LETTER TO THE EDITOR

Long-term survival after isolated liver transplantation for intrahepatic biliary papillomatosis

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Introduction

Since the first report in 1894 by Chappet [1] and the first anatomic description by Caroli in 1959 [2], about 60 cases of biliary papillomatosis (BP) have been reported. This disease is complicated mainly by the recurrent cholangitis and malignant transformation [3,4]. Localized BP may be treated by local resection, nevertheless only up to 40% of patients treated in this way survive for more than 5 years [5,6].

Case report

In 1984, a 58-year-old Caucasian woman was referred anicteric cholestasis (GGT 2xnrl; GPT 3xnrl). Previous history included a cholecystectomy with choledocotomy 18 years previously and an endoscopic sphincterotomy 7 years previously. Histological report of the gallbladder was not available.

Endoscopic retrograde cholangiography (ERC) showed a vermiform structure in the choledocal lumen, corresponding to a peculiarly shaped biliary stone, the intrahepatic biliary tree was poorly visualized (Fig. 1). Liver biopsy showed a picture of secondary biliary cirrhosis together with a periductular inflammatory infiltrate, suggestive of chronic-sclerosing cholangitis.

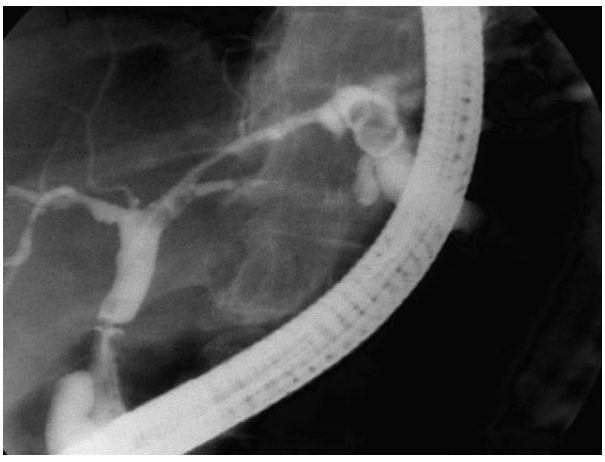

Figure 1 Retrograde cholangiography showing intrahepatic biliary papillomatosis (BP) at the level of the left hepatic duct and at the hepatic duct bifurcation.

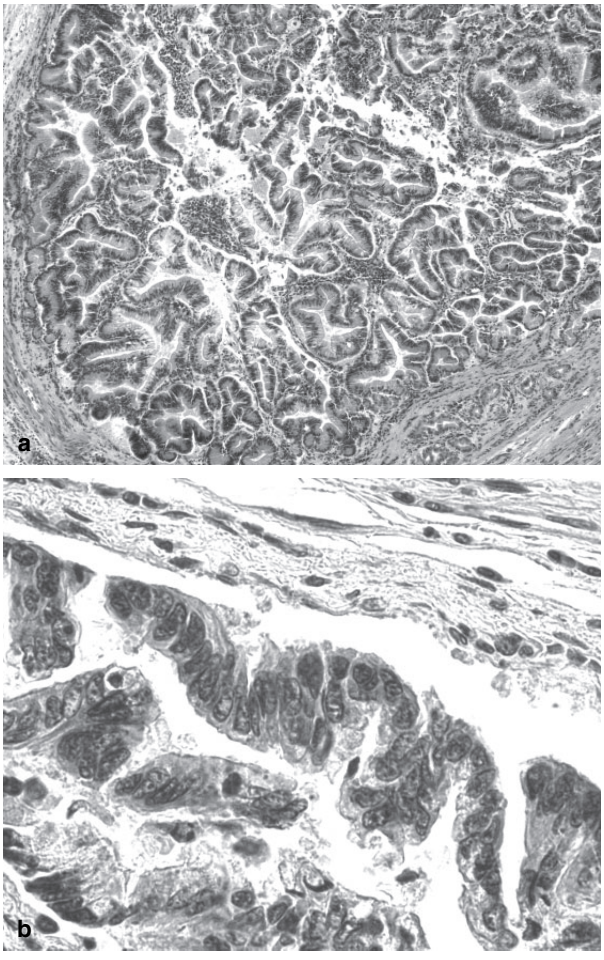

Figure 2 (a) Microscopic appearance of the left intra-hepatic bile duct filled with numerous papillary projections arising from the epithelial surface (Hematoxylin-eosin, original magnification ×10). (b) Higher magnification showing foci of high-grade dysplasia (Hematoxylin-eosin, original magnification ×40).

Table 1. Liver transplantation and diffuse biliary papillomatosis (BP) – literature review.

