Int J Clin Exp Pathol 2025;18(4):173-178
www.ijcep.com /ISSN:1936-2625/IJCEP0162302

Case Report

Intraductal papillary mucinous neoplasm of the intrahepatic bile duct: a case report and literature review

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Received November 27, 2024; Accepted March 29, 2025; Epub April 15, 2025; Published April 30, 2025

Abstract: Intraductal papillary mucinous neoplasm of the bile duct (IPMN-B) is a rare malignant tumor originating from the bile duct epithelium, characterized by its ability to secrete large amounts of mucin, which can lead to biliary obstruction. This paper presents a case involving a 69-year-old woman presenting with intermittent right upper abdominal pain, imaging revealed dilation of the left intrahepatic bile duct and the presence of a solid mass. We performed left lateral hepatectomy on the patient, and the postoperative pathological diagnosis was intraductal papillary tumor with associated invasive carcinoma. At the 6-month postoperative follow-up, the patient showed no signs of recurrence and was in good condition. This case underscores the high malignant potential of IPMN-B, emphasizing the importance of early surgical resection following diagnosis to achieve a favorable prognosis and improve patient outcomes.

Keywords: Intraductal papillary mucinous neoplasm of the bile duct (IPMN-B), liver, associated invasive carcinoma

Introduction

Intraductal papillary tumors of the bile duct (IPNB) constitute a premalignant pathological entity closely associated with cholangiocarcinoma, a condition that has garnered increasing clinical recognition in recent years. In 2010, the World Health Organization formally designated IPNB as a distinct classification within biliary tract tumors [1]. This neoplasm can manifest in both intrahepatic and extrahepatic bile ducts, which are anatomically continuous. Notably, approximately one-third of IPNB cases demonstrate mucin hypersecretion and are classified as intraductal papillary mucinous neoplasms of the bile duct (IPMN-B) [2, 3]. To date, documented cases of IPMN-B remain limited in the literature. Owing to its insidious clinical presentation, absence of pathognomonic symptoms, and nonspecific radiological features, IPMN-B is frequently subject to diagnostic oversight or misinterpretation. Herein, we report a case of intrahepatic cholangiocarcinoma initially detected due to abdominal pain, with subsequent histopathological evaluation confirming a diagnosis of intrahepatic IPMN-B with associated invasive carcinoma. Through a comprehensive analysis of the clinical diagnostic and therapeutic trajectory, imaging characteristics, and histopathological findings, this study provides a critical review of the current advancements in the understanding and management of IPMN-B.

Case report

A 69-year-old woman presented to the outpatient clinic with intermittent right upper abdominal pain. She had no significant medical history, including no history of smoking or alcohol use. Abdominal ultrasonography revealed a mixed cystic-solid mass in the dilated left hepatic duct, along with multiple gallstones in the gallbladder. Liver function tests and tumor marker levels were within normal ranges: alanine transaminase (ALT), 17.4 IU/L; aspartate transaminase (AST), 20.2 IU/L; and serum total bilirubin (TB), 20.3 μmol/L; γ-glutamyl transpeptidase, 39.2 IU/L; alkaline phosphatase, 88 IU/L. Tumor markers were unremarkable: alfa-fetoprotein (AFP), 1.27 IU/ml; carbohydrate antigen

