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Case Report

# Biliary Papillomatosis

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## ABSTRACT

Biliary papillomatosis is a disorder characterized by numerous adenomatous polyps of variable distribution and extent in intrahepatic bile ducts. It should be considered as a premalignant condition because a high proportion of the lesions undergo malignant transformation. In this report, we present a patient with abdominal pain and jaundice. According to his presenting signs and symptoms, ERCP was done for him and multiple biopsies were taken from the common bile duct. Due to high grade dysplasia in the pathological report, Whipple surgery was performed and specimens were sent for microscopic evaluation. Histological examination showed intraductal biliary papillomatosis.

***Keywords:*** Common bile duct, Gallbladder, Cholangiography

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## INTRODUCTION

Biliary papillomatosis (BP) is a clinicopathological condition characterized by multiple recurring papillary adenomas, which may involve extensive areas in extrahepatic bile ducts that furthermore may extend into the gallbladder and intrahepatic bile ducts as well. This disease affects both sexes equally. Most patients are adults aged 50-60 years. Complete excision of the multicentric lesions is difficult and local recurrence is common. The lesion consists of numerous papillary structures as well as complex glandular formations. Given severe dysplasia is often present, papillomatosis is difficult to distinguish from papillary carcinoma. Some researchers consider this lesion as a form of low-grade multicentric intraductal papillary carcinoma (1). It is a low-grade neoplasm with high malignant potential and should be regarded as a premalignant lesion. Recent studies suggest BP as having a rate of malignant transformation between 41% and 83%(2,3).

Herein, we describe a patient with abdominal pain and jaundice who was diagnosed as having biliary papillomatosis.

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## CASE REPORT

A 58-year-old man was admitted to our hospital with right upper quadrant abdominal pain and

**Table 1: Laboratory Data of the patient with biliary papillomatosis**

| Variable | Reference Range | Results |
|---|---|---|
| | **Adults** | |
| Hematocrit (٪) | 40.00-54.00 | 46.00 |
| Hemoglobin (g/dl) | 14.00-18.00 | 12 |
| White-cell count (per $mm^3$) | 4500-11,000 | 7800 |
| Differential count (٪) | | |
| Neutrophils | 40-70 | 55 |
| Lymphocytes | 22-44 | 35 |
| Monocytes | 4-11 | 7 |
| Eosinophils | 0-8 | 1 |
| Basophils | 0-3 | 2 |
| Platelet count (per $mm^3$) | 150,000-400,000 | 260,000 |
| Sodium (mmol/L) | 135-145 | 137 |
| Potassium (mmol/ L ) | 3.4-4.8 | 4 |
| Urea nitrogen (mg/dl) | 8-20 | 12 |
| Creatinine (mg/dl) | 0.60-1.50 | 1.20 |
| Glucose (mg/dl) | 70-110 | 135 |
| Bilirubin (mg/dl) | | |
| Total | 0.0-1.0 | 25 |
| Direct | 0.0-0.4 | 15 |
| Alkaline phosphatase (U/L) | 30-100 | 400 |
| Aspartate aminotransferase (U/L) | 9-32 | 208 |
| Alanine aminotransferase (U/L) | 7-30 | 840 |

yellowish discoloration of the skin since one month ago. He mentioned dark urine and alcoholic stool. He declared that cholecystectomy was done for him four years ago with preoperative assumption of gallbladder adenomyomatosis after which villous adenoma of gallbladder had been detected.

On admission, in light of physical examination, oral temperature was 37°C, blood pressure was 130/80 mm Hg, and pulse rate and respiratory rate were 96 and 18 beats per minute respectively. Furthermore, sclera was icteric, and abdomen was soft with mild tenderness in right upper quadrant. The rest of examination was unremarkable.

Laboratory findings showed a white blood cell count of 7800 cells/μL, a platelet count of 260000 cells/μL and a hematocrit of 46%. Blood urea nitrogen and creatinine levels were normal. Serum aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase were 208, 840, and 400 units/L, respectively. Serum total bilirubin was 25 mg/dL with a direct proportion of 15 mg/dL (Table 1). No other abnormality was found in the rest of laboratory data including tumor markers such as carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), and alpha fetoprotein.

In the next step, a computed tomography of abdomen and pelvis with oral and intravenous contrast was performed, which showed dilatation of common bile duct (CBD) and enlargement of head of pancreas.

