Biliary papillomatosis

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Abstract

Biliary papillomatosis (BP) is a rare disorder of the biliary tract characterized by the presence of multiple papillary adenomas spread along the biliary tree. Although benign, it carries a significant risk of malignant transformation. Due to low sensitivity and specificity of conventional radiologic modalities, the diagnosis as well as estimation of disease extent is difficult. Endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreaticography (ERCP) are superior although direct peroral cholangioscopy (POC) is currently the most accurate diagnostic method. Mainly because it provides more detailed information and makes targeted histological diagnosis possible. The treatment of biliary papillomatosis consists of surgical resection, liver transplantation (LT) or a combination of both. Unfortunately, the recurrence rate after radical surgery without LT remains high due to the diffuse distribution of the disease. (Acta gastroenterol. belg., **2023,** 86, **483-485**).

Keywords: Biliary papillomatosis, endoscopic ultrasound, endoscopic retrograde cholangiography, cholangioscopy, liver transplantation.

Introduction

Biliary papillomatosis was first described by Chappet in 1894 and is characterized by multiple adenomas of variable distribution and extent in the biliary tree (1,2). It mainly affects elderly males and an etiologic association with bile stasis and recurrent biliary tract infection is presumed (3,4). Although the lesions are considered benign, they have a high potential for malignant transformation. Diagnostic measurements to assess the disease extent and presence of high grade dysplasia or (in situ) carcinoma are still lacking (5). Cholangioscopy is superior to all other currently available diagnostic tools because of the direct visualization of the bile duct mucosa and additional histological diagnosis (6,7). The optimal therapeutical strategy for localized forms of biliary papillomatosis is still a matter of debate. Yet we do know that in patients with diffuse intra- and extrahepatic disease, liver transplantation is the treatment of choice due to the high recurrence risk (8).

Case series

Case report 1

A 72-year-old woman presented with jaundice after recent cholecystectomy due to symptomatic gallstone disease. Magnetic resonance imaging showed dilatation of the intrahepatic bile ducts and the common bile duct with a short, high grade stricture in the common bile duct. In addition, a thickening of the extrahepatic bile duct wall with an intraluminal hypo-echogenic papillary structure was seen with EUS. (Figure 1a) An urgent ERCP could confirm the stricture for which a plastic endoprothesis was inserted. Direct visualization of the bile duct mucosa was possible by using a single operator cholangioscope. (Figure 1b, c) This showed papillary mucosal projections consistent with biliary papillomatosis and a suspicious common bile duct stenosis with villous, hypervascular tissue. Targeted biopsies were taken, confirming the biliary papillomatosis without any degree of dysplasia nor carcinoma. The patient was referred for Whipple surgery. Unfortunately, the resection specimen did show pT2N0 cholangiocarcinoma in the distal common bile duct. Adjuvant chemotherapy was started.

Case report 2

A 74-year-old asymptomatic patient with no relevant medical history presented with mild cholestasis. Bile duct dilatation with contrast capturing mural nodules in the common bile duct was suspected on abdominal computed tomography and confirmed by EUS. With ERCP, dilatation of the common bile duct was seen with irregularly lining of the bile duct wall with multiple convex gaps. Additional cholangioscopy revealed multiple papillary mucosal projections in the common bile duct. (Figure 2a, b) The diagnosis of biliary papillomatosis was made and confirmed by histological analysis with focal high grade dysplasia. (Figure 2c, d) Surgery was recommended but the patient preferred a conservative treatment. He died one year later due to an unrelated cause. *This case (with different figures) was also reported by Struyve M. and Van Der Merwe S. in Dig. Endoscopy 2019* (6).

