Preoperative Diagnosis of Pancreatic Carcinoma by Percutaneous Aspiration Biopsy

MARTIN L. GOLDMAN, MD, ZUHER M. NAIB, MD, JOHN T. GALAMBOS, MD, JOE C. RUDÉ III, MD, KHEE-TIANG OEN, MD, EDWARD L. BRADLEY III, MD, ATEF SALAM, MD, and ANTONIO C. GONZALEZ, MD

Carcinoma of the pancreas and chronic pancreatitis may be extremely difficult to differentiate by standard diagnostic methods preoperatively as well as at the operating table. Operative pancreatic biopsy may have a high morbidity, rare mortality, and can be misleading. Percutaneous aspiration biopsy may be of great potential benefit. It provides additional histological material not usually available, and an accurate diagnosis of malignancy can be made. In select patients a needless laparotomy may be avoided. It appears to be a safe procedure that should be considered in the evaluation of the patient with suspected pancreatic malignancy in which a mass lesion is demonstrated by ultrasonography, computerized tomography, angiography, or retrograde pancreatography.

Both preoperative and intraoperative diagnosis of pancreatic carcinoma is difficult (1–4). Despite recent advances in angiography, retrograde pancreatography, ultrasonography, and computerized axial tomography, differentiation between chronic pancreatitis and pancreatic carcinoma remains uncertain in 15–20% of patients (5). Scattered reports indicate a high diagnostic accuracy of 75–80% with percutaneous pancreatic aspiration biopsy (4, 6–8). To evaluate the safety and effectiveness of this technique at our institution, we studied consecutive patients with suspected pancreatic neoplasms.

MATERIALS AND METHODS

The present report is based on 8 men and 5 women, aged 26–81 (median 61) with suspected pancreatic malignancy. The pancreatic cancer was localized for aspiration biopsy by the combination of ultrasonography and angiography (Figure 1) or cholangiography (Figure 2). Abdominal ultrasound B-scan using bistable oscilloscopic display was used for the anterior localization and depth of the lesion. The skin directly over the suspected mass was marked under ultrasonic guidance. A slight skin abrasion was made using a fine sterile needle and the skin stained with umbilical cord disinfectant (Triple Dye, Kerr Chemical Company, Northville, Michigan). This stain is not removed by sterilization preps. After the anterior localization point was marked, the depth of the lesion was obtained from both the A and B ultrasounds. Then, as the pancreatic lesion was demonstrated by angiography, the catheter in the artery was advanced as close to the suspected tumor mass as possible. The catheter thus served as the posterior marker of the pancreas. The aspiration biopsy was performed during the course of the angiogram or cholangiogram. The patient was kept in a supine position and the skin was prepped with betadine. A 3-mm superficial skin nick was made over the anterior skin marker. The depth of the needle penetration was estimated by the previous ultrasound and controlled by fluoroscopy, using the angiographic catheter as the posterior marker to guide the needle.

The anterior abdominal wall was punctured with a fine 23-guage 15-cm "Chiba" needle (Tanaka Sansei Do, Inc., Tokyo 113, Japan) (0.7 mm OD). To facilitate the puncture in an obese patient, a 20-gauge Medicut (Aloe Medical, St. Louis, Missouri 63103) intravenous cannula may

From the Departments of Radiology, Medicine, Pathology, and Surgery, Emory University Affiliated Hospitals, Atlanta, Georgia.

Address for reprint requests: Dr. Martin L. Goldman, Department of Radiology, Grady Memorial Hospital, 80 Butler Street, S.E., Atlanta, Georgia 30303.

