Clinical Case Report

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Occurrence of signet-ring cell carcinoma with cholangiocarcinoma 25 years after choledochal cyst excision

A case report

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Abstract

Rationale: Choledochal cysts are a risk factor for the development of cholangiocarcinoma. Hence, complete surgical excision is the preferred treatment in most cases. However, cholangiocarcinoma still can develop from the remnant biliary system after surgical excision. Signet-ring cell carcinoma is a rare type of cancer of the biliary system, and the occurrence of signet-ring cell carcinoma after surgical excision of choledochal cysts has not been reported in the English literature to date.

Patient concerns: We report a case of a 32-year-old woman who presented with a 1-month history of abdominal pain, obstructive jaundice, itching, and fever. The patient had undergone choledochal cyst excision and Roux-en-Y hepatico-jejunostomy 25 years previously and had now developed signet-ring cell carcinoma along with cholangiocarcinoma at the anastomotic site.

Diagnoses: signet-ring cell carcinoma along with cholangiocarcinoma.

Interventions: Interventions included laparotomy with evacuation,blood transfusion,and other adjuvant therapy.

Outcomes: The patient died five months later.

Lessons: Surgery is the best treatment for CCCs, and the surgeon should try to remove as much as of the bile duct cyst as possible.

Abbreviations: CA = carbohydrate antigen, CCCs = congenital choledochal cysts, GGT = γ-gluta-myltransferase, MRCP = magnetic resonance cholangiopancreatography, PET–CT = positron emission tomography-computed tomography, SRCC = signet-ring cell carcinoma.

Keywords: cholangiocarcinoma, choledochal cyst, signet-ring cell carcinoma

1. Introduction

Congenital choledochal cysts (CCCs) represent a rare biliary disorder characterized by cystic dilatations of the extrahepatic biliary tree, intrahepatic biliary ducts, or both. The incidence of CCCs has been reported to be as high as 1 in 13,500 in the United States and 1 in 15,000 in Australia.[1] Ohashi et al[2] divided CCCs into 5 categories. Given that CCCs indicate a precancerous condition, the recommended standard surgical treatment is excision of the dilated bile ducts with hepaticoenterostomy. Although it has been shown that some patients may still develop cholangiocarcinoma even after the operation,[1] the occurrence of signet-ring cell carcinoma (SRCC) after choledochal cyst excision has not been reported in the English literature to date. Here we report a case of SRCC co-existent with cholangiocarcinoma occurring 25 years after choledochal cyst excision.

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2. Case report

The study was approved by the Ethics Committee of First Hospital of Jilin University. Informed consent was obtained from the individual participant included in the study.

A 32-year-old woman was admitted to our hospital with a 1-month history of abdominal pain, jaundice, itching, and fever. She had undergone choledochal cyst excision and Roux-en-Y hepatico-jejunostomy 25 years previously. On clinical examination, the patient had icterus without any palpable abdominal lump. Blood chemistry tests showed a total bilirubin level of 75 mg/dL, aspartate amino-transferase (AST) level of 167 IU/L, alanine aminotransferase (ALT) level of 300 IU/L, alkaline phosphatase (ALP) level of 453 IU/L, γ-gluta-myltransferase (GGT) level of 390 IU/L, and total bile acid (TBA) level of 307 U/L. The level of carbohydrate antigen (CA) 19-9 was elevated up to 768.3 U/mL, and that of carbohydrate antigen (CA) 242 was 645.2 U/mL. The serum electrolyte, urea nitrogen, and creatinine levels were within normal ranges. Contrast-enhanced computed tomography revealed gross dilatation of the intrahepatic bile ducts with the presence of multiple stones within them. The wall of the common hepatic duct showed thickening with enhancement, raising the possibility of carcinoma. In addition, the lymph nodes in the periportal area and around the abdominal aorta were enlarged, ranging in diameter from 0.5 to 3 cm (Fig. 1). Magnetic resonance cholangiopancreatography (MRCP) revealed cystic dilatation of intrahepatic biliary system with the presence of multiple calculi within it. An irregular soft tissue shadow was visible at the hepatic hilum with poor visualization of the extrahepatic biliary system. Positron emission tomography-computed tomography (PET–CT) showed a soft tissue lesion

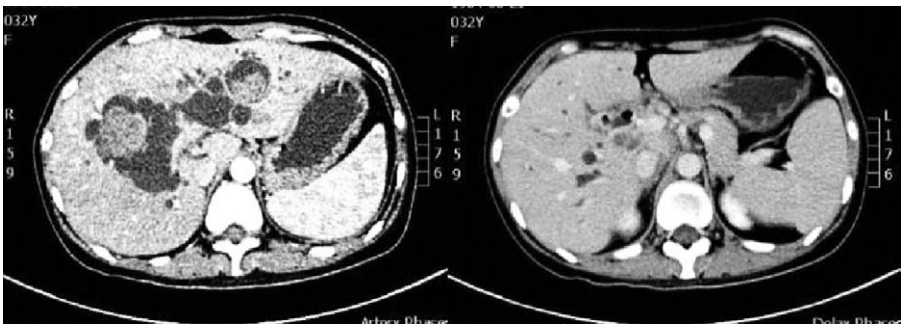

Figure 1. Contrast-enhanced CT showing cystic dilatation of intrahepatic bile ducts containing multiple stones (A). Presence of soft tissue lesion at the hepatic hilum, replacing the common hepatic duct (B). CT = computed tomography.

