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Cholangiographic findings of early-stage extrahepatic bile duct carcinoma

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Background. To clarify the cholangiographic findings of early-stage (T1, tumor confined to the mucosal or fibromuscular layer) extrahepatic bile duct carcinoma. ***Methods.*** Cholangiographic images were retrospectively analyzed without other information in 55 patients with extrahepatic bile duct carcinoma who underwent surgical treatment. Tumor stages were T1 (n = 10), T2 (n = 17), and T3 (n = 28). Cholangiographic findings were classified as "diffuse sclerosis," "stenosis," "papillary polypoid filling defect," or "nodular polypoid filling defect". "Papillary polypoid filling defect" was the term used when the width of the base was smaller than the width of the polypoid filling defect. ***Results.*** T1 patients showed papillary polypoid filling defects (n = 8) or nodular polypoid filling defects (n = 2) on cholangiography. When cholangiography showed papillary polypoid filling defects, 8 of the 14 resected patients showed T1 stage tumor histologically. ***Conclusions.*** In this study, 57% (8/14) of resected patients with papillary polypoid filling defects showed T1 stage tumor. No T1 stage tumor showed stenosis or diffuse sclerosis.

Key words: cholangiography, early stage, bile duct carcinoma

Introduction

Because endoscopy of the upper gastrointestinal tract is now a routine procedure, gastric cancer is commonly observed at an early stage. One can now easily distinguish between early-stage cancer and advanced disease by endoscopic findings. By contrast, in most patients with extrahepatic bile duct carcinoma the disease is diagnosed at an advanced stage;[1–8] no previous report has clarified the characteristics of bile duct cancer at an early stage, based on cholangiographic findings. Tio et al.[1] found that only 2 of 103 patients with bile duct carcinoma examined endosonographically were at the T1 stage (tumor confined to the submucosal muscular layer). Schoenthaler et al.[2] found none of 129 patients with bile duct carcinoma to be at the T1 stage. In this report, we retrospectively analyzed the cholangiographic images of extrahepatic bile duct carcinoma at the T1 stage.[9]

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Subjects and methods

Subjects

The cholangiograms of 55 patients with extrahepatic bile duct carcinoma who underwent surgical treatment between September 1992 and November 2000 were analyzed. There were 36 men and 19 women, with an average age of 66.3 years (range, 43 to 87 years). The patients' characteristics are summarized in Table 1. Patients with carcinoma of the intrahepatic bile ducts, gallbladder, pancreas, ampulla of Vater, or bile duct carcinoma associated with congenital bile duct dilatation were excluded from the study.

The patients underwent ultrasonography because of jaundice (n = 36), high serum biliary enzyme level (n = 15), abdominal discomfort (n = 3), or routine screening (n = 1). They underwent cholangiography because ultrasonography showed an intraductal mass (n = 36), bile duct dilatation (n = 18), or gallbladder stone (n = 1). Written informed consent was obtained from all patients prior to endoscopic retrograde cholangiography (ERC), endoscopic nasobiliary drainage, and percutaneous transhepatic biliary drainage (PTBD). Approval for the study from our institutional review board was

Table 1. Patients' characteristics

	Cancer stage		
	T1 (n = 10)	T2 (n = 17)	T3 (n = 28)
Age (years)	68.5	65.3	66.1
Sex (M/W)	8/2	11/6	17/11
Location of main tumor			
Right or left hepatic duct	2	2	4
Suprapancreatic duct	5	10	16
Intrapancreatic duct	3	5	8
Cholangiographic findings			
Diffuse sclerosis	0	0	0
Stenosis	0	8	25
Papillary polypoid filling defect	8	4	2
Nodular polypoid filling defect	2	5	1
Surgical results: pathology (main component)			
Well differentiated papillary adeno.	9	4	2
Well differentiated tubular adeno.	1	4	8
Moderately differentiated tubular adeno.	0	7	13
Poorly differentiated tubular adeno.	0	2	1
Exploration only	0	0	4
Surgical results: maximum diameter of the tumor			
Diameter <10mm	3	5	1
Diameter 10mm to <20mm	1	5	5
Diameter ≧20mm	6	7	18
Exploration only	0	0	4

T1, invasion of mucosa or muscular layer; T2, invasion of perimuscular connective tissue; T3, invasion of adjacent structures; adeno., adeno carcinoma

not required, because all of these modalities are considered standard care for such patients.

