Gastrointest Radiol 11:145–150 (1986)

Gastrointestinal Radiology

Fine Needle Aspiration Biopsy in Malignant Obstructive Jaundice

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Abstract. Percutaneous cytodiagnosis of malignancy in patients with biliary tract obstruction is often useful in planning subsequent therapy. Of 121 patients presenting for percutaneous transhepatic cholangiography and biliary drainage, 45 had fine needle aspiration biopsies. Forty-one patients had malignant obstruction of the biliary tree, while benign disease was present in 4 patients. Neoplasia was diagnosed in 12 of 13 patients with bile duct carcinoma, 16 of 22 patients with pancreatic cancer, and 3 of 6 patients with other malignancies. Radiologic biopsy sensitivity was only slightly inferior to surgical biopsy sensitivity in the same patient population. A scheme for biliary cytodiagnosis is presented, which uses a percutaneous approach for patients with suspected pancreatic carcinoma and a transcatheter approach for patients with suspected bile duct carcinoma. The utility of this procedure and the low complication rate are stressed.

Key words: Fine needle aspiration biopsy – Bile duct carcinoma – Pancreatic carcinoma – Obstructive jaundice.

Fine needle aspiration biopsy is frequently used for the preoperative diagnosis of abdominal malignancies in patients with obstructive jaundice. Numerous series have been reported in the medical, surgical, and radiologic literature with particular emphasis on the detection of pancreatic carcinoma. Percutaneous needle placement has been guided by percutaneous transhepatic cholangiography (PTC) (sensitivity, 52%) [1, 2], angiography (sensitivity range, 61–76%) [1–6], ultrasound (sensitivity range, 70–81%) [1, 4, 6–11], ERCP (sensitivity range, 88–93%) [1, 12, 13], and computed tomography (CT) (sensitivity range, 89–95%) [11, 14, 15]. Transcatheter brush and forceps biopsy techniques after percutaneous biliary drainage or T-tube insertions have also been reported [16–19], although total numbers of patients have not been large enough to determine meaningful sensitivities.

Differences in reported sensitivities may be explained by use of different biopsy methods, including varying numbers of needle passes, operator expertise, and criteria used by each cytopathologist in diagnosing malignancy, as well as by the use of the different imaging modalities for needle guidance. Of 121 patients presenting to the Duke University Medical Center for PTC and biliary drainage, 61 biopsy samples were obtained in 45 patients. Results were reviewed to assess the relative sensitivities in detecting the various malignancies causing biliary obstruction. The ability of the radiologist to detect and diagnose bile duct carcinoma as well as pancreatic carcinoma was specifically evaluated, and findings were compared with surgical biopsy results in the same patient population. A revised strategy for cytodiagnosis of obstructing malignancies has been adopted which should further minimize false-negative results.

Materials and Methods

One hundred twenty-one patients with obstructive jaundice presented to the Interventional Service for percutaneous transhepatic cholangiography and biliary drainage between January, 1979, and May, 1984. After initial evaluation by CT or ultrasound, PTC was performed with 21-gauge Cope or 22-gauge Chiba needles. Biliary drainage was performed as described previously [20, 21]. Either 8.3 Fr or 10 Fr Cope or biliary ring catheters were ultimately inserted with their tips in the

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duodenum whenever possible. The strictured area was negotiated in most cases. Biopsies were performed as discussed previously [4, 15]. Samples were obtained percutaneously with fluoroscopic guidance using transhepatic cholangiography, or alternatively, with ultrasound or CT guidance (Fig. 1). More recently, transcatheter brush or needle biopsies were also performed in certain patients (Fig. 2). Usually, 2–3 needle passes were made per sitting per patient. Twelve patients had 2 or more separate biopsy sittings. All aspiration biopsy specimens were placed in an iso-osmolar saline solution (Normosol®-R, Abbott Laboratories) and promptly transported to the cytopathology laboratory where they were evaluated according to techniques elucidated elsewhere [22, 23]. A cytologic result reported as "atypical" or "suspicious" was considered negative for the purpose of this study; however, in no case did a patient with such a result have benign disease when the final diagnosis was established. Final diagnoses were made at surgery and/or by clinical follow-up.

