

Cholangiocarcinoma

Role of Percutaneous Transhepatic Cholangiography in Determination of Resectability

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Exploratory laparotomy is frequently used to diagnose, treat, or palliate cholangiocarcinoma although surgery is rarely curative. In light of newly developed percutaneous and endoscopic approaches to diagnosis and therapy, we reviewed our experience with 35 cases of cholangiocarcinoma diagnosed and treated at the University of Michigan Medical Center from 1979 to 1984. Percutaneous transhepatic cholangiography (PTCA) was performed in 34 cases of which only four were resectable. All 22 patients who had preoperative cholangiograms suggesting unresectability had confirmation of this at surgery. Surgical palliation was accomplished with a combination of internal and percutaneous drainage in most cases. Angiographic, cytologic, and laboratory data are presented. PTCA accurately predicted unresectability of cholangiocarcinoma and is superior to angiography in this respect. In patients with cholangiocarcinoma, percutaneous and endoscopic approaches offer alternatives to surgery for diagnosis and palliation.

KEY WORDS: transhepatic cholangiography; cholangiocarcinoma obstructive jaundice; angiography; biliary cytology; biliary drainage; hypoalbuminemia.

Cholangiocarcinoma is the third most common cause of malignant biliary obstruction, exceeded only by carcinomas of the pancreas and gallbladder. Cholelithiasis, choledocholithiasis, and ulcerative colitis have been associated with increased risk of cholangiocarcinoma. Obstructive jaundice is the most common presentation. Since this carcinoma

typically invades local tissues early, most are not resectable even at presentation, although only 20% metastasize within the liver and to distant sites (1-4).

Visualization of the biliary tree is the pivotal step in the initial evaluation of obstructive jaundice and possible cholangiocarcinoma. Percutaneous transhepatic cholangiography (PTCA), has a success rate approaching 100% with bile duct dilatation, can assess the location and extent of biliary tract involvement, and has been proposed as a basis for determining surgical resectability (5-9).

Surgical excision with adequate surgical margins remains the optimal therapy and the only chance of cure; however, since the tumor is often unresectable at presentation, palliative drainage must be employed (10-18). Indications for surgery are the need for histologic diagnosis, curative resection,

Manuscript received July 31, 1986; revised manuscript received June 19, 1987; accepted August 3, 1987.

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TABLE 1. CHOLANGIOCARCINOMA: CHOLANGIOGRAPHY, ANGIOGRAPHY, AND SURGICAL RESECTABILITY AND PALLIATION

	Total cases	Cholangiographic patterns		
		Type I, intrahepatic and segmental ducts	Type II, right and left hepatic ducts, bifurcation and proximal 1 cm of common hepatic duct	Type III, common hepatic and common bile ducts excluding ampulla of Vater
Cholangiographic extent of disease	34	5	25	4
Angiograms*/evidence of unresectability	27/13	4/2	18/11	4/0
Percutaneous drainage/internal drainage accomplished	22/16	4/3	14/11	4/2
Exploratory laparotomy†/unresectable disease found	26/24	4/4	17/17	4/3
Postop drainage external/internal/both	1/6/16	0/1/3	1/3/13	0/2/1

*One patient had an angiogram without cholangiogram.

†Curative resections: one had type III cholangiogram, the other did not have a cholangiogram.

and palliative drainage. Histologic diagnosis may also be achieved by cytologic examination of biliary fluid in up to 50% of cases (10, 19). Palliative drainage usually done at the time of PTCA can be maintained for short- or long-term drainage (20–35).

This study reviews our experience with cholangiocarcinoma in light of these newly developed percutaneous methods of cholangiography, cytologic diagnosis, and palliative drainage. We assess the role of PTCA in the determination of tumor resectability in comparison with angiography and surgical findings.

MATERIALS AND METHODS

We retrospectively reviewed all patients with the diagnosis of cholangiocarcinoma who presented to the University of Michigan Medical Center between May 1979 and July 1984 for definitive diagnostic evaluation and therapy. Thirty-five cases were identified, 29 of which had cytologic, surgical tissue, or autopsy confirmation of the diagnosis. The other six patients had cholangiograms and clinical courses compatible with cholangiocarcinoma.

Cholangiograms as originally reported were classified according to the most proximal extent of the tumor: Group I had tumor in the intrahepatic and segmental ducts; group II involved the proximal extrahepatic ducts including the right and left hepatic ducts, the bifurcation and proximal 1 cm of the common hepatic duct; and group III included tumors limited to the distal extrahepatic ducts including the common hepatic duct and the common bile duct, excluding tumors of the ampulla of Vater.