As far as more investigation was concerned, magnetic resonance cholangiopancreatography (MRCP) showed dilatation of both intrahepatic bile ducts (up to 15 mm) and common bile duct (up to 26 mm in mid part). There was a cut-off with irregular border in the mid portion of CBD suggestive of tumoral involvement. Moreover, multiple stones were discovered as well (Figure1). Given the existence of probable tumoral involvement of the CBD, endoscopic retrograde cholangiopancreatography (ERCP) was performed and normal duodenal papilla and a large filling defect in distal part of the CBD was noted. Sphincterotomy and balloon extraction were performed, however, no stone or sludge was extracted. Multiple biopsies were taken from the

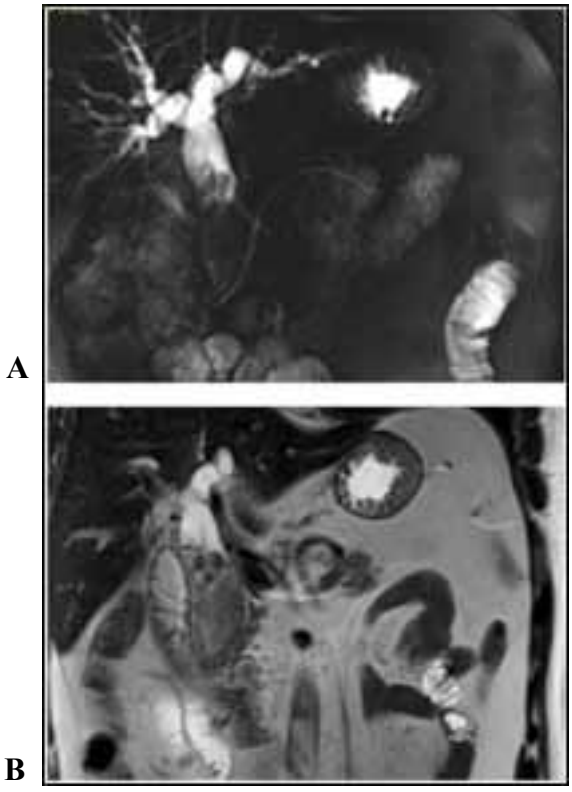


Fig.1: Magnetic resonance cholangiopancreatography (panel A and B, axial and 3-dimensional images) shows dilatation of both intrahepatic bile ducts (up to 15 mm) and common bile duct (up to 26 mm in mid part). There is a cut-off with irregular border in the mid portion of common bile duct suggestive of tumoral involvement.

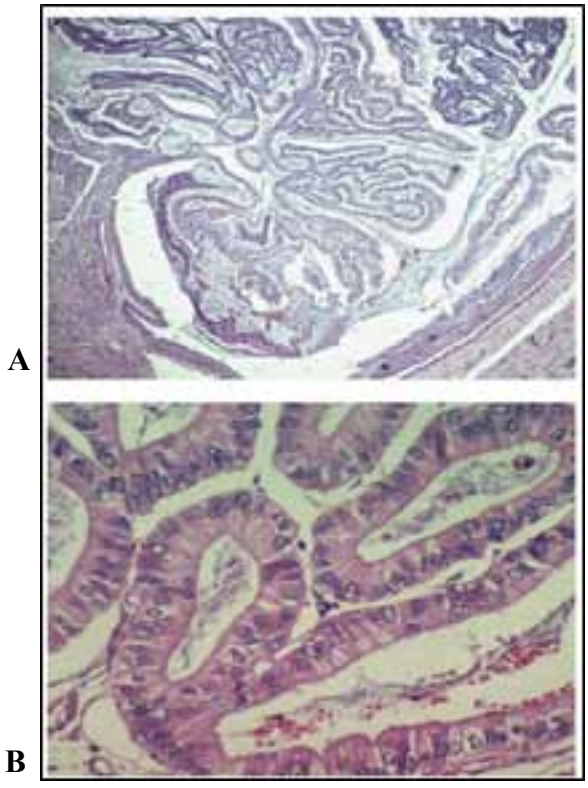


Fig.2: A section of intraductal lesion of common bile duct stained with hematoxylin and eosin: Panel A shows epithelial proliferation of a papillary lesion in the major duct. Panel B shows the same lesion in high power view.

distal part of the CBD. Pathological examination of biopsy specimens revealed glandular structures lined by atypical epithelial cells with large nuclei, irregular nuclear border, and prominent nucleoli, which could point to the diagnosis of at least high grade dysplasia. Considering the pathological findings, the patient underwent Whipple pancreaticoduodenectomy.

