Successful Treatment of Caroli's Disease by Hepatic Resection

Report of Six Patients

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Caroli's disease is a congenital disease of cystic or saccular dilatation of the intrahepatic bile ducts. There are two disease entities: a simple type and a periportal fibrosis type. Frequent complications with the simple type are recurrent cholangitis, liver abscess, intraductal lithiasis, abdominal pain, and fever that often lead to fatal sepsis. Development of portal hypertension and esophageal varices is usually a final feature of the periportal fibrosis type. Malignancies are also possible complications with Caroli's disease. During the recent 13 years, the author had experiences with eight patients with Caroli's disease of the simple type; six of these eight underwent hepatic resection: right lobectomy in two, left lobectomy in three, and left lateral segmentectomy in one. Other two patients died of sepsis and cholangiocellular carcinoma, respectively. All six patients with hepatic resections were relieved from the disabling symptoms after surgery and have had no recurrent hepatobiliary problems for 3 months to 13 years. Hepatic resection may be indicated for more patients than previously assumed in the treatment of Caroli's disease of the simple type.

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SINCE THE EPOCH-MAKING REPORT by Caroli and Couihaud[1] in 1958, a congenital disease of cystic dilatations of intrahepatic bile ducts has been widely accepted as Caroli's disease. Despite of a recent flurry of reports on Caroli's disease and intrahepatic stones, there are still essential problems to be solved in the diagnosis and treatment of these uncommon disorders. During recent years, the development and wide utilization of ultrasonographic and computed tomographic equipments have seemingly made it easier to discover and diagnose Caroli's disease.[2–5] On the other hand, the treatment of this disease is usually very difficult. Frequent complications in Caroli's disease are intraductal lithiasis, repeated cholangitis, and liver abscess. It is also reported that cholangiocellular carcinoma is occasionally complicated with Caroli's disease.[6] Although biliodigestive anastomoses are guaranteed by many authors as standard operation for this disease,[7–9] they are often unsuccessful in treating and preventing the above-mentioned complications. The incidence of suitable cases for hepatic resection may be low, but the most accurate and reliable treatment is undoubtedly removal of the diseased portion of the liver if possible as suggested by several investigators.[10–12] During the recent 13 years, we have experienced six successful hepatic resections in the treatment of Caroli's disease.

We assume it valuable to add our cases to the world literature not only because the role of hepatic resection seems to be underestimated, but also because there are as yet insufficient numbers of reports on resectional treatment of Caroli's disease.

Report of Patients

Case 1

A 31-year-old man presented with severe epigastric pain and high fever. Since 8 years of age, he had had an attack of upper abdominal pain once or twice a year, but its cause had not been elucidated. Emergency laparatomy was carried out under the diagnosis of perforation of peptic ulcer. There were no pathologic findings in the abdominal cavity except for a hard, irregular left hepatic lobe with marked fibrous reaction. The lesion was suspected to be a hepatic tumor and the abdomen was closed. Postoperative celiac angiography demonstrated only narrowing of the branches of the left portal vein (Fig. 1). Cholangiocellular carcinoma was doubted and reoperation was performed. As the lesion was confined in the left lateral segment, its resection was attempted. During parenchymal dissection, it proved that he had intrahepatic stones. The right hepatic lobe was normal on inspection and palpation. Postoperative course was uneventful except for wound infection. He has had no further problems for 13 years.

