

# An Intraductal Papillary Neoplasm of the Bile Duct at the Duodenal Papilla

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## Key Words

Intraductal papillary neoplasm of the bile duct · Duodenal papilla · Intraductal papillary mucinous neoplasm · Intraductal ultrasound · Peroral cholangioscopy

## Abstract

In recent years, the disease concept of intraductal papillary neoplasm of the bile duct (IPNB) has been attracting attention as a biliary lesion that is morphologically similar to intraductal papillary mucinous neoplasm (IPMN), which is considered to be a counterpart of IPMN. However, there are few reports on IPNB, and a consensus regarding the features of this disease is thus lacking. We experienced an extremely rare case of IPNB occurring in the bile duct at the duodenal papilla, which is a tumor presentation that has not previously been reported. Herein, we report this interesting case and discuss the possible association between IPMN and IPNB.

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## Case Report

Our patient was a 65-year-old male. Although he had suffered rectal cancer at the age of 44, no recurrence had been detected since his treatment. He reported no alcohol use but had a smoking history of 40 cigarettes per day for 33 years. His family history was unremarkable. Regarding the present illness, he visited a neighborhood clinic with the chief complaint of epigastric pain. Abdominal ultrasound revealed dilatation of the common bile duct, and a detailed examination was performed. However, because no causes were detected, he was referred to our hospital. Physical examination revealed no abnormal abdominal findings.

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Blood tests revealed no increase in hepatobiliary enzymes, the absence of jaundice, and no increase in inflammatory findings. The tumor marker levels (carcinoembryonic antigen and cancer antigen 19-9) were also normal. Abdominal ultrasound, CT, magnetic resonance cholangiopancreatography, and endoscopic ultrasound revealed marked dilatation from the common to the intrahepatic bile duct, but no tumor lesion was found (fig. 1). When endoscopic retrograde cholangiopancreatography was performed, the orifice of the duodenal papilla was dilated, and mucus secretion was observed. The common bile duct was markedly dilated, and a filling defect due to mucus was observed in the duct (fig. 2a). The pancreatic duct was normal without dilatation. When intraductal ultrasound (IDUS) was performed under suspicion of intraductal papillary neoplasm of the bile duct (IPNB), an exophytic papillary lesion was detected in the intrapancreatic bile duct (fig. 2b). Furthermore, peroral cholangioscopy (POCS) was performed revealing an exophytic papillary lesion at the same site (fig. 2c). The common bile duct was filled with abundant mucus. There were no lesions from the intrahepatic to the common bile duct. Thus, IPNB with the focal area located in the intrapancreatic bile duct was diagnosed. Although no apparent malignant cells were detected by cytology or biopsy, subtotal stomach-preserving pancreaticoduodenectomy was performed because of the high mucus-producing ability and concerns over malignant transformation (fig. 3a). The pathologic diagnosis was mild-to-moderate atypical tubular adenoma occurring in the bile duct at the duodenal papilla (fig. 3b). No apparent infiltration was observed. Based on immunostaining, the resected tissue was partially positive for mucin (MUC) 1, MUC2, MUC5AC, and MUC6.

## Discussion

Tumors with intrabiliary papillary growth have many morphological similarities to IPMN; and Chen et al. [1] called these tumors intraductal papillary neoplasia of the liver. Based on subsequently accumulated cases, such tumors were found to be characterized by intrabiliary papillary growth, the potential to progress to tubular or mucinous adenocarcinoma, and more favorable postoperative outcomes than conventional tubular adenocarcinoma. Their pathology is also similar to that of intraductal papillary mucinous neoplasm (IPMN) in many respects. Thus, in 2006, it was proposed that this group of diseases be called IPNB as a counterpart of IPMN [2–7]. Meanwhile, there are papillary tumors, also including many malignant cases, without overproduction of mucus in the bile duct. Considering IPNB to be a counterpart of IPMN is thus controversial [1–7].