The patients' surgical treatments were: hepatectomy with pancreatoduodenectomy (n = 1), hepatectomy (n = 10), pancreatoduodenectomy with portal vein reconstruction (n = 1), pancreatoduodenectomy (n = 3), pylorus-preserving pancreatoduodenectomy (n = 14), bile duct resection (n = 22), and surgical exploration (n = 4).

Techniques used for obtaining cholangiograms

Transpapillary biliary drainage was preferred in patients with distal bile duct obstruction. ERC was conducted using the standard technique.[4,10] After cannulation of the bile duct, contrast medium (60% meglumine sodium amidotrigoate) was injected to demonstrate the duodenal side of the stenosis, and the cholangiogram was recorded. Endoscopic nasobiliary drainage was performed with a 2.0-mm-diameter (6Fr) biliary catheter (PD-SS6.0; Catex, Tokyo, Japan) using techniques reported previously.[10] Side-holes in the catheter were positioned only at the proximal portion of the stenotic bile duct segment. Contrast medium was injected from the biliary catheter until it occupied the bilateral intrahepatic bile ducts, and images were recorded with the patients in the prone and right and left decubitus positions. To obtain clear cholangiograms, endoscopic biliary endoprostheses were not used during the initial endoscopic procedure.

PTBD was preferred in patients with proximal bile duct obstruction. It was performed under ultrasonographic or fluoroscopic guidance, using techniques reported previously.[10,11] A biliary catheter with a 2.7-mm diameter (Sumitomo Bakelite, Tokyo, Japan) or a biliary catheter with a 3.0-mm diameter (Create Medic, Yokohama, Japan) was used. Contrast medium (60% meglumine sodium amidotrigoate) was injected from the biliary catheter until it occupied the bilateral intrahepatic bile ducts, and images were recorded as noted above.

Study design

The cholangiograms were retrospectively reviewed by two experts, who had no other information (including surgical results and results of other imaging modalities). In 39 patients, cholangiograms obtained via an endoscopic nasobiliary drainage catheter and cholangiograms obtained during ERC were analyzed. In 15 patients, cholangiograms obtained via a PTBD catheter and cholangiograms obtained during ERC were analyzed. In the remaining patient, cholangiograms obtained via percutaneous transhepatic cholangiography and cholangiograms obtained during ERC were analyzed.

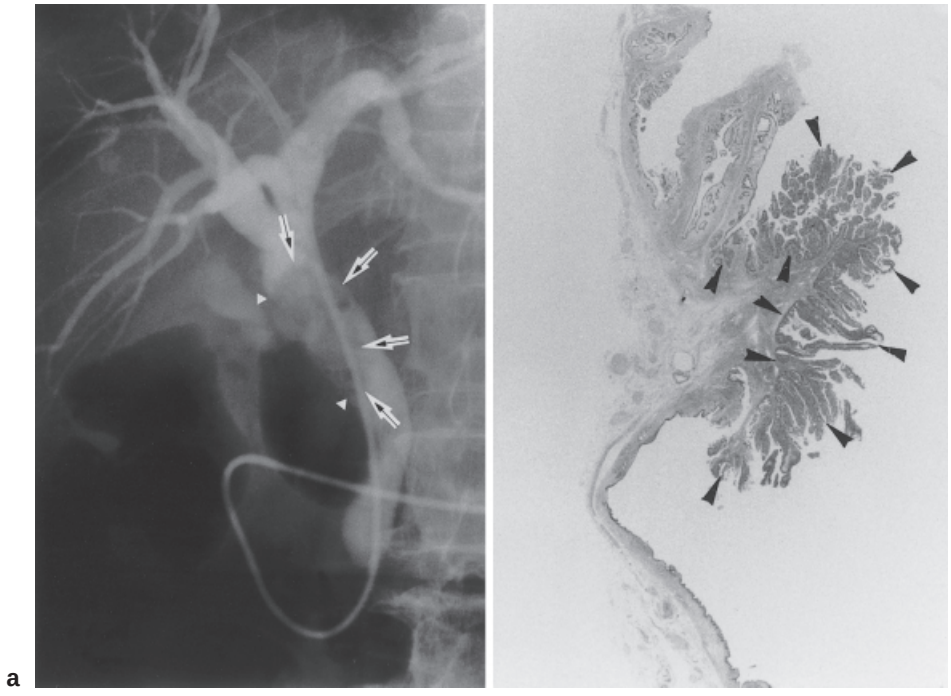

Fig. 1a,b. Findings in a 55-year-old man with high serum biliary enzyme level, and bile duct cancer at T1 stage (see Table 1 footnote for description of stages). **a** Cholangiography shows a papillary filling defect (*arrows*). The width of the base (*arrowheads*) was smaller than that of the polypoid filling defect. **b** Histologic findings of the resected specimen show well differentiated papillary adenocarcinoma confined to the fibromuscular layer (*arrowheads*). H&E, ×1