Case 2

A 40-year-old man had recurrent symptoms of severe epigastralgia and fever since he was a school boy. When he was 35 years old, he

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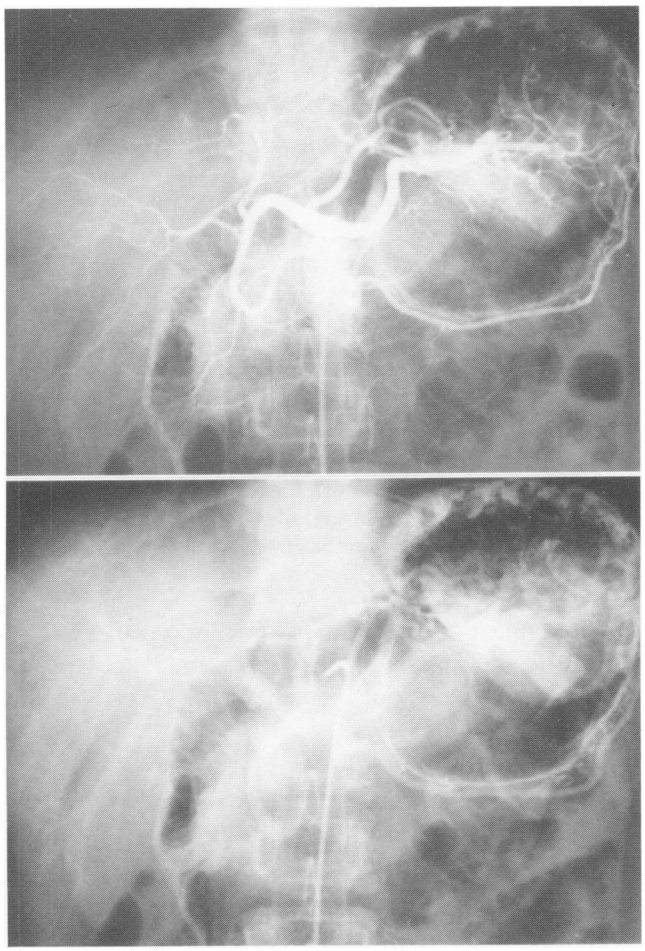

FIG. 1. Celiac angiography in Case 1. Atrophy of the left and hypertrophy of the right hepatic lobes were demonstrated. Narrowing of the left portal branches was a only positive finding.

was suspected to have cholelithiasis. Two months prior to this admission, he underwent cholecystectomy, but there were no stones in the gallbladder. The surgeon noticed a hard, fibrous left hepatic lobe and sent the patient to us. Liver scintigraphy showed weak and patchy uptake of the colloid in the left hepatic lobe (Fig. 2). Percutaneous transhepatic cholangiography was carried out without success. With the typical history indicating intrahepatic gallstones, laparotomy was performed. The left hepatic lobe was atrophic and its capsule was regionally fibrous and cicatrical. Cystic and cylindrical dilatations of the bile ducts filled with pigment stones were observed in the resected specimen. A biliary fistule occurred but it spontaneously subsided 4 weeks after operation. He has been doing well for 10 years.

Case 3

A 28-year-old woman was referred to us due to Caroli's disease of the left hepatic lobe. She had the first attack of epigastric pain, high fever, and jaundice when she was 14 years old. She suffered from similar symptoms several times a year, but the etiology was unknown. Two months before her admission to our clinic, she underwent cholecystectomy and choledocholithotomy. There was no stone in the gallbladder but two pigment stones were removed from the common bile duct. Intraoperative T-tube cholangiography demonstrated intra-

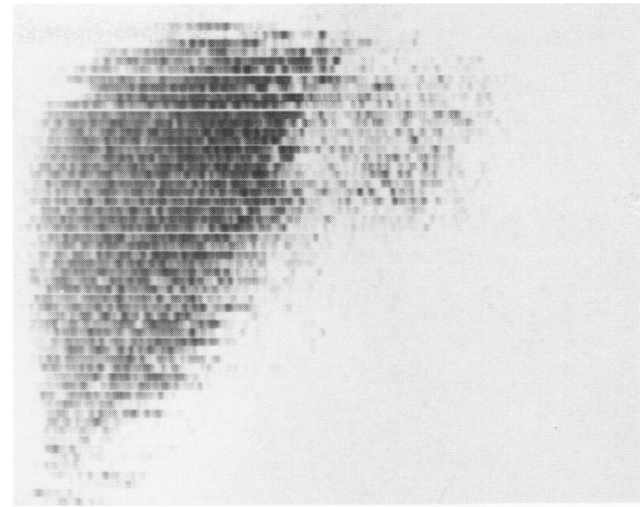

FIG. 2. Liver scintigraphy in Case 2. The left hepatic lobe was atrophic and patchy and irregular uptake of ^{99m}TC sulfur was demonstrated.

hepatic gallstones (Fig. 3). Left hepatic lobectomy was performed. She has been free from any complaints for 2 years and 5 months.

