—Case Reports—

A Case of Extrahepatic Bile Duct Wall Recurrence of Gastric Carcinoma that Was Treated with Pancreaticoduodenectomy

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Abstract

We report on a patient with obstructive jaundice caused by recurrence of gastric carcinoma in the wall of an extrahepatic bile duct more than 5 years after gastrectomy who was treated with pancreaticoduodenectomy. Histopathologic examination of the surgically resected specimen revealed a poorly differentiated adenocarcinoma with focal signet ring cells in the wall of the common bile duct which was histologically similar to the primary gastric carcinoma. To confirm the diagnosis, immunohistochemical staining was performed with antibodies against cytokeratins (CK7, CK20) and mucin peptide core antigens (MUC5AC, MUC6, MUC2). Based on the expression patterns of this monoclonal antibody panel, the final diagnosis of the common bile duct tumor was an isolated local recurrence of the gastric carcinoma. The patient has survived for more than 26 months after pancreaticoduodenectomy without recurrence.
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Key words: obstructive jaundice, pancreaticoduodenectomy, recurrent gastric carcinoma

Introduction

Gastric carcinoma that recurs after gastrectomy is an uncommon cause of obstructive jaundice. Most patients are not candidates for resection because they have widespread metastatic disease, and survival in such cases is usually poor[1]. We report on a patient with obstructive jaundice caused by gastric carcinoma that recurred in the wall of an extrahepatic bile duct more than 5 years after gastric resection who was treated with pancreaticoduodenectomy (PD) and has survived for more than 26 months without any evidence of recurrence.

Case Report

A 49-year-old woman was admitted because of painless jaundice. More than 5 years earlier, she had undergone distal gastrectomy with D2 lymph node dissection, including complete dissections of lymph node stations 8a and 12a, and Billroth I anastomosis for advanced gastric carcinoma (poorly differentiated

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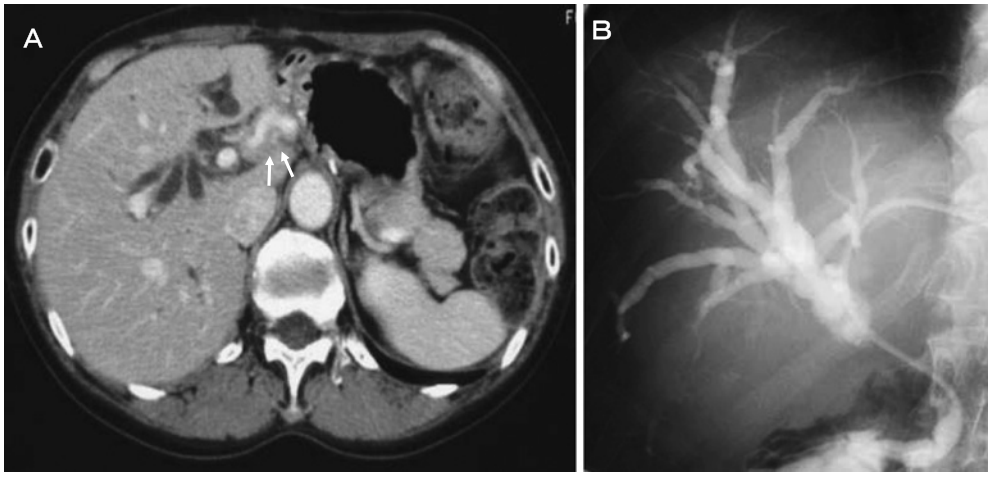

Fig. 1 **A**: Abdominal CT shows dilatation of the CBD and obstruction in the proximal CBD with enhanced wall thickening **(arrows)**. **B**: Direct cholangiography demonstrates a concentric stricture of the proximal CBD and dilatation of the intrahepatic bile duct.

adenocarcinoma with signet-ring cells, Borrmann type 2, located in the antrum, with lymph node metastasis at station 8a, pT2 pN2 M0) followed by 3 years of adjuvant chemotherapy (tegafur and uracil). The pathological results were recorded according to the *Japanese Classification of Gastric Carcinoma*[2]. On physical examination, she had icteric sclerae and skin. Abdominal examination revealed no palpable masses or tenderness. Laboratory tests showed elevation of total bilirubin (7.5 mg/dL, normal range, 0.3–1.2 mg/dL) and direct bilirubin (5.0 mg/dL; normal range, <0.4 mg/dL). The levels of other serum enzymes (alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and gamma glutamyl-transpeptidase) were moderately elevated. The levels of carbohydrate antigen 19-9 and carcinoembryonic antigen were within their normal ranges. Computed tomography showed dilatation of the common bile duct (CBD) and obstruction of the proximal CBD with wall thickening (**Fig. 1A**). Direct cholangiography demonstrated a concentric stricture of the proximal CBD and dilatation of the intrahepatic bile duct (**Fig. 1B**). Therefore, a proximal CBD carcinoma was suspected. However, cytologic examination of a bile brushing specimen revealed no malignancy. Although a definite diagnosis could not be obtained, on the basis of the preoperative diagnosis of an isolated, resectable CBD tumor, PD was performed.

