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ABOUT COVER

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Surgically treating a rare and asymptomatic intraductal papillary neoplasm of the bile duct: A case report

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Abstract

BACKGROUND

Intraductal papillary neoplasms of the bile duct (IPNBs) are rare and characterized by papillary growth within the bile duct lumen. IPNB is similar to obstructive biliary pathology. In this report, we present an unexpected case of asymptomatic IPNB and consolidate our findings with the relevant literature to augment our understanding of this condition. Integrating relevant literature contributes to a more comprehensive understanding of the disease.

CASE SUMMARY

A 66-year-old Chinese male patient was admitted to our hospital for surgical intervention after gallstones were discovered during a routine physical examination. Preoperative imaging revealed a lesion on the left side of the liver, which raised the suspicion of IPNB. A laparoscopic left hemihepatectomy was performed, and subsequent histopathological examination confirmed the diagnosis of IPNB. At the 3-mo postoperative follow-up, the patient reported good recovery and no metastasis. IPNB can manifest both latently and asymptotically. Radical surgical resection is the most effective treatment for IPNB.

CONCLUSION

Hepatic and biliary masses, should be considered to diagnose IPNB. Prompt surgery and vigilant follow-up are crucial in determining prognosis.

Key Words: Intraductal papillary neoplasm of the bile duct; Tumor; Surgical treatment; Prognosis; Case report

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Core Tip: Intraductal papillary neoplasms are relatively uncommon in clinical practice, often eluding detection by clinicians owing to the inadequacy of conventional imaging tests such as abdominal ultrasound and computed tomography, to identify and diagnose tumors. In the present case, the patient was asymptomatic. However, if the tumor was not detected and resected promptly, the patient could have lost the opportunity for surgical intervention when developing relevant biliary symptoms. Early detection and surgical intervention hold promise for a positive prognosis. Clinicians must further enhance their understanding of the clinical attributes and imaging indications to prevent missed diagnoses.

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INTRODUCTION

Intraductal papillary neoplasms of the bile duct (IPNBs) are rare tumors that predominantly affect middle-aged and elderly individuals. It exhibits a slightly higher prevalence in men than in women and has significant potential for malignancy. Most patients present with symptoms, such as epigastric pain, acute cholangitis, and jaundice, accompanied by elevated liver enzyme levels. However, asymptomatic cases are less frequent. Here, we report a case of asymptomatic IPNB and conduct a comprehensive review of the relevant literature to enhance our understanding of this disease.

CASE PRESENTATION

Chief complaints

A 66-year-old male patient was admitted to our hospital with a 7-year history of gallbladder stones, detected during a physical examination, leading to a proposed laparoscopic cholecystectomy.

History of present illness

Preoperative abdominal ultrasonography revealed multiple gallstones and cysts in the left lobe of the liver. Plain computed tomography (CT) of the chest and abdomen revealed low-density lesions in the left hepatic lobe, prompting the recommendation for an enhanced abdominal CT examination.

History of past illness

The patient had no prior history of surgery but had a history of multiple chronic conditions, including hypertension, diabetes, hyperlipidemia, and atrial fibrillation. The patient consistently adhered to the medication regimen and reported satisfactory management.

Personal and family history

The patient denied any family history of tumors.

Physical examination

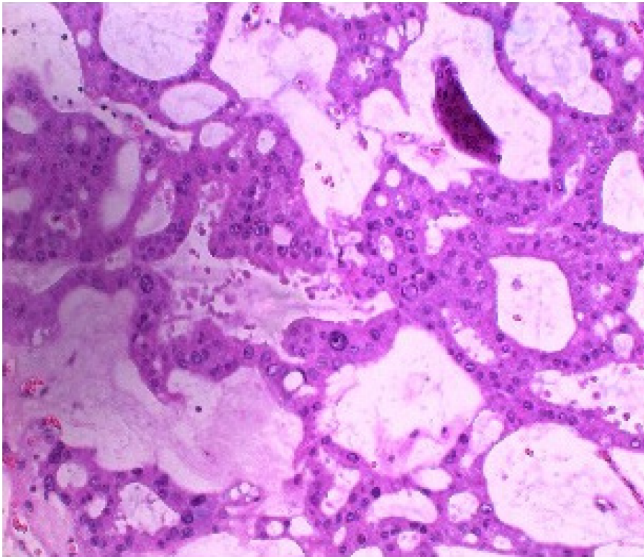
The patient was alert and in good condition. No abnormal symptoms such as jaundice, nausea, vomiting, or acid reflux were noted. An abdominal examination revealed no tenderness, rebound tenderness, or muscle tension. No abnormal masses were palpable, and the Murphy's sign was negative.

