

CASE REPORT

담도유두종 환자에서 광역학치료 후 간용적 보존 수술 1예

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Volume-reserving Surgery after Photodynamic Therapy for Biliary Papillomatosis: A Case Report

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Biliary papillomatosis is rare, and its pathogenic mechanisms are not yet clear. Because of its high risk for malignancy transformation, surgical resection is regarded as a standard treatment. Photodynamic therapy (PDT) has been used by the intravenous administration of hematoporphyrin derivative followed by laser exposure. A photochemical process causes disturbance of the microvascular structure and degradation of membrane. Cholangitis is a major complication after PDT. A healthy 56-year-old man was diagnosed with biliary papillomatosis involving the common hepatic duct, both proximal intrahepatic bile ducts (IHD), and the right posterior IHD. After biliary decompression by endoscopic nasobiliary drainage, PDT was performed to avoid extensive liver resection and recurrence using endoscopic retrograde cholangiographic guidance. After portal vein embolization, the patient underwent extended right hemihepatectomy. Following administration of chemoradiation therapy with tegafur-uracil and 45 Gy due to local recurrence at postoperative 13 months, there was no local recurrence or distant metastases. This is the first case report on PDT for biliary papillomatosis in Korea. Preoperative PDT is beneficial for reducing the lesion in diffuse or multifocal biliary papillomatosis and may lead to curative and volume preserving surgery. Thus, PDT could improve the quality of life and prolong life expectation for biliary papillomatosis patients. (*Korean J Gastroenterol* 2015;66:55-58)

Key Words: Papilloma, intraductal; Hepatectomy; Photochemotherapy

INTRODUCTION

Biliary papillomatosis, also known as benign papillary adenoma, is a rare disease characterized by multiple intraductal papillary tumors in the intrahepatic duct or extrahepatic duct with proliferated columnar epithelial cells.¹ However, it should be regarded as premalignancy disease with adenoma-carcinoma sequence.¹ Pathogenic mechanisms are not yet clear, although biliary papillomatosis is known to be associated with recurrent pyogenic cholangitis

and chronic biliary ductal inflammation.² Infection, clonorchiasis or pancreatic juice reflux causes extensive proliferation of biliary epithelial cells, followed by the dysplasia-carcinoma sequence.² Papillomatosis of the bile duct can cause bile duct obstruction and dilatation. Patients usually present with abdominal pain, jaundice, and acute cholangitis. Mechanical obstruction due to enlarging papilloma can cause septic cholangitis and hepatic failure.

Biliary papillomatosis is likely probably misdiagnosed often as biliary stones and typically remains unrecognized for

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a long time. Thus, patients typically experience aggravated papillomatosis before presenting, and have to undergo extensive liver resection after diagnosis. Naturally, due to worsening prognoses and delayed diagnosis, resection may not be possible.

The mean survival period following resection was 28 months; patients without resection had a survival period of less than 11 months.² Surgical resection has been considered the only therapeutic option for biliary papillomatosis patients. However, it can often remain incomplete because of high risk of recurrence or multifocality. Liver transplantation is also regarded as curative treatment.³ Patients could undergo percutaneous transhepatic biliary drainage (PTBD) to relieve their symptoms before surgery. Biliary papillomatosis is a disease of advanced age in the sixth-to-seventh decade of life and is twice as common in males as females.⁴ Preoperative evaluation includes CT scan, MRI, and/or ERCP.

CASE REPORT

A healthy 56-year-old man was diagnosed with common bile duct (CBD) stenosis by MRI during a routine checkup in December 2011. ERCP revealed a suspicious papillomatosis involving the common hepatic duct (CHD), both proximal intrahepatic bile ducts (IHD), and the right posterior IHD. Papillary dysplasia of CHD was confirmed by the biopsy. Tumor marker (CEA, 1.3 U/mL; CA 19-9, 8.0 U/mL) was normal. Serum AST/ALT was 28/25, and the cholestatic enzymes (ALP, 276 IU/L; GGT, 103 IU/L) were mildly elevated. After biliary decompression by endoscopic nasobiliary drainage, the patient was transferred to our institution for surgery (Fig. 1).

Before surgery, PTBD was performed at S3 IHD, and biliary

ductal dilatation was performed twice by 12 Fr and 18 Fr catheter at a two-day interval. Intraductal papillomatous change from distal CBD to right posterior IHD and left IHD 2nd portion was found on percutaneous transhepatic cholangioscopy (PTCS) (Fig. 2). Two weeks later, photodynamic therapy (PDT) was performed to avoid extensive liver resection and recurrence. First, PDT was performed from the point of the hilum to mid-CBD and the left and right IHD with 180 J for 450 seconds, three times during one day. One day later, a second round of PDT was performed only from the hilum to the left IHD twice at the same dosage. The patient presented with acute cholangitis with fever and bilirubin elevation (highest total bilirubin 7.2) after procedures. Symptoms disappeared, and bilirubin was down by administration of intravenous antibiotics.