Although there is no clear classification of IPNB on the basis of tumor location as in the case of the main-duct and branch-duct types of IPMN, IPNB is characterized by mucobilia, a condition associated with the secretion of abundant mucus; tumors with papillary growth are observed in the common bile duct, and many cases have imaging findings similar to those of the main-duct type IPMN in which the entire bile duct is dilated [8, 9]. Meanwhile, IPNB sometimes occurs in the peripheral bile duct. In such cases, tumors have a cystoid morphology, and those with a botryoid morphology similar to that of the branch-type IPMN have also been reported [8, 9]. In our case, abundant mucus secretion was documented, the common bile duct was dilated, and the image findings were similar to those of the main duct-type IPMN.

Regarding the clinical characteristics of IPNB, the peak onset age is in the seventh decade, and there is no sex difference. IPNB is often detected based on jaundice, liver dysfunction, and cholangitis symptoms. The primary sites are the intrahepatic bile duct in two thirds of cases and the extrahepatic bile duct in the remaining third, and IPNB is considered to

commonly occur in the left hepatic lobe. In contrast to IPMN, 80% of the IPNB cases show tissue atypism indicating malignancy [1–9]. Occurrence in the bile duct at the duodenal papilla, as in our case, is extremely rare. Despite marked mucus production, the absence of dilatation of the main pancreatic duct was assumed to be attributable to tumor occurrence in the bile duct at the papillary area. Moreover, our case had IPNB, which is often malignant, but was histologically identified as an adenoma.

Regarding the diagnostic imaging of IPNB, the detection of the disease is relatively easy because ultrasound and CT reveal dilatation from the common to the intrahepatic bile duct as well as cystoid dilatation of the intrahepatic bile duct. When contrast-enhanced CT is performed to diagnose papillary protrusion, a faint tumor stain is visible in cases with severe protrusion. However, small protrusions and superficial spreading are often difficult to detect even by cholangiography and IDUS. For the assessment of superficial spreading, observation under direct vision with percutaneous transhepatic cholangioscopy or POCS is useful [8]. A recent report stated that observation by cholangioscopy using narrow band imaging allows a clearer confirmation of the border between the superficial spreading lesion and normal tissue [10], and narrow band imaging is expected to contribute to the diagnosing progression of IPNB in the future. Although the localization of the lesion was difficult, IPNB was readily suspected in our case because dilatation from the common to the intrahepatic bile duct and retention of abundant mucus in the bile duct were observed. IDUS and POCS were found to be useful for localization, and the tumor was identified in the bile duct at the papillary area.

IPNB is pathologically similar to IPMN, of which the fundamental features are intraductal papillary growth and intraductal mucus retention, and IPNB is classified into four types based on the morphology of the tumor cells: pancreatobiliary type, intestinal type, gastric type, and oncocytic type. Since IPNB is frequently malignant and mainly of the intestinal and pancreatobiliary types, it is reportedly reasonable to regard this tumor as a counterpart of the main duct-type IPMN [4, 5]. The immunopathological characteristics of IPNB are similar to those of IPMN, and the tumor cells in IPNB are also known to frequently express MUC2, MUC5AC, and cytokeratin 20, which are the mucous phenotypes of the intestinal and gastric crypt epithelium [3]. Immunostaining of the specimen from our case was partially positive for MUC1, MUC2, MUC5AC, and MUC6.

Regarding treatment for this disease, because the prognosis after surgical resection of IPNB is more favorable than after resection of conventional cholangiocarcinoma, aggressive surgical resection is preferable despite the high frequency of malignant cases [4, 11, 12]. In our case, no recurrence has to date been detected in the 3 years since resection.

We experienced an extremely rare case of IPNB occurring in the bile duct at the duodenal papilla, which is a presentation of this tumor that has not previously been reported. We described this interesting case with a discussion of the association between IPMN and IPNB.

