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Differences in early imaging features and pattern of progression on CT between intrahepatic biliary metastasis of colorectal origin and intrahepatic non-mass-forming cholangiocarcinoma in patients with extrabiliary malignancy

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Abstract

Purpose: To assess the differences in early imaging features and progression pattern on CT between intrahepatic biliary metastasis (IBM) and non-mass-forming cholangiocarcinoma (NMFC) in patients with extrabiliary malignancy.
Methods: This retrospective study included 35 patients who were surgically and pathologically confirmed with IBM ($n = 14$) or NMFC ($n = 21$) at the time of or after surgery for extrabiliary malignancy. Two observers evaluated the following aspects of biliary lesions on initial or follow-up CT images: location, characteristics of intrahepatic duct (IHD) dilatation, presence of duct wall thickening, and periductal infiltration lesion or periductal expansile mass.
Results: All IBMs were associated with colorectal cancer ($p = 0.032$). As early imaging features on CT, smooth tapered localized IHD dilatation without duct wall thickening and peripheral duct involvement were observed significantly more often in IBM, and IHD dilatation with abrupt tapering or irregularity of transition site and bile duct wall thickening were significantly more common in NMFC (all $p < 0.05$). Regarding progression pattern, periductal expansile mass was present only in IBM, whereas periductal infiltrative lesion was present only in NMFC ($p < 0.001$).
Conclusion: In the differentiation between IBM and NMFC in patients with extrabiliary malignancy, the differences in early imaging features and progression pattern of the two diseases revealed in this study would be helpful for diagnosis.

Key words: Liver—Bile duct neoplasm—Metastasis—Cholangiocarcinoma—Computed tomography (CT)

Abbreviations

IBM	Intrahepatic biliary metastasis
NMFC	Non-mass-forming cholangiocarcinoma
IHD	Intrahepatic duct
CCC	Cholangiocarcinoma
CEA	Carcinoembryonic antigen
CA19-9	Carbohydrate antigen 19-9
TNM	Tumor, node, metastases
PACS	Picture archiving and communication system

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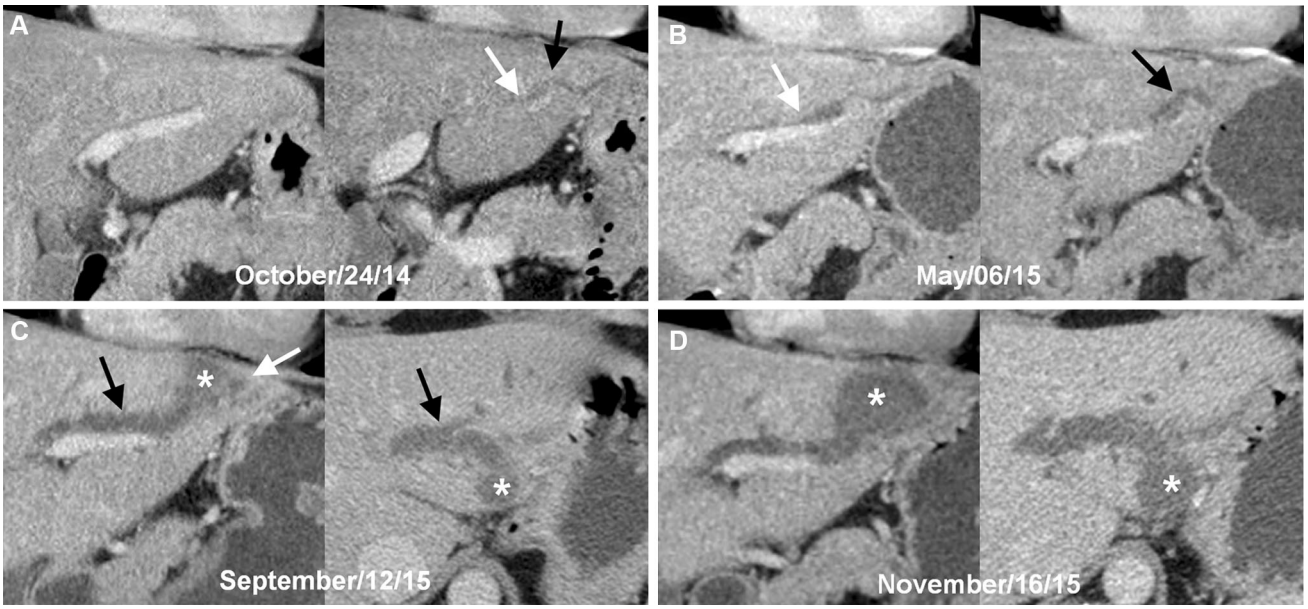

Fig. 1. A 43-year-old man with intrahepatic biliary metastasis from ascending colon cancer. **A** Coronal portal venous phase CT image obtained 18.2 months after right hemicolectomy for ascending colon cancer shows slightly localized dilatation of IHD in segment 2 of the liver. **B** Coronal CT image obtained 6.5 months after initial observation of localized IHD dilatation demonstrates the interval progression of localized dilatation of IHD. The smooth tapering of transition site (white arrows in a, b) and intraductal density greater than fluid density of localized IHD dilatation (black arrows in **A**, **B**) are noted. **C** On follow-up coronal (left image) and axial (right image) CT images, an approximately 2.4 cm-sized periductal expansile mass (asterisks) contiguous with dilated IHD was newly observed. Note that both the upstream (white arrow) and downstream ducts (black arrow) to the tumor are dilated. **D** The periductal expansile mass gradually increased in size on the last follow-up CT image (asterisks).