Cholangiographic findings[12,13] were classified as "diffuse sclerosis," "stenosis," "papillary polypoid filling defect," or "nodular polypoid filling defect." The term "papillary polypoid filling defect" was used when the width of the base was smaller than the width of the polypoid filling defect. Other polypoid filling defects were classified as "nodular polypoid filling defects." Typical cases are presented in Figs. 1, 2, and 3. When the cholangiographic findings were unclear because of abundant mucin, the patients were excluded. All data were analyzed using two-tailed Fischer's exact test. A P value of less than 0.05 was considered significant.

Results

Cholangiographic findings

As shown in Table 1, when cholangiography showed stenosis, there were no T1 lesions, and all patients with T1 disease showed polypoid filling defects ($n = 10$). When cholangiography showed papillary polypoid filling defects, 57% (8/14) of the resected patients showed T1 stage tumor histologically. In T1 patients, cholangiography showed papillary polypoid filling defects more frequently than in T2/3 patients (8/10, 80% vs 6/45, 13%, respectively; $P < 0.0005$).

Histologic findings of the resected specimens

As shown in Table 1, in T1 patients, histologic examination of the resected specimen showed papillary adenocarcinoma more frequently than in T2/3 patients (9/10, 90% vs 6/41, 15%, respectively; $P < 0.00001$). In T1 patients, the maximum diameter of the tumor in the resected specimen was 20 mm or larger in 60% of patients. There was no significant difference in the number of tumors 20 mm or larger between patients in T1 and T2/3 stages (6/10, 60% vs 25/41, 61%, $P > 0.5$).

Discussion

Bile duct carcinoma has been classified into three types based on the cholangiographic findings (polypoid, stenotic, and diffuse sclerosing types).[12,13] Nichols et al.[12] reported that prognosis was best for patients with polypoid carcinoma, and worst for those with diffuse sclerosing carcinomas. We further subclassified the polypoid type into two subtypes (papillary polypoid filling defect versus nodular polypoid filling defect). In our study, there were no subjects with diffuse sclerosis, a type that is rare in Japan. Our study suggests that patients with polypoid filling defects, especially those with papillary defects, should receive surgical treatment rather than radiotherapy and a biliary endoprosthesis, even if the maximum diameter of the tumor is greater than 20 mm. When a tumor occludes the bile duct, if the tumor base is small in area compared with its total volume, this tumor will be less invasive than tumors with a wide base.[8,14] Bile duct tumors with stenosis have wide bases compared with those with polypoid filling

