



A polypoid mass in the common bile duct

What is the diagnosis?

Question:

A 73-year-old woman with a prior history of cholecystectomy operation due to cholelithiasis was admitted to our clinic with complaints of abdominal pain in the epigastrium and right upper quadrant. Laboratory studies were unremarkable: Hb: 14.2 g/dL, hematocrit: 42.8%, WBC: 6000 / μ L, platelet: 167000/ μ L, AST: 14 U/L, ALT: 16 U/L, ALP: 69 U/L, GGT: 42 U/L, total bilirubin: 0.57 mg/dL, and direct bilirubin: 0.32 mg/dL. Ab-

dominal ultrasound examination showed dilatation of intrahepatic bile ducts. Endoscopic ultrasound (EUS) (Figure 1) and endoscopic retrograde cholangiopancreatography (ERCP) were then performed (Figure 2). During ERCP, the common bile duct was explored with a stone extraction balloon and a polypoid mass of 0.5 cm (Figure 3) came out of the common bile duct lumen, which was retrieved using a netted snare and sent to the pathology laboratory for histological examination (Figure 4).

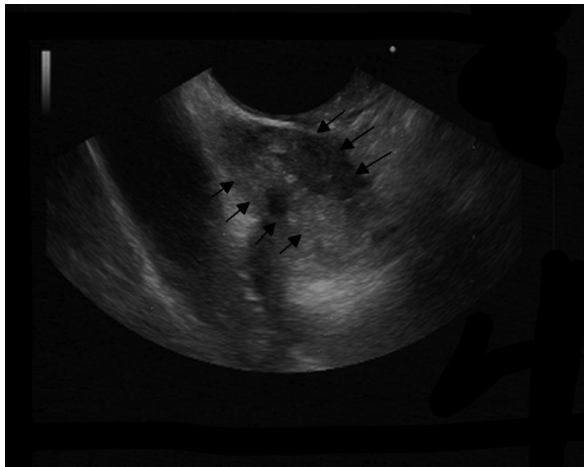


Figure 1. EUS. Proximal portion of the common bile duct is filled with echogenic material without any acoustic shadowing.



Figure 2. ERCP, cholangiogram. Multiple filling defects are observed in the proximal portion of the common bile duct.

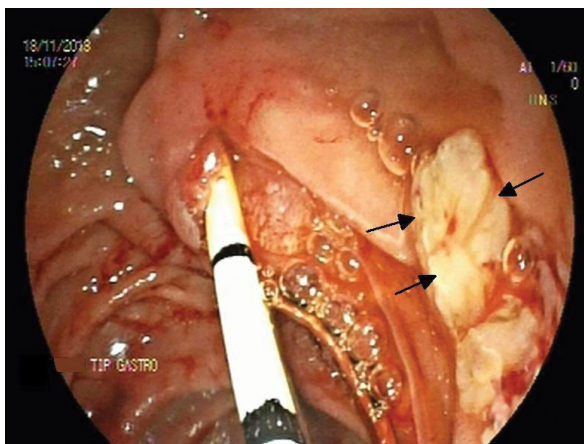


Figure 3. Polypoid mass retrieved from the common bile duct during ERCP when the common bile duct was explored with a stone extraction balloon.

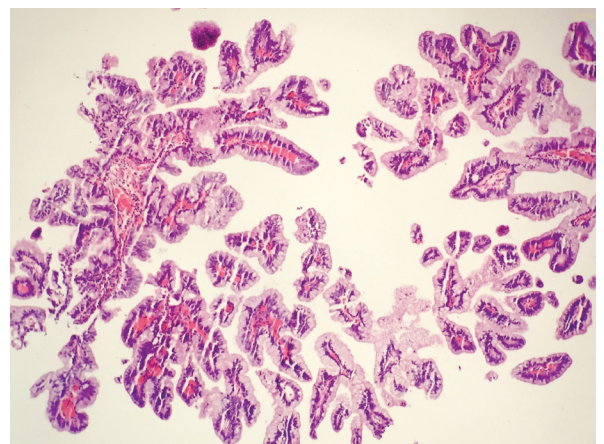


Figure 4. Histopathological examination specimen of the polypoid mass described in Figure 3 (Hematoxylin and eosin, x40). Ductal epithelial cells, with no apparent atypia, are seen forming papillary structures.