Intraoperative Findings

There was no evidence of extensive lymphadenopathy in the hepatoduodenal ligament, and no peritoneal carcinomatosis was detected intraoperatively. Cytological examination of peritoneal lavage fluid also revealed no malignancy. A firm elastic tumor was seen at the proximal CBD. Although the CBD tumor had invaded the pancreas, the CBD could be freed circumferentially. The hepatic artery and the anterior aspect of the portal vein were also identified at the upper border of the pancreas (**Fig. 2A**). Histological examination of the frozen section during surgery, showed no evidence that the tumor had invaded the region of the resected proximal CBD.

Pathological Diagnosis

The resected specimen showed diffuse thickening of the wall of the proximal CBD (**Fig. 2B**), and histologic examination showed poorly differentiated adenocarcinoma with focal signet-ring cells that were similar to the primary gastric carcinoma. The neoplastic tissue showed intramural infiltration with surrounding hepatobiliary ligamental involvement without mucosal epithelial replacement of the CBD wall. To confirm the diagnosis, immunohistochemical staining was performed with monoclonal antibodies against cytokeratins (CK7, CK20) and mucin peptide core antigens (MUC5AC, MUC6, MUC2). CK7 was expressed in the cytoplasm of the primary gastric

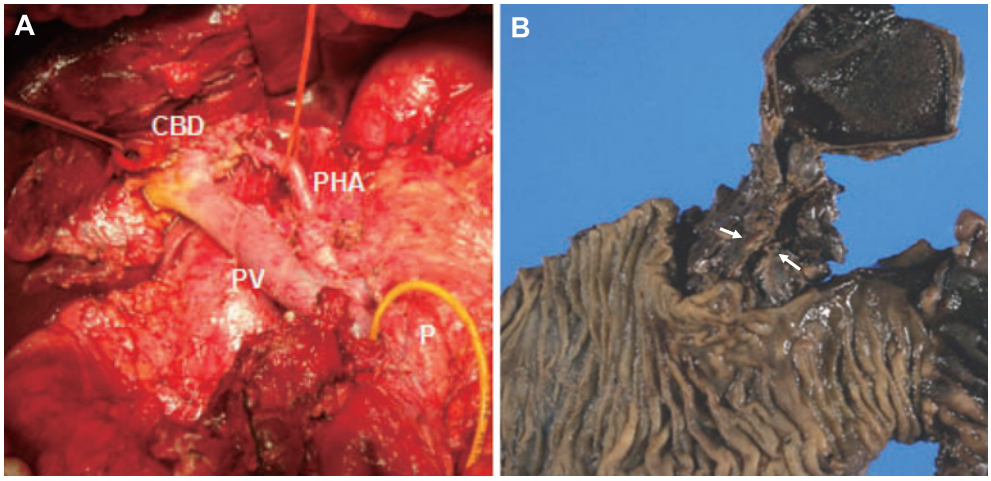

Fig. 2 **A**: The CBD could be freed circumferentially. The proper hepatic artery (PHA) and the anterior aspect of the portal vein (PV) are also identified at the upper border of the pancreas (P). **B**: The resected specimen shows diffuse thickening of the wall of the CBD (**arrows**).

	CK7	CK20	MUC5AC	MUC6	MUC2
Primary	+	-	+	-	-
CBD	+	-	+	-	-

+: positive, -: negative

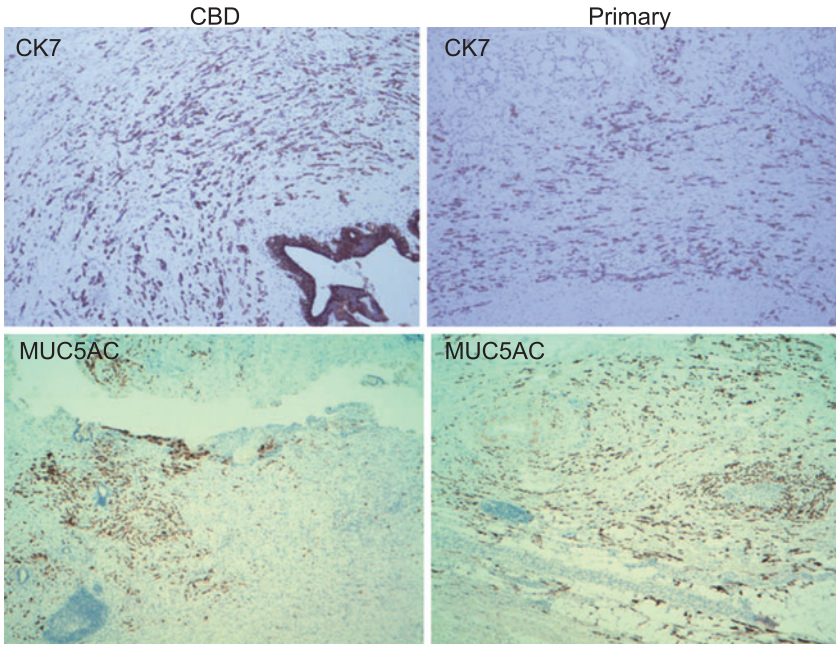

Fig. 3 Immunohistochemical staining: positive staining for CK7 and MUC5AC is observed both in the primary gastric carcinoma cells and the CBD tumor cells.