Survival as of December 1985 was determined either from the chart, tumor registry records, or telephone communication with the patient's relatives.

RESULTS

The median age of the patients was 64 years; patients were 20 men and 15 women. None had ulcerative colitis or sclerosing cholangitis, but a

history of choledocholithiasis was reported in five patients. The chief complaints at presentation were jaundice in two thirds of the patients, and weight loss and abdominal pain in the remainder. The duration of symptoms prior to initial presentation was a median of one month with a range of two weeks to two years. Eleven patients had surgical intervention for their disease prior to transfer. Of these, only two had a histologic diagnosis. The mean bilirubin on admission was 16.1 mg/dl, and in three cases the bilirubin was less than 3.0 mg/dl. Reports of biliary ultrasonography were available in 22 cases: 19 patients had dilated bile ducts and three reported no dilated ducts; two of these three were confirmed not to have dilated ducts by PTCA.

PTCA was generally the next step in the diagnostic work-up (Table 1). Thirty-four of 35 patients had cholangiography. Five had type I or intrahepatic involvement. Twenty-five had type II or proximal extrahepatic duct involvement; 19 of these had tumor involving both the right and left hepatic ducts, while six had tumor only at the bifurcation and proximal common hepatic duct. Four patients had tumor only in the distal extrahepatic ducts.

At the time of PTCA, percutaneous drainage was attempted in 22 patients with a 100% success rate. Sixteen patients had internal and external drainage and six patients had external drainage only. The mean duration of preoperative percutaneous drainage was eight days. During this period, the bilirubin fell from 14.5 mg/dl to 9.8 mg/dl ($P > 0.05$). For 19 patients where data were available, the albumin fell from 3.4 g/dl on admission to 3.0 g/dl preoperatively ($P < 0.01$). As a control for rehydration during this period, we found that the BUN decreased minimally from 15.8 mg/dl to 15.5 mg/dl ($P > 0.05$).

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TABLE 2. CYTOLOGIC DIAGNOSIS

	Total studied	Negative	Suspicious/positive
Biliary fluid	18	14	4
Positive surgical Bx*		13	2
Percutaneous aspirate	8	6	2
Positive surgical Bx		3	1
Brushings	2	2	0
Positive surgical Bx		2	0

*Bx: biopsy.

Cytologic specimens were obtained from 20 patients (Table 2). Biliary sampling was suspicious or positive in only 22% (4/18 samples obtained), and percutaneous needle aspirate was positive in 25% with only eight samples studied. Angiography was done in 27 of 35 patients. Evidence of tumor unresectability such as portal vein encasement, extrahepatic artery encasement, or distant liver metastasis (38–41) was reported in 13 of 27 cases.

Exploratory laparotomy was performed in 26 of 35 patients. Only two patients had attempted curative resection of their tumors. These two patients were clearly distinguished from the rest of our population. The first had a large liver mass in the right lobe that angiography reported as a resectable hepatoma. The patient underwent right lobectomy and, on pathology, adenocarcinoma of bile duct origin was found. This patient had a recurrence of this tumor in the left lobe and died of his disease 28 months after presentation. The second patient had carcinoma of the distal common bile duct. Cholangiography and angiography found no evidence of unresectability, and she underwent a Whipple procedure. She subsequently did poorly with much weight loss and died of sepsis at 13 months after surgery. There was no evidence of recurrence.

In the remaining 24 patients undergoing surgery, unresectable disease was found. Patients were considered unresectable because of lymph node involvement in six cases, vascular involvement (bilateral hepatic artery or portal vein) in four cases, bilateral ductal involvement in five cases, and extensive intrahepatic spread in eight cases. Biopsies were taken and a drainage procedure was done. Only one patient had internal drainage such as a Roux-en-Y hepatojejunostomy without a percutaneous tube, six had internal drainage in addition to a percutaneous tube, while 16 patients had external drainage via varying percutaneous drainage tubes. Nine patients had no surgery: one declined surgery; the other eight

were felt to have unresectable disease, and the decision was made not to attempt surgical palliation.

Exploratory laparotomy with biopsy provided tissue diagnostic for cancer in 16 of the 20 patients who had negative preoperative cytology or previous surgical biopsy. Overall four of 26 cases had surgical biopsies negative for cancer but were presumed to have the disease based on clinical and radiologic assessment and were treated accordingly. A surgical mortality of 4% was noted.