https://doi.org/10.62347/NZTK3263

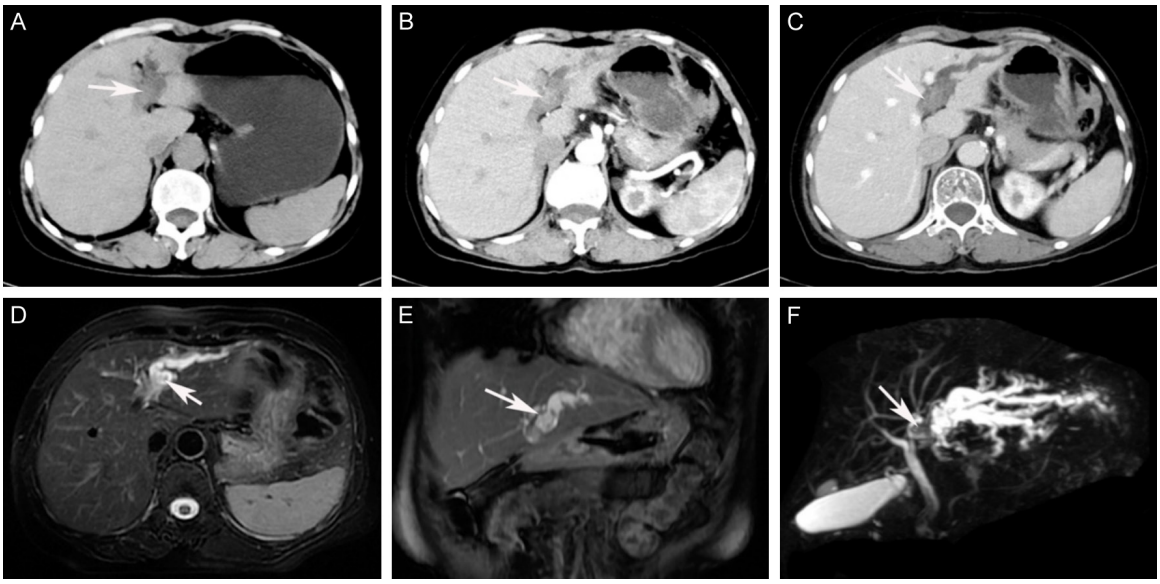

Figure 1. Preoperative imaging findings: A: Plain CT scan showing dilation of the left hepatic duct. B, C: Contrast-enhanced CT images demonstrating enhancement of the intraductal mass (white arrow). D, E: Axial and coronary MRI images revealing a cystic-solid mass in the left hepatic duct (white arrow). F: MRCP showing a mass obstructing the left hepatic duct (white arrow).

19-9 (CA19-9), 9.14 IU/ml; and carcinoembryonic antigen (CEA), 2.47 IU/ml.

Contrast-enhanced computed tomography (CT) revealed a tumor in the dilated left intrahepatic bile duct. The lesions demonstrated moderate enhancement in both the hepatic arterial phase and portal venous phase. In the hepatic arterial phase, the lesions exhibited slightly higher density compared to the liver parenchyma, while in the portal venous phase, the lesions showed relatively lower density than the liver parenchyma. Magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) further confirmed significant dilation of the peripheral biliary ducts in the left hepatic lobe, along with a 1.9 × 1.5 cm tumor within the ducts. The right intrahepatic bile duct and extrahepatic bile duct appeared normal (**Figure 1**).

Upon intraoperative inspection, a thick, jelly-like substance was observed flowing from the intrahepatic bile duct, and a papillary mass measuring of approximately 2 × 2 cm was identified in the left hepatic duct. The mass had a soft pedicle, raising suspicion of malignancy. Consequently, a left lateral hepatectomy was performed.

Pathological examination of the postoperative specimens confirmed an intraductal papillary neoplasm with high-grade intraepithelial neoplasia and focal invasive mucinous adenocarcinoma. Immunohistochemical analysis revealed strong positivity for CK19 in the tumor tissue. Other positive markers included CK8/18, CAM5.2, and CK, with partial positivity for CEA. The proliferative index, as determined by Ki-67 staining, was 30%. The tumor cells were negative for CK7, CDX-2, CK20, AFP, GCDFP-15, CA125, and P53. The patient was discharged on the 14th postoperative day and no recurrence was observed during the 6-month follow-up period (**Figure 2**).

