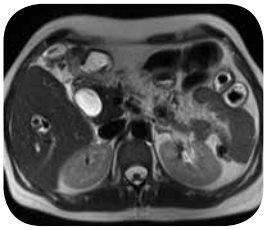

Biliary Papillomatosis: A Case Report

Papilomatosis biliar: presentación de un caso con trasplante hepático

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Key words (MeSH)

Dilatation
Bile ducts
Papilloma
Magnetic resonance imaging
Liver transplantation

Palabras clave (DeCS)

Dilatación
Conductos biliares
Papiloma
Imagen por resonancia magnética
Trasplante hepático

Summary

Intraductal papillary neoplasias of the bile ducts (IPNB), traditionally called "biliary papillomatosis", is a rare entity characterized by macroscopic papillary appearance and in many cases visible secretion of mucin. It occurs more frequently in patients with history of biliary lithiasis. We present the case of a 47 years old patient who underwent liver transplantation due to biliary cirrhosis secondary to intra- and extrahepatic lithiasis, which suffered for many years episodes of recurrent cholangitis managed among others, with a bilioenteric anastomosis. At pre-transplant imaging studies, in addition to changes due to cirrhosis, a significant intra- and extra- hepatic biliary tract dilation was found with multiple calculi within. Pathology results reported the presence of bile duct papillomatosis. The patient developed early recurrence into the native extrahepatic bile duct. She has so far received conservative management.

Resumen

Las neoplasias papilares intraductales de los ductos biliares (NPIB), tradicionalmente llamadas "papilomatosis biliar", son raras y se caracterizan por una apariencia macroscópica papilar y, en muchos casos, secreción visible de mucina. Ocurren con mayor frecuencia en pacientes con antecedente de litiasis biliar. Presentamos el caso de una paciente de 47 años de edad, a quien se le realizó un trasplante hepático por cirrosis biliar secundaria a litiasis intra y extrahepática, quien presentó durante muchos años episodios de colangitis recurrente, los cuales fueron manejados entre otros, con una anastomosis bilioentérica. En los estudios de imagen previos al trasplante, además de los cambios por cirrosis, se encontró una importante dilatación de la vía biliar intra y extrahepática, con cálculos de la vía biliar. La patología del explante mostró papilomatosis de la vía biliar. La paciente desarrolló recurrencia temprana en la vía biliar extrahepática nativa. Ha recibido manejo conservador hasta este momento.

Introduction

Biliary papillomatosis is a rare entity, of which there are only about 140 cases reported in the literature. It was first described by Chappet in 1894 and later by Caroli in 1959. Until 2007, only six cases with liver transplantation had been reported as treatment (1).

The term biliary papillomatosis has traditionally been used in both imaging and pathology for this type of injury, which is why we present our case with this name; however, the current recommendation is to use the term intraductal papillary neoplasms of the bile ducts (IPNB). The term IPNB was adopted in 2010 by the World Health Organization (2).

They are a different type of biliary tumor, which mainly affects the intrahepatic bile duct or the bile duct in the hilum and can be multifocal at the time of diagnosis. However, 80% of recurrences occur in the extrahepatic bile duct, as occurred in the case of this article (3).

IPNB may have similar characteristics to intraductal papillary mucinous neoplasms (IPMN) of the pancreas, with dilation of the affected ducts and intraductal papillary masses with hyperproduction of mucin. Its evolution and prognosis is better compared to cholangiocarcinoma (2).

Clinical case

A 47-year-old female patient who underwent orthotopic liver transplantation in May 2011, secondary to Child B biliary cirrhosis, MELD of 19, due to massive left intrahepatic lithiasis and episodes of recurrent cholangitis since 11 years.

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She was referred to the hepatology service with a history of open cholecystectomy and residual lithiasis. Served by recurrent episodes of cholangitis with antibiotic schemes, percutaneous stone extraction, biliary bypass catheters, in addition to a bilioenteric bypass performed years before in another institution, consisting of a latero-lateral choledochojejunal anastomosis.

She entered with progressive deterioration of the general condition, jaundice, itching of difficult handling and malnutrition, in addition of alteration of liver function tests, increase of transaminases ALT 256 and AST 194, cholestatic pattern, alkaline phosphatase of 807 and total bilirubin of 23.

