Intraholecystic Papillary-tubular Neoplasm of the Gallbladder Presenting with Jaundice

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Abstract

We herein report a case of intraholecystic papillary-tubular neoplasm (ICPN) of the gallbladder in which jaundice developed. A 58-year-old woman with jaundice was referred to our hospital. Computed tomography revealed a papillary tumor in the body of the gallbladder protruding into the bile duct. A transpapillary biopsy of the bile duct verified adenocarcinoma, and pancreatoduodenectomy with extended cholecystectomy was performed. The tumor spread macroscopically from the gallbladder body to the cystic duct, thus forming a polypoid mass protruding into the bile duct. This is a rare case of invasive carcinoma from ICPN leading to mechanical obstruction of the bile duct.

Key words: intraholecystic papillary-tubular neoplasms, ICPN, gallbladder cancer, mucin-producing tumor, intraductal papillary neoplasm of the bile duct, IPNB


Introduction

Intraholecystic papillary-tubular neoplasm (ICPN) of the gallbladder is a recently established tumor entity, previously referred to as mucin-producing tumor or papillary adenoma/carcinoma. ICPN is considered to be a subtype of intraductal papillary neoplasm of the bile duct (IPNB). In contrast to IPNB, in which jaundice generally develops, no cases of ICPN presenting with jaundice have thus far been reported. We herein report a patient with ICPN, forming a polypoid lesion, and presenting with jaundice.

Case Report

A 58-year-old woman complaining of itching was referred to our hospital due to jaundice. The laboratory data on admission showed the following abnormalities: total bilirubin 14.6 mg/dL, aspartate aminotransferase 299 IU/L, alanine aminotransferase 413 IU/L, lactate dehydrogenase 374 IU/L, alkaline phosphatase 744 IU/L, gamma glutamyl transpeptidase 871 IU/L, and carbohydrate-associated antigen 19-9 185 ng/mL.

The extracorporeal ultrasound showed an enlarged gallbladder with irregular wall thickening of the neck and body and debris-like echoes.
Figure 2. Computed tomography (CT) with contrast enhancement revealed a tumor occupying the bile duct (arrows) with irregular wall thickening of the neck and body of the gallbladder (arrow head). (a) The plane, (b) early phase, (c) delayed phase, and (d) portal phase views. (e) A tumor was confirmed in the region from the gallbladder (arrow head) to the bile duct in the coronal view of CT. The bile duct was filled with the tumor (arrows).

Figure 3. The magnetic resonance (MR) images showed a low intensity mass in the bile duct on the T1 (a) and T2 (b) weighted image (arrow). (c) A positive signal intensity on the diffusion-weighted imaging was detected in accordance with the tumor site. (d) MR cholangiopancreatography (MRCP) disclosed bile duct dilatation with an irregular defect from the middle bile duct to the neck of the gallbladder.
Endoscopic ultrasonography (EUS) demonstrated irregular wall thickening of the neck of the gallbladder (arrow) with debris-like echoes. (b) The iso-hyperechoic mass (arrow) filled the middle bile duct (arrow head). *Portal vein

Endoscopic retrograde cholangiopancreatography (ERCP) disclosed bile duct dilatation and a papillary-shaped defect in the bile duct without opacification of the gallbladder. Imaging showed positive signal intensity at the tumor site. Endoscopic ultrasonography (EUS) demonstrated a mass extending from the gallbladder body to the cystic duct forming a polypoid protrusion into the bile duct (Fig. 4). In addition, abundant mucus was confirmed in the gallbladder. Histologically, the tumor showed a tubulopapillary configuration with thin stalks, mucus, and focal invasion of the subserosa (Fig. 7). The results of immunostaining for mucus phenotypes (MUC1+/MUC2-/MUC5AC+/MUC6+) were compatible with pancreatobiliary-type ICPN (Table). The final diagnosis was minimally invasive papillary adenocarcinoma derived from ICPN as follows: G1, T2, N0, M0, Stage IB (1) and papillary-type adenocarcinoma with an infiltrating growth pattern, paptub, int, INFβ, GnlCGGbBm, 130×95×16 mm, ly0, v0, pn0, Sx, pHinf1a, pBinf0, pPanc0, pDu0, pPV0, pA0, pN0, pHM0, pDM0, pEM0, pT2, pStage II (2).

At the follow-up 16 months later, liver and nodal metastases were detected and the patient is currently undergoing chemotherapy (gemcitabine 1,000 mg/m² on day 1, 8 and 15, repeated every 28 days).