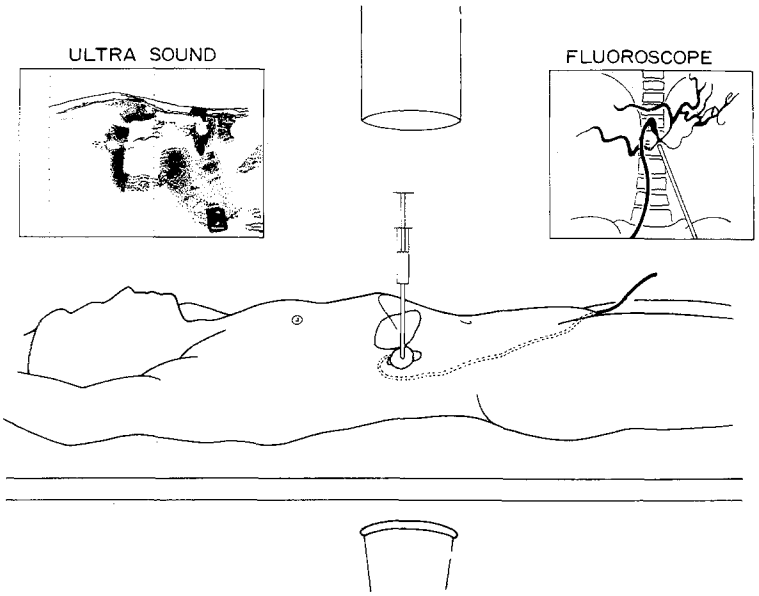

Fig 1. Technique of percutaneous aspiration biopsy of the pancreas. The skin directly overlying the main portion of the pancreatic mass (as determined by ultrasonography) is punctured with a Chiba needle. Under fluoroscopic guidance the needle is directed to the region of abnormal vessels seen by angiography. The needle may pass through stomach or liver prior to its entry into the pancreatic mass.

first be placed within the anterior abdominal wall at the point of the anterior skin marked. The Chiba needle can then be advanced through the Medicut catheter.

When the needle was advanced to its proper depth and the needle entered a firm gritty mass, the inner stylet was removed and continuous maximum suction was applied with a 10-cc syringe. During maximum suction over a few seconds, the needle was vigorously moved up and down several times over a 1-cm distance.

At the end of the aspiration pressure was still maintained on the syringe as the needle was removed from the pancreas. Aspirates only slightly more than what fills the contents of the lumen of the Chiba needle are obtained. The syringe and needle are separated. An air-filled syringe was attached to the needle and the aspirate was expressed into a jar of sterile saline, and then both the needle and syringe were flushed several times with saline into the collection jar. Four to five separate pancreatic punctures were performed. The technique of aspiration biopsy added approximately 10–15 min to the angiographic procedure.

The specimen was immediately carried to the cytology laboratory where the saline was passed through one or two membrane filters of 5-μm pore opening and the cells were promptly fixed and stained to avoid degeneration of cytogenic detail.

Patients were maintained at bedrest for 6 hr and were observed clinically over 3 days with daily serum amylase determinations. The only contraindication for this procedure was an increased risk of bleeding due to hemostasis.

RESULTS

In all of the 13 aspirations that were performed, recognizable pancreatic glandular and duct cells were obtained. Carcinoma of the pancreas was documented by angiography, clinical follow-up, or by histology in 11 patients (Table 1). In 6 of the 11 patients with carcinoma, positive cytology for adenocarcinoma was obtained (Figure 3). In a seventh patient the cytological material was suspicious of cancer. Two of the 6 positive cytologies were from patients with large tumors greater than 6 cm in diameter with extension outside of the body of the pancreas and encasement of major arteries and veins. Three of the 6 positive cytologies were from patients with medium-sized tumors 3–6 cm in diameter with extension outside of the head of the pancreas and encasement of the gastroduodenal artery, but with normal veins. One positive cytology was from a patient with a small tumor less than 3 cm in diameter localized within the head of the pancreas and encasement of only small pancreatic arteries. In the seventh patient in which cytology revealed suspicious cells, the tumor involved was also of moderate size. In the remaining 4 cancer patients in which