Complications of PTCA included fever $>101^{\circ}$ F in four patients. Death might have been related to complications in two additional patients. One had a low-grade fever on the day of PTCA, then a fever with positive blood cultures 11 days after PTCA, and died of sepsis one week later. The second had a subphrenic abscess thought to be an infected hematoma. This required surgical drainage, and the patient died two months after presentation.

Survival data were calculated based on known data of death in 31 of 35 patients. Two patients were still alive at the time of study. Two patients were lost to follow-up. Overall survival was 12.2 months. For patients who had surgery, the mean survival was 14.7 months, while those who did not have surgery had a mean survival of <1 month. The longest survivor is still alive at 61 months without evidence of recurrence.

DISCUSSION

Using cholangiographic locations of type I and II as evidence of unresectability, we find that all 22 patients with preoperative cholangiograms suggesting unresectability had confirmation of this at surgery. The surgical findings in our series always reported tumor as or more extensive than that demonstrated by cholangiography. Although the surgical extent of disease frequently was not precisely recorded, proximal extent of intraductal spread was generally the reason for unresectability. All 13 patients with evidence of unresectable disease demonstrated by angiography also had type I or II cholangiographic findings.

In the series of Nichols et al (6), of 69 patients with cholangiograms showing type I or II disease, only one patient had a possible surgical cure. In other series (10–18), many patients with type II disease underwent curative resections and their survival was about 17 months. Few if any had long-term survival. A recent series by Lai et al (42) found that even with aggressive curative resection

in 29 patients, the mean survival was 11.8 months with only one long-term survivor.

Histologic diagnosis by surgical biopsy can be difficult, with frequent false negatives. This is due to the scarring around the tumor and the patchy nature of the disease. Nonoperative histologic diagnosis can be made by a variety of percutaneous methods such as biliary fluid samples and needle aspiration of tumor. Harrell et al report positive cytology in 50% of biliary samples (19). Our findings are less than their results, with only 20% reported as positive or suspicious. Review of these specimens reveals many inadequate samples, typically with few or no epithelial cells. At our institution, much attention is currently being given to improving these cytologic results. Radiologists are being more aggressive in their efforts at washings and brushings during PTCA and obtaining multiple samples. A senior cytology staff physician currently prepares and reviews the specimens at the site in other radiologic diagnostic procedures. Naylor (unpublished data) reports a twofold increase in positive results since this practice was initiated. Application of these methods to biliary radiology could improve diagnostic cytologic yield.

Palliative drainage was generally achieved by a combination of percutaneous and surgically placed tubes in the patient undergoing surgery. In either case, external drainage in addition to internal drainage remained in place in most patients. External drainage is presumed to add an increased risk of infection but has the advantage of easy flushing or replacement if there is obstruction. It is not yet known how surgical and percutaneous placement of chronic drainage catheters would compare on a prospective basis.

Our finding of a fall in albumin during the period of preoperative percutaneous drainage has not been reported previously. It is presumably due to a combination of poor nutrition and external drainage of copious proteinaceous biliary fluid. This may be of clinical significance in light of reports that albumin is an independent predictor of poor prognosis (43-46). Emphasis needs to be placed on nutrition during this critical period, since protein needs may be additionally increased by biliary losses. While our study did not show a significant decrease in bilirubin during the period of percutaneous drainage, a previous study on an overlapping population did show a significant decrease (37).

Survival was lower in our group treated without surgery. This probably reflects the selection of this

group as poor surgical risk and thus poorer prognosis. All of the patients fit the criteria of Bonnel et al for poor operative risk (43).

Despite the generally high surgical risk of patients with cholangiocarcinoma, surgery is still frequently employed for assessment of extent of disease, tissue diagnosis, and palliative drainage. Percutaneous transhepatic cholangiography can reliably predict unresectability of cholangiocarcinoma. Advances in percutaneous methods of cytologic diagnosis and endoscopic and percutaneous techniques for palliative drainage offer alternatives to surgery. Utilization of endoscopic management of malignant biliary strictures has progressed recently. Palliation of biliary strictures, including hilar lesions, can be accomplished by the placement of biliary stents up to approximately 12 Fr with high rates of success and low mortality (47, 48). Percutaneous biliary drainage techniques including stent placement were introduced prior to endoscopic modalities and are used for chronic drainage; however, some studies suggest greater success, lower morbidity, and greater patient tolerance with endoscopic biliary prosthesis drainage (49).

Prospective studies are needed to compare surgical and nonsurgical approaches to palliation in the hope of improving the morbidity and poor prognosis of this uncommon disease.

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