In the imaging studies prior to transplantation, severe dilation of the intrahepatic biliary tract was detected, predominantly left, as well as dilation of the extrahepatic bile duct, with a bile duct of 28 mm. Also, changes due to chronic liver disease with hypertrophy of the caudate lobe (Figure 1).

Intrahepatic lithiasis was found, mainly in the radicals of the biliary tract of the right lobe of the liver, in the inferior and posterior right segments. The intra and extrahepatic bile duct was disproportionately dilated, compared to the size of the stones identified in the magnetic resonance imaging (MRI). Additionally, no calculations were identified in the distal common bile duct (Figure 2).

There were no signs of obstruction of the biliary anastomosis, which corresponded to a terminolateral anastomosis, between the middle third of the tortuous dilated bile duct and a jejunal loop (Figure 3).

Additionally, thickening of the walls of the bile duct, of left predominance and of the common hepatic duct at the confluence of the hepatic ducts was identified, which was attributed to cholangitis, without formation of abscesses or collections (Figure 4).

In May 2011 she underwent orthotopic liver transplantation, with terminoterminal anastomosis of the portal, anastomosis of the hepatic veins with the vena cava, with "piggyback" technique and terminoterminal anastomosis of the hepatic artery, without complications.

Due to the fact that the patient had undergone a biliary-enteric anastomosis, the biliary anastomosis was a type of choledochojejunostomy, in which the distal (native) choledochal was excluded, with the choledochojejunal anastomosis that she had.

The patient progressed satisfactorily and was discharged with clincal improvement and liver function tests.

The histologic report of the explanted liver described intraductal proliferation of epithelial lineage, in segments IV and II, which forms papillomatous structures that grow towards the lumen of the bile ducts, with low grade dysplastic changes, without invasion of the stroma. In addition, cholestasis was observed with biliary mucus plugs, fibrosis and slight lymphocytic inflammatory infiltrate, which led to the histological diagnosis of "biliary papillomatosis" (Figure 5).

Thirty days after the transplant, she was re-admitted due to deterioration of the liver profile, with ASA: 37, ALAT: 443, FA: 48, GGT: 965 and BT: 8.3; an ultrasound was performed with normal results. MRI was performed with contrast medium, with cholangioresonance sequences, in order to better assess graft anastomoses. The study identified a marked dilatation of the distal native choledochus that had been excluded, and in its wall, a lesion with a leafy, polypoid appearance that enhanced the contrast medium and that measured approximately 4.5 × 3.8 cm, a lesion that was not found in the studies prior to transplantation, so it was considered a recurrence of biliary papillomatosis (Figure 6).

The liver graft showed normal appearance, with permeability of all vascular structures. In cholangioresonance sequences, the biliary tract of the graft was identified, both intra and extrahepatic, without dilation and without signs of stenosis of the new bilioenteric anastomosis (Figure 7).

The liver biopsy performed showed moderate cellular rejection, for which he received medical management. She was discharged with improvement after treatment. Conservative management of tumor recurrence in the native bile duct has been carried out and clinical follow-up has continued, with MRI and positive evolution to date, without progression or malignant transformation.