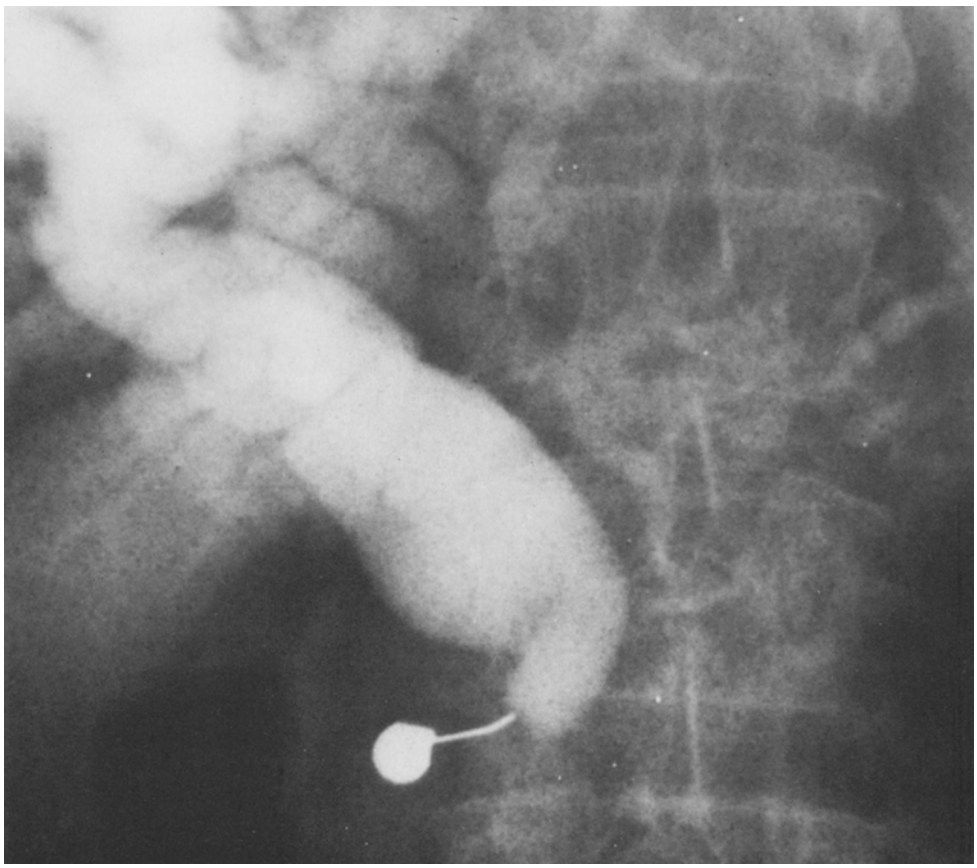

Fig 2. Successful percutaneous aspiration biopsy of the pancreas. The Chiba needle under fluoroscopic guidance is directed to the region surrounding the obstructed distal common bile duct.

aspiration biopsy was not diagnostic, the size of the carcinoma within the head of the pancreas was of large size in 1, moderate size in 1, and small in 2.

In 2 of the 13 patients, because of arterial irregularities, it was difficult to differentiate by angiography pancreatitis from carcinoma. In both cases the aspirate contained only normal pancreatic cells with an increased cellular debris, red blood cells, lymphocytes, and other monocytes. One of these patients died from liver failure, and an autopsy revealed chronic pancreatitis. The second patient underwent a laparotomy 18 months earlier for obstructive jaundice. The hard mass in the head of the pancreas at that time was interpreted as carcinoma, but operative biopsies of the mass showed only pancreatitis. His jaundice did not return, but he continued to have abdominal pain and weight loss. He was operated upon again and chronic pancreatitis was diagnosed after subtotal pancreatectomy.

Following percutaneous aspiration biopsy, none of the 13 patients had clinical or laboratory evidence of pancreatitis nor worsening of their clinical condition. Nine patients underwent laparotomy and one patient a postmortem examination. One patient developed a small hematoma 3 × 3 cm in the transverse mesocolon. In this patient, however, due to complete celiac artery stenosis, there was markedly increased vascularity in the region of the head of the pancreas because of collateral circulation from the superior mesenteric artery.

