A novel technique for endoscopic transpapillary "mapping biopsy specimens" of superficial intraductal spread of bile duct carcinoma (with videos)

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INTRODUCTION

Bile duct cancer (BDC) has a lower propensity for distant metastasis during the early part of its natural history, and local extension into adjacent vessels and longitudinal intraductal extension are of critical prognostic importance. Superficial intraductal spread (SIDS) is a characteristic feature of this tumor[1,2] and is associated with a more-differentiated phenotype and a less-aggressive clinical course.[3,4] However, the presence of SIDS correlates with positive resection margins after surgery. Hence, preoperative identification of the exact proximal and distal margins is important for deciding whether the surgical approach should comprise extrahepatic bile duct resection with or without pancreatoduodenectomy (PD) and whether right- or left-sided hepatectomy is needed.[5]

Direct cholangioscopic intraductal visualization, with or without narrow-band imaging, is important for evaluating SIDS.[5,6] Despite these enhanced imaging techniques, stent-induced or cholangitis-induced mucosal changes are often difficult to differentiate from neoplastic involvement in a segment of bile duct, without tissue sampling. The use of intraductal biopsy specimens for diagnosing SIDS of BDC can be performed by percutaneous transhepatic cholangioscopy, but this technique is time consuming, invasive, and might result in cancer seeding.[7,8] Hence, using an endoscopic route for obtaining transpapillary biopsy specimens may be preferable.[9]

Although the use of forceps biopsy in the diagnosis of stenotic bile duct lesions with fluoroscopic targeting or using per-oral cholangioscopy (POCS) has been described,[9-12] obtaining multiple directed intraductal biopsy specimens for evaluating SIDS, so-called mapping biopsy specimens, has not been previously reported. This method not only provides a tissue diagnosis of SIDS but also is less expensive and has widespread application to centers with limited resources, where POCS is unavailable. Herein, we tried to assess the mapping biopsy specimens method for defining the longitudinal extension of BDC.

METHODS

Patients

Between August 2010 and November 2013, 19 consecutive patients (17 men, mean age, 68.0 ± 6.4 years) who underwent preoperative transpapillary mapping biopsy procedures to assess SIDS of upper to lower BDCs were enrolled. Patients with hilar BDCs were excluded, because cancer in these locations has a propensity toward intraluminal growth that is undetectable by biopsy specimens.[3,13] All patients were preprocedurally assessed using CT scans and EUS. Proximal and distal bile duct wall thickness and/or papillary irregular mucosa identified on CT images and/or by EUS were taken as suspicious for SIDS. Seven of 19 patients had a biliary stent in situ for various periods. Four patients underwent POCS at the time of the mapping biopsy procedure per physician discretion using a video cholangioscope (model CHF-B260, diameter 3.4 mm; Olympus Medical Systems, Tokyo, Japan). Our institutional review board approved this study.

Study definitions

BDCs were classified as papillary or nodular based on a cholangiographic appearance of villous and irregular surface and a predominantly smooth or undulating intraluminal bulge, respectively. Intraluminal growth was diagnosed as significant wall thickening on CT images and/or luminal stricture by cholangiography. SIDS (Fig. 1) was defined as a contiguous, nonprotruding extension of at least 2 cm from

Abbreviations: BDC, bile duct cancer; IDUS, intraductal ultrasound; PD, pancreatoduodenectomy; POCS, per-oral cholangioscopy; SIDS, superficial intraductal spread.

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the main tumor of the bile duct.[3,6,7] SIDS was diagnosed pathologically either by preoperative intraductal biopsy specimen or after surgical resection.

Endoscopic retrograde cholangioscopy and biopsy protocol

Mapping biopsy specimens was done under fluoroscopic guidance after endoscopic retrograde cholangioscopy and intraductal ultrasound (IDUS) for estimation of right hepatic artery invasion. Biliary sphincterotomy was done only when required for POCS. From August 2010 to July 2013 we used the SpyBite mini-forceps (Boston Scientific, Natick, Mass) for mapping biopsy specimens. The SpyBite forceps was introduced into the bile duct inside a 6F Soehendra biliary dilation catheter (Cook Japan Ltd., Tokyo, Japan), which acted as a conduit for directing the forceps. The dilation catheter was cut just distal to a radiopaque marker (Fig. 2) to fluoroscopically determine the exact exit point of the SpyBite forceps. The modified dilation catheter was introduced to the desired site over a guidewire, followed by exchange of the guidewire for a SpyBite forceps.