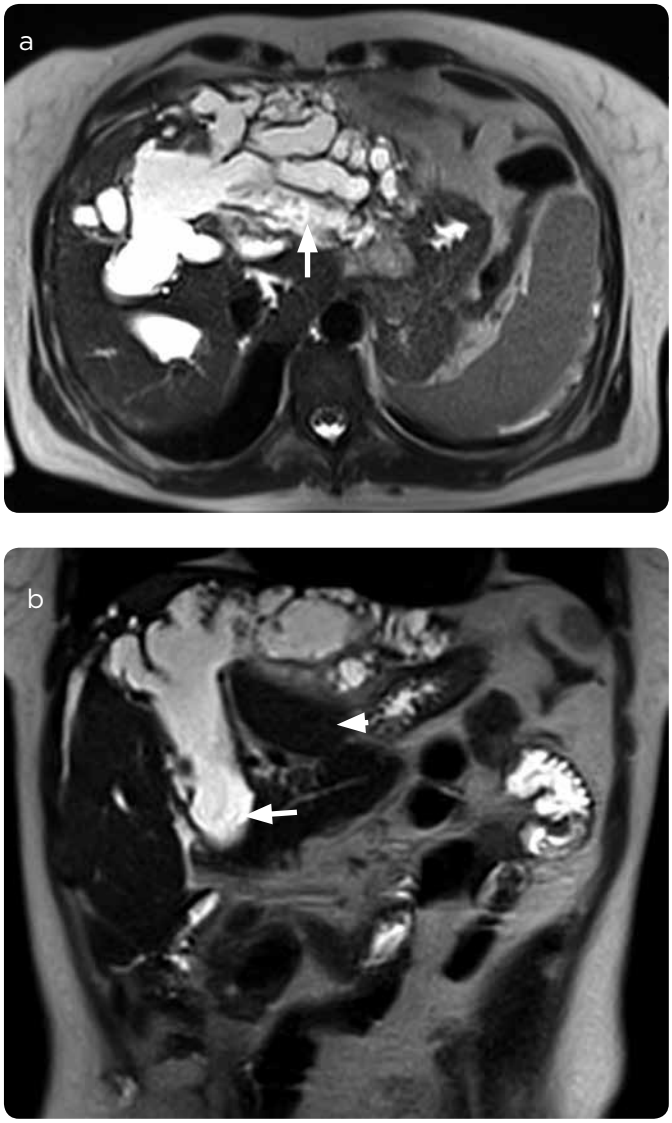

Figure 1. a) Axial section and b) coronal, T2 HASTE. Fusiform dilation of the intrahepatic bile duct, predominantly in the left hepatic lobe that is atrophied (arrow in a). Dilatation of the common bile duct (arrow in b), compensating hypertrophy of the caudate lobe (head of date in b).

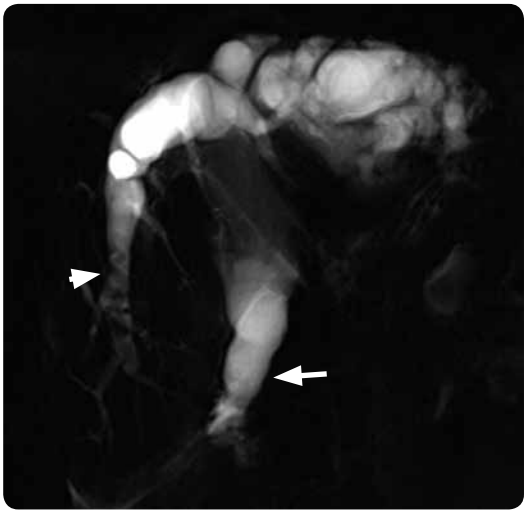

Figure 2. Cholangioresonance sequences: marked dilation of the bile duct with left predominance, intrahepatic lithiasis is observed mainly in radicals of the right lobe (arrowhead) and a dilated choledochus without stones (arrow).