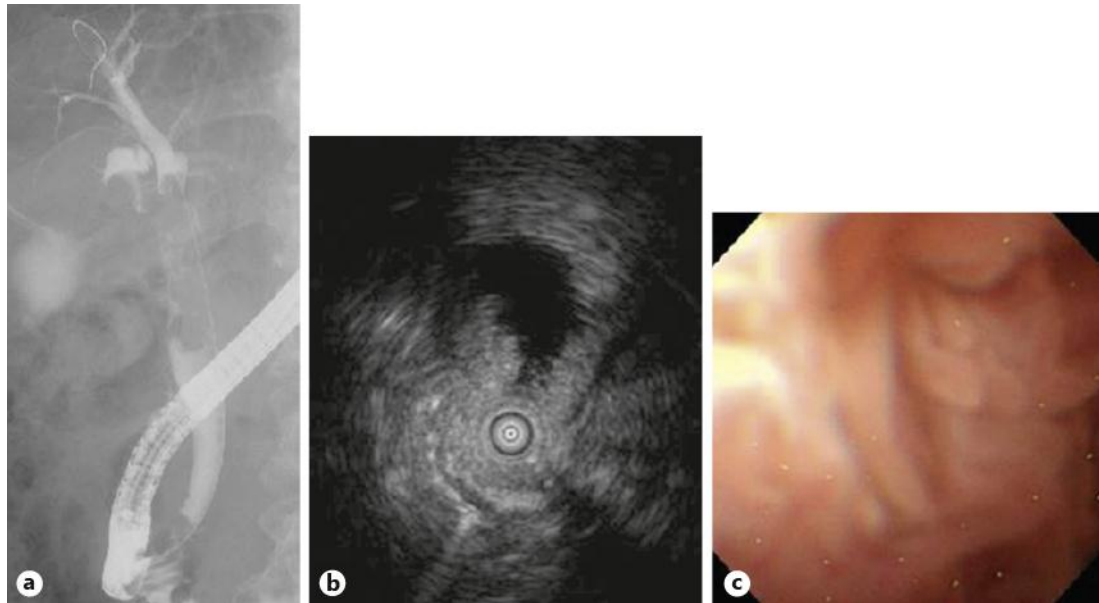
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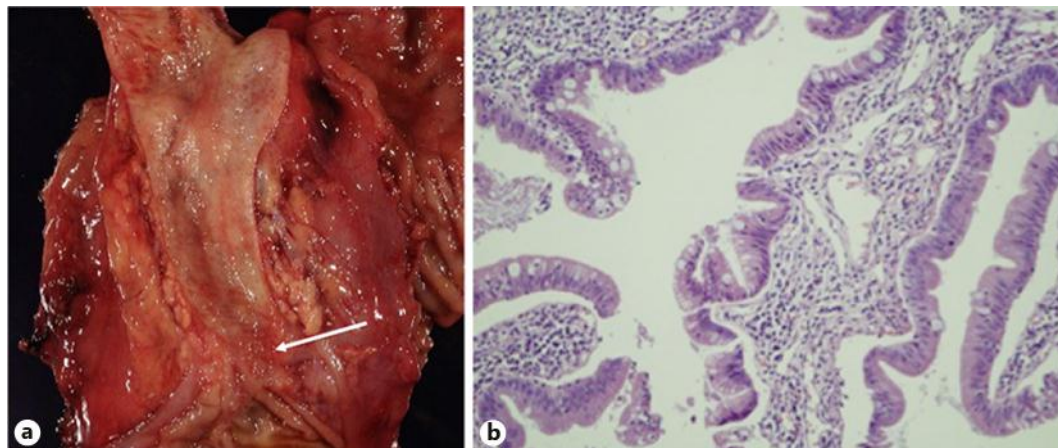
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**Fig. 1.** MRI revealed marked dilatation from the common to the intrahepatic bile duct, but no tumor lesion was found.



**Fig. 2.** **a** Endoscopic retrograde cholangiopancreatography revealed marked dilatation of the common bile duct with a filling defect due to mucus. IDUS (**b**) and POCS (**c**) revealed an exophytic papillary lesion in the intrapancreatic bile duct.



**Fig. 3.** **a** Subtotal stomach-preserving pancreaticoduodenectomy was performed because of the high mucus-producing ability and concerns over malignant transformation. The arrow shows the lesion in the intrapancreatic bile duct. **b** The pathologic diagnosis was mild-to-moderate atypical tubular adenoma occurring in the bile duct at the duodenal papilla. No apparent infiltration was observed.