

## Tubulopapillary adenoma of the gallbladder accompanied by bile duct tumor thrombus

Kentaroh Yamamoto, Fumio Yamamoto, Atsuhiko Maeda, Hirotsune Igimi, Mami Yamamoto, Ryosuke Yamaguchi, Yuichi Yamashita

Kentaroh Yamamoto, Fumio Yamamoto, Hirotsune Igimi, Mami Yamamoto, Department of Surgery, Yamamoto Memorial Hospital, Saga 848-0031, Japan  
Atsuhiko Maeda, Department of Internal Medicine, Maeda Hospital, Saga 848-0031, Japan  
Ryosuke Yamaguchi, Yuichi Yamashita, Department of Gastroenterological Surgery, Fukuoka University School of Medicine, Fukuoka 814-0180, Japan

Author contributions: Yamamoto K, Yamamoto F and Yamashita Y designed the report; Yamamoto K, Yamamoto M and Igimi H performed the genetic analyses; Yamamoto K, Maeda A and Yamaguchi R collected the patient's clinical data; Yamamoto K analyzed the data and wrote the paper.

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Correspondence to: Kentaroh Yamamoto, MD, PhD, Department of Surgery, Yamamoto Memorial Hospital, Hachiyakarami 88-4, Niri-cho, Imari, Saga 848-0031, Japan. [kentaroh-y@kenjin-kai.com](mailto:kentaroh-y@kenjin-kai.com)

Telephone: +81-955-232166 Fax: +81-955-224702

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**Key words:** Intraductal papillary mucinous neoplasm of the bile duct; Tumor thrombi

**Core tip:** Intraductal papillary mucinous neoplasm of the bile duct (IPNB) has relatively recently been recognized as a separate disease entity with an unclear pathogenesis. We present a case of IPNB developing from the gallbladder accompanied by a bile duct tumor thrombus in a 79-year-old female. Although this is not a malignant lesion, it has the potential to mimic a malignant lesion, and hence needs aggressive treatment.

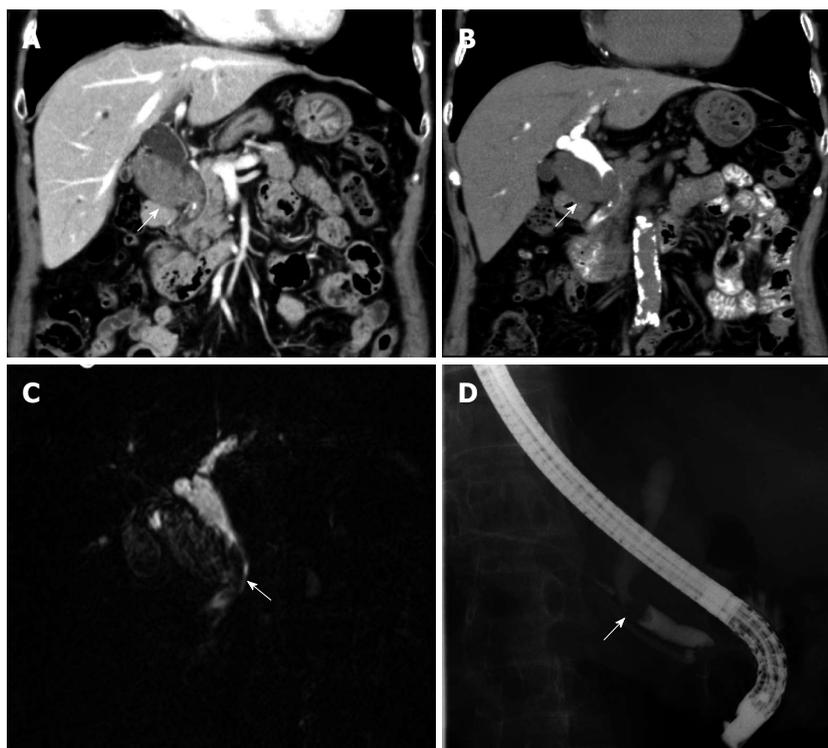
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### Abstract