The macroscopic examination of the resected specimen revealed a papillary tumor, 130×95 mm in size, located from the gallbladder body to the cystic duct forming a polypoid protrusion into the bile duct (Fig. 6). In addition, abundant mucus was confirmed in the gallbladder. Histologically, the tumor showed a tubulopapillary configuration with thin stalks, mucus, and focal invasion of the subserosa (Fig. 7). The results of immunostaining for mucus phenotypes (MUC1+/MUC2-/MUC5AC+/MUC6+) were compatible with pancreatobiliary-type ICPN (Table). The final diagnosis was minimally invasive papillary adenocarcinoma derived from ICPN as follows: G1, T2, N0, M0, Stage IB (1) and papillary-type adenocarcinoma with an infiltrating growth pattern, paptub, int, INFβ, GnlCGGbBm, 130×95×16 mm, ly0, v0, pn0, Sx, pHinf1a, pBinf0, pPanc0, pDu0, pPV0, pA0, pN0, pHM0, pDM0, pEM0, pT2, pStage II (2).

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**Discussion**

ICPN of the gallbladder was first described in the 2010 World Health Organization (WHO) classification. This rare tumor forms an intramucosal papillary or polypoid mass, often associated with various amounts of mucin. Adsay et al. stated that ICPN should be included in the same disease entity category as intraductal papillary mucinous neoplasm (IPMN) of the pancreas and IPNB based on the clinicopathological characteristics of these neoplasms (3). However, ICPN and IPNB have different characteristics, such as a predominant pancreatobiliary phenotype (4) and normal GNAS genes (5, 6). Further investigations are needed to confirm the characteristics of ICPN and IPNB as compared with IPMN.

Obstructive jaundice is rare in cases of ICPN. According
Figure 6. (a) A fresh specimen of the gallbladder, the bile duct, and gallstones. A polypoid lesion protruded from the cystic duct to the bile duct. (b) The histological mapping. A papillary cancer was identified in the area marked by the red line. Cancer invasion to the subserosa was detected at the flat lesion in the body of gallbladder (blue line).

Figure 7. (a) The pathological findings of ICPN. A pedunculated tumor with thin stalks was confirmed in the cystic duct (Fig. 6b segment D, Hematoxylin and Eosin (H&E) staining, 1.25×). (b) A high-powered view of the pedunculated tumor with a tubulopapillary configuration (Fig. 6b segment D, H&E staining 10×). (c-e) The immunostaining of the pedunculated tumor in the cystic duct (Fig. 6b segment D) for mucin: (c) MUC1, (d) MUC5AC, and (e) MUC6. (f) Focal invasion to the subserosa in the gallbladder body (arrows) (Fig. 6b segment J, H&E staining 5×). (g) A high-powered view of the focal invasion to the subserosa in the gallbladder body (arrow) (Fig. 6b segment J, H&E staining 10×).

to a PubMed search with the key phrase “mucin producing gallbladder carcinoma,” there were only two reported cases from 1979 to 2012. However, one case was complicated by primary sclerosing cholangitis (7), and the other was a case with carcinoma of the cystic duct (8). Therefore, no case of ICPN with obstructive jaundice due to the mechanical obstruction of the bile duct by an intraluminal polypoid tumor has been reported. Advanced gallbladder cancer often invades the bile duct directly and develops jaundice. In the present case, the unique tumor arose in the gallbladder neck and extended horizontally along the cystic duct mucosa, forming a protrusion into the bile duct, in contrast to the usual distribution of ICPN (the fundus or body) (3).

The establishment of a preoperative diagnosis of ICPN
The Results of Immunohistological Study of the Resected Specimen

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<th>Papillary tumor in the gallbladder neck</th>
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L.I.: labeling index, f: focal, d: diffuse

was difficult in this particular case although a diagnosis of adenocarcinoma was achieved by the transpapillary biopsy. A confirmation of mucin in the gallbladder and the bile duct was not possible with the applied diagnostic imagings. However, the recognition of mucin in the gallbladder by any of those examinations would have led to a precise diagnosis of ICPN.

The invasion was identified only at the flat lesion in the gallbladder body, not at the papillary lesion in the gallbladder or at the polypoid lesion in the cystic duct. Adsay et al. reported that invasive carcinoma, if present, was mostly at the base of the ICPN lesion (3). The p53 immunostaining of the tumor was diffusely positive in the gallbladder body while it was only focally positive in the cystic duct. Therefore, the flat lesion in the gallbladder had a more malignant potential than the polypoid lesion in the cystic duct.

The invasive carcinoma arising in ICPN usually has a better clinical outcome than ordinary invasive gallbladder cancer. In this particular case, however, metastases to the liver and lymph nodes were confirmed 16 months later in spite of minimal subserosal invasion without vascular invasion or lymphatic permeation as revealed in the resected specimen. Therefore, patients with ICPN should be carefully followed, namely in the same manner as for patients with ordinary gallbladder cancer.

We herein described a rare case of ICPN of the gallbladder causing jaundice. The ICPN showed interesting configurations extended superficially from the body of the gallbladder to the bile duct with a minimal invasion of the gallbladder body. A careful follow-up is required in cases of invasive carcinoma from ICPN regardless of the clinical outcome of ICPN.

The authors state that they have no Conflict of Interest (COI).

References


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