When incidental localized intrahepatic duct (IHD) wall thickening or dilatation without hepatic mass is observed on CT in patients with extrabiliary malignancy, it is difficult to determine whether it is caused by metastasis or primary biliary malignancy. Previous articles have reported that primary cancers of the lung, breast, gallbladder, stomach, colorectum, and pancreas can metastasize to the bile ducts [1, 2]. However, due to the rarity of intrahepatic biliary metastasis (IBM) from extrabiliary malignancy, primary biliary malignancy might be more likely.

However, IBM from colorectal cancer is increasingly being recognized [1–5]. Patients with IBM from colorectal cancer may be a candidate for peri-operative systemic chemotherapy to achieve resectability or to increase their long-term survival by reducing the risk of recurrence after resection [6, 7]. Therefore, pre-operative differentiation of IBM from primary biliary malignancy may have clinical significance. Lee et al. compared clinical and radiologic features between intraductal metastasis from colorectal cancer and double primary intraductal cholangiocarcinoma (CCC) and found that expansile intraductal lesion, presence of a contiguous parenchymal mass, and history of colorectal cancer favored intraductal metastasis [2]. However, expansile intraductal lesion and presence of a contiguous parenchyma mass would be seen only when metastasis has progressed; if there is only localized mild wall thickening or dilatation of IHD on abdominal CT, which could be early features of non-mass-forming cholangiocarcinomas (NMFCs) or IBM, it might be difficult to differentiate between the two diseases. In such cases, the biliary lesion would be followed up rather than adopting a surgical approach. Therefore, it is important to know the differences in early lesions and progression patterns of biliary lesions on CT between IBM and NMFC. However, to our knowledge, there has been no comparative study involving serial imaging observations to distinguish these two diseases in patients with extrabiliary malignancy. Accordingly, we performed this study to assess the differences in CT imaging features of early lesions and progression patterns of biliary lesions between IBM and NMFC in patients with extrabiliary malignancy.

Materials and methods

Patient population

This retrospective study was approved by our institutional review board, and the requirement for informed consent was waived. Using our institution's surgicopathologic and radiologic electronic database between January 2009 and July 2017, we retrospectively searched

for cases of surgically resected and pathologically proven IBM or NMFC in patients who underwent surgery for extrabiliary malignancy simultaneously or previously and identified 41 patients. Of them, 35 patients who had undergone pre-operative contrast-enhanced CT prior to hepatectomy according to our standard protocol within 1 month before surgery were included in this study. These 35 patients (27 men and eight women, median age, 67.0 years; range, 32–77 years) included 14 patients with IBM and 21 patients with NMFC. Three patients (one with IBM and two with NMFC) underwent surgery for extrabiliary malignancy and hepatectomy for biliary lesion simultaneously. The following clinical information, laboratory data, and pathologic results from electronic medical records were also assessed: time interval between the date of surgery for extrabiliary malignancy and the date of the first CT examination that showed localized wall thickening or dilatation of IHD; the number of follow-up CT examinations and overall follow-up period before hepatic resection after initial observation of localized wall thickening or dilatation of IHD; serum levels of carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) within 1 month of the last CT before hepatic resection; pathologic tumor, node, metastases (TNM) stage of extrabiliary malignancy; and history of chemotherapy for extrabiliary malignancy. At our institution, the definition of CEA and CA 19-9 elevation is serum level higher than 5 ng/mL and 37 U/mL, respectively.

CT technique

CT examinations were performed using various multidetector CT scanners: Philips Brilliance-40 detector (Philips Medical Systems, Cleveland, OH, USA), Toshiba Aquilion 64 detector (Toshiba Medical Systems, Tokyo, Japan), GE LightSpeed VCT 64 or GE Discovery CT 750 (GE Healthcare, Waukesha, WI, USA). Scanning parameters were as follows: 120 kVp, 189–200 mAs, 3 mm slice thickness, table speed of 26.5–39.37 mm per rotation (pitch 0.828–1.07), and a single breath-hold helical acquisition time of 4–6 s. For contrast-enhanced CT, a total of 120 mL non-ionic iodinated contrast material was administered through the antecubital vein with a power injector at a rate of 3–4 mL/s. All of the CT examinations that showed initial manifestation of localized IHD wall thickening or dilatation without a causative hepatic parenchymal mass for biliary lesion were single portal venous phase obtained at 70 s after the initiation of contrast material injection. Follow-up CTs after detection of intrahepatic biliary abnormality, CT examinations with liver CT protocol (quadruple-phase CT-unenhanced and contrast-enhanced arterial, portal, and equilibrium phases), or single portal venous phase were conducted based on the decision of the treating physicians. For CT with the liver protocol, hepatic arterial phase scanning began 30–40 s after injection of contrast agent by means of a bolus-triggered technique, and scanning of portal and equilibrium phases began 70 s and 180 s after the start of contrast injection, respectively. Unenhanced and contrast-enhanced multiphasic images were reconstructed at 3 mm intervals with a section thickness of 3 mm. Coronal and sagittal multiplanar reformation images with a 3 mm reconstruction interval were generated by one of our expert 3D technicians.

