Multiple Cancers of the Biliary Tract and Pancreatic Duct after Cholecystectomy for Gallbladder Cancer in a Patient with Pancreaticobiliary Maljunction

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Abstract

We herein report the rare case of a 76-year-old woman who underwent cholecystectomy with bile duct resection for advanced gallbladder cancer associated with pancreaticobiliary maljunction (PBM) and subsequently developed multiple cancers of the pancreaticobiliary system (the distal bile duct, intrahepatic duct and pancreatic duct) after the operation. We performed conventional endoscopic retrograde cholangiopancreatography (ERCP) using a side-viewing scope to evaluate the masses in the distal bile duct and the pancreatic duct. We also performed ERCP using double-balloon enteroscopy (DBE) to observe the mass in the intrahepatic duct. It was possible to directly observe the lesion using DBE and to perform a biopsy under visual control. All lesions were correctly diagnosed by the combination of ERCP using different endoscopes. The present case suggests that it is necessary to pay close attention (with regard to carcinogenesis) to the whole pancreaticobiliary system in patients with PBM. In addition, the combination of ERCP using DBE and a side-viewing scope may be useful for making a precise diagnosis in patients with altered biliary anatomy who have multiple cancers of the pancreaticobiliary system.

Key words: multiple cancers, pancreaticobiliary maljunction (PBM), direct cholangioscopy (DCS), double-balloon enteroscopy (DBE), endoscopic retrograde cholangiopancreatography (ERCP)

(Intern Med 55: 141-146, 2016)

DOI: 10.2169/internalmedicine.55.4706)

Introduction

It is widely known that pancreaticobiliary maljunction (PBM) is associated with carcinogenesis of the biliary system (1). The reflux of the pancreatic juice into the biliary duct is related to biliary carcinogenesis (2), thus multiple biliary cancers occasionally occur concomitantly with PBM (3-5). However, the relationship between pancreatic cancer and PBM is unclear.

In patients with a normal anatomy of the bile duct, it is useful to perform endoscopic retrograde cholangiopancreatography (ERCP) using a side-viewing endoscope to evaluate multiple biliary lesions. However, in patients who have already undergone bile duct resection and Roux-en-Y cholecystectomy, it is difficult to examine the entire biliary tree by the conventional ERCP method due to the long distance to choledocojejunostomy.

We herein report a rare case of multiple cancers of the pancreaticobiliary system associated with PBM diagnosed by the combined use of ERCP with double-balloon enteroscopy (DBE) and a side-viewing endoscope.

Case Report

A 76-year-old woman was referred to our affiliated hospital due to abdominal discomfort in 2010. Computed tomography (CT) of the abdomen showed a gallbladder mass (Fig. 1a, b). ERCP revealed that the pancreatic duct was joined to the bile duct without dilatation (Fig. 1c) and...
Figure 1. The findings of the preoperative examination. a, b) CT of the abdomen showed the mass in the neck of the gallbladder. c) An ERCP image showing only a smooth extrinsic compression of the bile duct (arrow). The gallbladder was not visualized by the injection of the contrast agent due to obstruction of the gallbladder neck. The pancreatic duct was observed to join the bile duct without dilatation.

Figure 2. The pathological findings of the resected gallbladder specimen revealed the presence of adenocarcinoma.

showed a smooth extrinsic compression of the bile duct, however, no mass lesion was detected. It was not possible to visualize the gallbladder due to the obstruction of the gallbladder neck caused by the mass. The patient was diagnosed with gallbladder cancer associated with PBM and underwent cholecystectomy with bile duct resection. Biliary reconstruction was performed using Roux-en-Y choledochojunostomy. The pathological findings of the resected specimen revealed moderately differentiated tubular adenocarcinoma of the gallbladder neck (Fig. 2). The tumor cells had spread to the gallbladder body and the cystic duct, but had not invaded the common bile duct. Therefore, the bile duct margin was negative and a radical excision was performed. Seven months after the operation, CT revealed a mass lesion in the distal bile duct and the main pancreatic duct at the pancreas head. Additionally, dilatation of the intrahepatic bile duct in the anterior superior segment (B8) was revealed. ERCP was attempted using a side-viewing duodenoscope in order to assess the masses in the distal bile duct and the main pancreatic duct (Fig. 3). ERCP showed multiple defects in the distal bile duct (Fig. 3a) and the main pancreatic duct at the pancreatic head (Fig. 3b). Biopsies of the bile duct and the main pancreatic duct at the pancreatic head were performed (Fig. 3c, d), which both revealed adenocarcinoma (Fig. 4). Although both of these lesions were diagnosed pathologically, making the correct pathological diagnosis by an endoscopic biopsy of the lesion in B8 was difficult due to the altered anatomy. Therefore, the patient was referred to our hospital for further studies, including endoscopic retrograde cholangioscopy (ERC) using DBE. Reexamination using CT was performed, which revealed the masses in the distal bile duct and the main pancreatic duct (Fig. 5a). In addition, CT revealed a low density mass in B8 with dilatation of the proximal intrahepatic bile duct (Fig. 5b). ERC using DBE was thus performed in order to obtain a histological diagnosis of the intrahepatic bile duct mass (Fig. 6). We used carbon dioxide insufflation during DBE. The scope could be advanced into choledochojejunal anastomosis via the R-Y limb. ERC was thus performed and showed a filling defect caused by an intraluminal mass (Fig. 6a, b). The scope was subsequently inserted into the bile duct, and a reddish tumor in B8 was observed directly, and a visually-guided biopsy
was performed (Fig. 6c), which revealed adenocarcinoma (Fig. 7). Therefore, multiple cancers of the pancreaticobiliary systems (the gallbladder, intrahepatic bile duct, extrahepatic duct and pancreatic duct) were pathologically confirmed. The patient refused a second operation and thereaf-
	er began chemotherapy with gemcitabine.