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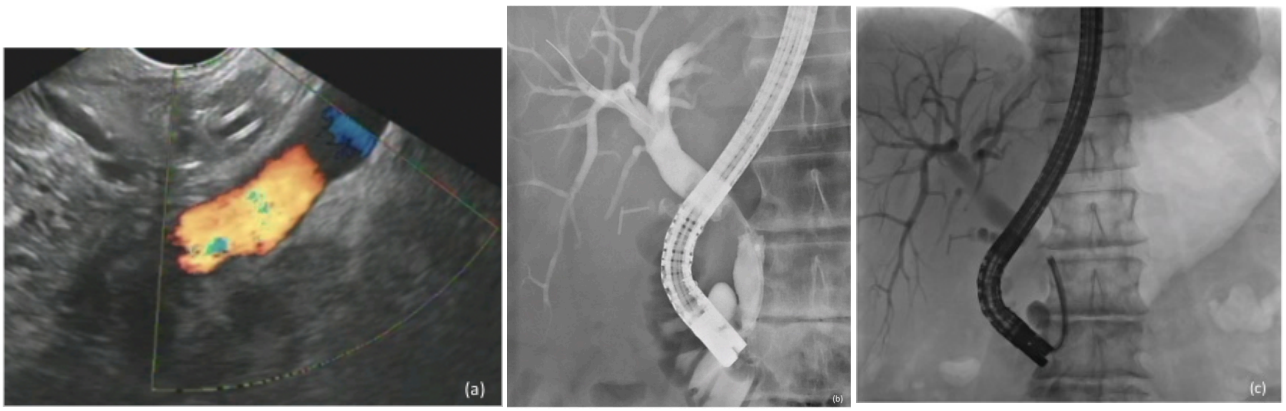

Figure 1. — (a) Endoscopic ultrasound (EUS) shows a plastic biliary endoprothesis. There is a thickening of the biliary wall with an intraluminal hypo-echogenic papillary structure. (b) Endoscopic retrograde cholangiography shows a high grade stricture in the common bile duct with massive intrahepatic bile duct dilatation. (c) Direct visualization in the bile ducts was performed by using a single operator cholangioscope.

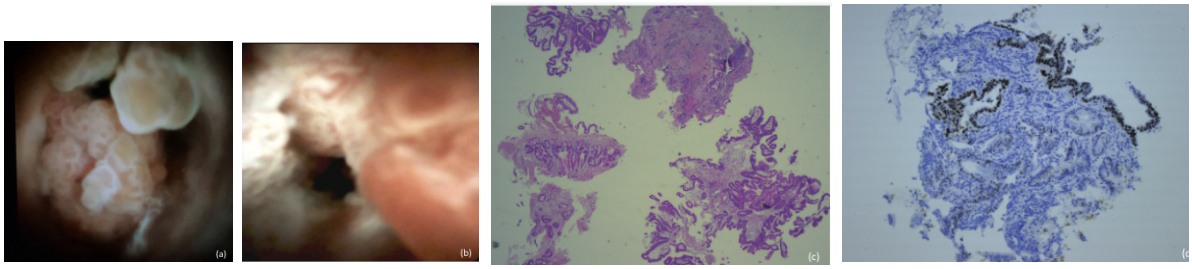

Figure 2. — (a,b) Cholangioscopic visualization of papillary mucosal projections in the bile ducts: biliary papillomatosis and a common bile duct stenosis with hypervascular tissue. (c) Histological proof of biliary papillomatosis with the typical papillary architecture (hematoxylin-eosin staining, x50). (d) P53 immunohistochemical staining showing an aberrant expression pattern consistent with high grade dysplasia.

Case report 3

A 78-year-old man with diabetes and ischemic heart disease was referred to the outpatient clinic because of elevated liver enzymes. MRI showed dilatation of the right intrahepatic bile ducts with a highly suspicious obstructive lesion covering the whole length of the right common hepatic duct. Oncologic staging showed no other lesions. The patient was referred for immediate surgery and a right hemi hepatectomy was performed. Pathology report showed intraductal biliary papillomatosis with only high grade intraepithelial neoplasia (pTisN0M0). He recovered well without any evidence of recurrence after 2 years of follow-up.

Case report 4

A 61-year-old man with a medical history of alcohol-related chronic pancreatitis presented with mild jaundice. Abdominal MRI showed a double duct sign located in the distal common bile duct and main pancreatic duct, but no tumoral pancreatic lesion could be seen on EUS. Diagnostic ERCP followed by direct cholangioscopy was performed with visualization of stenosing hyperemic and villous mucosal protrusions in the distal common bile duct. No other papillary lesions spread in the biliary tree were seen. Targeted intraductal biopsies and brushing samples were taken. Finally, a fully covered metallic biliary stent was placed to cover the stenosis. Histology report showed intraductal biliary papillomatosis with low grade dysplasia. The patient was referred for Whipple surgery. The definitive postoperative histology report showed chronic atrophying pancreatitis and biliary papillomatosis with low grade dysplasia. The patient had a good recovery and currently there is no evidence of recurrent disease after 2 years of follow-up.

