Tubulopapillary adenoma of the gallbladder accompanied by bile duct tumor thrombus

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Abstract
Intraductal papillary mucinous neoplasm of the bile duct (IPNB) is recognized as a precancerous lesion; however, both its pathogenesis and progression remain unclear. We present here a case of IPNB arising from the gallbladder accompanied by bile duct tumor thrombus in a 79-year-old female. The resected specimen revealed a tubulopapillary adenoma with no malignant cells. This case suggests that even in the absence of malignant cells, these tumors can behave as malignant tumors requiring aggressive treatment. Even if no malignant cells are present, intrapithelial neoplasms occurring in the ampullopancreatobiliary tract can behave as malignant tumors.

INTRODUCTION
Intraductal papillary mucinous neoplasm (IPMN) of the bile duct (IPNB) is a disease entity that was proposed in 2001 by Chen et al[1]. IPNB is regarded as a counterpart of IPMN of the pancreas, and is considered to be a precancerous lesion[2-5]. A similar spectrum of lesions also exists in the gallbladder[6]. However, these lesions have yet to be fully characterized and their pathogenesis and progression remain unclear. Most reported cases of invasive IPNB ultimately become cancerous. Generally, the tumors accompanied by a bile duct tumor thrombus are cancerous. Here we report a rare gallbladder tumor without cancerous changes accompanied by a bile duct tumor thrombus.
A 79-year-old female presented to our hospital for an incidentally-diagnosed gallbladder tumor. No abnormalities were seen in blood test results, including tumor markers. Laboratory data (normal range) were as follows: aspartate aminotransferase, 18 U/L (5-35 U/L); alanine aminotransferase, 14 U/L (5-30 U/L); alkaline phosphatase, 151 U/L (115-359 U/L); gamma-glutamyl transferase, 20 U/mL (0-50 U/mL); lactate dehydrogenase, 170 U/L (106-211 U/L); albumin, 4.0 g/dL (3.7-5.5 g/dL); and total bilirubin, 0.64 g/dL (0.2-1.0 g/dL). The concentrations of carcinoembryonic antigen and carbohydrate antigen 19-9 were 2.2 ng/mL (< 5.0 ng/mL) and 4.0 U/mL (< 37.0 U/mL), respectively. No serological evidence of hepatitis B or C was seen.

Contrast enhanced computed tomography (CT) revealed a tumor measuring 40 mm in diameter in the cystic duct, accompanied by a common bile duct tumor thrombus (Figure 1A). Drip infusion cholangiographic CT revealed a defect in the common bile duct (Figure 1B). Magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography revealed similar findings (Figure 1C and D). Cytological examination revealed the absence of malignant cells in bile. Without the evidence of malignant cells, we diagnosed it as gallbladder cancer or bile duct cancer because of the common bile duct tumor thrombus.

The patient underwent choledochectomy and cholecystectomy. Macroscopic examination of the resected specimen revealed a 40-mm tumor located in the neck of the gallbladder and a 30-mm tumor thrombus in the common bile, with rich mucilage (Figure 2). Microscopically, hematoxylin and eosin staining demonstrated the tumor to be a pyloric type tubulopapillary adenoma with moderate epithelial atypia, without evidence of stromal invasion (Figure 3). On immunological staining, the tumor cells were positive for MUC5AC, but negative for
A 79-year-old female with an incidentally-diagnosed gallbladder tumor accom-
panied by bile duct tumor thrombus.

**Clinical diagnosis**
The patient was diagnosed with gallbladder carcinoma by the imaging study.

**Differential diagnosis**
Differential diagnoses were bile duct carcinoma invaded to the gallbladder, malignant lymphoma and intraductal papillary mucinous neoplasm of the bile duct.

**Laboratory diagnosis**
All of the laboratory tests were within normal limits.

**Imaging diagnosis**
Computed tomography revealed a tumor measuring 40 mm in diameter in the cystic duct, accompanied by a common bile duct tumor thrombus. Drip infusion cholangiographic-computed tomography, magnetic resonance imaging, endoscopic retrograde cholangiopancreatography revealed a defect in the common bile duct.

**Pathological diagnosis**
Cytological examination revealed the absence of malignant cells in bile. Microscopically, resected specimen revealed a pyrhotic type tubulopapillary adenoma with moderate epithelial atypia.

**Treatment**
The patient underwent cholecystectomy and cholecystectomy.

**Related reports**
Intraductal papillary mucinous neoplasms of the bile duct are histologically classified as low- or intermediate-grade intraepithelial neoplasia corresponding to adenomas or borderline malignancy, high grade intraepithelial neoplasia corresponding to carcinoma in situ, or as having an associated invasive carcinoma. The neoplasms are regarded as precancerous lesions; therefore, radical resection is recommended in operable patients.

In our case, although the epithelial atypia was moderate, it was accompanied by a bile duct tumor thrombus. The neoplasms accompanied with tumor thrombus are often ordinary invasive carcinoma. What is curious is that no symptoms of biliary tract obstruction were observed in our patient, although we cannot rule out the possibility that such symptoms could have occurred in the immediate future. Furthermore, it is reported that pyrhotic type adenocarcinoma of the gallbladder has a poor prognosis. So, in our case, surgical treatment is considered reasonable and proper.

Even if no malignant cells are present, intraepithelial neoplasms occurring in the ampullopancreatictract can behave as malignant tumors. Hence, these patients should be treated aggressively.

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**DISCUSSION**
Recently, intraepithelial neoplasms occurring in the ampullopancreatictract have attracted a substantial amount of attention. These include the so-called IPNB, IPMN of the pancreas, intra-ampullary-tubulopapillary neoplasms (ITPN) of the pancreas, intra-ampullary-tubulopapillary neoplasms (IAPN) and intracytic papillary neoplasms (ICPN) of the gallbladder. IPNB, IPMN, and ITPN are recognized by the World Health Organization.

IPNbs are histologically classified as low- or intermediate-grade intraepithelial neoplasia corresponding to adenomas or borderline malignancy, high grade intraepithelial neoplasia corresponding to carcinoma in situ, or as having an associated invasive carcinoma. The neoplasms are regarded as precancerous lesions; therefore, radical resection is recommended in operable patients.

In our case, although the epithelial atypia was moderate, it was accompanied by a bile duct tumor thrombus. The neoplasms accompanied with tumor thrombus are often ordinary invasive carcinoma.

The patient underwent choledochectomy and cholecystectomy.

**Case characteristics**
A 79-year-old female with an incidentally-diagnosed gallbladder tumor accompanied by bile duct tumor thrombus.

**COMMENTS**

**Figure 3 Pathological examination of the tumor.** A: Hematoxylin and eosin staining demonstrated the tumor to be a tubulopapillary adenoma with moderate epithelial atypia (× 400); B: MUC5AC staining showing positive expression (× 600).
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