Discussion

Intraductal papillary mucinous neoplasm of the bile duct (IPMN-B) is defined analogously to its pancreatic counterpart, intraductal papillary mucinous neoplasm of the pancreas (IPMN-P). This similarity arises from their shared embryological origin, as both the bile duct and the pancreatic duct develop from the foregut mesoderm. Consequently, IPMN-B and IPMN-P exhibit overlapping pathological features, including excessive mucus secretion and subsequent ductal obstruction. Most critically, both entities are classified as precancerous lesions [3]. Although intraductal papillary mucinous neoplasm of the bile duct (IPMN-B) has gained increasing clinical recognition in recent years,

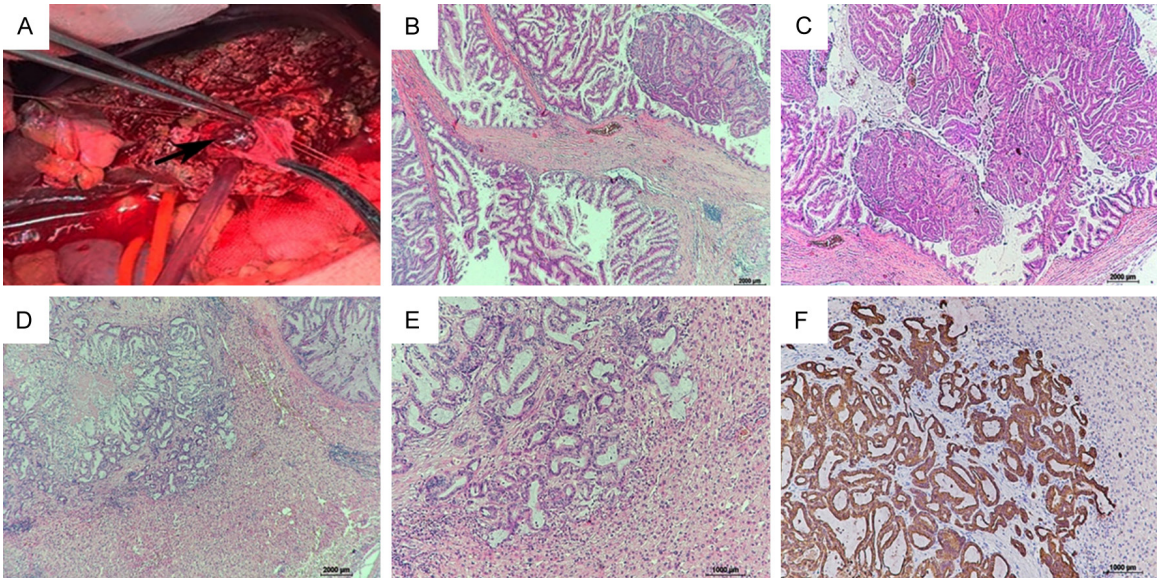

Figure 2. Surgical and pathological findings. (A) Intraoperative photograph showing a papillary mass (approximately 2 × 2 cm) in the left hepatic duct (black arrow). (B, C) Histopathological examination revealing papillary tumor structures with central fibrovascular cores (hematoxylin and eosin [H&E] staining; B, C ×40). (D, E) The tumor exhibited glandular structures with focal fusion and infiltration into the surrounding liver tissue (HE, D ×40, E ×100). (F) Immunohistochemical analysis demonstrating strong CK19 positivity in the tumor tissue (F ×100).

significant gaps remain in our understanding of its molecular mechanisms, natural history, and optimal management strategies. IPMN-B is rare in western countries, with a higher prevalence in Asian regions such as China, Japan, South Korea. Currently, there is a lack of large-scale epidemiological data on its population-based incidence. The disease primarily affects individuals aged 55-65 years, with no significant gender predilection [4, 5]. The pathogenesis of IPMN-B remains unclear; however, some studies suggest that the chronic inflammation caused by factors such as bile duct stones and Clonorchis sinensis infection may contribute to its development [6, 7]. Clinically, IPMN-B often presents with non-specific symptoms. In the early stages, patients may experience only intermittent upper abdominal pain. As the disease progresses, tumors growth and excessive mucus secretion can lead to complications such as fever, jaundice, and secondary pancreatitis. Additionally, approximately 10% of patients remain asymptomatic [8, 9].