DISCUSSION

Carcinoma of the pancreas is the fourth leading cause of death due to carcinoma in the United States (7). Angiography and retrograde pancreatography are useful diagnostic tools but do not always provide definite proof of cancer. Further-

TABLE 1. CASE SUMMARIES

Case	*Cytology**	*Ultrasound*	*Angiography†*	*Cholangiography†*	*Final diagnosis*
I	–	Mass in porta hepatis	Encasement of GDA, HA, SMV	Obstruction of CHD with encasement of intrahepatic ducts (Chiba needle)	Tumor-porta hepatis Signed out AMA
II	+	Mass in body of pancreas	Encasement of HA, SA, LGA, SV	Not performed	Pancreatic CA
III	–	Mass in head of pancreas	Encasement of small vessels within head of pancreas	Obstruction of distal CBD (Chiba needle)	Pancreatic CA
IV	+	Not performed	Encasement of GDA	Obstruction of distal CBD (Chiba needle)	Pancreatic CA
V	–	Mass in porta hepatis	Encasement of GDA	Incomplete obstruction of CBD proximal to ampulla of Vater (Chiba needle)	Pancreatic CA
VI	+	Mass in head of pancreas	Encasement of small vessels within head of pancreas	Obstruction of distal CBD (Chiba needle)	Pancreatic CA
VII	+	Mass in body of pancreas	Encasement of HA, SA, LGA, SV	Obstruction of distal CBD (Chiba needle)	Pancreatic CA
VIII	–	Mass in head of pancreas	Encasement of small vessels within head of pancreas	Obstruction of distal CBD (Chiba needle)	Pancreatic CA
IX	±	Mass in head of pancreas	Encasement of GDA	Obstruction of distal CBD (Chiba needle)	Pancreatic CA
X	+ –	Mass in porta hepatis	Irregularity of small vessels within head of pancreas	No obstruction (ERCP)	Chronic pancreatitis
XI	+ –	Mass in head of pancreas	Encasement of GDA, SMV	Not performed	Chronic pancreatitis
XII	+	Mass in head of pancreas	No vessel abnormalities	Obstruction of distal CBD (Chiba needle)	Pancreatic CA
XIII	+	No mass demonstrated	Encasement of small vessels within head of pancreas	Obstruction of distal CBD (Chiba needle)	Pancreatic CA

* – = negative; + = positive; ± = highly suspicious for tumor; + – = no evidence of tumor—increased inflammatory cells.
†LGA = left gastric artery; SA = splenic artery; GDA = gastroduodenal artery; HA = hepatic artery; SMV = superior mesenteric vein; SV = splenic vein; CBD = common bile duct; CHD = common hepatic duct.

more, their diagnostic accuracy varies. Even in experienced hands cancer cannot be differentiated from pancreatitis in every patient. Ultrasonography and computerized axial tomography are powerful diagnostic tools and usually can identify a pancreatic mass but not its histology. Not only do all these modern diagnostic methods fail to distinguish chronic pancreatitis from carcinoma in approximately 15–20% of patients (5), but also direct inspection and palpation of the pancreas during surgery often cannot differentiate between the hard fibrotic mass of chronic pancreatitis and carcinoma (9, 10). Even histological diagnosis based on pancreatic biopsy may be misleading because (1) frozen sections may be difficult to interpret as the distorted patterns found in chronic pancreatitis may simulate cancer, or (2) the neoplastic portion of the tumor may be comparatively small and deep-seated within a larger area of pancreatitis and biopsy material may miss the cancerous tissue in as many as 16–35% of cases, or (3) one may misinterpret pancreatitis as cancer in up to 7% of patients (2, 3, 9–11). Furthermore, biopsy of the pancreas by either the Vim-Silverman needle or wedge resection is associated with substantial risk: 5–20% of patients developed hemorrhage, pancreatitis, fistulas, or abscess formation after biopsy with mortality rate ranging from 1.7% to 3.8% (3, 9, 10). There is therefore an obvious need for a safe and accurate preoperative "biopsy" of the pancreas.

