

# Preoperative Diagnosis of Intraductal Papillary Neoplasm of the Bile Duct Followed by Laparoscopic Hepatectomy: A Case Report

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## ABSTRACT

**Introduction:** Intraductal papillary neoplasm of the bile duct (IPNB) is associated with better prognosis than biliary cancer after curative surgery.

**Case report:** We report a case of a 59-year-old woman who presented with an enlarging liver cyst with a mural nodule. Laboratory data indicated normal hepatobiliary function and tumor markers. Imaging revealed a lesion at liver segments 5 and 6, with dynamic computed tomography revealing slight enhancement of the nodule during the early phase, prolonged during the delayed phase.

**Results:** Magnetic resonance cholangiopancreatography revealed that the tumor was connected to segment 5 of the bile duct. Endoscopic retrograde cholangiopancreatography confirmed dilation of the bilateral intrahepatic bile duct owing to mucin obstruction from the tumor. Biopsy results were negative for malignancy, leading to a diagnosis of IPNB. Consequently, laparoscopic posterior segmentectomy and segment 5 resection were performed (operative duration: 433 min; intraoperative blood loss: 25 mL). Postoperative recovery was uneventful, and pathological examination indicated intestinal-type glandular epithelium with no invasive characteristics. The pathological diagnosis was IPNB without an invasive pattern. The surgical margin was clear, and no recurrence was observed 1 year postoperatively.

**Conclusion:** Although IPNB is rare and challenging to diagnose preoperatively, evaluation of horizontal tumor spread and laparoscopic hepatectomy are effective for noninvasive cases.

**Keywords:** intraductal papillary neoplasm of the bile duct, laparoscopic hepatectomy, preoperative diagnosis

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## INTRODUCTION

Intraductal papillary neoplasm of the bile duct (IPNB) was not clearly classified until 2010 when the World Health Organization proposed an integrated classification that recognized IPNB as a distinct entity. IPNB accounts for 10-15% of

all bile duct tumors (1). It is considered the counterpart of intraductal papillary mucinous neoplasm (IPMN) of the pancreas (P-IPMN). Treatment strategies for IPNB vary among different geographical locations. Although IPNB with an invasive pattern has a poor prognosis, aggressive surgical resection for IPNB is associated with a 5-year overall survival rate of approximately 50% (2,3).

Similar to IPMN, IPNB can be classified into intestinal, gastric, biliopancreatic, and acidophilic subtypes (4). It can also be categorized by location as intrahepatic, extrahepatic, and diffuse (4-6). Recently, biliary pathologists in Japan and Korea have proposed subclassifying IPNB into types I and II based on growth morphology and atypia. The World Health Organization has adopted this subclassification in its 2019 revision (5<sup>th</sup> edition) and described its characteristics (4).

In this report, we present the case of a patient with a preoperative diagnosis of IPNB who underwent laparoscopic hepatectomy. We also present a review of the literature on IPNB.