Laboratory examinations

Total bilirubin, 20.6 $\mu\text{mol/L}$ (reference range: 0-23 $\mu\text{mol/L}$); direct bilirubin, 7 $\mu\text{mol/L}$ (reference range: 0-4 $\mu\text{mol/L}$); indirect bilirubin, 13.6 $\mu\text{mol/L}$ (reference range: 0-17 $\mu\text{mol/L}$); alanine transaminase (ALT), 13 U/L (reference range: 9-50 U/L); aspartate transaminase (AST), 19 U/L (reference range: 15-40 U/L); carcinoembryonic antigen (CEA), 5.46 ng/mL (reference range: 0-5 ng/mL); alpha fetoprotein, 2.61 ng/mL (reference range: 0-20 ng/mL); carbohydrate antigen 199 (CA199), 29.88 U/mL (reference range: 0-37 U/mL). The rest of the laboratory results were normal. Pathological examination of the lesion revealed an IPNB with severe epithelial dysplasia or high-grade intraepithelial neoplasia (Figure 1).

Imaging examinations

Abdominal enhanced CT arterial phase (Figure 2A), abdominal enhanced CT venous phase (Figure 2B), and an initial diagnosis of a cystic, solid lesion in the left lobe of the liver with dilatation of the distal intrahepatic bile ducts were made; cholangiocarcinoma was ruled out, and magnetic resonance (MR) enhancement examination was recommended. Subsequently, abdominal MR imaging (MRI) + MR cholangiopancreatography (MRCP) (enhanced) examination



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Figure 1 The pathological result suggestive of IPNB (hematoxylin-eosin × 400).

(Figure 2C-E) confirmed the presence of cystic and solid lesions in the left hepatic lobe, along with dilation of the left intrahepatic bile duct, indicative of IPNB.

FINAL DIAGNOSIS

The patient was diagnosed with IPNB, accompanied by severe epithelial dysplasia and high-grade intraepithelial neoplasia.

TREATMENT

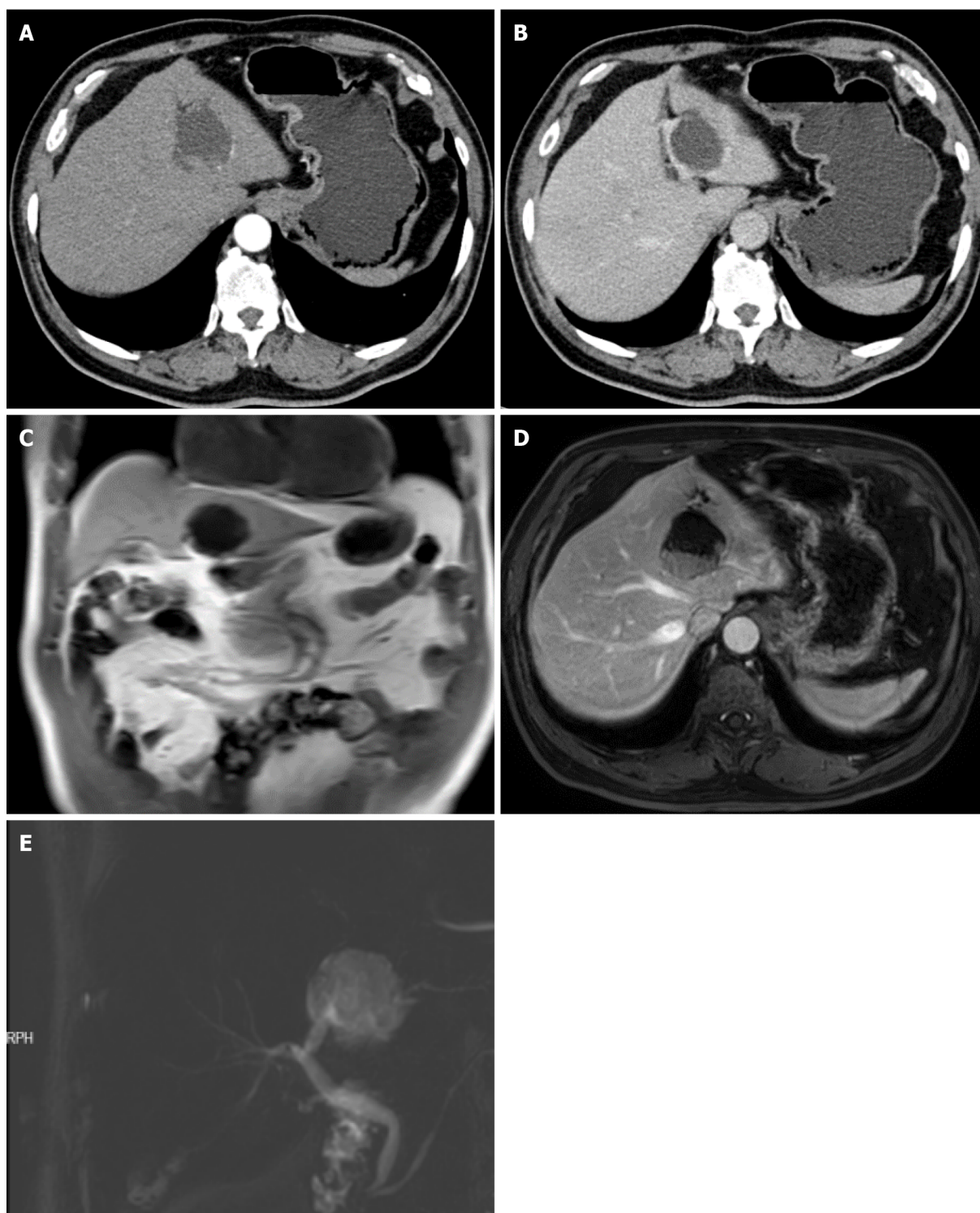
The patient underwent a laparoscopic left hemihepatectomy and cholecystectomy. No additional masses were identified perioperatively, and no subsequent treatment was required.