The reliability of cytologic diagnosis of cancer is well established. It has been utilized successfully in the diagnosis of cancer of the breasts, lymph nodes, subcutaneous tissue, and prostate (1, 12–14). This

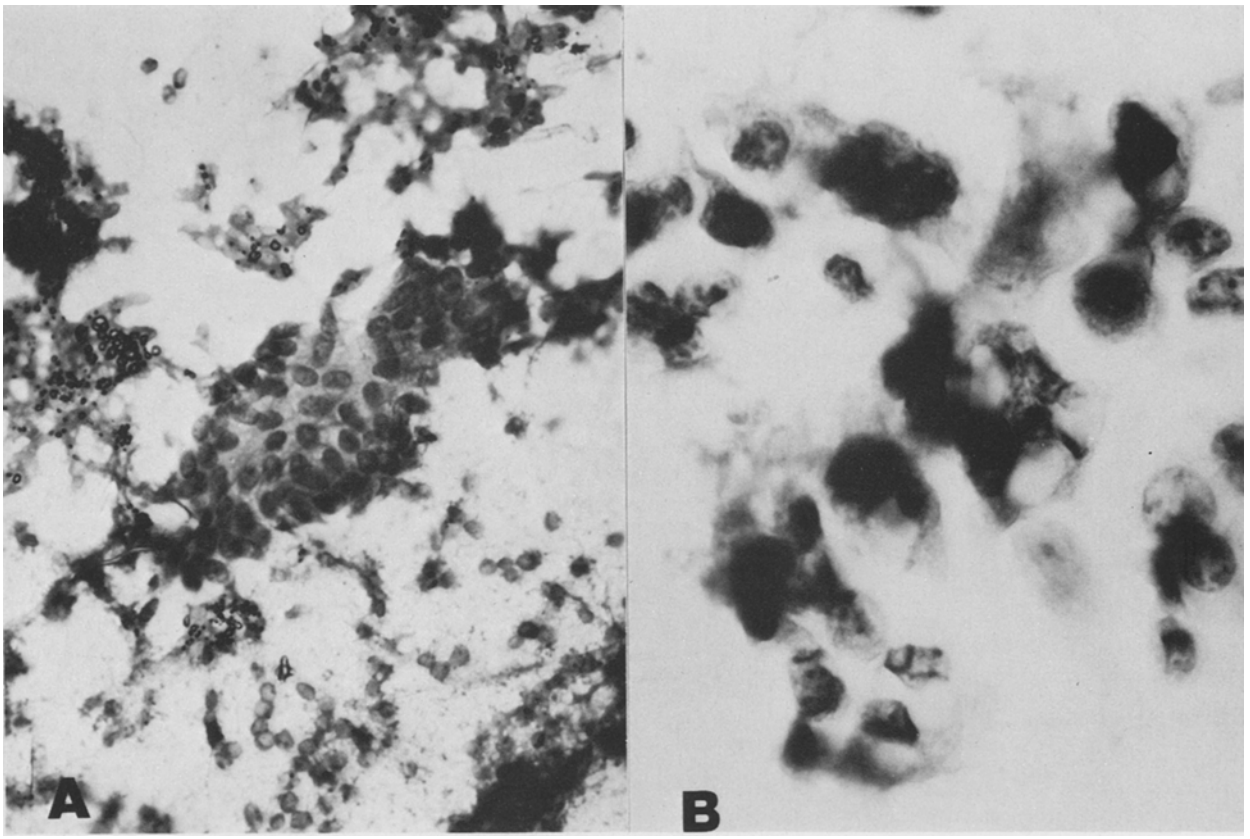

Fig 3. Pancreatic cells obtained by percutaneous aspiration biopsy. (A) Sheet of normal pancreatic cells (×250). (B) Cluster of malignant pancreatic cells (×750). Note the large irregular nuclei and chromatin clumping.

technique is based on aspiration and smear rather than resection of small pieces of tissue. One of the main advantages of cytology is the cells originate mainly from the glands and the scar and fibrous tissue which is a handicap for the histological diagnosis is not present. In the histological section one of the most important criteria of malignancy is the demonstration of the infiltration of the cancer cells to the surrounding tissue and blood vessels. This is not available in the aspirated cells and the cytologist has to rely on the minute morphological changes of the individual cells. Their interpretation is not as difficult as generally thought. Pathologists experienced in recognizing tumor cells in Pap smears will have little difficulty in differentiating the malignant pancreatic cells from benign ones. In cases of pancreatitis there is an increase of degenerative changes which are also easy to recognize and can be readily appreciated from the malignant changes.