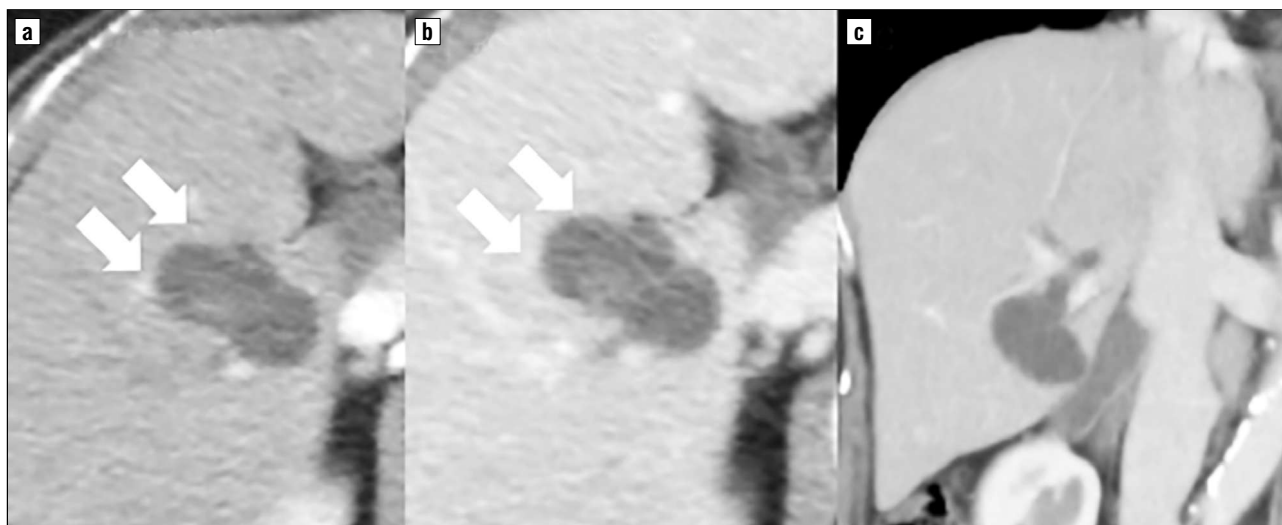
## CASE REPORT

A 59-year-old woman presented to our hospital with an enlarging liver cyst comprising a mural nodule. The cyst was observed during a routine examination and followed up annually. The size of the cyst had increased over 2 years, and the mural nodule appeared within the cyst. Her medical history included hypothyroidism, acute appendicitis, and uterine fibroids. Laboratory test results indicated normal hepatobiliary enzymes and

tumor markers, Child-Pugh grade A, liver damage grade A, and an indocyanine green retention rate at 15 min of 6.5%. Her family history was unremarkable.

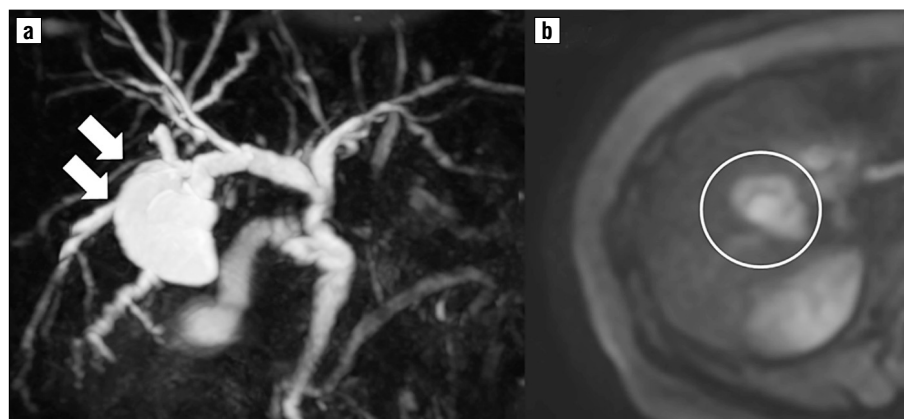
Abdominal ultrasonography identified a space-occupying lesion at liver segments 5 and 6, measuring 30 × 30 mm in diameter, with a mural nodule. Dynamic computed tomography indicated that the mural nodule inside the cyst was slightly enhanced during the early phase; this enhancement was prolonged during the delayed phase (*fig. 1 a-c*). Magnetic resonance cholangiopancreatography revealed that the tumor was connected to the biliary duct of segment 5 (*fig. 2 a, b*). Endoscopic retrograde cholangiopancreatography revealed that the intrahepatic bile duct was dilated owing to mucin produced by the tumor and that the tumor was connected to segment 5 of the biliary duct (*fig. 3*). A step biopsy of the liver hilum, branches of the anterior and posterior bile ducts, and right main bile duct demonstrated no malignancy. Intraductal ultrasonography revealed an approximately 10-mm highly echogenic nodular lesion within a multifocal cyst. The nodule exhibited no intramucosal invasion of the intrahepatic bile duct (*fig. 4*). Therefore, IPNB was diagnosed.