Image analysis

Two radiologists (K.T.W. and J.H.M. with 10 and 9 years of abdominal imaging experience, respectively) reviewed all serial CT images in consensus. In cases of disagreement, a third reviewer (S. H. K. with 19 years of abdominal imaging experience) was asked for an opinion, and a consensus was reached. The radiologists were blinded to all clinical and pathologic features, but were aware that the study population had either IBM or NMFC. All images were assessed using a picture archiving and communication system (PACS) (Centricity Radiology RA 1000; GE Healthcare, Chicago, IL), with adjustment of the optimal window setting in each case. To reduce learning bias, the study coordinator (J. K. M. with 18 years of abdominal imaging experience) showed the reviewers a series of sample images of CT features to be analyzed. The reviewers assessed the presence of localized dilatation or wall thickening of IHD, the presence of periductal infiltrative lesion or periductal expansile parenchymal mass, the location of initial biliary lesion, and the presence of imaging findings of *Clonorchis sinensis* infestation. The pattern of transition site of localized dilated IHD, intraductal feature of dilated IHD, and bile duct wall thickening or periductal lesion were categorized according to the criteria defined in Table 1. The presence of localized IHD dilation was defined as presence of dilatation mainly in the upstream intrahepatic bile duct, while the downstream bile duct was not dilated or less dilated. The presence of wall thickening of IHD was determined visually compared with adjacent normal bile duct wall. Periductal infiltrative lesion was defined as an area of periductal thickening and increased enhancement with irregular narrowing of involved bile ducts and upstream bile duct dilatation [8]. Periductal expansile parenchymal mass was defined as a parenchymal solid mass contiguous with the intraductal mass [2]. The location of the initial localized dilatation or wall thickening of IHD was categorized into central (involvement of the first-order) versus peripheral (involvement of second-order and smaller bile ducts) according to the starting point of the biliary lesion [5]. The characteristic imaging feature of *Clonorchis sinensis* infestation was the presence of diffuse, uniform dilatation of the small IHDs with no or minimal dilatation of

Table 1. Assessed imaging parameters and definitions

Parameters	Definition
Pattern of transition site of dilated IHD	
T1	Smoothly tapering at the site of transition
T2	Abrupt tapering or irregularity at the site of transition
Intraductal feature of dilated IHD	
L1	Intraductal fluid density
L2	Intraductal density greater than fluid density without discrete nodular projection
L3	Intraductal density greater than fluid density with discrete nodular projection, or interval increased intraductal density
Bile duct wall thickening or periductal lesion	
W1	No bile duct wall thickening
W2	Only bile duct wall thickening
W3	Periductal infiltrative lesion
W4	Periductal expansile mass
Final imaging features before hepatectomy	
Intraductal type	IHD dilatation with or without intraductal mass No bile duct wall thickening No periductal infiltrative or expansile mass
Stricture or periductal infiltrative type	Bile duct wall thickening as a cause of IHD dilatation or presence of periductal infiltrative lesion
Periductal expansile type	Presence of periductal expansile mass

IHD, intrahepatic duct

the large bile ducts and no focal obstructing lesion [9]. In the follow-up CTs, we evaluated whether the existing biliary lesion had progressed or new imaging parameters listed in Table 1 had emerged. In addition, final imaging features of the biliary lesion before hepatectomy were classified into intraductal type, stricture or periductal infiltrative type, and periductal expansile type (Table 1). Of 35 patients in this study, four (one with IBM, three with NMFC) who underwent hepatectomy immediately after the first observation of biliary lesion on CT were excluded from the evaluation of follow-up CT examinations.

Pathologic analysis

During study period, one of experienced pathologists (C.K.P. and K.T.J., with 38 and 20 years of experience in hepatobiliary pathology, respectively) thoroughly evaluated all resected hepatic tumors. The resected tumor specimens were fixed in formalin, stained with hematoxylin–eosin, and cut into 5 mm-thick slices. Immunohistochemical staining such as cytokeratin (CK)-7 and CK-20 was performed to differentiate IBM from NMFC.

Statistical analysis

The clinical and imaging features were compared using the χ^2 or Fisher-exact test for categorical variables and the Mann–Whitney test for continuous variables. Statistical analyses were performed with statistical software (SPSS version 12.0, SPSS). A value of $p < 0.05$ was considered to indicate statistical significance.

Results

Clinical features

The clinical characteristics of the patients with IBM and NMFC are summarized in Table 2. Of 21 NMFCs, 13

Table 2. Patient characteristics and clinical features

Characteristics	Biliary metastasis (N = 14)	Non-mass-forming cholangiocarcinoma (N = 21)	p value
Age (year)[a]	67.5 (32–73)	67.0 (40–77)	0.329
Male:Female	11:3	16:5	1.000
Extrabiliary malignancy			0.032
Colorectal cancer	14 (100)	13 (61.9)	
Stomach cancer	0 (0.0)	4 (19.0)	
Others	0 (0.0)	4 (19.0)	
History of chemotherapy for extrabiliary malignancy	10 (71.4)	9 (42.9)	0.166
CEA elevation (cut off, 5 ng/mL)[b]	3 (21.4)	1 (4.8)	0.279
CA 19-9 elevation (cut off, 37 U/mL)[b]	3 (21.4)	6 (28.6)	0.704
Time interval (months)[c]	28.5 (0.0–63.5)	19.8 (0.0–148.9)	–
Follow-up period (months)[d]	9.2 (0.0–50.1)	11.4 (0.0–46.7)	–
Follow-up CT number[e]	2 (0–9)	2 (0–5)	–

Continuous variables are described as median with range in parentheses and categorical variables are described as number of patients with percentage in parentheses

CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9

[a]Age at the time of hepatectomy

[b]Serum levels of CEA and CA19-9 within 1 month of the last follow-up CT before hepatic resection. Variables are described as number of patients with elevated indices and percentage in parentheses

[c]Time interval between the date of surgery for extrabiliary malignancy and the date of the first CT examination that showed localized wall thickening or dilatation of IHD

[d]Overall follow-up period before hepatic resection after initial observation of localized wall thickening or dilatation of IHD

[e]The number of follow-up CT examinations and overall follow-up period before hepatic resection after initial observation of localized wall thickening or dilatation of IHD

