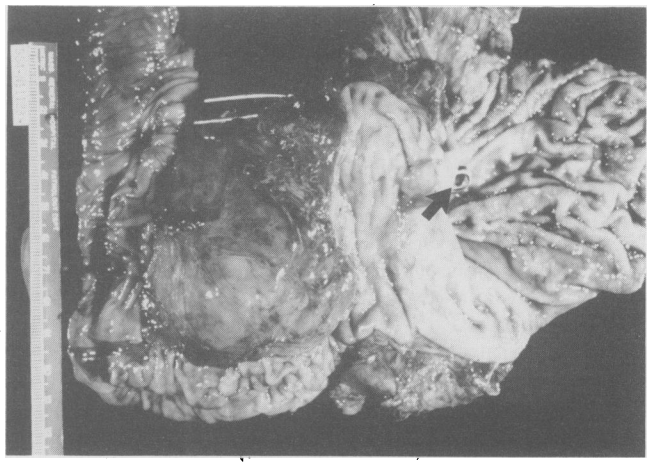
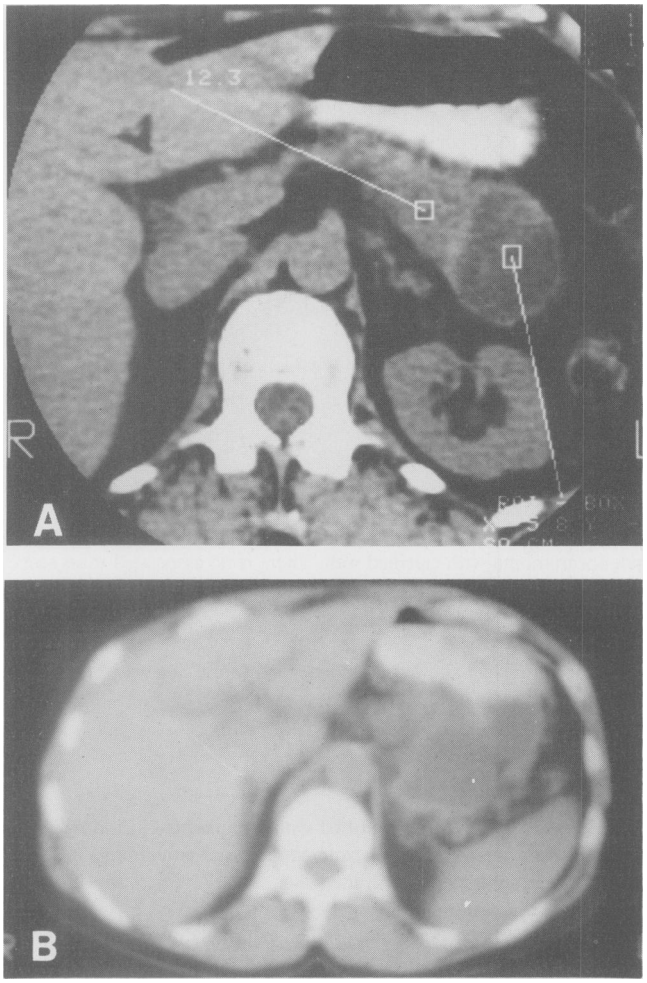


FIG. 4. Resected head of the pancreas and distal stomach (case 4). The cystadenoma had been anastomosed to the posterior gastric antrum 1 year before. The pin (arrow) lies in the persistent communication between the stomach and the cyst cavity.



FIGS. 5A and B. *A.* A CT scan showing a single cyst in the tail of the pancreas. This was drained into a Roux-en-Y jejunal loop (case 7). *B.* CT scan 1 year later now showing a multiloculated cystic tumor in the body and tail of the pancreas.

His recovery was initially uncomplicated. The drainage tract healed over, and at 2 weeks ultrasound examination showed no residual cyst.

