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Bile Duct Carcinoma in Association with a Choledochal Cyst ——Report of a Case——

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ABSTRACT. A case of bile duct carcinoma associated with a pre-existing type I-A choledochal cyst is reported here. A 38-year-old man who had received a Roux-en-Y hepaticojejunostomy for a cyst of the common bile duct 11 years earlier was revealed to have metastatic carcinoma in the lungs. The primary site of the carcinoma was clinically undetermined, but was found by autopsy to be in the bile duct. Although the relation between these two lesions was unclear, circumstantial evidence suggested that they were related to each other. A persistent chronic inflammatory irritation in this area was considered to be responsible for development of the tumor.

Key words : bile duct carcinoma — choledochal cyst

Biliary tract cysts, most of which are choledochal cysts, are relatively rare. About 1,500 cases have been reported in the world literature, and more than two thirds of them were from Japan.[1,2] It has been noted that bile duct carcinoma may arise as a long-term complication of choledochal cysts. Sixty-seven such cases, 2.5 per cent of all reported choledochal cysts, have been documented.[2] In most of these patients, choledochal cysts were found during adulthood. The average age for patients with bile duct carcinoma and a choledochal cyst was much younger than that for those with bile duct carcinoma without a choledochal cyst. The youngest patient with both a choledochal cyst and carcinoma was 15 years old. The most common histologic type among associated carcinomas was adenocarcinoma, but squamous cell and undifferentiated carcinomas were also reported.

Recently we encountered a patient with bile duct adenocarcinoma who had a cholecystectomy, a lithotomy and a Roux-en-Y hepaticojejunostomy for choledocholithiasis, a type I-A choledochal cyst and repeated cholangitis, 20, 7, and 6 years prior to his demise, respectively. Although there was no clearcut evidence of a direct relationship between the presence of the choledochal cyst and the development of bile duct carcinoma, we considered that the latter developed on the basis of the former. The rarity of such an association prompted us to present our case and discuss the possible etiological relation between the carcinoma and the choledochal cyst. Persistent chronic inflammatory irritation was considered to be responsible for the development of the tumor.

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AUTOPSY FINDINGS

The right upper abdomen was markedly adhesive. The gallbladder had been removed, and the area in which it seems to have been present was adherent to a fibrous mass in the hepatic hilus. The upper portion of the extrahepatic biliary tract was embedded within this dense connective tissue and could not be identified (Fig. 1). A 1 cm long segment of the lower part of the common bile duct with a circumference of 1 cm was embedded within the fibrous tissue, and contained a black gallstone, 0.3 cm in diameter. The mucosal surface of the duct was grossly unremarkable as was the papilla of Vater. No anomalous arrangement of the pancreaticobiliary system was seen. Although it was not apparent grossly, the fibrous tissue was revealed to have an adenocarcinoma microscopically. The tumor was a well-differentiated tubular adenocarcinoma, scattered within the desmoplastic fibrous connective tissue (Fig. 2). Invasion to the adjacent hyperplastic nerve bundles was prominent. The liver was directly infiltrated by a tumor through the area of adhesion. The mucosal surface of the common bile duct was lined with a single layer of columnar epithelium and was free of tumor. Metastatic foci were noted in the lungs, pleura, esophagus, and pancreas, as well as in the hepatic hilar, mediastinal and peripancreatic lymph nodes. No metastasis was present in the bone. Although examination of the multiple metastatic lesions in the lungs revealed tumor cells growing along alveolar walls with some resemblance to bronchiolo-alveolar carcinoma of the lung, none of the organs other than the bile duct was considered to be a primary site.