**Discussion**

In patients with a previous history of cancer, it is some-

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**Figure 3.** The findings of ERCP using a side-viewing duodenscope. a, b) ERCP showed multiple defects in the bile duct (a) and the main pancreatic duct at the pancreatic head (b). c, d) Biopsies of the lesions of the bile duct (c) and the main pancreatic duct (d) were performed.

**Figure 4.** Biopsies of lesions of the bile duct (a) and the main pancreatic duct (b) both revealed adenocarcinoma.
times difficult to distinguish primary cancer from metastasis when new cancerous lesions occur. Warren and Gates first reported the criteria for multiple primary malignant tumors (6), however, their criteria did not allow for a definitive conclusion regarding whether the multiple tumors were primary or metastatic. This was because one of their criteria, that the possibility of metastases must be excluded, is sometimes difficult to prove, in particular if all tumors have the same pathological findings. In the present case, multiple cancerous lesions, which were all adenocarcinoma, occurred in the biliary tract and pancreatic duct seven months after the operation for the original gallbladder cancer. We speculated that this case had multiple primary cancers of the gallbladder, intrahepatic bile duct, extrahepatic bile duct and pancreatic duct because PBM is associated with an increased risk of biliary cancer (1) due to the reflux of pancreatic juice (7). However, multiple metastases of the original gallbladder cancer could not be completely ruled out because all lesions were simultaneously detected within a short time after the operation, and they shared pathological similarities with gallbladder cancer. The definitive distinction between multicentric primary cancers and gallbladder cancer metastases is difficult.

Although biliary cancer in patients with PBM is occasionally encountered, pancreatic cancers in patients with PBM
are rare (8-12). Funabiki et al. (13) reported that the incidence of pancreatic cancer is higher in patients with PBM than in patients without PBM. They suspected that the reflux of bile into the pancreatic duct may cause chronic inflammation and cancer of the pancreas. However, the relationship between pancreatic cancer and PBM remains controversial and unclear. In addition, cases of double cancer of the biliary system and the pancreas is extremely rare in patients with PBM (8, 10-12), despite occasional reports of multiple cancers of the biliary system in patients with PBM (3-5). The present case suggested that careful attention should be paid to the whole pancreaticobiliary system with regard to carcinogenesis, however, further case studies are needed.

In the present case, the multiple cancerous lesions of the intrahepatic bile duct, extrabiliary duct and pancreatic duct were detected after gallbladder cancer surgery bile duct resection with Roux-en-Y choledochojejunostomy. Because of the surgical reconstruction, the pathological diagnosis of the intrahepatic lesion was difficult using a side-viewing duodenoscope. In general, ERCP in patients with altered surgical anatomy is difficult due to the long distance to the papilla of Vater or choledochojejunal anastomosis. However, following the report by Haruta et al. in 2005 (14) where ERCP using DBE was performed in a child after liver transplantation, the success rate of ERCP in patients with altered surgical anatomy has recently increased due to the use of DBE (15). In our patient, who underwent biliary reconstruction with Roux-en-Y choledochojejunostomy with wide cholangio-jejunal anastomosis, we successfully performed ERC, direct cholangioscopy (DCS), and a visually-guided biopsy for the tumor in B8 using DBE. DCS using DBE (DBE-DCS) was a very useful method to evaluate the tumor, which provided high-quality images and allowed us to perform a visually-guided biopsy. Okabe et al. previously reported successful DBE-DCS in a patient who had a previous history of choledochojejunostomy for previous intraductal biliary carcinoma (16). However, it is difficult to perform DBE-DCS in patients with an intact papilla or narrow anastomosis. Therefore, we have not been able to successfully perform DBE-DCS in every patient. In difficult cases of DBE-DCS, switching from DBE to an ultrasmall endoscope is useful to allow DCS to be performed (17, 18). DBE-DCS can potentially cause adverse events, such as perforation, bleeding, and cholangitis. Therefore, all procedures should be performed as carefully as possible. In addition, hemiparesis caused by an air embolism after direct cholangioscopy with an intraductal balloon anchoring system was reported (19). In the present case, we performed DBE-DCS with carbon dioxide insufflation in order to prevent an air embolism.

The presence of multiple cancers in the pancreaticobiliary system in patients with PBM is rare. PBM carries a high risk of biliary cancer, however, the relationship between pancreatic cancer and PBM is controversial. The present case suggested that the reflux of either pancreatic juice or bile into the opposite duct may cause carcinogenesis. Therefore, close attention should be paid to the whole pancreaticobiliary system in patients with PBM. In addition, multiple carcinogenesis may occur metachronously. Thus, multiple cancers may occur in the pancreaticobiliary system after bile duct resection of the first biliary cancer (as observed in the present case). In such cases, a combination of ERCP using DBE and a side-viewing scope can be useful for the precise diagnosis.

The authors state that they have no Conflict of Interest (COI).

References


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