Discussion

Biliary papillomatosis is a rare but premalignant condition consisting of numerous biliary papillary adenomas having the tendency to spread superficially along the biliary tree. There is a male predominance (2:1) with a mean age of 50-70 years old (3,4). Two entities are known: the mucin-hypersecreting type (MBP) and a non-mucin producing type (NMBP) (2). Besides, there are localized versus more diffuse forms, with combined intra- and extrahepatic disease manifestation estimated in 58% of cases (9). Bile stasis and recurrent biliary infections, hepatolithiasis, chlonorchiasis and

pancreatic juice reflux are associated with the development of BP (2,3).

The clinical features of biliary papillomatosis range from asymptomatic to acute obstructive symptoms (e.g. biliary colics, jaundice) to more chronic symptoms (e.g. pruritus, weight loss…). Acute cholangitis due to bile duct obstruction is more frequent in the MBP-group while one third of patients with NMBP is estimated to be asymptomatic (2).

Radiology as well as endoscopic methods can be used for the diagnosis of BP, with bile duct dilatation as a classic first sign. Abdominal ultrasound (US) and computed tomography (CT) may show thickening of the bile duct walls and sometimes even intraductal masses (7). MRI can demonstrate T2 hyperintense, T1 hypointense, diffusion restrictive intraluminal papillary signal voids. Unfortunately, the sensitivity and specificity of both radiologic and endoscopic methods is low and the differentiation of benign from malignant disease is even more difficult (4,7). However in experienced hands, EUS can diagnose the intraductal papillary masses, possible invasion into the duct wall and pathologically enlarged lymph nodes. When using contrast enhancement EUS, the contrast capturing within the intraductal masses is a good marker to differentiate from bile sludge for example. EUS is therefore more accurate in determining the etiology of biliary obstruction than US or CT with more than 80% accuracy of predicting malignancy (7). With ERCP, multiple small filling defects, a serrated irregularity of the bile duct wall, bile duct dilatation and mucin hypersecretion through a wide-open ampulla can be visualized (2,6,7).

The newest and most accurate diagnostic method is direct peroral cholangioscopy (POC). Detailed information about the bile duct mucosa can be obtained with histological diagnosis of suspect mucosal lesions (2,6,7). Besides, mapping of the biliary tree (including main intrahepatic branches) is possible to define surgical resection margins (10). Optical cholangioscopic diagnosis of malignancy has a sensitivity and specificity of nearly 90%, which is even more compared to visually directed biopsy taking with the rather small biopsy forceps (sensitivity 60%, specificity 98%) (10). Of course, visual findings always require biopsy confirmation in the setting of BP. There seems to be an added value of narrow band imaging (NBI) during cholangioscopy in terms of mucosal characterization, although only several case reports are available in the current literature (11,12).

The optimal therapeutical strategy for localized BP is still controversial because of the risk of underestimating multifocality and presence of possible malignancy. Aggressive treatment is absolutely necessary to achieve full resection of all the affected areas (13).

Currently, radical surgical resection is the main treatment strategy, although liver transplantation could be considered (8,14). A 5-year survival rate of 81% is reported in cases of R0 radical resection of localized BP lesions (15).

In cases with diffuse biliary papillomatosis including the intrahepatic biliary tree, a referral to tertiary hepato-biliary centers is necessary to evaluate the need for liver transplantation (8,13,14). Because the extrahepatic bile ducts are only partially removed in LT, a concomitant whole duodenopancreatectomy may represent the most effective surgical strategy for diffused lesions (15). To avoid unfavorable results after liver transplantation, Vibert and colleagues (8) recommend patient selection eligible for LT by first step radical resection to exclude advanced tumor invasion or positive lymph nodes.

In the current literature only a handful cases in which BP patients receive liver transplantation are reported. The prognosis in cases of malignant recurrence after liver transplantation is unfortunately very poor, probably due to the use of immunosuppressant therapy (13).

In inoperable patients, endoscopic biliary drainage combined with clinical, radiological and/or endoscopic follow-up is recommended.

Potential competing interests

None.

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