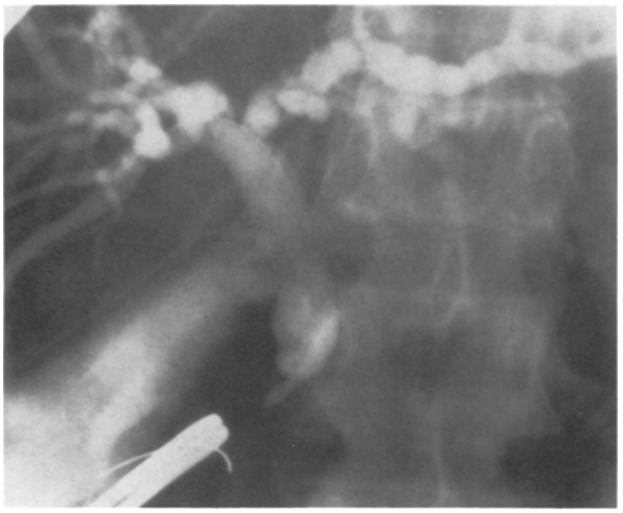

Fig. 1. Percutaneous fine needle aspiration biopsy in a patient with pancreatic carcinoma. Forceps are seen guiding the Chiba needle into the region of the obstructing mass.

Results

Sixty-one samples were obtained in 45 patients. Forty-one patients (91%) were ultimately determined to have malignancy. Twenty-two patients had pancreatic carcinoma, 13 patients bile duct carcinoma, 5 patients metastatic disease, and 1 patient a hepatoma. The remaining 4 patients had benign disease. A total of 57 samples were obtained from the 41 patients with malignant disease. These were positive 33 times (sensitivity, 58%). Transcatheter biopsies were positive 8 of 12 times (sensitivity, 67%) and percutaneous biopsies 25 of 45 times (sensitivity, 56%).

Cytologic examination was positive in 31 patients. There were no false-positive results. Overall sensitivity was 76%. There were 10 patients with false-negative and four with true-negative cytologic findings. Therefore, although the positive predictive value was 100%, the predictive value of a negative result was only 29% (Table 1).

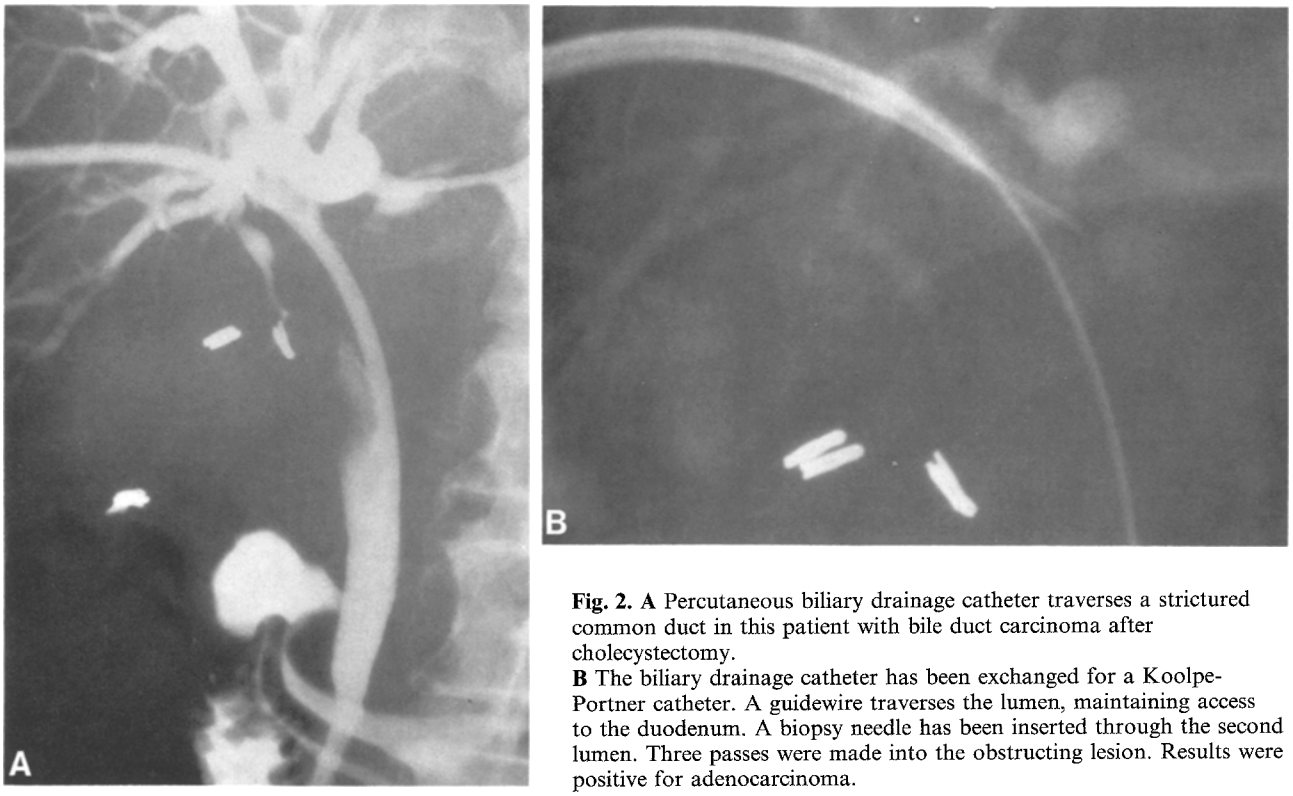

Fig. 2. A Percutaneous biliary drainage catheter traverses a strictured common duct in this patient with bile duct carcinoma after cholecystectomy.
B The biliary drainage catheter has been exchanged for a Koolpe-Portner catheter. A guidewire traverses the lumen, maintaining access to the duodenum. A biopsy needle has been inserted through the second lumen. Three passes were made into the obstructing lesion. Results were positive for adenocarcinoma.