Author	Year	Sex	Age	Symptoms	Diseases of	Anatomo-pathology	Lymph node metastasis	Biliary anastomosis	Technique	Recurrence	Outcome	Actual IS
Gigot [7]	1989	F	60	Right upper quadrant pain Jaundice	Extra- and intrahepatic	Glandular carcinoma Papillar lesion at section margin	Absent	Hepatico-jejunostomy	OLT	Yes Distal in biliary tract remnant	Death 1 year	–
Bottger [8]	1989	M	49	Choletasis Colicky pain Previous partial bile duct removal; local chemotherapy	Extra- and intrahepatic gallbladder	Diffuse papillomatosis Well-differentiated adenoma	/	/	OLT	Yes	Death (chronic rejection) delay unknown	/
Dumortier [9]	2001	F	61	Right upper quadrant pain Jaundice	Extrahepatic bile duct and proximal part of left and right intrahepatic bile ducts	Three foci of invasive carcinoma	Absent	Hepatico-jejunostomy	OLT and cephalic duodeno-pancreatectomy	No	Alive 46 months	Tacrolimus MMF
Beavers [10]	2001	M	59	Cholestasis Cholangitis Liver abscess Previous Roux-Y choledoco-jejunostomy and left hepatectomy	Extra- and intrahepatic bile ducts	Multifocal adenomatosis	/	Hepatico-jejunostomy	OLT	No	Alive 9 months	
Ciardullo [11]	2003	M	60	Cholestasis Cholangitis	Extra- and intrahepatic bile ducts	Difuse papillomatosis	Absent	Hepatico-jejunostomy	OLT	No	Alive 9 months	
Present case	2003	F	64	Cholestasis Ascites Upper GI-bleed because of portal hypertension	Left intrahepatic bile duct Bile duct bifurcation	Two foci of high grade dysplasia (*in situ* carcinoma)	Absent	Choledocho-choledochostomy	OLT	No	Alive 16 years	Infratherapeutic Cya

She rapidly developed progressive liver dysfunction complicated by ruptured esophageal varices. Liver transplantation (LR) including partial excision of the main bile duct was performed in May 1989. Because of the absence of any type of macro- and microscopic lesions in the lower part of the common bile duct, duodenopancreatectomy was not performed. Biliary tract continuity was restored using the choledoco-choledocostomy with T-tube drainage.

The hepatectomy specimen, weighting 750 g showed features of secondary biliary cirrhosis. The bile duct lumen was partly obstructed by pus; the left intra-hepatic duct was found to be lined by a massive papillary proliferation of epithelial cells extending from the bile duct bifurcation; two areas were characterized by high grade dysplasia of the papillary epithelium (adenocarcinoma *in situ*) (Fig. 2). The common and right intrahepatic bile ducts and lymph nodes were disease-free.

At 6 and 11 years post-LT, she presented with cholestasis caused by choledochal and intrahepatic stones; these were removed by endoscopy and lithotripsy. During the 16 year follow-up period, an NMR and ERC did not detect recurrent tumor disease. The patient is, however, currently recovering from a low anterior resection and a partial hepatectomy performed for a distal rectal cancer with synchronous liver metastases.

Discussion

Biliary papillomatosis is characterized by a proliferation of the bile duct columnar epithelium with papillary formations that extend into the lumen. The typical mucoid secretions and tumor growth cause bile duct obstruction, which sometimes leads to secondary biliary cirrhosis [8]. Malignant transformation, observed in 25–50% of patients with long-term follow-up, is difficult to demonstrate even when the results of cytological or intra-operative examinations are available. In order to assess the real nature and degree of infiltration of these lesions, analysis of the complete resected specimen is necessary [4,8].

Many radiological or surgical interventions are palliative measures looking only at temporary improvements to bile duct drainage. Surgical resection is the only curative treatment, the extent of which must be adapted to the localization of the lesions [4]. The disease must be treated aggressively as even complete resection of a localized, unilobar or extrahepatic BP is associated with a very high incidence of recurrence (up to 50%) and BP has a high incidence of dissemination and degeneration. An LT, curiously reported only five times in literature, should be considered as the treatment of choice, especially for intrahepatic or both intra- and extrahepatic lesions as it guarantees the best, long-term survival.

The necessity to totally resect both intra- and extrahepatic bile ducts during total hepatectomy and duodenopancreatectomy remains unclear [7–11] (Table 1). In cases where BP does not extend distal to the bile duct bifurcation, both macro- and microscopically, the distal choledocus can be preserved. In such cases, choledococholedocostomy is preferred to hepatico-jejunostomy as the method of biliary reconstruction in order to retain endoscopic access to the remaining bile duct. Despite its limitations (related to incomplete opacification), an ERC with direct visualization of BP lesions and of the typical mucus hypersecretion remains even today, the best way to diagnose (recurrent) BP [12–15]. In cases where BP extends below the biliary bifurcation, total hepatectomy and duodenopancreatectomy should be proposed.

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