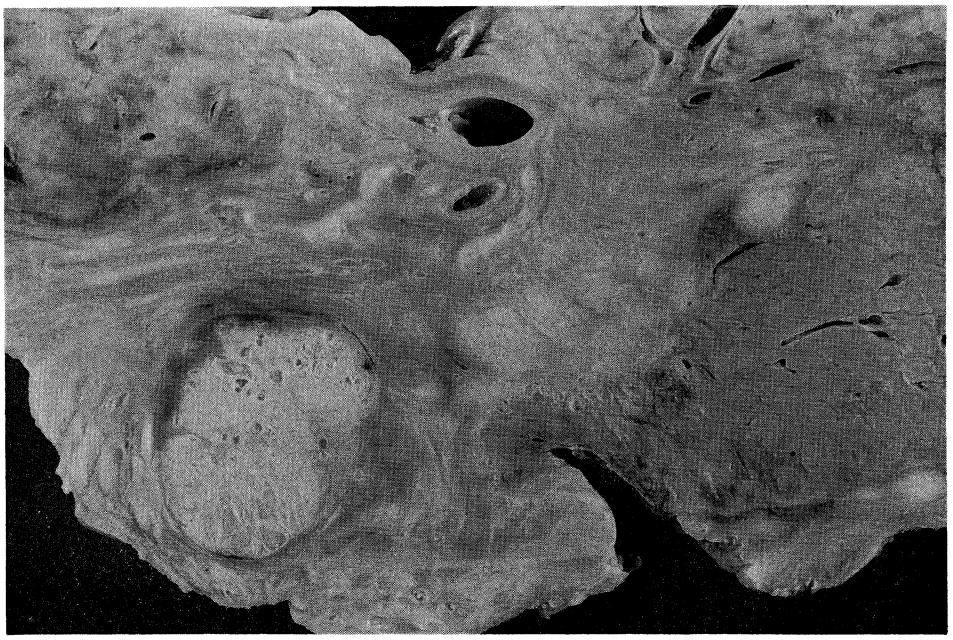

Fig. 1. A cut surface of the liver and its hilus. The hilus has been replaced by dense connective fibrous tissue.

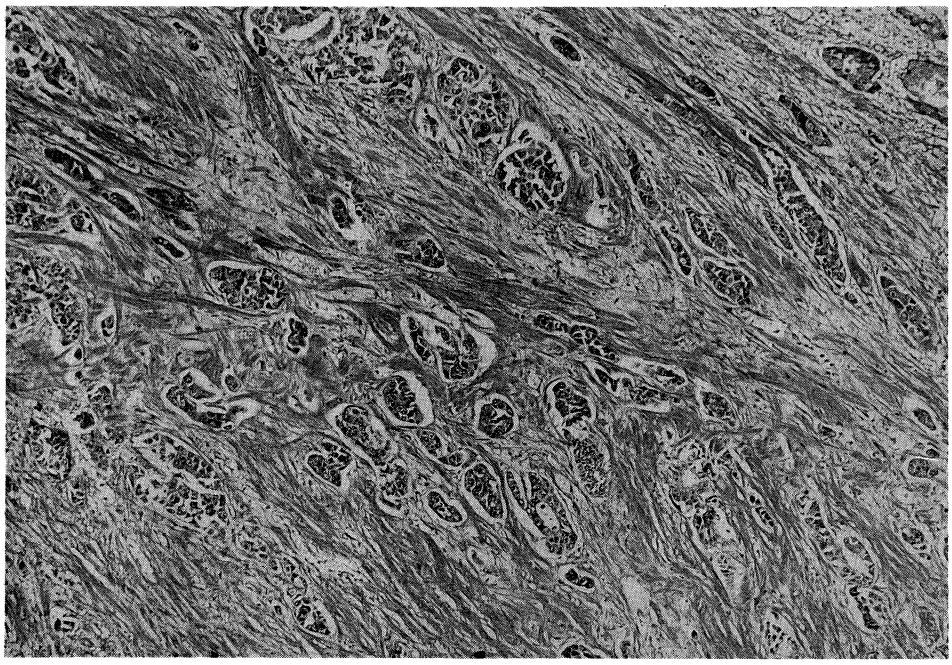

Fig. 2. Microscopic appearance of the hilus of the liver. Well-differentiated adenocarcinoma showing tubular structures is present in the dense connective tissue. (H-E stain, ×150)

REPORT OF A CASE

A 37-year-old man was admitted to the Kawasaki Medical School Hospital (January 21, 1985) because of severe lumbago, anorexia and weight loss. He had a history of a cholecystectomy for unknown reason twenty years earlier. Thirteen years later, he suffered right shoulder pain and jaundice, and was admitted to another hospital, where a lithotomy for choledocholithiasis was performed. One year later (at the age of 32), he received a Roux-en-Y hepaticojejunostomy following a diagnosis of chronic cholangitis due to a type I-A choledochal cyst at the other hospital. At that time, no malignancy was histologically demonstrated in the removed choledochal cyst, and no detailed information is available. He was well for the next eleven years. One year before admission, repeated episodes of right lumbago appeared. There was a history of anorexia and weight loss of 16.0 kg during the past year.

On admission, the patient was fair in appearance. His body temperature was 36.4°C, his pulse 70/min and his blood pressure 110/60 mmHg. No lymphadenopathy was found. The head, neck and lungs were normal. A systolic heart murmur was slightly audible at the apex. The liver was palpated by one finger breadth at the right midclavicular line. There was no abdominal mass, tenderness, or ascites. His hematocrit was 33.4 per cent. The white-cell count was 4500/mm^3, with a normal differential count. His platelet count was 1,290,000/mm^3. Serum protein was 6.9 g/dl, albumin 3.9 g/dl, globulin 3.0 g/dl, bilirubin 0.5 mg/dl, gamma-GTP 101 IU/1, GPT 37I U/1, GOT 24 IU/1, CEA 16.0 ng/ml, and CA19-9 1,700 u/ml. Urinalysis and stool

examination were normal. X-ray films of the chest revealed multiple small nodular shadows in the lungs. Abdominal echography and a computed tomographic scan disclosed a swelling of a para-aortic lymph nodes, splenomegaly, dilatation of the portal vein and a left renal cyst. Cytological examination of his sputum revealed an adenocarcinoma. Despite extensive searches, the primary site remained undetermined. The lumbago gradually increased and continuous epidural injection of analgesics was necessitated. Four months later the patient was discharged on analgesics. Three months after discharge, his lumbar pain became severe and uncontrollable. He returned to our hospital on September 4, 1986. His general condition gradually deteriorated and he died of pneumonia a month after the second admission. An autopsy was performed 3 hours after his demise.