Twenty-five patients with carcinoma were diagnosed at the first sitting (first-sitting sensitivity, 67%). Of 10 patients with malignancy who had initially negative findings on cytologic study, and who were subjected to repeat biopsy, tumor cells were subsequently identified in 6. Six of 10 false-negative results occurred in patients who underwent only 1 biopsy sitting.

Radiologic biopsy sensitivity was highest in patients with bile duct carcinoma, in whom 12 of 13 malignancies were detected (92%). Neoplastic cells were isolated from 16 of 22 (73%) patients with pancreatic carcinoma, 2 of 5 patients with metastatic disease, and the 1 patient with a hepatoma. No significant complications were encountered.

Surgical biopsy sensitivity in the same patient population was 88% (35/40). The surgeons obtained positive histologic or cytologic samples in all 19 patients with bile duct carcinoma, and in 16 of 21 patients (76%) with pancreatic carcinoma including 2 of 5 patients with negative radiologic biopsy findings. Not surprisingly, few patients with metastatic disease underwent surgery, and none of these few had diagnostic biopsy specimens taken (Table 2).

Table 1. Patients undergoing fine needle biopsy

	Malignancy	Benign disease	Total
(+) Cytology	31	0	31
(−) Cytology	10	4	14
Total	41	4	45

Sensitivity, 76%; specificity, 100%; positive predictive value, 100%; negative predictive value, 29%; accuracy, 78%.

Table 2. Comparison of radiologic and surgical biopsy results

	Radiologic biopsy		Surgical biopsy			
	Number	%	After negative radiologic biopsy	After positive or without radiologic biopsy	Total	%
Bile duct carcinoma	12/13	92	0/0	19/19	19/19	100
Pancreatic carcinoma	16/22	73	2/5	14/16	16/21	76
Metastatic disease	2/5	–	0/0	0/0	0/0	–
Hepatoma	1/1	–	0/0	0/0	–	–
Total	31/41	76	2/5	33/35	35/40	88

Discussion

Fine needle aspiration biopsy has been accepted as a safe and effective technique for diagnosis of the common malignancies that cause biliary obstruction. It is often desirable to obtain a definite cytologic diagnosis of carcinoma in patients who are not surgical candidates [24]. Differentiation of benign from malignant disease by radiologic imaging may also be impossible in more than 10% of patients with pancreatic masses [25, 26], and in selected patients with biliary ductal strictures [27]. Biopsy may be required in these cases to establish a diagnosis of malignancy.

The overall sensitivity of 76% obtained here is similar to that reported elsewhere. The individual sensitivity of 73% in detecting pancreatic carcinoma rivals that reported by others (60% [2]–86% [11]) who used multiple modalities for needle guidance, but is lower than that obtained in series using ERCP or CT alone (88% [12]–95% [14]). This suggests that the latter 2 techniques are superior in permitting accurate needle placement into malignant, noninflammatory, nonnecrotic tissue.

Most pancreatic neoplasms are enveloped by thick rinds of inflammatory tissue due to pancreatitis resulting from pancreatic ductal obstruction by tumor [28]. Much of the mass effect, vascular change, and even the biliary ductal obstruction may be caused by this surrounding pancreatitis [6]. In several series it has been noted that false-negative biopsy results often occurred in patients with particularly desmoplastic pancreatic tumors [5, 6]. Obviously, CT can more easily delineate the full extent of the pancreatic cancer than can other modalities. The radiologist can subsequently define and biopsy the epicenter of the tumor, which potentially yields the highest percentage of true-positive results [24].

While ultrasound imaging is similar to CT, there may be technical difficulties in visualizing the entire pancreas and the tumor itself, due to attenuation of the sound waves by surrounding bowel gas. This may account for the somewhat lower sensitivities obtained when ultrasound is employed for needle placement. The extremely high sensitivities obtained with ERCP may reflect the fact that the vast majority of pancreatic neoplasms are ductal in origin and that the site of pancreatic ductal obstruction more frequently indicates tumor location than does, for example, the site of biliary ductal obstruction. PTC-guided biopsy would there-

fore be expected to provide lower biopsy sensitivities since neither tumor margins nor the site of pancreatic duct obstruction is defined by this modality.