The usefulness of pancreatic cytology was first demonstrated by Dreiling et al (15) in 1960. Utilizing the exfoliative cytological technique of duodenal aspirations, a positive diagnosis of pancreatic cancer was made in 78% of patients (47 of 60), but with a false-positive diagnosis in 5.6% of patients with a normal pancreas. Goldstein in 1968 (16), utilizing exfoliative cytology following secretin stimulation, made a diagnosis of pancreatic cancer in 18 of 24 patients (75%) without any false-positive diagnoses. There are, however, technical difficulties in cell sampling from the duodenum (9). The success of this procedure requires the positioning of the sampling tube in the duodenum (which may be easy or impossible) and an unobstructed pancreatic duct which communicates with the cancer. After the tumor occludes the duct pancreatic secretions cannot carry malignant cells to the duodenal tube.

Arnesjo et al (9) utilized fine-needle aspiration

biopsy of the pancreas during operation and compared it with tissue biopsy in the same patients. They found aspiration biopsy to be comparable to biopsy with positive diagnosis on cytology in 16 of 18 patients (88%). Other groups have substantiated the clinical usefulness and reliability of pancreatic aspiration biopsy performed peroperatively or at autopsy. By this technique Christofferson documented malignancy in 68 of 72 cases (17), Koivoniemi in 16 of 18 cases (18), Forsgren in 28 of 29 cases (19), Kline in 11 of 12 cases (18), and Shorey in 18 of 21 cases (20). In these series there were no reported false-positive diagnoses and in the operative patients no reported complications. Because of its high diagnostic yield, multiple punctures of deeply seated lesions are permitted with a lack of complications. Peroperative aspiration biopsy has been modified and a percutaneous approach has been attempted. The initial reports have been very encouraging. Holm et al (6) reported a positive diagnosis of pancreatic carcinoma in 17 of 21 patients, Tylen et al (8) reported a positive diagnosis in 22 of 29 patients with a lesion being as small as 3 cm, and Smith et al (7) reported a positive diagnosis in 5 of 6 cases. There were no known false-positive diagnoses in these series. In all patients the procedure was accomplished with a minimum of pain. The only reported complications were minor and included in 1 patient the passage of a single blood clot per rectum 2 days after biopsy, but no drop in hematocrit (7), and in 1 patient with chronic pancreatitis an elevation of serum amylase 1 day after puncture (6). In patients who underwent surgery shortly after biopsy there was sometimes noted a punctate bleeding point that was considered insignificant (8).

As in other series (4, 6–8), we have noted no significant complications in our 13 patients. In 2 of the patients studied the lesion proved nonresectable by angiographic criteria. Thus an unnecessary laparotomy was avoided and palliative chemotherapy and radiotherapy was initiated. In 2 additional patients the aspirate contained normal pancreas cells with an increased cellular debris of red blood cells, lymphocytes, and other monocytes. In both these patients pancreatitis was proven histologically. We are presently performing aspiration biopsies on autopsied patients to see if these are consistent findings in pancreatitis.

The technique of percutaneous aspiration biopsy requires experience. Until recently we have been altering our techniques and are hopeful of achieving a higher diagnostic accuracy. In addition to proper localization of the tumor mass by using better ultrasonic (Grey scale) equipment, it is important to feel a hard gritty sensation as the needle is entering the mass.

It has been demonstrated experimentally (12) that microscopic seeding of the tumor cells occurs during aspiration biopsy. However, in large studies there has been no clinical evidence that aspiration biopsy alters the incidence of survival or of local tumor extension in carcinoma of the breast, kidney, salivary glands, prostate, or metastatic lymph nodes (1, 12, 19). Seeding is clinically insignificant probably because only a few cells enter the needle track and these cells are destroyed before they can give rise to local tumor growth. Although there are scattered reports of tumor growth along tracks of needles used for biopsy, there are no definite reports of local tumor extension caused by fine-needle 18- to 22-gauge aspiration biopsies (6, 12, 20).