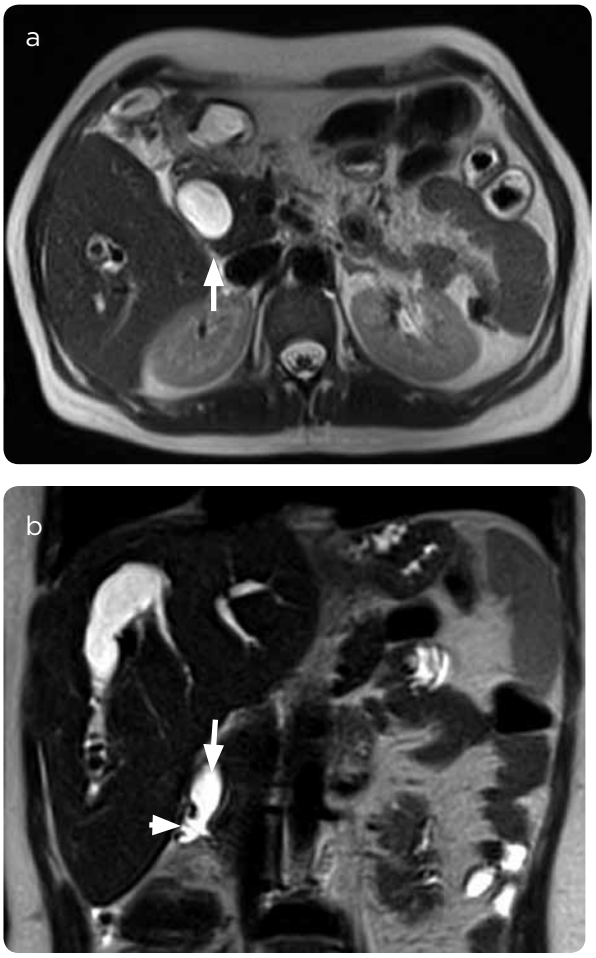

Figure 3. Axial and coronal sequences HASTE. a) Dilated distal bile duct, without stones (arrow). b) The terminolateral anastomosis without stenosis is identified, otherwise wide, with dilation of the common bile duct (arrow), connivent valves of the jejunal loop (arrow head).

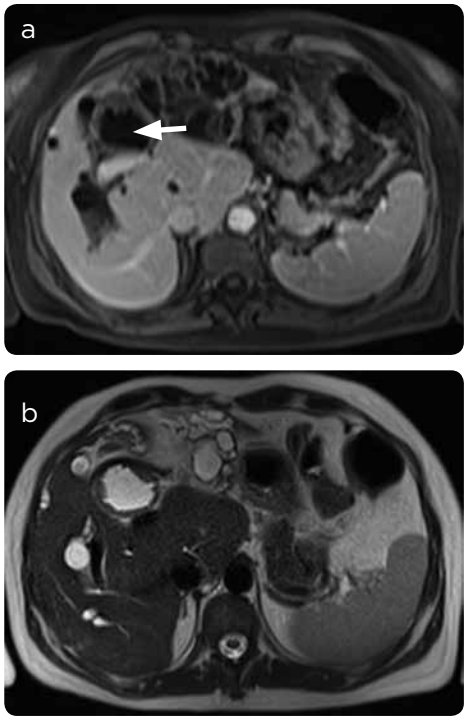

Figure 4. T1 a) Axial contrast medium in portal phase. b) Axial HASTE in the upper abdomen. Thickened walls of the left bile duct and of the walls of the common hepatic duct are identified immediately after the confluence of the hepatic ducts, where the wall measures up to 5 mm (arrow), with enhancement after the administration of contrast medium.

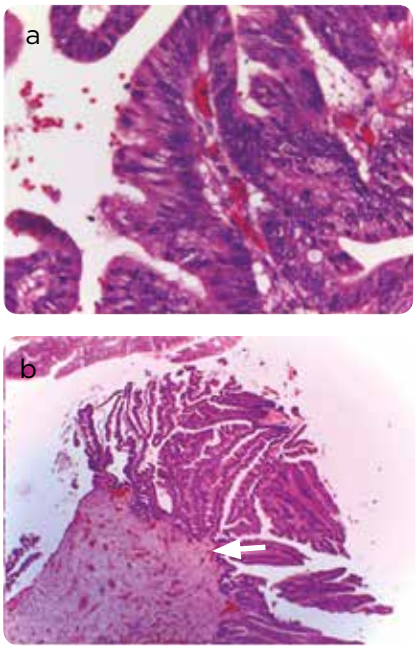

Figure 5. Histological sections of the liver and bile duct. Intraductal proliferation of epithelial lineage that forms papillomatosis structures that grows towards the lumen of the bile ducts, with low-grade dysplastic changes without invasion of the stroma (arrow). In addition, cholestasis, biliary plugs, fibrosis and mild lymphocytic inflammatory infiltrate, consistent with diagnosis of biliary papillomatosis.