DISCUSSION

Choledochal cyst or congenital cystic dilatation of the bile duct is the second most common anomaly in the extrahepatic biliary system. To date, 1500 biliary tract cysts have been recorded in the world literature, and most of them (77.7%) have been choledochal cysts.[1,2] Surprisingly, they seem to be more prevalent in Japan, with more than two-thirds of the reported cases being from Japan. Patients ranged in age from neonates to 80 years old. Forty to sixty per cent of the patients were diagnosed before the age of ten. Seventy-five per cent of the patients with choledochal cysts were female, and the cysts occurred in all parts of the bile duct between the liver and the duodenum. Various anatomic forms of bile duct cysts have been reported. The classification proposed by Todani *et al.*,[3] which divides these into eight types, is most often used: Type I; common type, (A) choledochal cyst in a narrow sense, (B) segmental choledochal dilatation, and (C) diffuse or cylindrical dilatation, Type II; diverticulum type in the whole extrahepatic duct, Type III; choledochocele, Type IV-A; multiple cysts at the intra- and extrahepatic ducts, Type IV-B; multiple cysts at the extrahepatic duct only, Type V; intrahepatic bile duct cyst (single, or multiple). Our case corresponds to type I-a.

Choledochal cysts may be associated with a variety of complications, such as stone formation, malignant tumors, cholangitis, biliary cirrhosis, portal hypertension or portal vein aneurysm. Stone formation, occurring in an estimated 8 per cent of choledochal cysts, is the most common complication.[1] The second common complication is development of malignant tumors. It was reported in 2.5 per cent of patients with bile duct cysts, and its incidence was much higher than the incidence in those without a choledochal cyst, which was estimated to be 0.012-0.48 per cent.[4] Voyles *et al.* reviewed a total of 67 carcinomas with choledochal cysts.[5] The average age of such patients (37 years old) was younger than that of those with ordinary bile duct carcinoma. In about half of the cases, bile duct cysts were recognized during the first decade of life. Most cysts associated with carcinoma tend to be found after reaching associated with carcinoma tend to be found after reaching adulthood, and carcinomas usually arise from such cysts several years later with high incidence (84 per cent) in cysts classified as type I or IV-A. The most common histologic type of developing malignant tumor was adenocarcinoma,

squamous cell and undifferentiated carcinomas were also reported.

Our patient exhibited the typical features of "carcinoma arising in association with choledochal cyst". He was found to have a choledochal cyst when he was 32 years old, at which time the cyst was removed. The period from his first operation to his last was 14 years, and six years after his last operation, metastatic adenocarcinoma of the lung was detected. The choledochal cyst was found at the last operation. Carcinoma may arise on the wall of a choledochal cyst or after the choledochal cyst has been removed. The interval between removal of the cyst and development of carcinoma varies in patients, ranging from one month to 12 years (average 5 years).[1] The interval has generally been longer in patients operated on during the first decade of life, and such patients carry a lower risk of carcinoma.[5]

Carcinoma of the biliary tree is associated with a variety of conditions, including sclerosing cholangitis, congenital hepatic fibrosis, biliary atresia, anomalous arrangement of the pancreaticobiliary system, chronic cholangitis and choledochal cyst.[5,6] Factors common to all these lesions include bile stasis, persistent chronic inflammatory irritation, infection over a prolonged period or pancreatocholedochal reflux.[6] Any one of these factors may have had a carcinogenic effect. In our case, it is difficult to demonstrate whether the development of carcinoma had an immediate connection with the pre-existing choledochal cyst. Our patient had a history of chronic cholangitis, choledocholithiasis and some surgery of the biliary tract, and the choledochal cyst was removed at the age of 32. It is speculated, therefore, that such chronic inflammatory irritation for a long period may have played a part in the development of bile duct carcinoma in our case. Although it is said that the excision of the cyst and Roux-en-Y hepaticojejunostomy which our patient received are the best procedure for choledochal cyst,[1] this procedure may not be perfect and/or may be too late to prevent malignant change.

The primary site of the carcinoma remained clinically undetermined. If a more serious view had been taken regarding his history of choledochal cyst, a more appropriate and speedier diagnosis might have been entertained. Clinicians should be aware of the carcinogenic risk factors related to this condition, and should pay more attention to the patient's history.

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