Case 4

A 37-year-old man was operated on for cholelithiasis 5 years before this admission. He had occasionally had upper abdominal pain since 10 years of age. At the time of cholecystectomy, he was noted to have an atrophic left hepatic lobe. Although he had no symptoms after operation, the history and operative findings suggested the presence of Caroli's disease in his left hepatic lobe. Therefore, he was called and studied precisely. Ultrasonography and computed tomography (Fig. 4) showed positive findings. For fear of development of malignancy, left lobectomy was carried out. He has been well for 1 year after the hepatectomy.

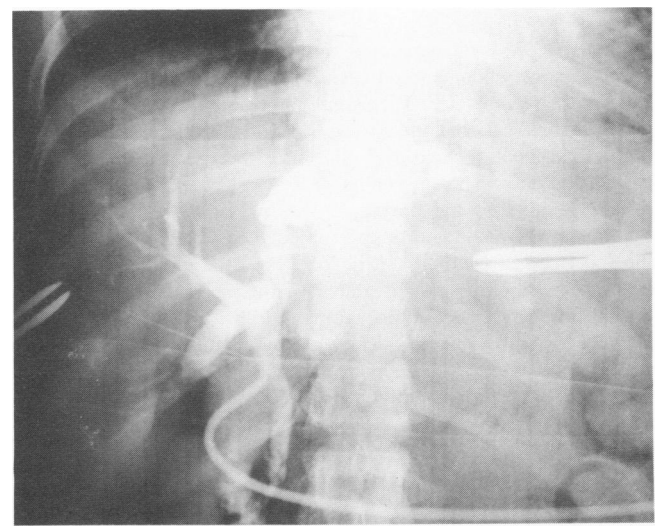

FIG. 3. Intraoperative T-tube cholangiography in Case 3. Note the saccular dilatation of the left hepatic duct and intraductal lithiasis.