One month after the drainage operation, the patient was readmitted with recurrent discharge from the drain site. CT scan now revealed a multiloculated cyst in the lesser sac. At re-operation there was a thick-walled cyst in the lesser sac, once again believed to be a pseudocyst. A cyst-gastrostomy was created. Nonetheless, the patient had persistent and sometimes profuse bloody drainage *via* the old external drainage tract and was re-operated on an additional time in an unsuccessful attempt to control this discharge. After transfer to the MGH, CT scan showed a large multiloculated cyst with solid components behind the stomach. The serum amylase level was normal. Gastroscopy documented persistence of the communication between the stomach and cyst cavity. Angiographic examination showed tumor vessels within the mass. At exploration there was a 15-cm cystic mass in the lesser sac, adherent to the stomach and transverse colon, but separate from the pancreas. The tumor was resected along with the attached distal stomach and transverse colon. The histologic diagnosis was debated but finally determined to be most likely leiomyoblastoma.

Six months later he was readmitted with metastatic tumor in the mediastinum. Despite chemotherapy he died 1 year after resection of the tumor.

Discussion

There is apparently a tendency among physicians and surgeons to assume that a cyst discovered in the pancreas is probably a pseudocyst and to make treatment decisions accordingly. More than half of the neoplastic cysts of the pancreas we have seen in the last 10 years have been misdiagnosed and maltreated in this way. Analysis of this experience makes a number of lessons and guidelines clear.

1. The clinical syndrome associated with cystic neoplasms of the pancreas has relatively consistent characteristics.[7] All seven patients with pancreatic cystadenomas or cystadenocarcinomas were women. Five of the seven patients had vague abdominal pain and five of the seven patients had significant weight loss. None had a history of pancreatitis or identifiable antecedent factors such as alcoholism, gallstones, or trauma.

2. The serum amylase level was normal in all of our patients. Approximately 50–75% of patients with pseudocysts will have an increased serum amylase level.[2,3,5,7]

3. Ultrasound and CT scans may fail to show a solid mass component of the tumor,[8] but multiple cysts or internal septa (Fig. 5B) should raise the suspicion of tumor (6 of 8 patients had one or both of these findings). Multiple pseudocysts occur less frequently than single pseudocysts.[8,9]

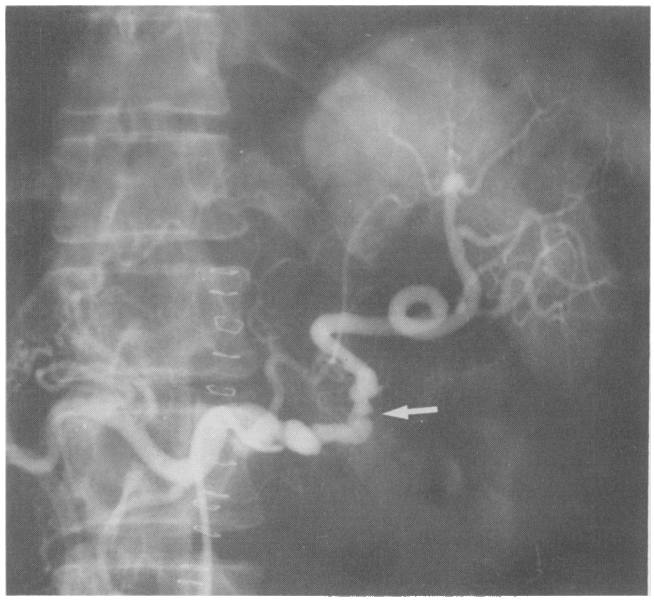


FIG. 6. Celiac arteriogram (case 7) showing encasement at the origin of the splenic artery (arrow) by a cystadenocarcinoma.

