CASE REPORT

Unusual presentation of a low-grade intraductal papillary neoplasm of the bile duct

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Summary Intraductal papillary neoplasm of the bile duct usually manifests as abdominal pain, jaundice, and cholangitis but rarely presents as hemobilia. In this article, we present the case of a 74-year-old man with a 2-year history of repeated hemobilia without a definite diagnosis. A cholangiogram revealed a left intrahepatic duct dilatation with a filling defect, and computed tomography revealed a hyperdense lesion in the left lateral liver segment, which was subsequently resected. Histopathological examination revealed focal low-grade intraductal papillary neoplasm of the bile duct and markedly dilated bile ducts with a ruptured blood vessel. The postoperative course was uneventful. Clinicians should comprehensively evaluate cases of unusual and recurrent gastrointestinal bleeding by considering this diagnosis.

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1. Introduction

Intraductal papillary neoplasm of the bile duct (IPNB) has been defined as a "biliary epithelial tumor with exophytic nature exhibiting papillary mass within the bile duct lumen and with prominent intraductal growth pattern". The most
common manifestations are abdominal pain, jaundice, and cholangitis; however, hemobilia has occasionally been observed.\textsuperscript{2,3} Definitive clinical and radiological diagnosis is difficult in IPNB. Because malignant components are present in over half of all IPNB cases, a complete surgical resection is typically necessary.\textsuperscript{2,3} In this article, we report the surgical treatment of an IPNB presenting as recurrent hemobilia.

2. Case report

A 74-year-old man with a 2-year history of recurrent upper gastrointestinal (GI) bleeding and cholangitis presented with epigastric pain, jaundice, and tarry stool. On examination, he had icteric sclera, pale conjunctiva, and local epigastric tenderness. Laboratory tests revealed that the serum bilirubin and hemoglobin levels were 3 mg/dL and 10.2 g/dL, respectively. An upper GI endoscopy revealed a large blood clot in the second portion of the duodenum near the papilla of Vater. Angiography did not show any vascular lesion from the branches of the celiac trunk and superior mesenteric artery. Abdominal ultrasonography and contrast-enhanced computed tomography (CT) revealed bilateral intrahepatic biliary tree dilatation with no intrahepatic lesion. Endoscopic retrograde cholangiopancreatography revealed bilateral intrahepatic biliary tree dilatation with filling defects in the distal common bile duct (CBD); although a few stone fragments were extracted, the filling defects remained. Choledochoscopy revealed minimal blood clotting in the CBD and some blood flow from the left intrahepatic duct; a T-tube was placed in the CBD after removing the clot, but after 1 month, a filling defect was observed again in the left intrahepatic duct (Fig. 1). Contrast-enhanced CT revealed a hyperdense lesion in the left lateral liver segment (Fig. 2), which was subsequently resected. Grossly, intrahepatic bile ducts were markedly dilated and a papillary tumor measuring 1.0 cm × 0.9 cm × 0.8 cm was observed along with an atrophic and fibrotic appearance of periductal liver parenchyma (Fig. 3). Microscopically, a focal low-grade IPNB (Fig. 4A) was evident along with markedly dilated bile ducts, granulation tissue, and vessel rupture (Fig. 4B). The histopathological diagnosis was pancreaticobiliary-type IPNB (Fig. 4C). The postoperative course was uneventful, and the patient was discharged on postoperative Day 7; no recurrence was observed at the 1-year follow-up examination.
3. Discussion

Hemobilia is a crucial differential diagnosis for the etiology of upper GI bleeding. The clinical triads are upper GI bleeding, jaundice, and right upper quadrant pain. However, only some patients present with all of these classic symptoms at the same time. Hemobilia is usually caused by trauma (iatrogenic, blunt, and penetrating injury), inflammation (gallstone disease, cholangitis, vasculitis, and parasitic infection), coagulopathy, or hepatic neoplasm (benign and malignant). The diagnosis can be made using various diagnostic tools, including upper GI endoscopy, endoscopic retrograde cholangiopancreatography (ERCP), angiography, abdomen ultrasound, CT, magnetic resonance cholangiopancreatography (MRCP), and choledochoscopy. Upper GI endoscopy can be used to rule out other gastro-duodenal lesions. In addition, ERCP may play a role in revealing the etiology of hemobilia, such as stones or tumors. Angiography can simultaneously reveal vascular lesions and facilitate embolization. Abdomen ultrasound examination and CT can reveal intrahepatic tumors, intraluminal clots, biliary dilatation, and hematoma. When the etiology is uncertain, MRCP may further differentiate stones from hematomas. Surgical cholecdochoscopy is an additional choice for diagnosing hemobilia.