carcinoma cells and the CBD tumor cells; MUC5AC was also expressed in both. On the other hand, there was no staining for CK20, MUC6, or MUC2 in cells of either the primary or CBD tumor **(Fig. 3)**. Based on the expression pattern of this monoclonal antibody panel, the final diagnosis of the CBD tumor was an isolated local recurrence of gastric carcinoma.

Postoperative Course

The patient was discharged on the 25th postoperative day without severe complications. The patient has been followed up in the outpatient clinic, where she has received 1 year of adjuvant chemotherapy with S-1 (28-day courses of 100 mg/day at 14-day intervals). She has survived for more than 26 months without any evidence of recurrence.

Discussion

Malignant biliary obstruction is frequently caused by metastatic disease[1]. The primary carcinomas causing metastatic biliary obstruction can include carcinomas of the stomach, colon, lung, uterus, and breast[3]. The incidence of extrahepatic biliary obstruction associated with the local recurrence of gastric carcinoma has been reported to be 1.4% to 2.3%[1,4]. It has been reported that the causes of bile duct obstruction are lymph node metastases (93%) in the hepatoduodenal ligament and direct invasion of the primary gastric tumor or recurrent tumor (7%)[4]. Most patients are not candidates for resection because they have widespread metastatic disease, with extensive lymph node metastasis in the hepatoduodenal ligament, sometimes associated with peritoneal dissemination[4].

Many authors have reported the usefulness of percutaneous transhepatic biliary drainage for patients with obstructive jaundice caused by metastatic disease[5,6]. The median survival time of patients with obstructive jaundice caused by local recurrence of gastric carcinoma and treated with external biliary drainage alone has been reported to be 2.0 to 4.2 months[5]. In addition, with chemoradiotherapy (combining external radiation with cisplatin, 5-fluorouracil, and leucovorin) after percutaneous transhepatic biliary drainage survival is prolonged to 14.4 months[6].

Infrequently, patients may present with isolated metastatic or recurrent tumors requiring PD for tumor clearance. However, the appropriate role of PD in the treatment of nonperiampullary tumors, including recurrent gastric carcinoma, is unclear[7]. In recent years, there has been a marked decrease in the hospital morbidity and mortality rates after pancreatic resection, with several large series documenting a mortality rate of less than 4% after PD[8]. In the present case, it is unclear whether surgical resection, especially PD, is warranted on the basis of an analysis of risks and benefits. One cannot recommend PD as a therapeutic option for recurrent gastric carcinoma on the basis of only a single case. However, PD was necessary to diagnose the cause of the obstructive jaundice accurately in this case. As a result, our patient survived for more than 26 months without recurrence.

Differentiating a primary CBD neoplasm from a metastatic or locally recurrent malignancy was difficult. The diagnosis of extrahepatic biliary recurrence from gastric carcinoma must rely on clinical and radiographic findings. However, because the CBD tumor presented as a single, isolated lesion and was considered technically resectable, PD was performed for tumor clearance.

Several recent histopathological studies have addressed the role of cytokeratins and mucin expression in gastric carcinoma[9,10]. Kocer et al.[10] evaluated the expression of MUC5AC in gastric carcinoma on the basis of different clinicopathological variables and prognosis. Their results showed that MUC5AC mucin expression correlates mainly with advanced stage, presence of synchronous liver metastases, and moderate or poor differentiation of the tumor.

In the present case, immunohistochemical analysis of the surgical specimen confirmed that the final diagnosis of the resected CBD tumor was a recurrent gastric carcinoma. However, the mechanism by which a slowly growing tumor recurred in the wall of the CBD more than 5 years after primary gastric resection is unclear. Histopathological analysis of the surgical specimen

did not reveal continuous spread from the gastroduodenal anastomosis through the CBD. It should be noted that the present case is unusual with respect to tumor biology. Although the reason for this discrepancy cannot be explained at present, further histopathological studies, as well as large-scale clinical studies, may be required to clarify the significance of surgical resection of recurrent gastric carcinoma. Furthermore, these studies might also clarify the appropriate postoperative follow-up and the need for additional therapy, such as chemotherapy, for new, recurrent malignancies postoperatively.

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