There was no evidence of obstruction, severe stricture, or remnant papillomatosis of the CBD and both IHD on PTCS one month after the second round of PDT, and all of the previously detected papillomatosis lesions were improved. After portal vein embolization, the patient underwent extended right hemihepatectomy in June 2012. There was no intraperitoneal metastasis, and complete resection was performed (Fig. 2). Pathologic results showed total necrotic change of IHD with chronic cholangitis, hepatolithiasis, and foreign body reaction was observed, and there was no lymphatic metastasis.

After postoperative 13 months, PTCS was followed and granulomatous tissue and IHD stones were found on the left main duct. The biopsy result showed local recurrence with papillary atypical epithelial proliferation from anastomosis site to left IHD. After postoperative 13 months, chemoradiation therapy with tegafur-uracil and 45 Gy was ad-

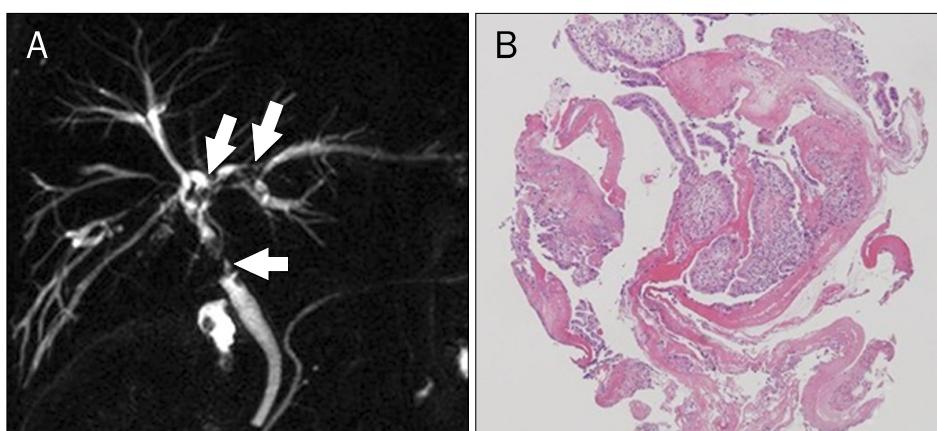


Fig. 1. (A) Two-dimensional thick-section rapid acquisition with relaxation enhancement image shows an irregular intraluminal filling defect in the common bile duct and left intrahepatic duct (arrows). Both intrahepatic ducts are dilated. (B) Papillary atypical epithelial proliferation in the left intrahepatic duct 1st portion before photodynamic therapy (H&E stain, $\times 100$).