Accordingly, Laparoscopic posterior segmentectomy and anatomical resection of segment 5 were performed. The operative duration was 433 min, and the intraoperative blood loss was 25 mL. Pathological examination indicated that the tumor was lined with glandular epithelium with intestinal-type characteristics and that the nuclei were arranged basolaterally while maintaining polarity (*fig. 5*). Intra-

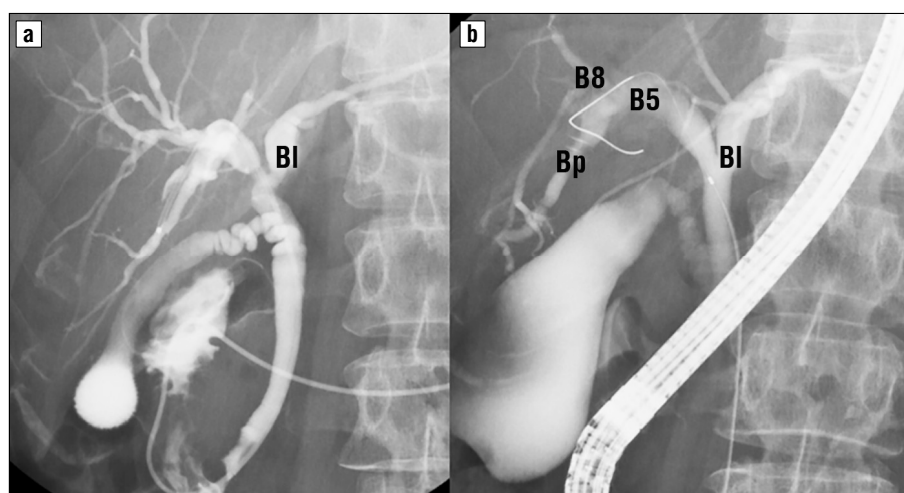


**Figure 1 - Abdominal computed tomography findings. (a) and (b):** A multilobular 30- X 30-mm tumor with adjacent lesions detected in liver segments 5 and 6. The arrows (→) indicate where the mural nodule inside the cyst is slightly enhanced during the early phase. This enhancement was prolonged during the delayed phase. (c): This image reveals dilatation of the right hepatic duct

**Figure 2 - Magnetic resonance cholangiopancreatography (MRCP).**  
 (a): MRCP shows a 30-mm multifocal cyst at segment 5 with a liquid reservoir inside.  
 (b): Diffusion-weighted image (DWI) reveals a pale abnormal signal from the mural nodule within the cyst



**Figure 3 - Endoscopic retrograde cholangiopancreatography.** (a) and (b): a cystic mass traversing the biliary duct of segment 5 (B5). No bile duct anomalies are observed. The results of step biopsy and bile cytology tests are negative for the left bile duct (B1), B8, and posterior branch of the bile duct (Bp)



