The Role of Surgery in Caroli’s Disease

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BACKGROUND: Caroli’s disease is a rare congenital disorder characterized by multifocal segmental dilation of the intrahepatic bile ducts. Whether conservative or surgical strategies should be preferred is still a matter of debate. The aim of this study was to evaluate the role of surgery in the management of Caroli’s disease.

STUDY DESIGN: From April 1998 until August 2005, 12 consecutive patients with Caroli’s disease were treated in the Department of General, Visceral, and Transplantation Surgery, University Hospital Essen, Germany. All patients were intended to receive liver resections or liver transplantsations.

RESULTS: There were seven men and five women, with a median age of 39 years (range 7 months to 70 years). Eight patients had monolobar and four patients had bilobar liver involvement. All patients had a history of recurrent cholangitis, with up to 16 unsuccessful conservative treatment attempts. Nine patients (75%) underwent liver resection and two (17%) had liver transplantation. Intraoperatively, three patients (25%) were found to have cholangiocarcinoma, of which one was unresectable. There was no mortality and only low morbidity (16%) postoperatively. After a median followup of 31 months, 11 patients are well with no recurrent symptoms.

CONCLUSIONS: Surgery can offer a definite therapy, with an acceptable morbidity and virtually no mortality in localized Caroli’s disease. In diffuse disease, the use of extended resections or liver transplantation can provide good longterm results. (J Am Coll Surg 2006;202:928–932. © 2006 by the American College of Surgeons)
association with other clinical conditions, choice of surgical technique, subsequent complications, and recurrence rates. If possible, supplementary information was obtained from referring general practitioners. Evaluation of the hepatobiliary system included ERCP, percutaneous cholangiography, ultrasonography, CT, or MRI, performed either at the referring hospital or at our institution. These imaging studies were able to delineate the localization of Caroli’s disease before the elective operation was planned. Operations were tailored to the individual patient according to their preoperative evaluations.

RESULTS

Patient data
We treated seven male and five female patients with a median age of 39 years (range 7 months to 70 years). Most patients showed symptoms starting at a median age of 28 years, with recurrent cholangitis, pain, and jaundice being the most frequent symptoms. Eleven of 12 patients had been experiencing recurrent symptoms for 1 to 29 years before surgical treatment. The distribution of Caroli’s disease was bilobar in four patients and monolobar in eight. In patients with monolobar disease, only the left lobe was affected. Two patients presented with associated CHF (Table 1).

Interventional and conservative treatment
Between 2 and 16 ERCP interventions were performed per patient. Additional treatment interventions included papillotomy in six patients, stone extraction in four, stenting in two, and extracorporeal shock wave lithotripsy in two patients. All patients received antibiotic treatment over a prolonged period of time; five patients received it for 1.5 to 2 years (Table 1).

Indications for surgery
Indications for resection were failure of conservative treatment, suspected malignancy, or symptoms associated with CHF. Eleven patients presented with recurrent cholangitis, nine with pain, and seven with episodes of jaundice. Both patients who received a liver transplantation (LT) had associated CHF and recurrent cholangitis. In the adult patient, the periportal fibrosis was associated with recurrent gastrointestinal bleeding.

Surgical treatment
Operations were tailored to the individual patient according to our preoperative evaluation and are outlined in Table 2. Three patients (25%) received a left lateral sectionectomy (segments II/III) and four (33%) a left hepatectomy (segments II/III/IV). One patient (8%) underwent a left hepatectomy including segments I to IV and another had a multisectionectomy with resection of segments II, III, IVa, and VII (Fig. 1). One patient (8%) was found to have unresectable, bilateral cholangiocellular carcinoma (CCC) at the time of operation (Fig. 2). Two patients (16%) who received a left hepatectomy were found to have an incidental CCC. All patients (n=5, 41%) in whom a bile duct revision or exploration was necessary received a T-tube for decompression of the bile duct. Two patients (17%) underwent LT. One of them was a child, who received a living donor liver transplantation (LDLT) from his mother.
Morbidity/mortality
Postoperative complications occurred in one patient (8%) who had a biliary leak that was treated conservatively and required no reintervention, a pleural effusion, and a pneumothorax from a central intravenous line. One patient suffered from a minor wound infection. There was no postoperative mortality (Table 2).

Followup
Overall median followup was 31 months. Eleven patients (92%) are currently alive. The patient with unresectable CCC died 5 months after diagnosis. Two patients (17%) had an incidental CCC in the resected specimen (pT1NxMX, R0 and pT2NxMx, R0) and are currently well 6 and 11 months, respectively, after the operation. Postoperative staging revealed no distant metastases. Comparing pre- and postoperative symptoms, none of the patients experienced additional episodes of cholangitis, pain, or jaundice. No patients showed disease recurrence in the remnant liver (Table 2).