Currently, the preoperative diagnosis of IPMN-B remains challenging. Laboratory tests often reveal abnormal liver function indices and elevated CA19-9 levels, which are primarily caused by bile duct obstruction. However, CA19-9 elevation cannot reliably distinguish between benign or malignant lesions [10]. Imaging modalities also lack specificity for IPMN-B diagnosis. Ultrasonography (US) is the most cost-effective imaging method and can demonstrate intra- and extrahepatic bile duct dilation as well as heterogeneous echogenic masses within the bile ducts. However, its accuracy is often compromised by intestinal gas interference and the presence of bile duct stones.

CT is the most widely used diagnostic tool for IPMN-B. It can detect focal or diffuse bile duct dilation and visualize intraluminal masses. On contrast-enhanced CT, the masses typically show mild enhancement during the arterial phase but no significant enhancement in the delayed phase. MRI and MRCP can clearly delineate the biliary tree and identify filling defects within the bile ducts. According to a literature review by Ritchie et al., the hallmark imaging features of IPMN-B include bile duct dilation and intraluminal mass [11].

Positron emission tomography-computed tomography (PET-CT) is currently the most accurate modality for differentiating benign from malignant tumors and assessing metastatic potential. A comparative study by Ikeno et al. demonstrated that preoperative PET-CT can distinguish non-invasive IPMN-B from invasive IPMN-B [12].

ERCP may reveal mucin extrusion from the duodenal papilla and biliary filling defects on cholangiography in some patients. Although choledochoscope-guided biopsy, provides a definitive diagnostic approach, its clinical application is limited due to technical challenges, such as the risk of iatrogenic pancreatitis and procedural complexity.

Based on its pathological characteristics, IPMN-B can be classified into four distinct subtypes: pancreatobiliary (PB), gastric, intestinal, and oncocytic [13]. Among these, the PB and intestinal type are the most frequently observed. Additionally, IPMN-B can be stratified according to the degree of cellular atypia into low-grade and high-grade intraepithelial neoplasia, with the latter often associated with invasive cancers [14].

The PB subtype histologically resembles pancreatobiliary epithelium and is immunohistochemically positive for MUC1, MUC5AC and CK7. In contrast, the intestinal subtype mimics colonic intraepithelial tumors, typically expressing MUC2 and MUC5AC, but lacking MUC1 expression. The gastric subtype is characterized by gastric foveolar-like epithelium, which commonly expresses MUC6, MUC5AC, and CK7, but rarely MUC1 or MUC2. Finally, the oncocytic subtype is composed of cuboidal or columnar cells with abundant cytoplasm, exhibiting diffuse MUC5AC expression and focal positivity for MUC1 and/or MUC2 [15-17].

In 2020, the Japan Biliary Association and the Korea Hepatobiliary and Pancreatic Surgery Association jointly proposed updated histopathological diagnostic criteria, formally establishing Type 1 and Type 2 IPMN-B as distinct entities [18]. Type 1 IPMN-B is histologically defined by copious mucin production, papillary/villous/tubular architecture, and thin fibrovascular stalks within papillae. This subtype is predominantly associated with intestinal or gastric epithelial differentiation. In contrast, Type 2 IPMN-B exhibits minimal mucin secretion and demonstrates complex histomorphological patterns, including cribriform, densely tubular, solid, or macrocystic components. Notably, the PB subtype is significantly overrepresented in Type 2 lesions, and nearly all Type 2 cases (93.6%) were associated with invasive carcinoma at diagnosis. Although no significant difference in recurrence rate (RR) between the two subtypes, Type 2 demonstrated a markedly higher lymph node metastasis rate compared to Type 1. Furthermore, Type 2 patients exhibited significantly inferior 1-, 3-, and 5-year overall survival (OS) and disease-free survival (DFS) outcomes relative to Type 1 counterparts.