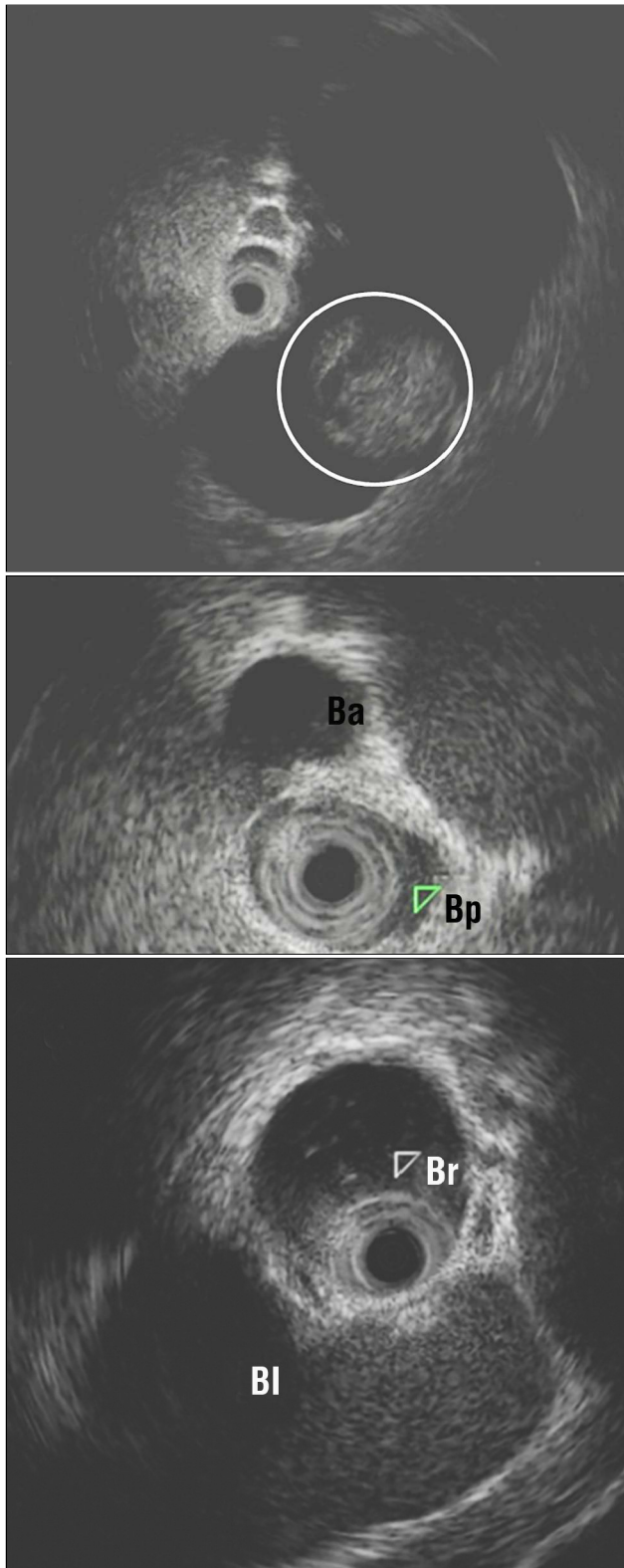
epithelial carcinoma components were not observed. An immunohistochemical analysis revealed no estrogen receptors or progesterone receptors in the tumor. The pathological diagnosis was IPNB without an invasive pattern. The surgical margin was free from tumor invasion. The postoperative course was uneventful, and the patient was discharged 8 days postoperatively.

## DISCUSSION

Symptoms of IPNB, including abdominal pain and jaundice, vary among patients. Therefore, a precise pre-operative diagnosis, which is important for ensuring optimal surgical treatment, can be difficult. The prognosis of IPNB is better than that of biliary cancer; however, progression to adenocarcinoma is associated with a poorer prognosis (7). Risk factors for recurrence in patients with IPNB include R1/R2 resection, lymph node metastasis, and invasive patterns (8). Additionally, the presence of invasive components in the surgical margin can affect recurrence (9). The presence of minimal dysplasia in the surgical margin is reportedly

associated with a poor prognosis (7). In our case, the tumor did not invade the anterior branch of the biliary duct, as confirmed via a preoperative biliary biopsy. Instead, the tumor occupied the posterior segment, necessitating posterior segmentectomy and segment 5 resection for tumor-free margins. The surgical margin was pathologically free from tumor invasion. Other factors that predict the prognosis include MUC2 positivity, type I disease, and intestinal patterns (8), and our case was categorized as type I IPNB based on the immunohistochemical staining pattern.