DISCUSSION
Optimal management of patients with Caroli’s disease is still a matter of debate because time and severity of onset seem to vary tremendously. Because of the disease’s rarity and rather unspecific symptoms, diagnosis is often delayed, but the medical history in our patients showed that nearly all of them had been experiencing Caroli’s symptoms for a long time (1 to 29 years).

It is probably safe to state that patients with symptomatic Caroli’s disease should first undergo a conservative or interventional attempt, as shown by our own data, in which almost all patients were treated conservatively. Ross and associates' treated 12 patients with ursodeoxycholic acid and reached dissolution and sustained clinical remission in all of them. Caroli-Bosc and
coworkers\textsuperscript{8} reported complete stone removal with no morbidity or mortality in 100% of their six patients treated with ERCP. On the other hand, there is clear evidence that some patients do not benefit from sole conservative or interventional treatment options. Recurrent cholangitis may evolve into hepatic abscesses, septicaemia, secondary biliary cirrhosis, portal hypertension, variceal bleeding, and hepatic failure.\textsuperscript{9,10} Benhidjeb and coworkers\textsuperscript{11} reported a late mortality rate of 23.5\% in 4 of 17 patients in whom a resection could not be performed. Despite achieving better results in removing intrahepatic stones,\textsuperscript{12,13} internal biliary drainage operations either with or without hepatic resection have morbidity. In a study by Dagli and colleagues,\textsuperscript{14} 5 of 10 patients with internal drainage required additional procedures and had ongoing sepsis.

Additionally, Caroli’s disease poses another life-threatening problem: it has a relatively high incidence of intrahepatic malignant tumors. Dayton and associates\textsuperscript{5} showed that of all 142 patients reported in the literature, malignancies of the liver or biliary tract developed in 10 (7\%). Other authors have found CCC in 11\% to 14\% of patients, suggesting that the risk of malignant tumors developing is 100 times greater than that of the general population.\textsuperscript{15,16} In our own study, CCC developed in three patients (25\%) on the basis of Caroli’s disease (Fig. 2), even though we cannot deny the possibility of a bias in our series because all patients were referred after other treatment strategies failed. Several hypotheses have been postulated as to the etiology of this malignant transformation. One of them suggests that the bile fluid itself could be carcinogenic, or that bile stasis could induce neoplastic changes in the cysts. This hypothesis is supported by the rather low incidence of malignancy in liver cysts, which do not contain bile fluids.\textsuperscript{17} Another theory states that congenital malformation per se may be responsible for the predisposition to malignant transformation, because even after internal drainage operations, CCC can develop in the remaining cysts.\textsuperscript{18,19} Last but not least, chronic inflammation has long been suggested to have premalignant potential.\textsuperscript{20}

We cannot confirm that malignancy develops only in patients with long lasting, insufficiently treated Caroli’s disease. Although one patient did have Caroli’s symptoms for more than 2 decades, the one patient with unresectable CCC had Caroli’s disease for only 2 years and the other had been diagnosed 2 months before. Maybe there are subgroups of Caroli’s disease that have a more aggressive malignant transformation potential, which cannot be identified purely on the clinical symptoms.

Despite the proved association between Caroli’s disease and malignant intrahepatic tumors, the unpredictable onset of development, as seen in our series, makes it difficult to advocate prophylactic surgery.

Notwithstanding, it seems more than justified to advocate a rather aggressive surgical strategy in symptomatic patients who have had several futile conservative treatment attempts. In patients with Caroli’s disease confined to one lobe, this can be achieved by a hemihepatectomy, left or right, with low morbidity and virtual no mortality. So far, there has been no report of malignant tumors arising after surgical resection.

In contrast, diffuse Caroli’s disease is still difficult to manage. Despite the advances in medical and endoscopic treatment options, they are seldom able to guarantee permanent recovery from symptoms of Caroli’s disease. Depending on the biologic age and health status of these patients, only an extended resection might be able to remove all stones and cysts. In our own study, one of the patients (8\%) needed a multisectionectomy (Fig. 1) to remove all diseased liver parenchyma. Such treatment resulted in complete and long lasting relief of symptoms, which could also be confirmed by others.\textsuperscript{4,10,21} For patients with diffuse involvement of both liver lobes in association with cirrhosis, or for those with symptoms of associated hepatic fibrosis, LT has been successful.\textsuperscript{22,23}

Asymptomatic patients in whom there is no indication for liver resection or transplantation should at least be followed up regularly on an outpatient basis to detect any kind of deterioration or malignant transformation as early as possible.

In summary, our policy on the basis of our own series favors a rather aggressive treatment that includes hepatic resection when the disease is confined to one lobe. Patients with diffuse involvement are difficult to manage, but the possibility of an extended resection or multisegmentectomy has to be considered. Despite the unpredictable right timing, and exposing otherwise fairly healthy individuals to the risk of transplantation and their associated consequences, LT or living donor liver transplantation is the ultimate treatment option for patients with Caroli’s disease complicated by recurrent cholangitis, not amenable to conservative treatment and early sclerosing cholangitis or biliary cirrhosis.
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REFERENCES