Answer: Intraductal papillary neoplasia of the bile duct (IPNB)

Intraductal papillary neoplasia of the bile duct (IPNB) is a very rare tumor of the biliary tract characterized by exophytic growth of tumor cells into the biliary tree forming papillary structures. Various nomenclatures such as biliary papillomatosis, mucin-producing cholangiocarcinoma, mucin-producing bile duct tumor, and mucin-hypersecreting bile duct tumor have been used in the literature to define IPNB (1-5). In the 2010 World Health Organization Classification of biliary tumors, IPNB was included as a separate clinical entity covering intraductal papillary cholangiocarcinoma and its precursor lesions (6). IPNB may be associated with mucin secretion, and similar to other mucin-producing tumors, it also has a premalignant potential. Papillary cholangiocarcinoma is the malignant counterpart of IPNB. IPNB is considered as the biliary variant of intraductal papillary mucinous neoplasia (IPMN) of the pancreas, and both share common microscopic, macroscopic, and clinical characteristics. Four different subtypes of IPNB have been defined: gastric, pancreato-biliary, intestinal, and oncocytic (7). IPNB can occur anywhere along the biliary tract; however, extra-hepatic IPNB has been reported to be more frequent (8). In studies from Eastern countries, IPNB has been shown to be associated with hepatolithiasis and clonorchiasis; however, such an association has not been reported from Western countries.

Intraductal papillary neoplasia of the bile duct is derived from the biliary epithelium. It progresses from low-grade, intermediate, and high-grade intraepithelial neoplasia to invasive carcinoma. TP53, p16, KRAS, and SMAD4 mutations have been shown to be associated with the carcinogenesis sequence of IPNB (9). Because both the bile ducts and pancreas develop from the ventral endoderm of the foregut, it has been suggested that similar genetic and molecular oncologic pathways are involved in IPNB and IPMN (10).

Although some patients can be totally asymptomatic, the majority of patients with IPNB present with signs and symptoms related to biliary obstruction. Abdominal pain, repeated acute cholangitis episodes, and obstructive jaundice are the most commonly reported clinical manifestations (11).

The diagnosis of patients with IPNB is usually challenging. Routine laboratory tests may show the presence of obstructive jaundice; however, these tests are not useful in differential diagnosis. Carbohydrate antigen 19-9 (CA 19-9) may be elevated in some patients; however, it is also not a specific marker, and CA 19-9 levels can be found to be elevated in several neoplastic and non-neoplastic diseases. Abdominal ultrasound may show biliary dilatation; however, the presence of an intraluminal mass can be demonstrated only in a small percentage of patients. Abdominal computed tomography and magnetic resonance imaging can also be used to demonstrate intraluminal mass and other findings associated with IPNB. Endoscopic ultrasound and intraductal ultrasound (IDUS) are probably the

most important techniques for the diagnosis and work-up of patients with IPNB. In addition to the demonstration and characterization of the intraluminal mass within the biliary tree, depth of invasion and involvement of the lymph nodes can also be assessed and can respectability be judged using EUS and IDUS. In our patient, EUS showed that the proximal portion of the common bile duct was filled with an echogenic mass (Figure 1) without any acoustic shadowing.

Endoscopic retrograde cholangiopancreatography is also usually required in the work-up of patients with suspected IPNB for both diagnostic purposes and also to re-establish compromised biliary drainage. IPNB appears as intraluminal filling defects in the direct cholangiogram. Mucobilia, which is characterized by diffuse dilatation of the bile duct with an amorphous filling defect, can also be noticed in some patients during ERCP. Endoscopic examination of the papilla may also reveal a dilated papillary orifice with mucin (12). Cholangioscopy is also useful in the diagnosis of IPNB with direct visualization and biopsy of the intraluminal lesion. In our patient, multiple filling defects were noticed in the common bile duct during ERCP (Figure 2), but exploration of the common bile duct with a stone extraction balloon catheter did not retrieve any stones. One last point to emphasize is that histologic examination of the polypoid material coming out of the bile duct during ERCP was the mainstay of the diagnosis in our patient. Ductal epithelial cells, with no apparent atypia, forming papillary structures were seen in the histopathological examination of the polypoid material (Figure 4). We could not find any report describing a similar occurrence in the literature.

All patients with IPNB are candidates for treatment, because as previously stated, in addition to the usually associated biliary obstruction and recurrent cholangitis, IPNB is considered to be premalignant. Moreover, even in patients with benign biopsy results, concomitant malignant transformation can be present in other sites. The definitive treatment is surgery. Patients without distant metastasis and eligible for surgery should be considered for surgical resection. The prognosis of patients with IPNB has been reported to be better than conventional bile duct cholangiocarcinomas (13). Our patient was also referred to surgery and resection was performed. Histological examination of the resection material showed the presence of concomitant malignant transformation in other parts of the tumor.

In conclusion, IPNB is a very rare bile duct tumor with unique clinical characteristics. Diagnosis is usually difficult and requires extensive work-up. Since IPNB is considered as a premalignant lesion, all eligible patients should be judged for surgery. Awareness of the clinicians would also contribute to early and correct diagnosis in patients with IPNB.

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Informed Consent: Written informed consent was obtained from patients who participated in this study.

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