Percutaneous aspiration biopsy of the pancreas may be a reliable diagnostic aid in the evaluation of a patient with a pancreatic mass. It is a rapid, easily tolerated, inexpensive procedure that appears to be safe, but should be performed only if there is no evidence of liver metastasis. Liver biopsy in these patients would then be the diagnostic procedure of choice. Only a positive cytological diagnosis is of value and a negative result does not exclude a pancreatic malignancy. A positive cytological report not only helps the surgeon with his operative procedure plan, but also allows him to discuss in greater depth with his patient the operative approach that will be utilized. In addition a needless laparotomy may be avoided and palliative chemotherapy or radiotherapy instituted in patients with far advanced carcinoma. This includes primarily patients in whom angiography demonstrates a nonresectable tumor of the body or tail of the pancreas and who do not have obstructive jaundice or gastric outlet obstruction. It also includes, however, the patient with obstructive jaundice who in addition to his pancreatic carcinoma may have on cholangiography complete or partial malignant obstruction to his common hepatic duct making a biliary bypass procedure unlikely to succeed. This patient may receive palliation without surgery by prolonged percutaneous biliary drainage.

REFERENCES

1. Berg JW, Robbins GF: A late look at the safety of aspiration biopsy. Cancer 15:826–827, 1962

2. Bowden L: The fallibility of pancreatic biopsy. Ann Surg 139:403–408, 1954
3. Lightwood R, Reber HA, Way LW: The risk and accuracy of pancreatic biopsy. Am J Surg 132:189–194, 1976
4. Oscarson J, Stormby N, Sundgren R: Selective angiography in fine needle aspiration cytodiagnosis of gastric and pancreatic tumours. Acta Radiol 12:737–749, 1972
5. Anacker H: Efficiency and Limits of Radiologic Examination of the Pancreas. Massachusetts, Thieme-Edition/Publishing Sciences Group, Inc., 1975, pp 273–276
6. Hancke S, Holm HH, Koch F: Ultrasonically guided percutaneous fine needle biopsy of the pancreas. Surg Gynecol Obstet 140:361–364, 1975
7. Smith EH, Bartrum RJ, Jr, Chang YC, et al: Percutaneous aspiration biopsy of the pancreas under ultrasonic guidance. N Engl J Med 292:825–828, 1975
8. Tylen U, Arnesjo B, Lindberg LG, et al: Percutaneous biopsy of carcinoma of the pancreas guided by angiography. Surg Gynecol Obstet 142:737–739, 1976
9. Arnesjo B, Stormby N, Akerman M: Cytodiagnosis of pancreatic lesions by means of fine needle biopsy during operation. Acta Chir Scand 138:363–369, 1972
10. Schultz NJ, Sanders RJ: Evaluation of pancreatic biopsy. Ann Surg 158:1053–1057, 1963
11. Rosen PP: Histologic diagnosis of pancreatic disease (correspondence). N Engl J Med 293:97, 1975
12. Engzell U, Esposti PL, Rubo E, et al: Investigation of tumour spread in connection with aspiration biopsy. Acta Radiol 10:385–398, 1971
13. Franzen A, Zajicek J: Aspiration biopsy in diagnosis of palpable lesions of the breast. Acta Radiol 7:241–262, 1968
14. Kline TS, Neal HS: Needle biopsy—a pilot study. JAMA 224:1143–1146, 1973
15. Dreiling DA, Nieburgs HE, Janowitz HD: The combined secretin and cytology test in the diagnosis of pancreatic and biliary tract cancer: Med Clin North Am 44:801–815, 1960
16. Goldstein H, Ventzke LE: Value of exfoliative cytology in pancreatic carcinoma. Gut 9:316–318, 1968
17. Christofferson P, Poll P: Peroperative pancreas aspiration biopsies. Acta Pathol Microbiol Scand (Suppl) 212:28–32, 1970
18. Kline TS, Goldstein G, Neal HS: Pancreatic carcinoma, pancreatitis, and needle aspiration biopsy. Arch Surg 109:578–579, 1974
19. Forsgren L, Orell S: Aspiration cytology in carcinoma of the pancreas. Surgery 73:38–42, 1973
20. Shorey BA: Aspiration biopsy of carcinoma of the pancreas. Gut 16:645–647, 1975