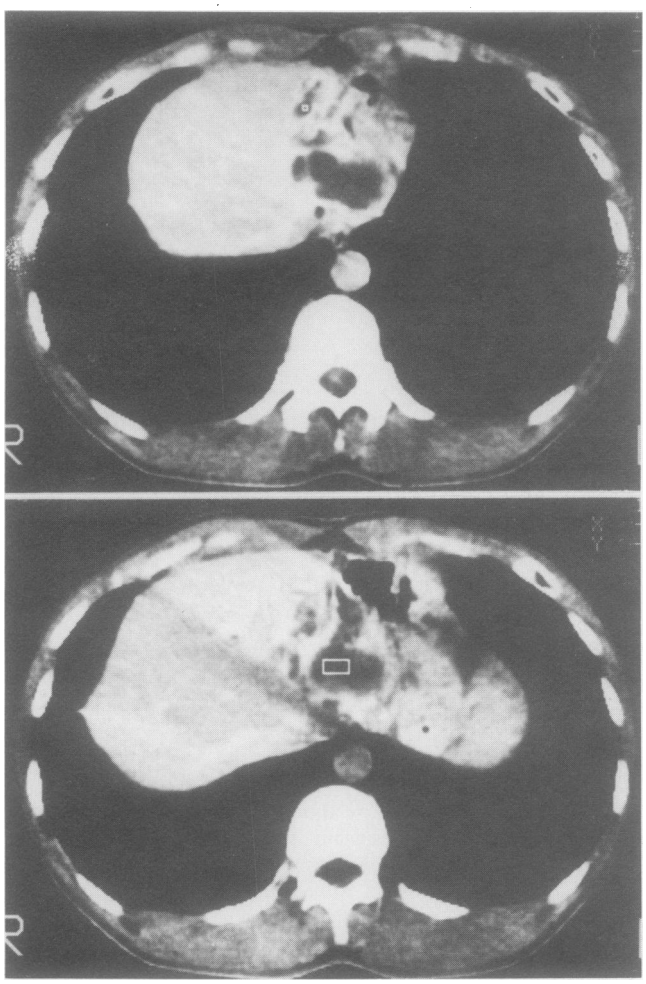

FIG. 4. Computed tomography in Case 4. There were many cystic or saccular dilatations of intrahepatic ducts of the left hepatic lobe.

Case 5

A 36-year-old woman first had an episode of high fever and pain at the right upper abdomen and back following the delivery of her first child at 28 years of age. The symptoms recurrently occurred during the following years but the etiology was obscure. Under a suspected diagnosis of choledocholithiasis, she underwent cholecystectomy and choledochotomy. There were no stones in the extrahepatic biliary system. Soon after the operation, she had an attack of the same symptoms, and computed tomography demonstrated cystic lesions in the upper part of the right hepatic lobe (Fig. 5). She was referred to us for further investigation and treatment. Ultrasonography showed several dilated intrahepatic bile ducts and stone echos inside them (Fig. 6). She underwent a right hepatic lobectomy. Right subphrenic abscess ensued but was successfully drained by reoperation. She has been free from complaints for 6 months.

Case 6

A 45-year-old woman first had jaundice of unknown causes when she was 14 years old. Since 20 years of age, she had recurrent episodes of fever and pain at the right back and upper abdomen. At 43 years of age, she was diagnosed to have choledocholithiasis and Caroli's disease in the posterosuperior segment of the right hepatic lobe (Fig. 7). She was treated by cholecystectomy, choledocholithotomy, and choledochojejunostomy (Roux-en-Y). Intrahepatic stones were removed as far as possible using a balloon catheter under choledochofiberscopy. Postoperative course was uneventful, but she had persistent pain and discomfort at the right back. Accordingly, a right hepatic lobectomy was performed (Fig. 8). Postoperative course was uneventful except for wound infection. She has been relieved from the pain after surgery.

Results

Clinical Manifestation

Clinical features of all patients are summarized in Table 1. All patients had recurrent episodes of pain and fever. Jaundice was noted only in one patient. The symptoms started at their childhood in all patients except for one. Five patients had undergone some sorts of biliary operation previously.

Biochemical Tests

Biochemical determinations were not specific for Caroli's disease. Hepatic functions were completely normal in five cases. Only one patient (Case 4) had slightly abnormal functions such as elevated levels of serum bilirubin and liver enzymes.

Radiologic Examination

Liver scanning with ^{99m}Tc sulfur was performed in three patients. Patchy and weak uptake of the colloid and atrophy of the diseased segment of the liver were depicted in all. Ultrasonography correctly revealed dilated

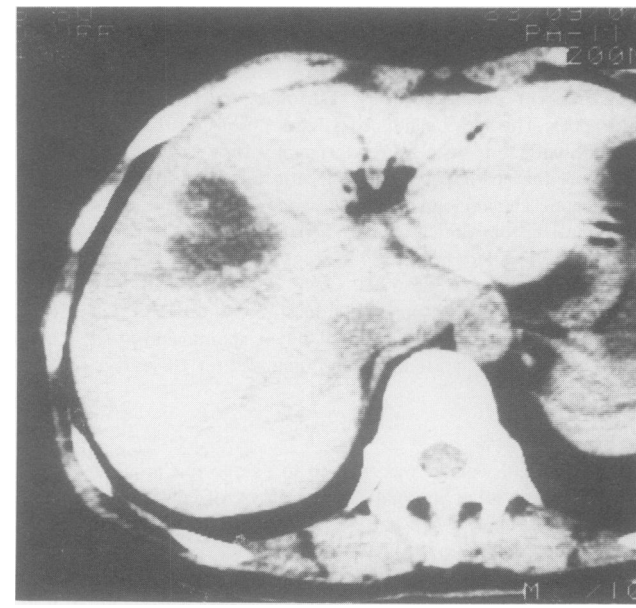

FIG. 5. Computed tomography in Case 5. There were cystic dilatations of bile ducts containing stones in the right hepatic lobe.