Lymph node dissection is important for achieving a good long-term prognosis for intrahepatic cholangiocarcinoma (ICC) (10). Various studies have reported that lymph node metastasis negatively affects the recurrence-free survival of patients with ICC. However, Luvira et al. (10) concluded that routine lymph node dissection is not necessary for IPNB, as metachronous lesions in the remaining liver can affect survival, even in patients with nonmalignant IPNB. They also noted that IPNB has a low propensity for lymph node metastasis. Our patient did not undergo lymph node dissection



**Figure 4 - Intraductal ultrasonography showing an approximately 10-mm highly echogenic nodular lesion within a multifocal cyst. The nodule exhibits negative intramucosal invasion of the intrahepatic bile duct. Ba: anterior bile duct; Bl: left bile duct; Bp: posterior branch of the bile duct; Br: right bile duct.**

**Figure 5 - Pathological results.**  
The nodules are basolaterally aligned glandular epithelial nuclei with intestinal morphology and no polarity disorder.  
(a): A formalin-fixed macrospecimen is presented. (b): The glandular epithelial nuclei with intestinal-type characteristics are arranged basolaterally and show no polarity disorder. No intraepithelial carcinoma components are observed in this tissue specimen



because the preoperative diagnosis was IPNB without an invasive pattern. Considering the favorable prognosis of IPNB, routine lymph node dissection is unlikely to influence long-term outcomes. However, as discriminating between nonmalignant IPNB and IPNB with invasive patterns is difficult, further prospective studies are required to evaluate the effect of routine lymph node dissection on long-term prognosis.

IPNB is usually associated with a higher pancreaticobiliary type than IPMN. Aoki et al. (11) reported the presence of high-grade dysplasia and invasive types in IPNB, whereas low-grade and intermediate-grade dysplasia were not observed. In the present case, the

patient had intrahepatic type I IPNB and mucin hypersecretion. The prognosis of type I IPNB is similar to that of IPMN, and type II IPNB has a poorer prognosis than type I IPNB. Moreover, the expression of MUC5AC and MUC6 significantly affects the long-term prognosis of IPNB (11). Although the prognostic values of these mucins vary among studies, there is limited literature on the prognostic significance of MUC6 expression. Moreover, previous studies have shown inconsistent results regarding the clinical impact of MUC5AC expression on the surgical outcomes of ICC and pancreatic neoplasms, including P-IPMN. MUC5AC expression is strongly associated with a high American Joint Committee on Cancer tumor category, lymph node metastasis, and worse postoperative survival with ICC, as well as with decreased lymph node metastasis, decreased incidence of vascular invasion, and better postoperative survival with pancreatic neoplasms, including that of P-IPMN (12).

Recent advances in laparoscopic liver resection have led to improved postoperative outcomes, including fewer postoperative complications and shorter hospital stays, without increasing the blood loss volume and mortality (13). Malignancies, particularly colorectal liver metastasis (CRLM) and hepatocellular carcinoma (HCC), are the most common indications for laparoscopic major hepatectomy (LMH) (14). Considering oncological efficacy, LMH is associated with long-term survival rates comparable to those of open hepatectomy in CRLM and HCC cases (15-19). Matono et al. (20) reported the first case of branch-type IPNB after laparoscopic anatomical resection, although previous reports have described open hepatectomy for such cases. Laparoscopic hepatectomy results in a shorter postoperative hospital stay and lower intraoperative blood loss than open hepatectomy (21).

Patients with branch-type IPNB without an invasive pattern are good candidates for laparoscopic hepatectomy, and a precise horizontal tumor spread of the bile duct is important for achieving R0 resection. Accurate diagnosis of IPNB and thorough evaluation of tumor spread are crucial; laparoscopic hepatectomy may be the optimal option for noninvasive cases.

### *Author's Contributions*

MT and TA conceived the presented idea, developed the theory, and performed the computations. MI, MK, RH, KT, and TT provided encouragement to investigate specific aspects of the case and supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

### *Conflict of Interest*

The authors declare that they have no competing interests.

### *Ethical Statement*

All procedures performed during this research were approved by the Ethical Committee of our institution.

### *Informed Consent*

Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

### *Availability of Data and Materials*

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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