Therefore, IPMN-B is recognized as a significant precursor to cholangiocarcinoma. The exact rate of malignant transformation remains poorly quantified; however, Kubota et al. reported that among 119 surgically treated IPMN-B patients, approximately 36% were pathologically diagnosed with invasive carcinoma postoperatively [8]. Consequently, active intervention should be pursued when clinical suspicion of IPMN-B arises. Differential diagnosis of IPMN-B is essential to distinguish it from other cholangiocarcinoma subtypes, bile duct stones, and cystic lesions, particularly mucinous cystic neoplasms (MCN). Pathologically, MCN is characterized by the presence of ovarian-type stroma (OS), which serves as the most critical distinguishing feature from IPMN-B.

Radical surgical resection remains the gold standard for IPMN-B management. We reviewed English cases of IPMN-B with associated invasive carcinoma in the PubMed database and found that surgical resection as the cornerstone of management for patients with invasive cancer, and curative surgery can achieve better prognosis (**Table 1**). The surgical approach is determined by the lesion's anatomical location and extent. For localized intrahepatic lesions with negative frozen-section margins intraoperatively, hepatectomy (segmentectomy or lobectomy) is recommended. In cases involving the extrahepatic bile duct, pancreatoduodenectomy (Whipple procedure) is the preferred intervention. For patients with diffuse bile duct involvement, liver transplantation represents the sole curative option [9, 19]. Although Lymph node metastasis in IPMN-B is uncommon, the utility of regional lymphadenectomy remains debated. However, Jarnagin et al. advocate for systematic lymph node dissection in tumors involving the hilar or distal bile ducts [19]. For non-resectable cases, palliative biliary drainage (e.g., stenting) should be prioritized to mitigate biliary infections, optimize hepatic function, and reduce complications rates. Studies demonstrate that aggressive surgical intervention achieves 1-, 5-, and 10-year survival rates of 96%, 84%, and 81%,

Table 1. IPMN-B with associated invasive carcinoma cases reported in English

Author	Year	Age	Sex	Symptoms	Location	Treatment	Prognosis (months)
Ogiso T	2024	80	M	Liver tumor	LBD	Right hepatectomy	Alive (36)
Miry N	2024	65	F	Jaundice	CBD	Bile duct resection and Roux-en-Y	NM
Mukaida E	2021	57	F	Liver tumor	CBD	Laparoscopic right liver lobectomy	NM
Estanqueiro LR	2021	64	M	Abdominal pain Jaundice	CBD	Bile duct resection and Roux-en-Y	Dead (60)
Takasaki T	2022	82	M	Abdominal pain	LBD	Left hepatectomy	NM
Fujino R	2020	60	M	Liver tumor	RBD	Right hepatectomy	Alive (64)
Ikenaga N	2019	70	M	None	LBD	Left hepatectomy	NM
Ikenaga N	2019	70	F	Liver tumor	LBD	Left hepatectomy	NM
Takahashi G	2015	57	F	Hemobilia	RBD	Right hepatectomy and caudate lobectomy	Dead (36)
Date K	2015	69	F	None	RBD	Right hepatectomy combined with bile duct resection	Dead (12)
Current study	2025	69	F	Abdominal pain	LBD	Left lateral hepatectomy	Alive (6)

IPMN-B, intraductal papillary mucinous neoplasm of the bile duct; NM, no mentioned; LBD, left intrahepatic bile duct; RBD, right intrahepatic bile duct; CBD, common bile duct.

respectively, underscoring its prognostic significance [8].

Conclusion

In conclusion, IPMN-B remains a poorly understood and rare biliary tract tumor. For elderly patients, imaging findings such as bile duct wall masses and biliary ductal dilatation should raise clinical suspicion for this disease. The recent introduction of Type 1 and Type 2 subclassifications, which emphasize histopathological and clinical features of IPMN-B, may serve as robust predictors of patient outcomes. Early radical surgical resection, aimed at relieving biliary obstruction, can significantly improve prognosis and ensure favorable long-term results.

Disclosure of conflict of interest

None.

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