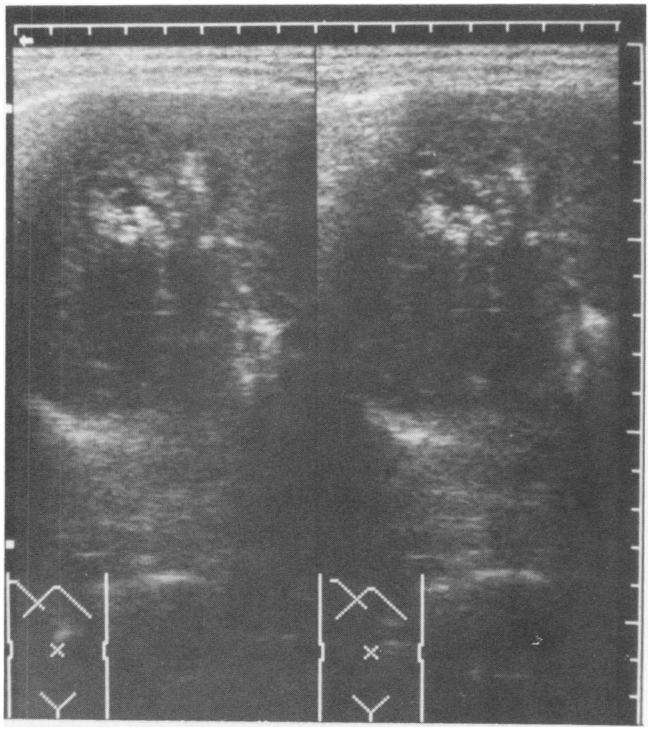

FIG. 6. Ultrasonography in Case 5. Cystic dilatations filled with stones were found in the right hepatic lobe.

ducts and stones inside them in all four cases tested. Computed tomography, which was done in three patients, also demonstrated the lesions well in all. Angiography was carried out on the initial three patients in order to differentiate the lesions from hepatic tumors, but no specific findings were observed. Endoscopic retrograde cholangiography was performed in two patients (Cases 5 and 6), but the lesions were not visualized in both of them. Intraoperative cholangiography with high pressure, however, demonstrated the cistern in one of them. Intraoperative cholangiography depicted the lesions in another two patients (Cases 3 and 4). Only one patient had a cyst of the right kidney (Case 5). This patient also had an abnormal anatomy of the bile duct; the bifurcation of the right and left hepatic ducts was located very low and the cystic duct was from the right duct. Obvious choledochal cyst was not seen in any of the patients although the diameter of the choledochus in Case 6 was 27 mm.

Histopathologic Finding

Cylindrical or cisternal dilatations of the intrahepatic ducts were found in three patients with the disease in the left lobe and in one patient with the disease in the right lobe. Cystic dilatations were noted in two patients, one in the right and the other in the left hepatic lobe. Pigment stones were present in all cases. Purulent bile