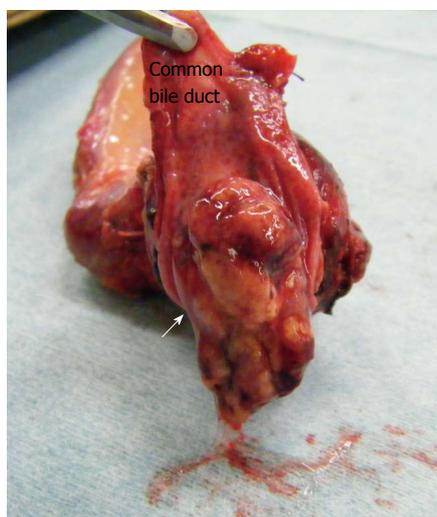
Intraductal papillary mucinous neoplasm of the bile duct (IPNB) is recognized as a precancerous lesion; however, both its pathogenesis and progression remain unclear. We present here a case of IPNB arising from the gallbladder accompanied by bile duct tumor thrombus in a 79-year-old female. The resected 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, intraepithelial 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*<sup>[1]</sup>. IPNB is regarded as a counterpart of IPMN of the pancreas, and is considered to be a precancerous lesion<sup>[2-5]</sup>. A similar spectrum of lesions also exists in the gallbladder<sup>[6]</sup>. 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.



**Figure 1** A 79-year-old female presented to our hospital for an incidentally-diagnosed gallbladder tumor. A: Coronal contrast-enhanced computed tomography (CT) image. The white arrow points to the gallbladder tumor with bile duct tumor thrombus; B: Coronal drip infusion cholangiographic CT image. The white arrow indicates the gallbladder tumor with bile duct tumor thrombus; C: Endoscopic retrograde cholangiopancreatography image. The white arrow indicates the defect due to the bile duct tumor thrombus; D: Magnetic resonance cholangiopancreatography image. The white arrow indicates the defect due to the bile duct tumor thrombus.



**Figure 2** The resected specimen. Dissection of the common bile duct demonstrated a mucin-producing tumor thrombus.

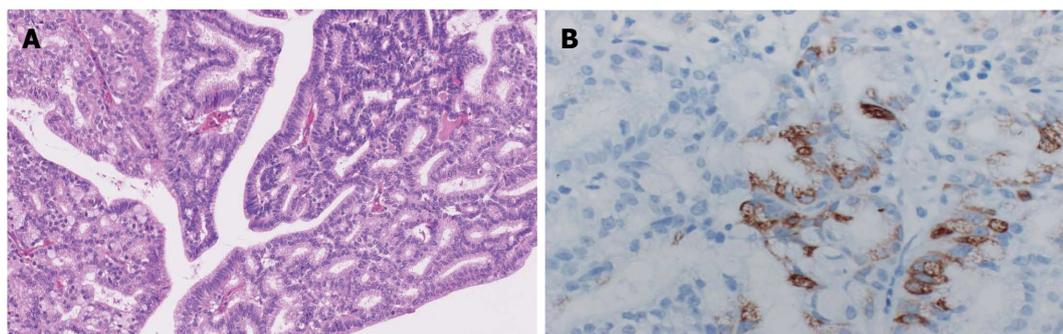
## CASE REPORT

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



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

MUC1 and CK20.

## DISCUSSION

Recently, intraepithelial neoplasms occurring in the ampullopapillary tract have attracted a substantial amount of attention. These include the so-called IPNB, IPMN of the pancreas, intraductal tubulopapillary neoplasms (ITPN) of the pancreas, intra-ampullary-tubular neoplasms (IAPN) and intracystic papillary neoplasms (ICPN) of the gallbladder<sup>[1-6]</sup>. IPNB, IPMN, and ITPN are recognized by the World Health Organization<sup>[7]</sup>. IPNB, on the other hand, is a relatively recently proposed (in 2001) disease entity<sup>[1]</sup> which has been shown to be histologically similar to IPMN<sup>[2-5]</sup>. A similar spectrum of lesions also exists in IAPN and ICPN; however, these have not been fully characterized<sup>[6]</sup>.

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<sup>[5,6]</sup>. The neoplasms are regarded as precancerous lesions; therefore, radical resection is recommended in operable patients<sup>[4,5,8,9]</sup>.

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<sup>[10,11]</sup>. 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 pyloric type adenocarcinoma of the gallbladder has a poor prognosis<sup>[12]</sup>. So, in our case, surgical treatment is considered reasonable and proper.

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

## COMMENTS

### Case characteristics

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 pyloric type tubulopapillary adenoma with moderate epithelial atypia.

### Treatment

The patient underwent choledochectomy 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 accompanied with tumor thrombus are often ordinary invasive carcinoma.

### Term explanation

Intraductal papillary mucinous neoplasm of the bile duct is a recently recognized disease entity whose behavior is still unclear.

### Experiences and lessons

Although the epithelial atypia was moderate, it was accompanied by a bile duct tumor thrombus. Even if no malignant cells are present, intraepithelial neoplasms occurring in the ampullopapillary tract can behave as malignant tumors. Hence, these patients should be treated aggressively.

### Peer review

This article applies the validity of surgical treatment for intraepithelial neoplasms occurring in the ampullopapillary tract, even if it is an adenoma.

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