Metachronous Bile Duct Cancer in a Patient Surviving for a Decade and Undergoing Curative Surgery Twice

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We report a 75-year-old woman with metachronous bile duct cancer who underwent curative resection twice and has survived for a decade. In 1989, she was admitted because her serum alkaline phosphatase level was elevated. Computed tomography (CT) showed a low-density mass, 2 cm in diameter, at the left hepatic duct and intrahepatic bile duct dilatation in the left lobe. We diagnosed the lesion as an intrahepatic bile duct cancer and performed extended left hepatic lobectomy with systematic lymph node dissection. The histological diagnosis was a well differentiated cholangiocellular carcinoma with hepatic hilar and celiac lymph node metastases (T1N2M0, Stage IVB). In 1996, she was re-admitted with obstructive jaundice. CT showed a slightly enhanced mass, 4 cm in diameter, in the pancreatic head. After reducing the jaundice by percutaneous transhepatic biliary drainage, pancreatoduodenectomy was performed. The histological diagnosis of this lesion was a moderately differentiated adenocarcinoma originating from the intrapancreatic bile duct. Ten years after the first operation, she is leading a normal daily life with no cancer recurrence. These findings suggest that repeated curative surgery can result in a long-term survival of patients with metachronous bile duct cancer.

Key words: intrahepatic bile duct cancer - lymph node metastasis - metachronous - surgery

INTRODUCTION

Intrahepatic bile duct cancer accounts for about 6-16% of primary liver cancers (1-3), but little is known about its etiology and associated pathogenic factors. Surgery is the only curative treatment for patients with intrahepatic bile duct cancer (4-6), but the prognosis is poor. The five-year survival rates after resection have been reported to range from 27 to 44% (3,7,8). The prognosis of patients with lymph node metastasis is extremely poor (4,9). Moreover, to the best of our knowledge, metachronous carcinoma of the bile duct that has been surgically treated has not been reported. This is the case report of repeated curative operations for metachronous bile duct cancer with lymph node metastasis in a patient who has survived for over a decade since the first operation. We believe this is the first report of operations for metachronous bile duct cancer.

CASE REPORT

In 1989, a 67-year-old woman was admitted with mild liver dysfunction and dilatation of the intrahepatic bile duct in the left lobe. On admission, she had high alkaline phosphatase (463 IU/ml, normal: 60-320), total bilirubin (1.2 mg/dl, 0.2-1.1); and carbohydrate antigen (CA) 19-9, (419 IU/ml, <37.0) levels. Ultrasonography showed low echoic mass at the site of the left bile duct and intrahepatic bile duct dilation limited to the left lateral segment. Computed tomography also revealed a low density mass and bile duct dilatation in the left lateral segment (Fig. 1). Percutaneous transhepatic cholangiography (PTC) and endoscopic retrograde cholangiography (ERC) in combination showed complete obstruction of the left bile duct (Fig. 2). Cholangiocellular carcinoma in the left liver was diagnosed and extended left lobectomy including the caudate lobe was performed. Lymph node dissection from the hepatic hilus to the celiac axis was carried out and the surgical margin of the bile duct was confirmed to be cancer free by a frozen section. Macroscopic examination revealed a nodular infiltrative type bile duct cancer, 20 x 20 x 15 mm in diameter, in the left intrahepatic bile duct and microscopy revealed it was a well differentiated tubular adenocarcinoma with perineural invasion (Fig. 3). Two of 15 hilar and celiac lymph nodes were metastasis positive and, according to the pTNM pathological classification, the tumor was classified as pT1N2M0, stage IVB (10).
Metachronous bile duct cancer

Figure 1. Abdominal CT in 1989 revealed a low density mass and bile duct dilation in the left lateral segment.

Figure 2. In 1989, PTC and ERC showed segmental obstruction of the left bile duct with dilatation of the left ductal system.

She was followed up in the outpatient clinic every 4 months, when ultrasonography or CT was performed. In 1996, she was re-admitted with obstructive jaundice. On admission, her serum levels were: glutamic oxaloacetic transaminase 99 IU/ml (0-40), glutamic pyruvic transaminase 113 IU/ml (0-40), alkaline phosphatase 528 mU/ml, total bilirubin 8.5 mg/dl, direct bilirubin 6.7 mg/dl (0-0.6), carcinoembryonal antigen (CEA) 4.3 ng/ml (<5.0) and CA 19-9 770 IU/ml. Percutaneous transhepatic biliary drainage was performed and cholangiography showed complete obstruction of common bile duct at the distal portion (Fig. 4).

Ultrasonography disclosed a 4-cm-diameter low echoic mass and CT showed an enhanced tumor, 4 cm in diameter, in the pancreatic head (Fig. 5). Angiography demonstrated no tumor stain or vascular encasement. This lesion was diagnosed preoperatively as a pancreatic head cancer and pancreatoduodenectomy with peripancreatic lymph node dissection was performed. The pathological diagnosis was a moderately to poorly differentiated adenocarcinoma of the extrabiliary bile duct with pancreatic and duodenal invasion (Fig. 6) and it was classified as T3N0M0, stage IVA. The origin was considered to be the intrapancreatic bile duct for the following reasons: 1) the main pancreatic duct was free from cancer by pathological examination, 2) the bile duct was obstructed completely at the intrapancreatic portion and the cancer was observed circularly in the lumen of the bile duct, and 3) the cancer was located at the bile duct in the pancreatic head and the differentiation of the cancer was different from that of the first lesion. Her postoperative course was uneventful and, 10 years after the first operation, she is well without recurrence.

DISCUSSION

Several studies have shown factors influencing the prognosis of patients with bile duct cancer. The intraductal growth type of cholangiocarcinoma, a well differentiated lesion, no lymph node metastasis and a cancer-free surgical margin and mucobilia appear to be factors associated with a good prognosis (2,11-14). However, the outcome for patients with intrahepatic bile duct cancer is poor. In the review of the international literature, only two patients with lymph node metastasis-positive intrahepatic bile duct cancer survived for longer than 5 years (4,9). Bhuya et al. reported that the 5-year survival rate of patients with perineural...
invasion (32%) was significantly lower than that of those without perineural invasion (67%, P < 0.05) (15). They also observed a significant association between perineural invasion and vascular and lymphatic vessels involvement. The pathological findings in our patient were perineural invasion and metastasis-positive lymph nodes in the hilar and the celiac regions. According to the UICC TNM classification, the celiac node is not included in the regional lymph nodes affected by intrahepatic bile duct cancer. This is a very rare case of a long-term survivor after resection of an intrahepatic bile duct cancer and despite the presence of remote lymph node metastasis. Our findings possibly indicate that radical surgery with systematic lymph node dissection may be the only means of achieving long-term survival of patients with bile duct cancer. Therefore, providing diffuse spread is clinically absent, surgical resection may be indicated even in a patient with metachronous multicentric bile duct cancer.

If the survival of patients with cholangiocarcinoma is prolonged, then the occurrence of a second primary cancer may become more common, as has been observed with other cancers. Therefore, we consider it important to check for second primary cancers, as well as recurrence, in long-term survivors of bile duct cancer. Resection may be the only means of achieving long-term survival of patients with bile duct cancer. Therefore, providing diffuse spread is clinically absent, surgical resection may be indicated even in a patient with metachronous multicentric bile duct cancer.

**References**