(61.9%) were associated with colorectal cancer and four (19.0%) with stomach cancer, whereas all 14 IBMs were associated with colorectal cancer ($p = 0.032$). Among 35 patients, ten (71.4%) of 14 patients with IBM and nine (42.9%) of 21 patients with NMFC had a history of chemotherapy for extrabiliary malignancy. Three (14.3%) of 21 patients with NMFC were receiving chemotherapy for extrabiliary malignancy at the time of hepatic resection. Elevation of CEA and CA 19-9 in the two groups was not significantly different. Elevation of both CEA and CA 19-9 was observed in two (14.3%) patients with IBM and one (4.8%) with NMFC. In patients with IBM and NMFC, the median follow-up periods between initial observation of biliary lesion on CT and hepatic resection were 9.2 months (range 0.0–50.1 months) and 11.4 months (0.0–46.7 months), respectively. Two (14.3%) of 14 patients with IBM and six (28.6%) of 21 patients with NMFC underwent surgery 2 years after the initial observation of localized wall thickening or dilatation of IHD on CT.

Imaging features on CT

The imaging features of patients with IBM and NMFC are summarized in Table 3. On initial CT, all 14 (100%) IBMs and 18 (85.7%) of 21 NMFCs showed localized dilatation of IHD. Among them, 13 (92.9%) of 14 IBMs appeared as T1 pattern of transition point (Fig. 1),

Table 3. Imaging features on CT of biliary metastases and non-mass-forming cholangiocarcinomas

	Biliary metastasis	Non-mass-forming cholangiocarcinoma	*p* value
On initial CT			
Patients No.	14	21	
Localized dilatation of IHD[a]	14 (100)	18 (85.7)	0.259
Pattern of transition site			< 0.001
T1	13 (92.9)	6 (33.3)	
T2	1 (7.1)	12 (66.7)	
Intraductal features of dilated IHD			< 0.001
L1	0 (0.0)	11 (61.1)	
L2	13 (92.9)	3 (16.7)	
L3	1 (7.1)	4 (22.2)	
IHD wall thickening or periductal lesion			0.005
W1	13 (92.9)	9 (42.8)	
W2	0 (0.0)	11 (52.4)	
W3	0 (0.0)	1 (4.8)	
W4	1 (7.1)	0 (0.0)	
Location of initial localized wall thickening or dilatation of IHD			0.027
Central duct	0 (0.0)	7 (33.3)	
Peripheral duct	14 (100)	14 (66.7)	
Clonorchiasis sinensis infestation	1 (7.1)	7 (33.3)	0.108
Emerging imaging features on follow-up CTs[b]			
Patients No.[b]	13	18	
Pattern of transition point			–
No dilatation → T1	N.A.	1 (33.3)	
No dilatation → T2	N.A.	2 (66.7)	
T1 → T2	4 (30.8)	2 (33.3)	
Intraductal features of dilated IHD			0.150
L1	0 (0.0)	2 (11.1)	
L2	0 (0.0)	2 (11.1)	
L3	1 (7.7)	4 (22.2)	
IHD wall thickening or periductal lesion			< 0.001
W2	0 (0.0)	0 (0.0)	
W3	0 (0.0)	7 (38.9)	
W4	6 (46.2)	0 (0.0)	
On last CT before hepatectomy			
Patients No.	14	21	
Final imaging types before hepatectomy			< 0.001
Intraductal type	7 (50.0)	8 (38.1)	
Stricture or periductal infiltrative type	0 (0.0)	13 (61.9)	
Periductal expansile type	7 (50.0)	0 (0.0)	

Categorical variables are described as number of patients with percentage
IHD, intrahepatic duct; T1, smoothly tapering at the site of transition; T2, abrupt margin or irregularity at the site of transition; L1, intraductal fluid density; L2, intraductal density, greater than fluid density without discrete nodular projection; L3, Intraductal density, greater than fluid density with discrete nodular projection, or interval increased intraductal density; W1, no bile duct wall thickening; W2, only bile duct wall thickening; W3, periductal infiltrative lesion; W4, periductal expansile mass
[a]If localized IHD dilatation was observed, the pattern of transition point and intraductal features of dilated IHD were assessed
[b]The evaluation of new emerging imaging features with progression was conducted only in patients who have follow-up CT examinations before hepatectomy. One patient with biliary metastasis and three patients with non-mass-forming cholangiocarcinoma were excluded for analysis because they did not undergo follow-up CT