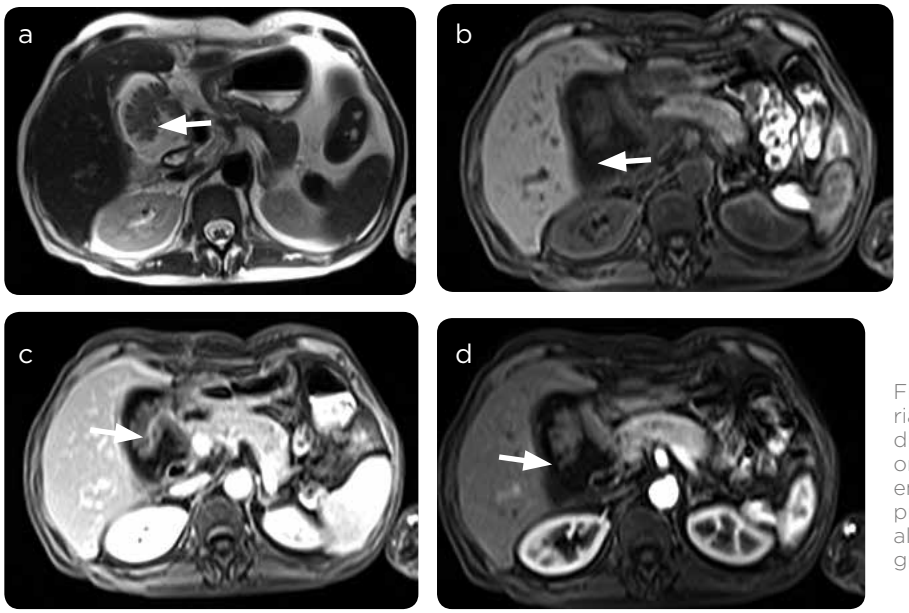

Figure 6. a) T2 axial, b) T1 VIBE simple, c) arterial and d) portal. Dilation of the extrahepatic distal common bile duct (native). Depending on its wall, a mass (arrow) appears leafy, with enhancement of the contrast medium, which protrudes toward its light, 4.5 × 3.8 cm. No alterations of the intrahepatic bile duct of the graft were observed.

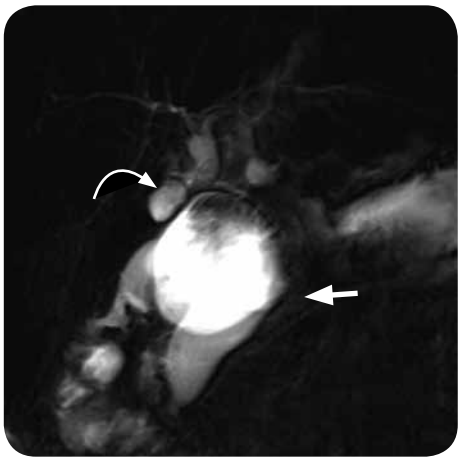

Figure 7. Cholangioresonance sequence. The bile duct of the normal caliber graft is identified, the intrahepatic bile duct is not dilated (curved arrow) and there are no signs of stenosis of the new bilioenteric anastomosis. The markedly dilated native bile duct is observed, with lesion of polypoid aspect depending on its wall (arrow).

probably due to the greater frequency in these areas of patients with hepatolithiasis and clonorchiasis, which are considered the main risk factors (2).

IPNBs are relatively rare neoplasms and represent 9% to 38% of all ductal carcinomas. They occur between the sixth and eighth decade of life and slightly more frequent in men. The most common clinical manifestations are intermittent abdominal pain, cholangitis and jaundice. 30% of patients have a history of gallstones or present concomitantly (4,5).

The counterpart of the IPMN of the pancreas has been considered, since both originate within the ducts and have a predominantly papillary, intraductal growth pattern. In terms of histological classification, IPNB have four subtypes: gastric, intestinal, pancreatobiliary and oncocytic (5,6).

These neoplasms produce mucin in abundant quantity. Up to 33% produce large amounts of mucin, which is secreted into the bile duct (7); this probably explains the marked dilation of the biliary tract that the patient had, including the important dilation of the choledochojejunal anastomosis.

Depending on the location of the tumor, dilation of the bile duct can be from an isolated segment or from the entire system. Another of its characteristics is the friability of the tumor, which tends to detach itself causing intermittent biliary obstruction, simulating gallstones or recurrent pyogenic cholangitis. The definitive diagnosis is often made by surgery (8).

Despite the increase in these neoplasms, the clinical and imaging characteristics and their prognosis are less well known than that of the IPMN of the pancreas.