The surgical biopsy sensitivity in diagnosing pancreatic neoplasm of 76% was not significantly different from that obtained by radiologic biopsy in this study. This value is slightly lower than that reported in the surgical literature for wedge biopsy (46–90%) [29–31], and for aspiration biopsy (71–100%) [29, 32–35]. Only 2 of 5 patients with negative radiologic biopsy specimens who went on to surgery had positive findings on surgical biopsy specimens.

Surgical biopsy of pancreatic neoplasms may be quite difficult, particularly for those lesions located deep within the pancreas, and those surrounded by inflammation and fibrosis. In several of the cases reported here, the surgeons palpated rock-hard pancreatic masses described as typical ductal adenocarcinomas. Although multiple surgical biopsies revealed only inflammatory tissue, the subsequent clinical course of these patients was entirely compatible with the surgeon's impression of malignancy. Thus, surgical biopsy may not represent the "gold standard" to which the successes and failures of radiologic biopsy can be compared. Clinical follow-up is occasionally required to confirm a diagnosis of malignancy.

Obtaining cytologic diagnoses of malignancy in 12 of 13 patients with bile duct carcinoma represents a significant improvement from results reported by Evander et al., who were able to isolate malignant cells in only 10 of 19 patients (53%). In the latter study, biopsies were performed percutaneously with use of angiography and/or PTC to localize the tumor [2]. As our experience increased, transcatheter biopsies were performed exclusively when possible.

We believe that use of this technique explains our much greater sensitivity in detecting these small tumors. The transcatheter approach allows even the tiniest of lesions responsible for biliary ductal obstruction to be biopsied. Localization of such a neoplasm via a percutaneous route may be difficult if not impossible, particularly when biplane fluoroscopy is not available. Sensitivity in detecting bile duct carcinoma at surgery was equally high: malignant tissue was obtained by the surgeons from all patients undergoing laparotomy. The number of patients with metastatic disease was too small to allow us to calculate a meaningful sensitivity.

The lack of significant complications directly attributable to percutaneous biopsy is in agreement with several series previously reported [14, 22, 34, 36]. Many have, in fact, stressed the absence of any significant organ injury in patients who subsequently required surgery. Although a recent report has suggested that hematocrit drops of >3 may occur in as many as 2.5% of patients [37], we have found no demonstrable alteration in the clinical course of any of the patients we biopsied. One case each of post-biopsy sepsis, abscess formation, and fatal necrotizing pancreatitis has been described [11, 37]. No patients in this series developed any such complications directly attributable to the biopsy procedure.

The theoretical risk of needle tract tumor implantation has been frequently stated. Ferrucci et al. have reported the only recorded case observed with 22-gauge fine needles to date. In their series of 100 cases, 1 patient had 10 passes made into a pancreatic carcinoma within 2 days. Three months later, recurrence along the needle tract was demonstrated [39]. Kline and Neal failed to observe any such seeding in a series of 3,267 patients who had chest and abdominal lesions biopsied [35]. Ho et al. similarly reported no needle tract tumor implantation in 1,500 patients who had lung, thyroid, or breast biopsies [12], nor did Lalli et al. in a series of 1,223 lung biopsies [22], nor Engzell et al. in their group of 626 abdominal biopsies [36]. The other infrequent reports of seeding have occurred in patients who had biopsies with 18–20-gauge aspiration or core biopsy needles [40–42]. While transcatheter biopsy itself is believed to have no significant risk, there are several reports of probable tumor seeding along biliary drainage catheter tracts [43–45], including a group of 3 patients included in this series of 121 patients [46]. Since this report, a 4th such patient has been discovered. (Only 1 of these 4 patients has had a transcatheter aspiration biopsy.)

Our approach for cytodiagnosis of patients with obstructive jaundice presenting for PTC and drainage is to obtain up to 3 samples of bile for cytologic analysis on successive days, when possible. If these are negative, fine needle aspiration biopsy is performed. If the patient's hospital stay must be shortened, biopsy may take place at the same time the bile samples are collected. A percutaneous approach under CT or ultrasound guidance is recommended for patients with obstructive jaundice and pancreatic head masses. A transcatheter approach is preferred, when feasible, for patients with portal masses, or in whom no mass is visualized by the preliminary imaging procedure. Ferrucci et al. have shown that up to 4 passes should be made at each biopsy sitting [11]. We have also

found that 2 separate sittings are often helpful, as was the case in 6 of 10 patients with malignancy. It is likely that such a scheme for cytodiagnosis will serve to improve upon an already respectable sensitivity rate of 73% for this procedure.

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Received: December 17, 1984; accepted: March 8, 1985