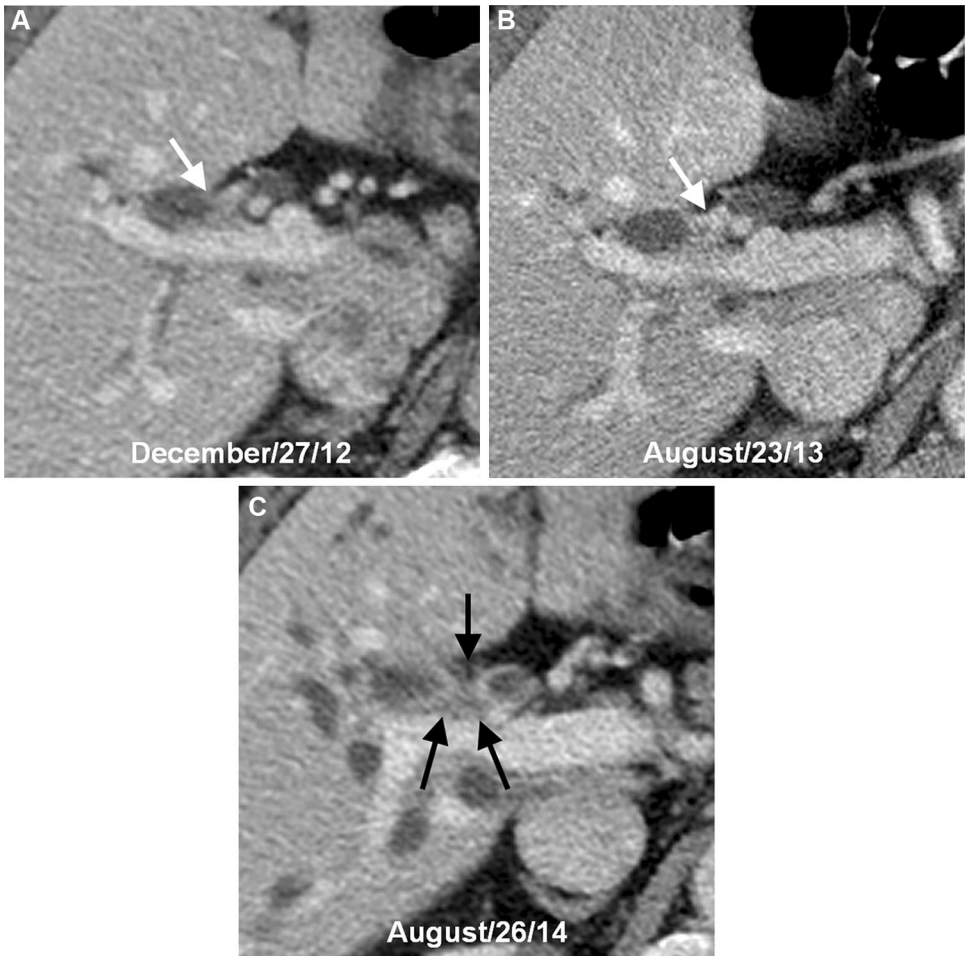

Fig. 2. A 67 year-old man with double primary non-mass-forming cholangiocarcinoma and descending colon cancer. **A** Axial portal venous CT image obtained 51.5 months after operation for colon cancer shows duct wall thickening of right lobar duct and upstream IHD dilatation with abrupt tapering at transition site (arrow). **B** Follow-up CT image obtained 8 months after initial observation of biliary lesion demonstrates the interval progression of bile duct wall thickening (arrow). **C** Last follow-up CT image shows periductal infiltrative lesion (black arrows) and the more thickened wall of the right lobar duct.

whereas 12 (66.7%) of 18 NMFCs showed a T2 pattern of transition point ($p < 0.001$) (Fig. 2). Regarding the intraductal features of dilated IHD on initial CT, 13 (92.9%) of 14 IBMs appeared as L2 type, and 11 (61.1%) of 18 NMFCs showed L1 type ($p < 0.001$). Bile duct wall thickening and periductal infiltrative lesion were observed in 11 (52.4%) and one (4.8%) of 21 NMFCs, respectively (Figs. 2, 3), whereas periductal expansile mass was seen only in one (7.1%) of 14 IBMs on initial CT ($p = 0.005$) (Fig. 1). Two patients with periductal infiltrative lesion or periductal expansile mass underwent surgery for extrabiliary malignancy and hepatectomy simultaneously. All IBMs involved the peripheral duct (Fig. 1), whereas central duct involvement was observed only in seven (33.3%) of 21 NMFCs on initial CT ($p = 0.027$) (Fig. 2). One (7.1%) of 14 IBMs and seven (33.3%) of 21 NMFCs had imaging features suggestive of *Clonorchis sinensis* infestation on initial CT ($p = 0.108$).

The progression of 13 IBMs and 18 NMFCs during the follow-up period is summarized in Table 3 and Fig. 4. Localized dilatation of IHD with T2 pattern of transition point developed in two (66.7%) of three NMFCs that did not show localized dilatation of IHD on initial CT (Fig. 3). Among emerging imaging features during the follow-up period, periductal infiltrative lesion occurred in only seven (38.9%) of 18 NMFCs (Figs. 2, 3), whereas periductal expansile mass occurred in six (46.2%) of 13 IBMs ($p < 0.001$) (Fig. 1, Table 3). During the follow-up period, four (30.8%) of 13 IBMs and seven (38.9%) of 18 NMFCs showed stability in imaging features of biliary lesions for more than 6 months. Among these, two (15.4%) of 13 IBMs and two (11.1%) of 18 NMFCs were stable for more than 18 months (Fig. 4).

On the last CT before hepatectomy, the intraductal type was seen in seven (50.0%) of 14 IBMs and eight (38.1%) of 21 NMFCs. Stricture or periductal infiltrative