OUTCOME AND FOLLOW-UP

The patient exhibited favorable postoperative recovery and underwent regular follow-ups at our outpatient clinic for three months using abdominal CT, with no evidence of metastasis or recurrence.

DISCUSSION

According to the latest WHO classification, IPNB, recognized as a precancerous lesion in cholangiocarcinoma (CCA), is predominantly characterized by papillary or villous growth within the bile duct lumen[1]. More than 30% of patients with IPNB exhibit significant mucus secretion into the lumen[2]. The pathogenesis of IPNB remains unclear; however, investigations have identified major risk factors, including hepatic bile duct stones, hepatic schistosome infection, primary sclerosing cholangitis, congenital biliary anomalies, and exposure to substances, such as chlorinated organic solvents. Other contributing factors include bile duct malformations, familial adenomatous polyposis, and Gardner's syndrome. The progression of IPNB is gradual, and is initiated by inflammation due to biliary stasis, biliary infections, and CCAs, ultimately culminating in a multistage transformation of the bile ducts, marked by proliferation, heterotopic hyperplasia, and carcinoma development[3]. Molecular studies have identified mutations in CTNNB1, STK11, and GNAS in patients with IPNB concurrently with intraductal papillary mucinous neoplasm (IPMN)[4]. Kirsten rat sarcoma viral oncogene mutations are risk factors for IPNB progression and offer potential diagnostic and therapeutic avenues[5]. Tanaka *et al*[6] identified EVI1 expression in IPNB, highlighting its potential as a prognostic marker. Notably, patients with MUC1-expressing IPNB tumors have a more unfavorable prognosis[7]. Owing to the relatively subtle clinical symptoms of IPNB compared with those of other tumors, a significant number of patients with IPNB are diagnosed after the disease has advanced, leading to bile duct obstruction. Subsequently, these patients gradually develop associated



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Figure 2 Abdominal enhanced computed tomography and magnetic resonance imaging + magnetic resonance cholangiopancreatography (enhanced) examination. A and B: The initial diagnosis of a cystic solid lesion in the left lobe of the liver with dilatation of the distal intrahepatic bile ducts. Cholangiocarcinoma was ruled out, and a magnetic resonance enhancement examination was recommended; C-E: Presence of cystic and solid lesions in the left hepatic lobe and dilation of the left intrahepatic bile duct, indicative of intraductal papillary neoplasms of the bile duct.

biliary symptoms, including jaundice, abdominal pain, and cholangitis[8]. The current study's findings indicate a higher prevalence of IPNB in East Asia, particularly in regions such as Japan, Korea, and Thailand, where intrahepatic bile duct stones are prevalent[9]. IPNB is also considered the biliary counterparts of IPMNs of the pancreas because of their mucin-hypersecretory properties[10]. To enhance staging and prognostic accuracy, IPNB has been further classified into four distinct subtypes: Pancreaticobiliary, intestinal, eosinophilic, and gastric; the intestinal subtype is the most prevalent and displays the highest incidence of malignancy. Currently, the commonly used modified IPNB staging systems include types 1 (intrahepatic biliary) and 2 (extrahepatic biliary). Approximately 40% of IPNB cases were classified as type 1, and