The most common radiological findings in patients with IPNB are dilation of the bile ducts and intraductal masses. Several patterns have been reported, including: diffuse dilation of the bile duct with visible mass, diffuse dilation without visible mass, focal dilatation with visible mass, intraductal lesion in the mold and sclerosing lesion with proximal focal dilatation. The first two patterns are the most common (5). These types of patterns have been found in cholangiography, tomography and with special detail in MRI studies (9).

Due to the excess of mucin produced by this type of lesion, dilation of the bile duct is not proportional to the size of the mass, which is why one of the most important characteristics are the dilated bile ducts without complete obstruction of the same (9).

In imaging studies, the main feature is segmental or lobar dilatation of the bile duct with or without a visible mass, and with severe atrophy of the affected liver parenchyma (10).

Large tumors can be seen on ultrasound, tomography, ERCP, and cholangiography or MRI. In contrast, small tumors or tumors that spread through the mucosal surface are difficult and sometimes impossible to visualize by any modality (8).

Ultrasound is sensitive in the detection of dilation of the bile duct, but only detects mass within it in 41.2% of cases. With respect to computed tomography (CT), it can detect tumors larger than 1 cm and dilated bile ducts, with a sensitivity of 50% (11).

Since MRI provides excellent resolution of contrast and multiparameter information, which includes the diffusion, dynamic and cholangioresonance sequences, this diagnostic method has an advantage over the others in the characterization of these lesions and especially has advantages to differentiate between the calculations in the bile duct and polypoid lesions. CT may have difficulty in differentiating lithiasis from the bile duct and stone molds, lesions or polypoid masses, something that should be considered especially when they may be associated and coexist (9).

Differential diagnoses include recurrent pyogenic cholangitis and biliary mucinous cystic neoplasms (cystadenomas and cystadenocarcinomas).

It is confused with recurrent pyogenic cholangitis, and with stones because both pathologies produce intermittent and incomplete biliary obstruction, in addition to intraluminal masses or filling defects. Ultrasound and cholangiography confuse the mucus plugs with stones (8,11).

Cystadenomas and biliary cystadenocarcinomas are characterized by cystic lesions, which may be septate or multiloculated, contain mucin and wall nodules or excrescenses in the wall, which may also be papillary in appearance; however, they do not communicate with the bile ducts. Additionally, cystadenoma and cystadenocarcinoma, in histology, have tissue similar to the ovarian stroma in their wall, unlike IPNB (13) which are characterized by being papillary tumors, which grow inside the bile ducts, with a thin center fibrovascular and an excessive production of mucin by the neoplastic cells, which produces a tubular or cystic dilation of these ducts (14).

Unlike IPMN of the pancreas, all IPNB require treatment, since this neoplasm, especially with its high production of mucin, causes recurrent cholangitis and obstructive jaundice, even if they do not have malignant transformation. The risk of malignant transformation is high, between 20-50%, reason why surgery is the treatment of choice (1,2)

It is important, then, to perform histological staging by means of biopsy, in order to know important histological factors, for example, that the frequency of invasive carcinoma in pancreaticobiliary type papillomatosis was significantly higher than in the gastric and intestinal types (15,16). Consequently, management depends on the degree and histological type, the extent of superficial dissemination and the degree of invasion, ranging from limited resections to liver transplantation (2,11).

Liver transplantation is indicated when the lesions are diffuse and the same criteria are considered as for primary cancers, that there is no metastatic disease or regional vascular or ganglion invasion. Recurrent cholangitis, the development of portal hypertension and chronic malnutrition affect the decision (14).

Because there was recurrence of the tumor after the transplant, close monitoring of this patient was decided through the clinic and the images that have shown stability in these five years. She has rejected new surgical interventions, the graft works well and her quality of life improved ostensibly.

Conclusion

Biliary papillomatosis is a relatively rare entity and it is currently recommended to use the term IPNB. They should be suspected in patients with marked dilation of the bile duct, even if they have intrahepatic lithiasis since they are frequently associated.

Liver transplantation has been performed in multifocal disease with recurrent infections and development of biliary cirrhosis.

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Received for evaluation: February 22, 2017
Accepted for publication: February 7, 2018