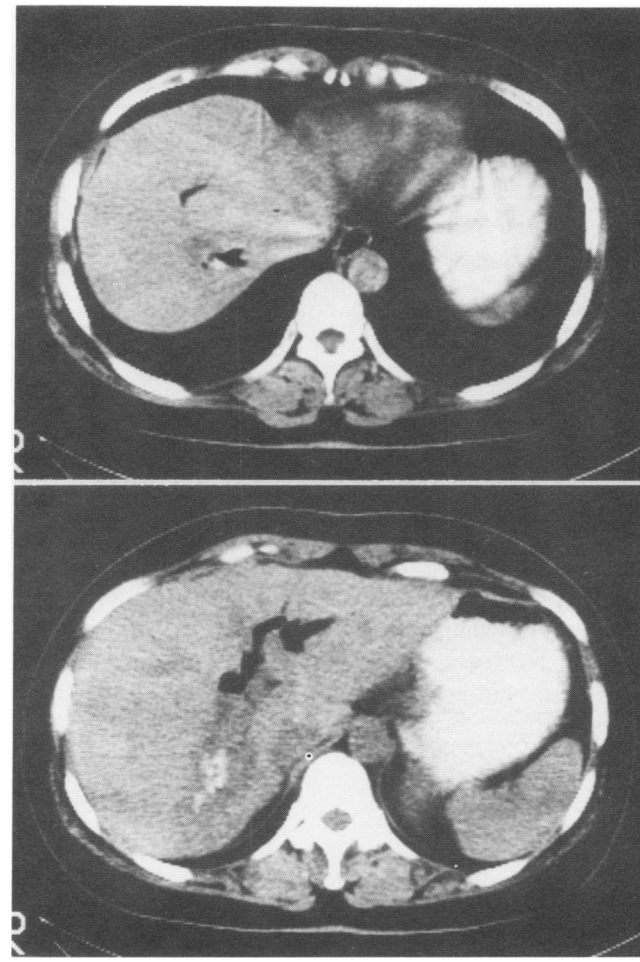

FIG. 7. Computed tomography in Case 6. Note cystic dilatations with stones in the posterosuperior segment of the right hepatic lobe.

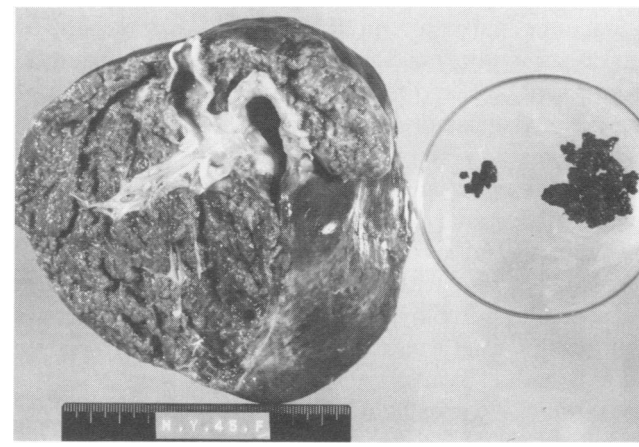

FIG. 8. Resected specimen in Case 6. There were two cystic dilatations of bile ducts in the upper part of the right hepatic lobe. The cysts were filled with bilirubin stones and whitish pus. Scar formation was noted at the diseased portion of the liver but the remaining part was normal macro- and microscopically.

TABLE 1. *Clinical Data of Six Patients with Caroli's Disease*

Case No.	Age (yrs)	Sex	Symptoms	Age at First Symptoms (yrs)	Previous Operations	Site of Caroli's Disease
1	31	M	Epigastralgia, fever	8	Exploratory laparotomy at 31 years	Left lateral segment
2	40	M	Epigastralgia, fever	10	Cholecystectomy at 40 years, no stones	Left lobe
3	28	F	Epigastralgia, fever, jaundice	14	Choledocholithotomy at 28 years	Left lobe
4	37	M	Epigastralgia	10	Cholecystectomy at 32 years, stones (+)	Left lobe
5	36	F	Pain at right upper abdomen and back, fever	28	Cholecystectomy at 36 years, no stones	Superior segment of right lobe
6	45	F	Pain at right upper abdomen and back, fever	14	Cholecystectomy, choledocholithotomy, choledochojejunostomy at 43 years	Superior segment of right lobe.

was accumulated in the lesions in four cases. Histologically, acute and chronic inflammation, fibrosis, and degenerative changes were found in the lesions of all patients. However, there was no neoplastic lesion in all cases. Also, periportal hepatic fibrosis was absent in all instances.