60% as type 2. Notably, mucin hypersecretion is more prevalent in type 1 IPNB (I-IPNB) compared to type 2[11,12]. Recent studies have demonstrated that the modified two-tier grading system effectively reflects postoperative survival compared to the traditional grading approach, contributing to a comprehensive postoperative assessment of IPNB[13]. Additionally, one research team discovered that the survival rate for type 1 was notably superior to that for type 2 by employing a scoring system encompassing six pathological characteristics (such as location, mucin secretion, and tissue structure)[14]. Compared with CCA, IPNB generally exhibits a more favorable overall prognosis. However, given the potential for malignant transformation, early diagnosis and prompt treatment of IPNB remain central to ongoing research. Our case was incidentally discovered when the patient was admitted to the hospital for surgical treatment of gallbladder stones. The majority of cases were identified as a consequence of disease progression, presenting with biliary symptoms that led them to seek medical attention for laboratory and imaging assessments. Nonetheless, routine laboratory tests, such as ALT/AST/alkaline phosphatase and tumor markers CEA/CA199, lack distinct specificity and often exhibit elevated levels in many patients with typical biliary inflammation[15]. CT and MRI are remain the primary diagnostic tools for imaging evaluation. However, patients with IPNB often present with concurrent biliary inflammation and stones, resulting in a low rate of early clinical diagnosis. Currently, choledochoscopy should be employed in conjunction with CT and MRI for the precise localization of IPNB. Transoral cholangioscopy (POCS) enables the assessment of the scope of bile duct lesions, thereby facilitating the formulation of a tailored surgical strategy[16]. In IPNB cases characterized by substantial mucin secretion, percutaneous transhepatic cholangioscopy (PTCS) offers greater advantages than POCS[17]. The 2012 guidelines identified pertinent predictors, such as obstructive jaundice, duct size, wall nodules, and abrupt size changes, as potential indicators of the extent of malignancy in IPNB[18]. A recent study conducted by a Korean research team revealed that of the 116 cases of I-IPNB, 62 (53.4%) exhibited invasive carcinomas, whereas 61 (76.3%) of the 80 cases of type 2 extrahepatic IPNB displayed invasive carcinomas. Multifactorial analysis indicated that mural nodules of < 12 mm and intensified mural nodules were predictors of malignancy in I-IPNB and type 2 IPNB, respectively. In addition, 43.7% of patients with nonsurgical mucosal alloplastic hyperplasia would develop malignancies within three years[19].

Prompt initiation of surgical treatment is imperative for patients diagnosed with IPNB, likely achieving complete margin-negative (R0), significantly enhancing patient prognosis[20]. Conventional surgical approaches include partial hepatectomy, choledochotomy, pancreaticoduodenectomy, hepatopancreaticoduodenectomy, and liver transplantation. The optimal surgical choice is determined through preoperative multidisciplinary team discussions, PTCS, and POCS integrated with intraoperative cholangioscopy. Recently, a Japanese research team effectively employed red dichroic imaging technology for precise tumor extent assessment during preoperative POCS in a 75-year-old IPNB patient, consequently facilitating a successful pancreaticoduodenectomy[21]. Palliative modalities are frequently employed in patients with severe preoperative bile duct inflammation or in advanced cases that are not amenable to surgical intervention. These include endoscopic nasobiliary drainage and endoscopic retrograde cholangiopancreatography biliary stenting aimed to mitigate the patient's symptoms. Innovative techniques, such as radiofrequency ablation and photodynamic therapy have emerged as viable treatment alternatives[22,23]. A Korean research team successfully alleviated jaundice in a patient with advanced IPNB using argon plasma coagulation, and the current follow-up period extends beyond two years[24]. Advancements in novel technologies have the potential to enhance patient survival significantly. Despite IPNB's notably improved overall prognosis compared with CCA, with a 5-year survival rate exceeding 80%[25], ongoing regular follow-up remains imperative. Notably, approximately 13%-29% of patients with surgically resected IPNB experience recurrence within a short timeframe. This recurrence rate escalates to 47%-62% in cases where the patient is diagnosed with invasive IPNB[26].

CONCLUSION

In conclusion, IPNB, recognized as a precancerous lesion, has a favorable overall prognosis. However, the precise pathogenesis and mechanisms underlying IPNB progression remain unclear. Furthermore, nonspecific clinical manifestations pose a challenge for early diagnosis. Meticulous preoperative imaging, intraoperative cholangioscopy, and prompt pathological evaluation of resection margins are crucial for the informed selection of an appropriate surgical strategy. A comprehensive exploration of molecular targeted therapy coupled with vigilant postoperative monitoring will aid in formulating a more informed and rational treatment protocol for individuals affected by IPNB.

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FOOTNOTES

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