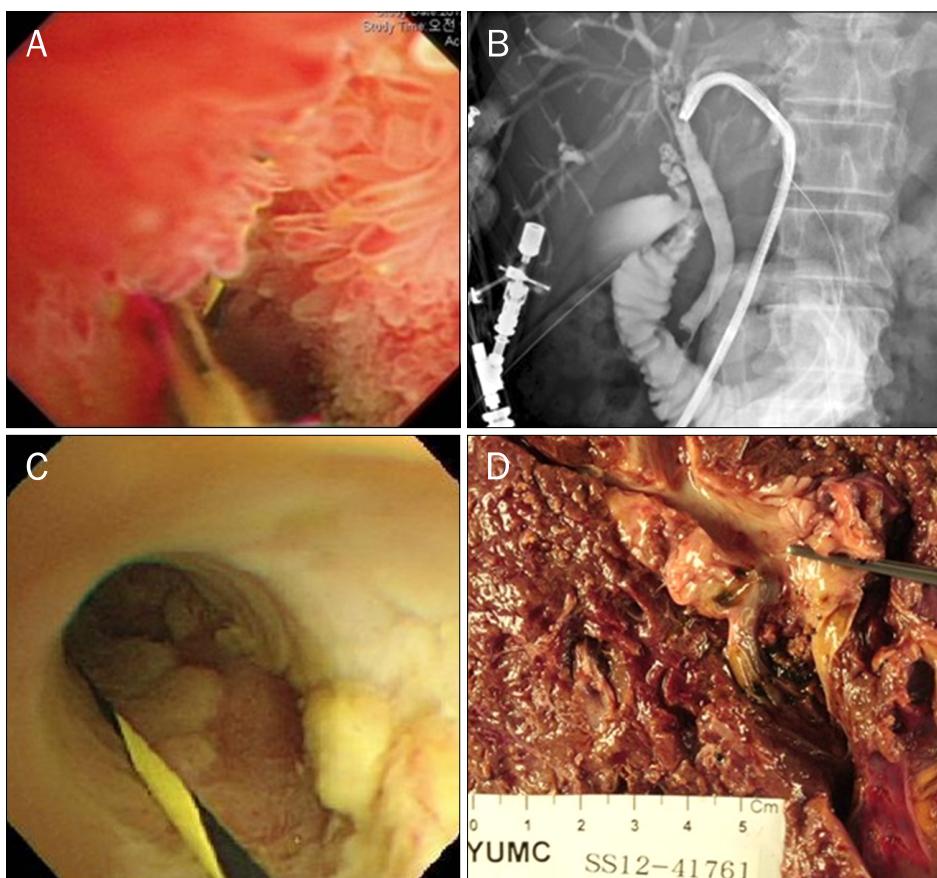


Fig. 2. (A, B) Percutaneous transhepatic cholangioscopy before photodynamic therapy (PDT) shows diffuse biliary papillomatosis from the distal common bile duct to the left intrahepatic duct 2nd portion. (C) Damaged epithelial cells and scars after PDT, and there is no evidence of remnant papillomatosis. (D) Pathologic specimen from right extended hepatectomy.

ministered due to local recurrence. There were no local recurrences or distant metastases afterwards.

DISCUSSION

This study is the first case report on PDT with volume reserving surgery in Korea. The patient was still alive over 30 months despite local recurrence. Biliary papillomatosis had been regarded as benign or low malignant potential, but a recent review reported a high rate of malignant occurrence (41%),^{2,5,6} and a single center in Korea reported malignant occurrence in 83% of 58 patients.⁷ Resection is usually recommended for treatment of biliary papillomatosis, and resectability depends on the location and extent of disease because of the malignancy, high recurrence rates, and multifocality.

PDT was established for treatment of Barrett's esophagus, lung cancer, and bile duct cancer⁸ and was first reported in 1991 by McCaughey et al.⁹ for treatment of extrahepatic bile duct cancer. It may be a suitable therapeutic choice for patients with recurrent biliary papillomatosis after resection or

who are not eligible for surgery. PDT has been used by means of intravenous administration of hematoporphyrin derivative and followed by laser exposure with proper wavelength. After local application, a photosensitizing agent concentrates in the lesion.

In general, the argon dye laser has been used with continuous wave and penetrates with the thermal change in the biliary papillomatosis lesion.¹⁰ The pulsed excimer dye laser penetrates into deeper layers and activates the photosensitizer more effectively without thermal change.¹⁰ The subsequent destruction of neoplastic tissue is a photochemical process which contributes to disturbance of the microvasculature and degradation of membrane by oxygen radicals.⁸ PDT was performed using ERCP guidance. Cholangitis is a major complication after PDT,¹⁰ thus biliary drainage is inevitably required for prevention of cholangitis and biliary sepsis.

Diffuse biliary papillomatosis shows a high recurrence rate after surgical resection. Thus, radical hepatectomy or liver transplantation is the preferred therapeutic choice for bilobar or recurrent disease. Successful PDT can be ancillary for

achievement of R0 resection, avoiding extensive resection or re-operation in advanced intrahepatic and extrahepatic papillomatosis. It can give good results for the patient in terms of better quality of life and prolonged lifespan.

The mean survival period following resection was 28 months; patients without resection had a survival period of less than 11 months.² Surgical resection has been considered the only therapeutic option for biliary papillomatosis patients. However, surgical resection can often remain incomplete, with a high risk of recurrence or multifocality. Thus, liver transplantation is also considered to be curative treatment.³ In this case, the patient had PDT, and extensive surgical resection was avoided.

Some patients could not be treated surgically because of their comorbidities, such as cardiopulmonary disease, and the extent of the carcinoma. PDT could have been used as a local cancer therapy, especially for elderly patients. Suzuki et al.¹⁰ reported on the efficacy of PDT for bile duct carcinoma in four elderly patients for whom surgery was not possible. Three of four patients survived over 20 months without surgical resection, showing improvement in survival compared with 11 months survival without resection. In another case report of a successful PDT for biliary papillomatosis in the distal CBD in Turkey, the patient survived for 10 years.⁸ This patient underwent the Whipple procedure in 1996 and a 2nd operation, right hepatectomy and hepaticojejunostomy was performed in 2002 because of recurrence. Due to recurrence again in 2004 and 2005, photodynamic therapy was administered, because repeated operations were no longer possible. After three applications of PDT, bile duct epithelium showed normal macroscopic and histological appearance. He died in 2006 of multi organ failure because of pneumonia and decompensated liver cirrhosis.

Nevertheless, this case also shows that PDT could improve the quality of life and prolong life expectation when compared with median survival rate. In Korea, only a few biliary papillomatosis cases have been reported. However, most of them underwent surgical resection or palliative drainage for obstruction.

In conclusion, biliary papillomatosis has malignant potency. It is easily misdiagnosed, even in patients with typical symptoms or when proper preoperative evaluation has been performed. Once diagnosed, surgical resection is considered the only therapeutic option for biliary papillomatosis, and the survival rate is very low after resection. Furthermore, many patients require repeat or extensive surgery because of recurrence after resection. Therefore, PDT can be considered as a beneficial treatment for patients with bilobar or recurrent biliary papillomatosis after resection. It can show good results in terms of quality of life and prolonged lifespan.

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