Operative Results

Postoperative complications occurred in four patients: wound infection in two, right subphrenic abscess in one, and biliary fistula in one. All of them were successfully treated by reoperation or conservation treatments. All patients were discharged from hospital and have had no recurrent hepatobiliary problems for 3 months to 13 years.

Discussion

Since his first report in 1958,[1] Caroli has recognized two disease entities associated with congenital dilatation of intrahepatic bile ducts.[13] The first is a "simple type" that is not associated with periportal fibrosis or cirrhosis. It is, however, very important clinically because of its frequent association with recurrent cholangitis, liver abscess, abdominal pain, and fever, which often lead to fatal sepsis. The second is a "periportal fibrosis type" that is associated with congenital hepatic fibrosis. Development of portal hypertension and esophageal varices is usually a final feature of this type. All of our six patients had a "simple type" disease.

As there are excellent descriptions concerning the etiology of Caroli's disease,[14,15] we do not repeat it here. But our patients also support the theory that the disease is of congenital origin because the first symptoms began in their childhood in five of six cases. All patients had recurrent attacks of pain, fever, or jaundice for many years. A pitfall in diagnosis of Caroli's disease is apparently in unawareness of this disease. As easily recognized by reviewing the world literatures, unnecessary or fruitless operations are not infrequently performed or repeated, as was so in our own cases. Physicians should always consider a possibility of Caroli's disease when a patient has the typical symptom of recurrent pain, fever, and/or jaundice from his or her childhood. Surgeons should investigate the liver when they can not find any pathology in the extrahepatic biliary system in a patient who has presented with a typical clinical manifestation of gallstones.

Ultrasonography and computed tomography (CT) may be useful tools for the diagnosis of Caroli's disease, as recently suggested by several authors.[2-5] In fact, these two methods demonstrated the lesions most correctly also in our patients. Endoscopic retrograde cholangiography, percutaneous transhepatic cholangiography, or even operative cholangiography often fail to delineate the lesions since proximal orifices of the diseased ducts are frequently stenotic or obstructed by stones or debris. Nevertheless, these examinations are useful and may give a definitive information that the cystic lesions in the liver are communicated with the biliary system. In order to obtain this conclusive finding, CT cholangiography may also be useful if contrast medium is excreted in the dilated ducts.[4]

The standard methods of treatment of Caroli's disease involve external drainage by means of a T-tube in the common bile duct[8,9] and internal drainage by biliodigestive anastomoses.[7-9] External drainage may produce a temporary effect, but is usually not very effective. Intrahepatic stones associated with recurrent biliary infections are usually bilirubinate,[16] and chemical irrigation is ineffective in dissolving them. Choledochoduodenostomy, Roux-en-Y choledochojejunostomy, and Roux-en-Y hepaticojejunostomy are the most commonly used

methods of internal drainage for Caroli's disease. However, these procedures often result in incomplete decompression of the biliary tree since the diseased intrahepatic ducts frequently have stenotic segments that cause bile stasis, sludge formation, recurrent infection, and intrahepatic stones.

Important therapeutic points of Caroli's disease are to relieve disabling clinical symptoms such as pain, fever, or jaundice and to cure or prevent cholangitis and liver abscess, which may lead to life-threatening sepsis. As pointed out recently by Dayton et al.,[6] it is also very important to prevent the development of cholangiocellular carinoma. Squamous cell carcinoma is also reported to be complicated with Caroli's disease.[17,18] In fact, we lost two patients with Caroli's disease during the same period of this series; one due to systemic sepsis from suppurative cholangitis and the other due to cholangiocellular carcinoma. Both patients are not included in the current series. The diagnosis of Caroli's disease was made only at autopsy in the former case and that of cholangiocellular carcinoma in the latter patient was obtained at exploratory laparotomy.