at the hepatic hilum and enlarged periportal and paraaortic lymph nodes with high radiolabeled [18F]-2-fluoro-2-deoxy-D-glucose (FDG) uptake suggestive of metastatic cholangiocarcinoma. Intraoperatively, a tumor was found at the site of the hepaticojejunostomy and was biopsied. The dilated hepatic duct proximal to the anastomosis was opened, and T tube drainage was performed. Additionally, biopsy of Group 8 lymph nodes (lymph nodes along common hepatic artery) was performed. Histological examination of the neoplasm (Fig. 2) revealed SRCC coexisting with cholangiocarcinoma. The lymph nodes showed metastatic deposits of both SRCC and cholangiocarcinoma. On immunohistochemistry, the tumor cells showed positive staining for AE1/AE3, CK19, CK7, and Ki-67, where staining for p53 was negative. The patient was alive at 5 months after the operation.

3. Discussion

CCCs are characterized by single or multiple congenital dilations of the extrahepatic and/or intrahepatic biliary tree. The most common types are I and Iva, in which there is dilatation of the extrahepatic bile duct or both the extrahepatic and intrahepatic bile ducts, respectively.[3] CCCs are rare in Western countries, with an incidence of 1: 100,000 to 1: 150,000, and account for approximately 1% of all benign biliary diseases, but they are less uncommon in Asian countries. Although CCCs can be diagnosed by ultrasound, CT, and MRCP, approximately 20% of cases remain undiagnosed. Once the disease is diagnosed, complete cyst removal is essential, because of the inherent 20% to 30% risk of developing biliary tract malignancy.[2] However, cholangiocarcinoma rarely occurs following choledochal cyst resection, with reported rates of only 0.7% to 6%.[2] Bile duct infection, pancreatic enzyme stimulation, recurrent cholestasis, and excessive bile acid concentration are considered to be carcinogenic risk factors. A case of cholangiocarcinoma was reported to have arisen from the remnant intrapancreatic part of a CCC 12 years after the first operation for removal of the CCC.[4] Kumamoto et al[5] reported that the duration between initial surgery and the diagnosis of cancer can range from 2 to 26 years. Hence, surgery is the best treatment for CCCs, and the surgeon should try to remove as much as of the bile duct cyst as possible.

SRCC is a unique pathological subtype of cancers characterized by the presence of intracytoplasmic mucin, which pushes the nucleus to one side of the cell, giving the cells an appearance like that of a ring.[6] SRCC most commonly arises from the stomach, and SRCCs of other digestive organs grow rapidly and have a poor prognosis.[7] SRCC of the bile ducts is very rare, and most SRCCs of the biliary system originate from the gallbladder.[8] Five cases of primary biliary SRCC have been reported in the English literature to date.[8–12] However, there has been no report of cholangiocarcinoma co-existing with SRCC after CCC excision. Also, this is the first case of primary SRCC of the bile duct after presentation of a choledochal cyst to be reported in the literature. A previous study[13] reported that the origin of SRCCs in the periampullary area is poorly understood and suggested 2 possible explanations: one is that the tumors arise from the ectopic gastric mucosa, and the second is that there may be development of gastric-type epithelial metaplasia, which later turns malignant. However, in our case, the patient underwent excision of the CCC with no evidence of ectopic gastric mucosa

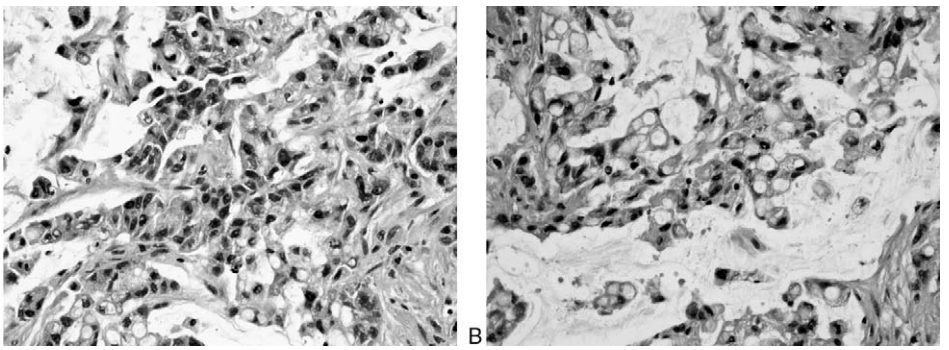

Figure 2. (A) Signet ring cells co-existing with cholangiocarcinoma in the bile duct mucsa (H&E staining; magnification, ×40). (B) Signet ring cells (H&E staining; magnification, ×100).

or gastric metaplasia on the biopsy. Hence, the origin of SRCC in our case is difficult to ascertain.

In conclusion, we report a case of SRCC coexisting with hilar cholangiocarcinoma and occurring 25 years after excision of a CCC. The origin of SRCC in the setting of a CCC is not known and needs to be evaluated in future studies.

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