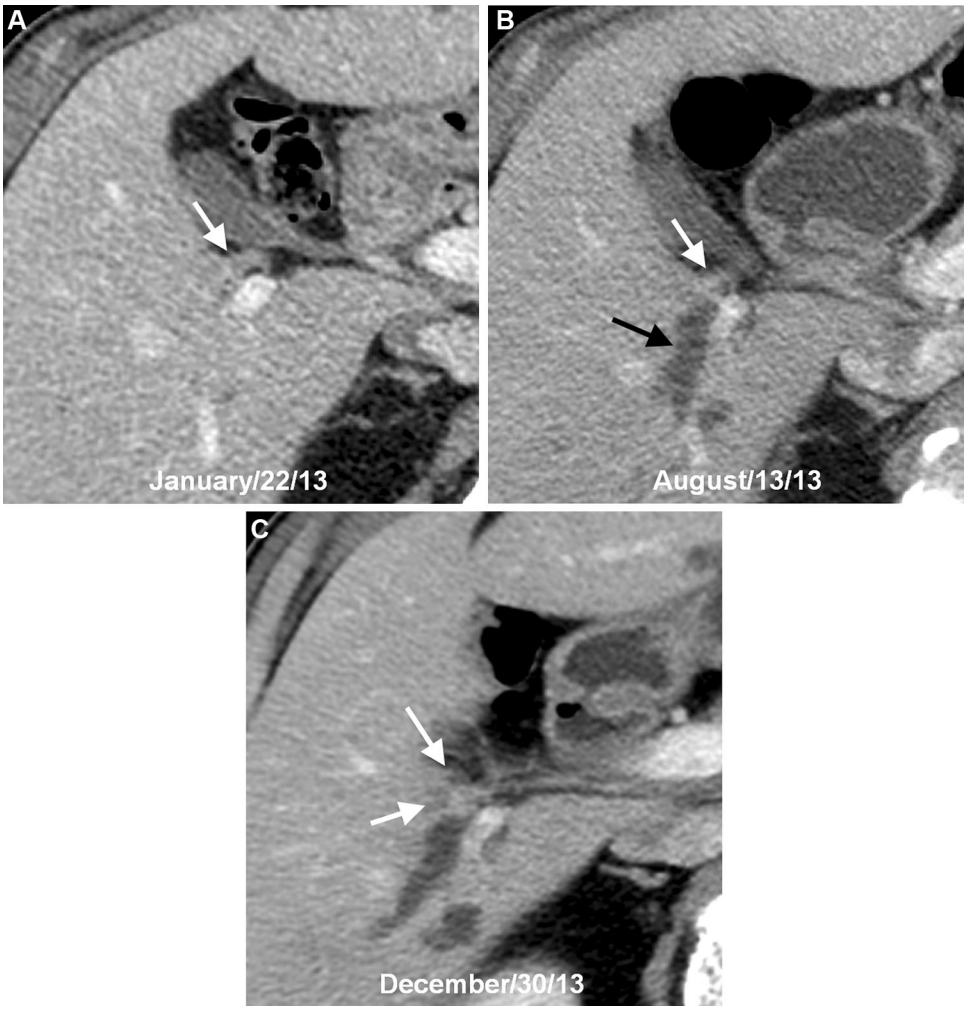

Fig. 3. A 70 year-old man with double primary non-mass-forming cholangiocarcinoma and rectal cancer. **A** Axial portal venous phase CT image obtained 48.9 months after lower anterior resection for rectal cancer shows bile duct wall thickening of the right posterior duct (arrow). **B** Follow-up CT image obtained 6.8 months after initial observation of biliary lesion shows increased bile duct wall thickening (white arrow). Upstream right IHD dilatation (black arrow) with abrupt tapering at transition site is shown. **C** Last follow-up CT image obtained 11.4 months after initial observation of biliary lesion shows the periductal infiltrative lesion (white arrows).

type appeared in only 13 (61.9%) of 21 NMFCs (Figs. 2, 3), whereas periductal expansile type appeared in only seven (50.0%) of 14 IBMs ($p < 0.001$) (Fig. 1).

Discussion

This study demonstrated that there were significant differences in the early imaging features and progression pattern on CT that could be useful for differentiation between IBM and NMFC in patients with extrabiliary malignancy. In the early imaging features of biliary lesions, localized IHD dilatation accompanying findings of smooth tapering of transition site, intraductal feature with greater than fluid density and without discrete nodular projection, no duct wall thickening, and peripheral duct involvement were significantly more common in patients with IBM ($p < 0.05$). In contrast, localized IHD dilatation accompanying findings of abrupt tapering or irregularity at transition site and duct wall thickening were significantly more common in patients with NMFC ($p < 0.05$). Regarding the progression pattern and final imaging features, periductal expansile mass was observed only in IBMs, whereas periductal infiltrative lesion was seen only in NMFCs ($p < 0.001$).

On pathology, intrabiliary tumor growth of IBM usually consists of two components: intraluminal and intraepithelial extension [2, 10–12]. The major component of IBM is known to be an intraluminal extension, and macroscopic intraluminal extension is consistently accompanied by intraepithelial extension [2, 11]. In intraluminal extension, tumors grow in the bile duct lumens, resembling tumor thrombi, and the IBMs from colorectal cancer tend to completely obstruct the lumen