4. Endoscopic retrograde pancreatography showed no communication between the pancreatic duct and the cysts of these tumors, and the duct showed no obstruction or other changes suggestive of chronic pancreatitis in any of our patients. Sixty per cent or more of patients with pseudocysts will show a communication with the duct system[2,10] and various ducts abnormalities are characteristic of patients with chronic pancreatitis.[2,10,11]

5. Angiographic evaluation may show evidence of hypervascularity and tumor vessels (Cases 1 and 4) or vascular encasement (Fig. 6) (Cases 4 and 7).[12] Arteriography in patients with pseudocysts instead show hypovascularity and displacement of vessels.[13]

6. The gross appearance of neoplastic cysts in most cases differs from pseudocysts. The latter tend to be thick-walled, opaque, and adherent to adjacent viscera, especially the stomach. The rest of the pancreas is most often indurated and distinctly abnormal. Neoplastic cysts usually have a thin glistening wall that is often transparent; adherence to the stomach is not the rule, and the pancreas adjacent to the cyst has a normal texture.[14]

7. The fluid in the cystic neoplasm is usually clear and mucoid, whereas pseudocyst fluid is gray and opalescent, or may contain old blood and necrotic debris. The amylase content of pseudocyst fluid is very high, but is low (equal to or less than the serum level) in neoplastic cysts.[15] This difference allows for the possibility of differential diagnosis by needle aspiration of the cyst contents. Although "amylase-poor" pseudocysts have been reported,[16] they are very much the exception. Schwerk[15] found that all of ten pseudocysts had an elevated amylase concentration, whereas both of two cystadenoma fluids did not. Cytologic examination may add confirmation if epithelial cells or tumor cells are identified in the fluid (Case 5).

8. Biopsy of the cyst wall with frozen section examination will usually make the differentiation. If an epithelial lining is present, neoplasm should be presumed. In two of our patients, that information was available but not appreciated.

The absence of an epithelial lining in a limited biopsy specimen does not rule out the diagnosis of a cystic tumor. Compagno and Oertel[17] found that the epithelial lining can be discontinuous and patchy so that even multiple biopsies can miss it. Two patients in our series had single biopsies that did not demonstrate epithelium, and consequentially had the wrong operative procedure performed. The epithelial lining was eventually proven in all our patients.

9. Surprisingly, one still encounters published recommendations to treat large cystic neoplasms of the pancreas by internal drainage into a viscus, either as a definitive procedure or planned first stage, preliminary to later resection.[18] This suggestion seems entirely misconceived because internal drainage will inadequately control symptoms (and even create a painful "ulcer" as in Case 4), potentially lead to infection (Case 3), fail to cure a curable cancer, and inadequately drain a lesion that is or may become multiloculated (Case 7). A pseudocyst adequately drained either externally or internally into a viscus quickly collapses. The cavity shrinks to a slit or heals within 1–3 weeks.[5,19] The finding of a persistent cavity in spite of adequate decompression should strongly imply a stiff neoplastic wall. In three of our cases (Cases 3, 4, and 6), the persistence of the cavity was appreciated as an important diagnostic clue. The most striking of these was Case 4, in which the retrogastric cyst cavity could be entered and examined with a gastroscope 6 and 14 months after the cyst-gastrostomy.

10. The natural history of these tumors may be exceedingly slow and indolent, extending over a documented period of several years (more than 7 years in Case 3).[6] The slow growth, tendency *not* to infiltrate adjacent structures, and relatively low likelihood of metastases all make second chances possible in many cases. Resection for probable cure was still accomplished 1–7 years after cyst-gastrostomy or cyst-jejunostomy in three cases, including a carcinoma (Case 4), and after 3 years observation of a carcinoma in a fourth (Case 2). Neither tumor size nor previous violation should preclude an attempt at curative removal.[18] Unfortunately the error of missing the correct diagnosis does cost dearly on occasion. Two of our patients (Cases 5 and 7) had metastases at the time of the second operation, 6 to 8 months later.

11. Finally, other cystic lesions beside those arising from the pancreas may mimic pseudocysts. Case 8 illustrates the therapeutic errors and misadventures related to misdiagnosing what proved to be a cystic leiomyoblastoma of the stomach. Simple mesenteric cysts have also been mistaken and mishandled in this fashion.

Conclusions

Pancreatic neoplastic cysts differ in many characteristic ways from pseudocysts. The true diagnosis usually should be made from the outset, but errors can often be corrected in time.

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