IPNB is a papillary tumor containing biliary epithelium and grows within the bile duct. It can spread everywhere along the extra- and intrahepatic bile duct epithelium. IPNB has been categorized into a spectrum ranging from premalignant lesions to invasive cholangiocarcinomas. Intraductal papillary neoplasm, low-, intermediate-, high-grade intraepithelial neoplasia, and invasive carcinoma have been defined in the World Health Organization International Classification of Diseases.

The most common manifestations of IPNB are abdominal pain, jaundice, and cholangitis. Hemobilia has been rarely observed in IPNB. Several case reports have described unusual presentations of IPNB. In cyst-forming IPNBs, mucinous fluid has been associated with hemorrhage in two of nine cases, with bleeding mimicking a hepatic hemorrhagic cyst. Sen et al reported a rare case of benign biliary papillomatosis in a choledochal cyst presenting with hemobilia. In the current case, the papillary tumor dilated the bile duct and ruptured a blood vessel, causing hemobilia.

Clinically, diagnosing IPNB definitively is difficult. Our patient presented with repeated upper GI hemorrhage and cholangitis, which were misleading. The tumor caused intermittent partial obstruction of the bile duct mimicking bile duct stones; therefore, imaging may be beneficial. Ultrasonography revealed nonshadowing intraductal echogenic lesions and CT showed intraductal noncalcified soft-tissue masses with asymmetric wall thickening. Cholangiography revealed an intraductal papillary mass and a serrated bile duct margin. However, several studies have reported that intraductal masses were evident in only 41.2%...
and 50% of ultrasonography and CTs, respectively. Biliary tract dilatation is the most common radiological finding in IPNB.

IPNB has been histologically classified into four types: pancreaticobiliary, intestinal, gastric, and oncocytic. More than half of all cases contain malignant components, with these being most common in the pancreaticobiliary type. Most cases of IPNB are intraductal papillary neoplasm with high-grade intraepithelial neoplasia or an associated invasive carcinoma. A complete surgical resection with negative margin may provide a survival benefit. Because the current case presented with repetitive hemobilia and cholangitis and was of a pancreaticobiliary type, we performed a left lateral liver segmentectomy and achieved a negative resection margin.

All IPNBs should be treated because, with or without mucus secretion, they often repeatedly cause obstructive jaundice and cholangitis, even if the tumor is benign. If surgery is planned, preoperative cholangioscopic examination is crucial. The extent, spread, and location of a tumor must be carefully evaluated. Preoperative CT can be used to assess the depth of invasion and involvement of lymph node metastasis. Patients with distant metastasis should be ruled out prior to surgery. IPNB should be treated as a similar level of cholangiocarcinoma if surgery is indicated. Major hepatectomy or limited resection can be considered for the surgical procedure. A frozen section examination of the cut surface of the bile duct may be performed intraoperatively to achieve a malignancy-free margin of resection. Regional lymph node dissection also should be performed.

Several studies have demonstrated that IPNBs originate from normal epithelium and proceed to low-, mid-, and high-grade intraepithelial neoplasia and to invasive carcinoma. Biliary intraepithelial neoplasia (BilIN) is a precursor related to the development of invasive carcinoma. Numerous similar molecular genetic changes occur in the BilIN and IPNB lineages. However, certain authors have reported differences and inconsistent results in the molecular genetic changes between the two lineages. Cyclin D1, a regulator of the cell cycle, plays a role in the development and progression from low grade to the invasive carcinoma in both the IPNB and BilIN lineages. The positive rate of cyclin D1 expression is found to be similar to that in IPNB (53%) and BilIN (43%); however, Itatsu et al reported a different outcome, 65% in IPNB and 20% in BilIN lineages. The expression rate of the other molecular events, such as p16, c-myc, b-catenin, SMAD4/DPC4, and p53, are also reported differently by some authors.

4. Conclusion

Definitive clinical and radiological diagnosis is difficult in IPNB. Surgeons should comprehensively evaluate recurrent GI bleeding and cholangitis. Because malignant components are present in more than half of all IPNB cases, complete surgical resection is necessary.

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