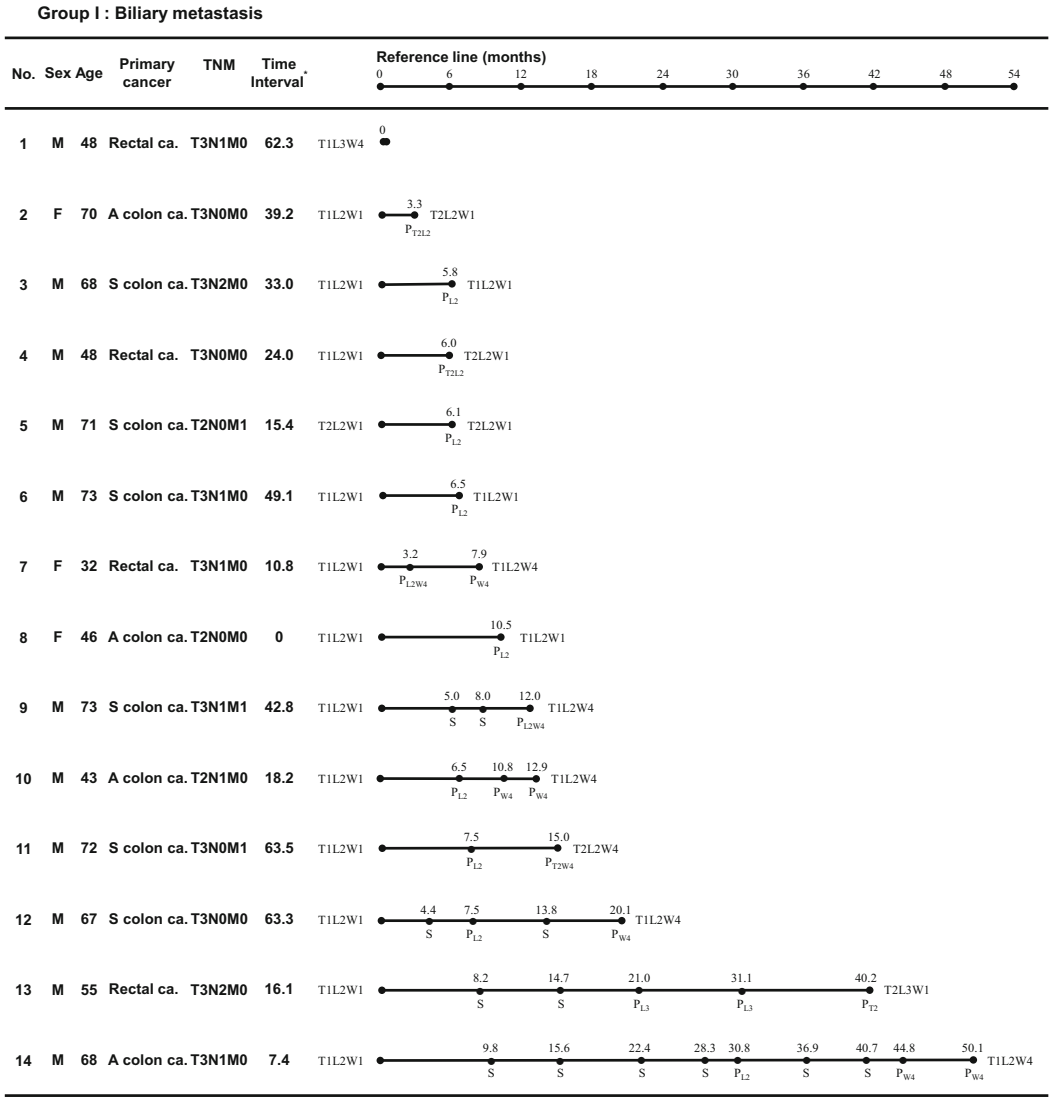

Fig. 4. Clinical and serial CT imaging features of 35 patients with intrahepatic biliary metastasis and non-mass-forming cholangiocarcinoma. **A** Intrahepatic biliary metastasis. **B** Intrahepatic non-mass-forming cholangiocarcinoma. *Note* Numbers above the points marked on the straight line indicate elapsed time after the date of the first CT examination that showed localized wall thickening or dilatation of IHD. The meanings of abbreviations below or beside the point marked on the straight line are as follows: P, Progression; S, Stable; T1, smoothly tapering at the site of transition; T2, abrupt margin or irregularity at the site of transition; L1, intraductal fluid density; L2, intraductal density, greater than fluid density without discrete nodular projection; L3, Intraductal density, greater than fluid density with discrete nodular projection, or interval increased intraductal density; W1, no bile duct wall thickening; W2, only bile duct wall thickening; W3, periductal infiltrative lesion; W4, periductal expansile mass.

of the involved bile duct [3]. This would be the reason for localized IHD dilatation with diffuse increased intraductal density greater than that of fluid rather than discrete intraductal nodular density. In intraepithelial extension, tumor cells advance along the intact basement membrane and replace the non-neoplastic biliary ductal epithelium [10]. The smooth tapered IHD dilatation without duct wall thickening and periductal infiltrative lesion might be due to the intact basement membrane.

In this study, periductal expansile mass was only seen in IBMs, which is consistent with findings of a previous study [2]. Lee et al. reported that, after the appearance of expansile intraluminal extension, progression to a parenchymal mass contiguous with the intraductal lesion was observed. In contrast, IHD wall thickening or dilatation with abrupt tapering or irregularity at transition site appeared significantly more often in early imaging features of NMFCs, which corresponds to the early imaging features of periductal infiltrating CCC [13].