We obtained 1 to 3 biopsy specimens each from the confluence of B2+B3 (Fig. 3A), B4 (Fig. 3B), the anterior and posterior segmental ducts (Fig. 3C), and the main right and left hepatic ducts (Fig. 3D) to define proximal tumor extension (Video1, available online at www.giejournal.org) and from the inferior bile duct if needed (Video 2, available online at www.giejournal.org). These are important intraductal landmark sites for deciding the extent of liver resection (Fig. 4), such as left-sided hemihepatectomy or left-sided trisegmentectomy,[6] and deciding whether PD was needed. We did not take biopsy specimens from a liver lobe when it was already in the proposed resection field. For instance, when right-sided hemihepatectomy was needed because of right hepatic artery invasion, we did not obtain biopsy specimens from the right hepatic ducts. Likewise, when PD was needed, we did not perform biopsy from the distal side of primary lesion. To prevent false-positive results arising because of cross-contamination, we collected biopsy specimens from the distal side to the proximal side.

Experienced cytopathologists (W.H. and Y.Y.) with complete knowledge of the clinical and endoscopic data evaluated the cytologic and biopsy specimens. The results of biopsy described as "suspected carcinoma" and "carcinoma" were considered as malignant for the purposes of analysis. For sampling adequacy, a "sufficient" biopsy was defined as the inclusion of submucosal tissue in the biopsy and "insufficient" biopsy by the absence of stromal components. The main study parameters were tumor extension pattern related to the macroscopic tumor type, sampling adequacy rates, and diagnostic yield of the mapping biopsy method.

Statistical analysis

Frequencies, proportions (%), and means are used as appropriate for descriptive analyses. The results of mapping biopsy procedures were compared with the histopathologic results obtained after surgical resection. Both ends (most proximal and distal) of the biopsy sites diagnosed as SIDS by intraductal biopsy samples with subsequent postsurgical confirmation were considered true positive. Those with a final postsurgical diagnosis of benign were considered false positive. Likewise, lesions categorized as benign by endoscopic retrograde cholangioscopy with a final diagnosis of benign were considered true negative, and those with a final diagnosis as SIDS were considered false negative. Data were analyzed using the χ^2 test. $P < .05$ was considered significant.

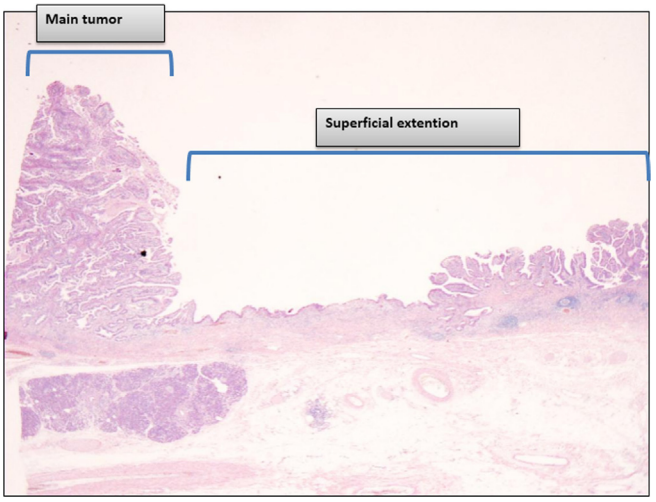

Figure 1. Microscopic view of an example of intraductal superficial spread more than 2 cm.

Figure 2. SpyBite mini-forceps with cut Soehendra biliary dilator.

RESULTS

Primary lesions included upper to middle BDCs (n = 10) and lower BDCs (n = 9). Of the 19 patients, 4 (21%) underwent hepatic resection with extrahepatic bile duct resection, 11 (57%) underwent PD (traditional or pylorus-preserving), and 4 (21%) were treated by hepatectomy and PD. Macroscopic tumor types were nodular in 14 patients (73.6%) and papillary in 5 (26.4%) (Table 1).