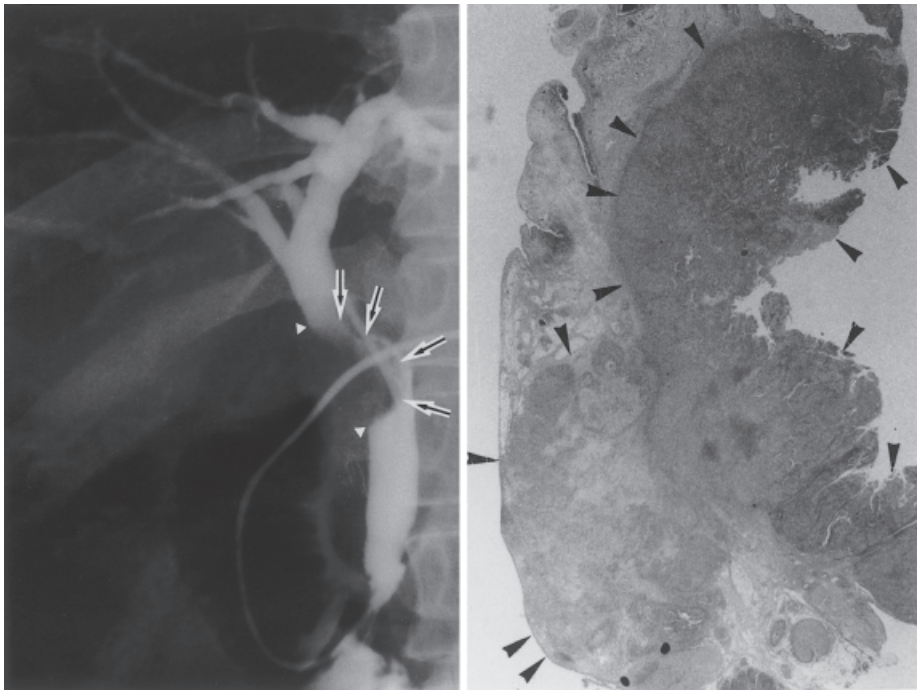

Fig. 2a,b. Findings in a 67-year-old man with jaundice, and bile duct cancer at T2 stage. **a** Cholangiography shows a nodular filling defect (*arrows*). The width of the base (*arrowheads*) was larger than that of the polypoid filling defect. **b** Histologic findings of the resected specimen show moderately differentiated tubular adenocarcinoma that had invaded the perimuscular connective tissue (*arrowheads*). H&E, ×1

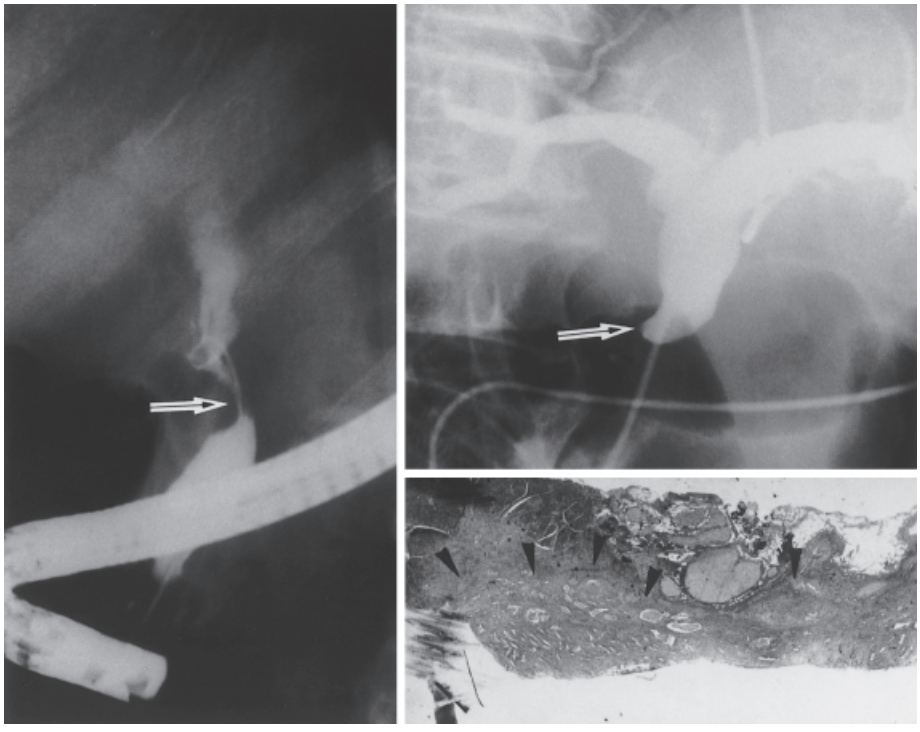

Fig. 3a–c. Findings in a 69-year-old man with jaundice, and bile duct cancer at T3 stage. **a**,**b** Cholangiography shows a stenosis (*arrows*). **c** Histologic findings of the resected specimen show moderately differentiated tubular adenocarcinoma that had invaded the pancreatic parenchyma (*arrowhead*). H&E, ×1

defects. In the resected specimens, nine of the ten T1 patients showed papillary adenocarcinoma, reflecting the characteristic cholangiographic findings. In this study, differentiation between stage T2 bile duct cancer versus stage T3 by cholangiographic findings was not analyzed, because the frequency of tumor invasion to adjacent structures would be different according to the location of the tumor, clearly an important prognostic factor.[3,5,7]

Recently, intraductal ultrasonography using a high frequency, thin-caliber ultrasonic probe has been reported to be useful in differentiating between bile duct cancer at stage T2 versus stage T3.[14–17] However, differentiating between stage T1 and stage T2 has been limited, because some T2 tumors, as well as most T1 tumors, show preserved wall structures by intraductal sonography.[18] Therefore, our study may compensate for this limitation.

In conclusion, 57% of resected patients with papillary polypoid filling defects by cholangiography showed T1 stage tumor. No T1 stage tumor showed stenosis or diffuse sclerosis.

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