Group II : Non-mass-forming cholangiocarcinoma

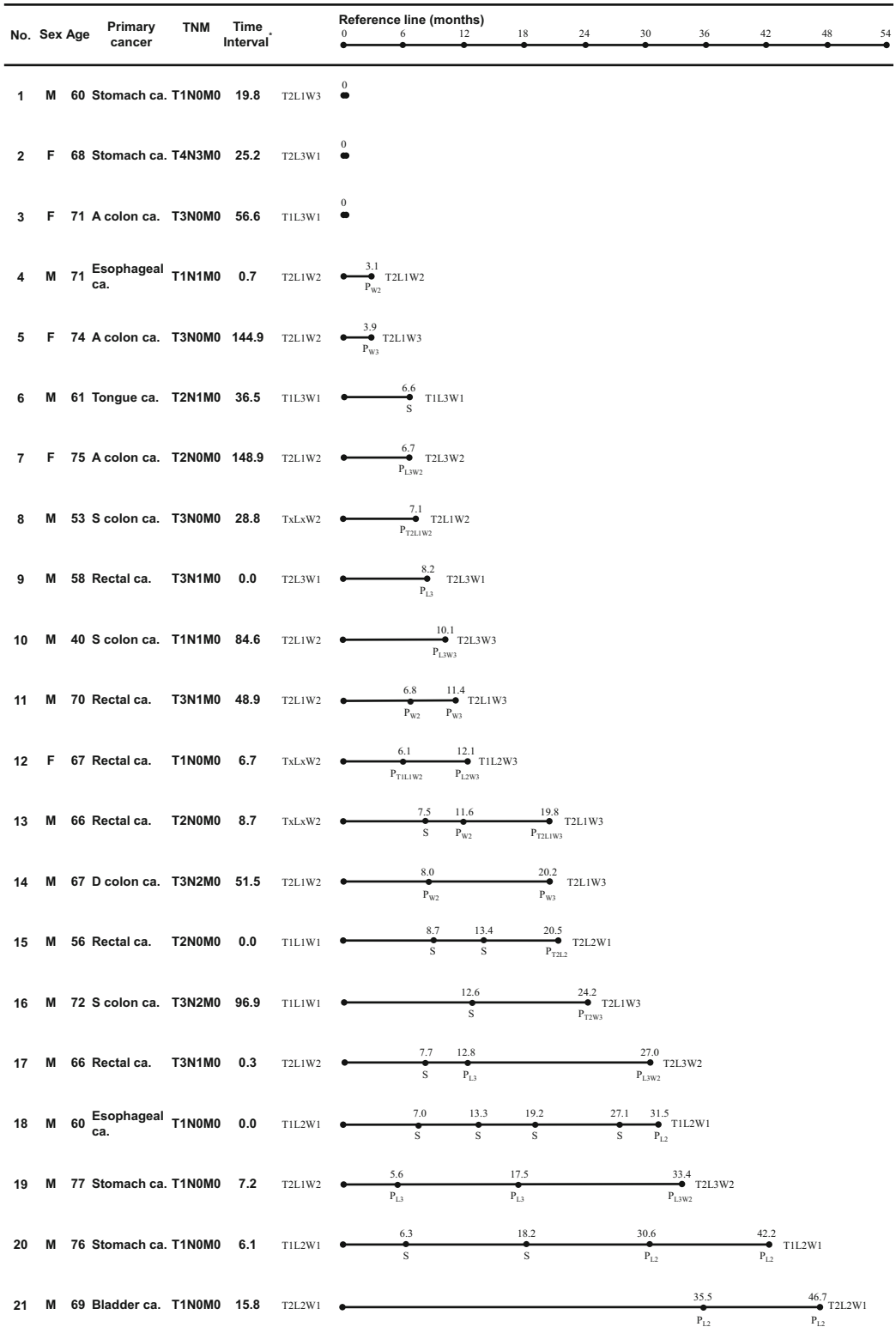

Fig. 4. continued.

Periductal infiltrating CCC initially grows along the bile duct wall and causes concentric bile duct wall thickening. As the tumor progresses, the involved bile ducts become narrow, the upstream bile ducts are dilated, and periductal infiltrative lesion appears [13]. The periductal infiltrative lesion on CT reflects the tumor spread via the perineural tissue, periductal connective tissue, and lymphatics. If localized IHD dilatation progresses only axially or longitudinally while remaining intraductal lesion with smooth tapering and without bile duct wall thickening, or a periductal infiltrative or expansile mass, it would be difficult to differentiate between IBM and NMFC. In such cases, the site at which the lesion originated may help to differentiate between IBMs and NMFCs.

In this study, four (30.8%) of 13 IBMs and seven (38.9%) of 18 NMFCs showed stability of biliary lesions for more than 6 months, and two (15.4%) of 13 IBMs and two (11.1%) of 18 NMFCs were stable for more than 18 months on follow-up CT. Therefore, when new mild dilatation or wall thickening of IHD occurs in patients with extrabiliary malignancy, it is recommended to follow-up with observations at least every 6 months for at least 2 years.

In this study, all IBMs were associated with colorectal cancer, similar to a previous report by Lee et al. [2]. Many clinical, pathologic, and radiologic studies have reported that colorectal liver metastases that are mainly confined to the bile duct can resemble CCC [10, 12, 14–18]. Estrella et al. reported a relatively high prevalence of intrabiliary growth in colorectal liver metastases (3.6–10.6%) compared with non-colorectal liver metastasis (0.7–1.9%) [3]. In general, it can even be challenging to distinguish between IBM from colorectal cancer and CCC with a conventional histological examination, and careful examination including immunohistochemical staining using CK-7 and CK-20 is needed [3, 14, 17, 19]. In addition, IBMs from colorectal cancer can occur even when many years have elapsed since resection of the primary cancer [3, 10]. In this study, in three (21.4%) of 14 IBMs, initial biliary lesions were detected on CT more than 5 years after resection of the primary colorectal cancers.

There were several limitations to our study. First, because it was a retrospective study and only available data could be analyzed, selection bias may have existed. In particular, we only included the surgically resected IBMs or NMFCs. The patients who eventually did not undergo hepatic resection due to the rapid progression of biliary lesion were not evaluated. This would predispose to select patients with slowly progressive disease in our study. Second, the number of patients was small due to the rarity of the diseases. However, there have been only a few reported cases of IBM without a hepatic parenchymal mass. Regarding the imaging and clinical features, we included the largest number of IBMs to date in this study. Further study with a larger sample is needed to generalize our results. Third, although it is known that various types of malignant tumor can show IBM, colorectal cancer was the only primary tumor associated with IBM in this study. This disparity may be because we included only surgically proven cases, and aggressive metastasectomy has been widely accepted only for colorectal hepatic metastasis.

In conclusion, in the differentiation between IBM and NMFC in patients with extrabiliary malignancy, the differences in early imaging features and progression pattern of the two diseases revealed in this study would be helpful for diagnosis.

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Compliance with ethical standards

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Ethical approval Research involving human participants and/or animals: Research involving human participants. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent This retrospective study was approved by our institutional review board, and the requirement for informed consent was waived.

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