During the surgery, a mass like lesion was found in the CBD and remnant of cystic duct. Other parts, however, were normal. Surgery was continued with the resection of head of pancreas, duodenum, CBD, and remnant of cystic duct and the tissues were sent to be analyzed by pathologist.

On microscopic examination of the mass, an intraductal lesion was found, which was composed of proliferation of atypical epithelial cells in predominantly papillary structures. Focal high grade dysplasia was found without evidence of progression to adenocarcinoma. Pancreatic and duodenal tissues were free of tumor (Figure2). The final diagnosis of pathologist was consistent with intraductal BP (intraductal papillary neoplasia) without frank adenocarcinoma.

## DISCUSSION

BP is a disorder characterized by numerous adenomatous polyps of variable distribution and extent in intrahepatic bile ducts (4). It should be considered as a premalignant condition because a high proportion of these lesions undergo malignant transformation (5,6).

Most affected patients die within 3 years due to cholangitis and hepatic failure. Treatment of BP is difficult because of its propensity to grow and spreading along the biliary tree. Liver transplantation may be helpful in this regard.

Our patient was presented with jaundice and abdominal pain. MRCP and ERCP were performed, and because of the presence of dysplasia in distal portion of the CBD, Whipple surgery was done. In

literature, we have found some other patients in whom clinical manifestations were various and diagnosis and treatment were difficult as well. Guglielmi and colleagues reported a case of papillomatosis of the biliary tract in a 75-year-old woman, who presented with jaundice, pruritus, and fever. The surgical treatment consisted of cholecystectomy, choledochotomy, and positioning a definitive T-Tube for the patient (7).

Between March 1995 and January 2003, Lee and co-workers reviewed 58 patients who were diagnosed as having BP by cholangioscopic and histological findings at a tertiary referral center. The authors retrospectively reviewed the medical records to obtain demographic, radiological, cholangioscopic, and pathological data. The common clinical manifestations of the patients at the presentation were repeated episodes of abdominal pain, jaundice, and acute cholangitis. Acute cholangitis was more common in patients with mucin-hypersecreting BP (MBP), whereas patients with non-mucin-producing BP (NMBP) were more asymptomatic. Papillary adenocarcinoma and mucinous carcinomas were detected in 48 patients (83%) with papillary adenomas. Although clinical presentations were somehow different for patients with NMBP and MBP, the long-term survival rate was similar (4).

Therapeutic strategy should be selected preoperatively among resection, transplantation, or stent. In many cases surgical strategy is preferred, considering the mass extension, local infiltration, and patient's age, and when possible, with the aid of extemporaneous histological examination. We preferred to perform Whipple pancreaticoduodenectomy for our case in the light of the involvement of distal part of CBD in early pathology.

Sotona and colleagues reported a case of papillary adenoma of the extrahepatic biliary tract presenting with obstructive jaundice. The diagnosis was based on the ERCP and cholangioscopy. The patient was treated with bile duct resection with Roux-en-Y hepaticojejunostomy (8).

Forlano and co-workers reported a case of biliary papillomatosis of common hepatic duct in an 82-year-old man presented with obstructive jaundice and abdominal pain. They firstly performed cholecystectomy and positioning of T-tube and then due to the presence of filling defect in CBD, resection of CBD and hepaticojejunostomy at the hepatic pedicle was done. The histological examination showed a villous adenoma of the common bile duct with high grade dysplasia (9).

Imvrios and colleagues presented a case of a 43-year-old white man with papillomatosis of intra and extrahepatic biliary tree who sought care for repeated episodes of obstructive jaundice and cholangitis. The diagnosis was suspected after the ERCP and confirmed by liver and common bile duct biopsies. The patient underwent orthotopic liver transplantation with Roux-en-Y hepatico-jejunostomy to treat end-stage liver cirrhosis (10).

Finally, we conclude that BP is characterized by multicentric papillary lesions of intra and extrahepatic biliary epithelium with a high rate of malignant transformation. Moreover, as it is multifocal and has a propensity to grow and spread along the biliary tree, treatment is somehow difficult.

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