Considering these and those problems, resection of the diseased segment or lobe of the liver is apparently advantageous. It is generally said that the incidence of suitable patients for hepatic resection is low, but we were able to perform hepatic resection in six of eight patients experienced during the recent 13 years. We feel that more patients than previously assumed are indicated to undergo hepatic resection. Postoperative morbidity, especially of infectious complications, was high in our series. This was obviously due to persistent intrahepatic infections. Not only extensive pre- and postoperative chemotherapy with broad-spectrum antibiotics but careful operative maneuver may be important to reduce or eliminate these complications. There was no operative death. The long-term follow-up of the patients revealed satisfactory results. All patients are alive and rehabilitated without recurrent hepatobiliary problems for 3 months to 13 years.

The current study may indicate that hepatic resection should be aggressively performed in selected patients with Caroli's disease of the "simple type."

References

1. Caroli J, Couihaud C. Une affection nouvelle, sans doute congenitale, des voies biliares: la dilatation kystique unilobaire des canaux hepatiques. Sem Hop Paris 1958; 14:496–502.
2. Kaiser JA, Mall JC, Salmen BJ, Parker JJ. Diagnosis of Caroli's disease by computed tomography: report of two cases. Radiology 1979; 132:661–664.
3. Mittelstaedt CA, Volberg FM, Fischer GJ, McCartney WH. Caroli's disease: sonographic findings. Am J Roetgenol 1980; 134:585–587.
4. Musante F, Derchi LE, Bonati P. CT cholangiography in suspected Caroli's disease. J Comput Assist Tomogr 1982; 6:482–485.
5. Sorensen KW, Glazer GM, Francis IR. Diagnosis of cystic ectasia of intrahepatic bile ducts by computed tomography. J Comput Assist Tomogr 1982; 6:486–489.
6. Dayton MT, Longmire WP Jr, Tompkins RK. Caroli's disease: a premalignant condition? Am J Surg 1983; 145:41–48.
7. Pridgen JE Jr, Aust JB, McInnis WD. Primary intrahepatic gallstones. Arch Surg 1977; 112:1037–1043.
8. Simi M, Loriga P, Basoli A, et al. Intrahepatic lithiasis: study of thirty-six cases and review of the literature. Am J Surg 1979; 137:317–322.
9. Sato T, Suzuki N, Takahashi W, Uematsu I. Surgical management of intrahepatic gallstones. Ann Surg 1980; 192:28–32.
10. Schrumpf E, Bergan A, Blomhoff JP, et al. Partial hepatectomy in Caroli's disease. Scand J Gastroenterol 1981; 16:581–586.
11. Vallent K, Vadon G, Szebeni A, et al. Mit hepato-lobektomie operierter fall einer congenitalen, cystischen, intrahepatischen gallengangserweiterung (Caroli-Syndrom). Chirurg 1982; 53:131–136.
12. Adson MA, Nagorney DM. Hepatic resection for intrahepatic ductal stones. Arch Surg 1982; 117:611–616.
13. Caroli J. Disease of the intrahepatic biliary tree. Clin Gastroenterol 1973; 2:147–161.
14. Glenn F, Moody FG. Intrahepatic calculi. Ann Surg 1961; 153:711–724.
15. Longmire WP Jr, Mandiola SA, Gordon HE. Congenital cystic disease of the liver and biliary system. Ann Surg 1971; 174:711–726.
16. Nagase M, Hikasa Y, Soloway RD, et al. Gallstones in Western Japan: factors affecting the prevalence of intrahepatic gallstones. Gastroenterology 1980; 78:684–690.
17. Chaudhuri PK, Chaudhuri B, Schuler JJ, Nyhus LM. Carcinoma associated with congenital cystic dilatation of bile ducts. Arch Surg 1982; 117:1349–1351.
18. Song E, Kew MC, Grieve T, et al. Primary squamous cell carcinoma of the liver occurring in association with hepatolithiasis. Cancer 1984; 53:542–546.