Transpl Int (1997) 10: 241–244

BRIEF REPORT

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Liver transplantation in patients with Caroli's disease and recurrent cholangitis

Received: 16 July 1996
Received after revision: 4 February 1997
Accepted: 5 February 1997

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Abstract Caroli's disease is an uncommon congenital disorder of the intrahepatic biliary tree. It is characterized by multiple and segmental dilatations of the bile ducts. The clinical course of Caroli's disease is often complicated by recurrent episodes of bacterial cholangitis that seriously impair the patient's quality of life. Despite wide spectrum antimicrobial agents, medical treatment of cholangitis is frequently unsuccessful in patients with Caroli's disease due to the persistence of bacteria in dilatated bile ducts. Other therapies, including internal or external biliary drainages and various surgical or endoscopic procedures, have been used in the treatment of Caroli's disease, with poor results. There are no previous reports in the literature of liver transplantation for recurrent cholangitis in patients with Caroli's disease. We present two such cases, in which cholangitis is resolved.

Key words Liver transplantation, Caroli's disease · Caroli's disease, liver transplantation · Cholangitis, Caroli's disease, liver transplantation

Introduction

Caroli's disease is a rare congenital disorder of the intrahepatic biliary tree characterized by multiple, saccular, segmental cystic dilatations of the bile ducts that are joined with the remainder of the biliary drainage system [3, 4]. Patients with this disease usually present with abdominal pain and fever due to acute bacterial cholangitis, intrahepatic lithiasis and liver abscesses in early childhood. Development of recurrent bacterial cholangitis, despite antibiotic treatment, is frequent and seriously impairs the quality of life of the patient. Treatment of Caroli's disease is difficult and depends on the location and extent of the disease. The administration of ursodeoxycholic acid and various surgical procedures, including external biliary drainages, internal drainages with biliodigestive anastomoses, sphyncterotomies and hepatic resections, are effective in only some patients [3, 7, 10, 12–19, 24, 26, 27].

We present, to the best of our knowledge, the first two cases of orthotopic liver transplantation (OLT) for recurrent bacterial cholangitis in patients with Caroli's disease.

Case reports

Patient no. 1

A 62-year-old woman was diagnosed as having Caroli's disease in 1988 after her first cholangitis episode. The diagnosis was based on ultrasonography and computerized tomography findings, which showed widespread cystic dilatation of the intrahepatic bile ducts with intrahepatic lithiasis (Fig. 1). A few days later, a Roux-en-Y hepaticojejunostomy was performed. During the 18 months fol-

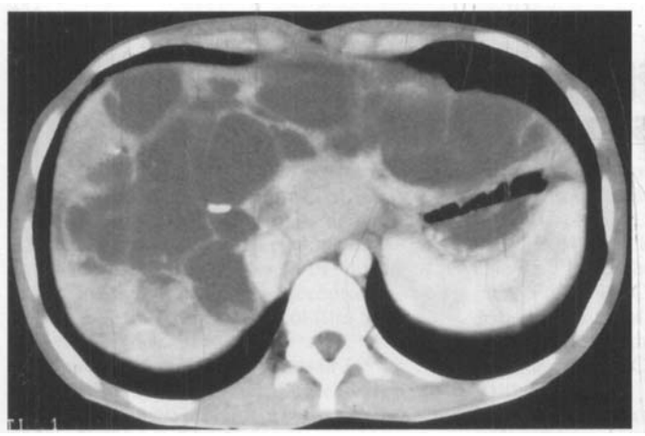

Fig. 1 Abdominal computerized tomography in patient 1. Liver cystic dilatations are shown as large hypodense areas that contain several intrahepatic lithiases appearing as hyperdense nodules

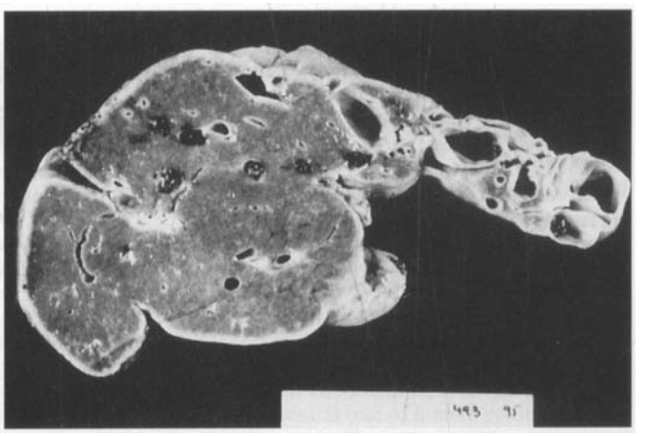

Fig. 2 Section of the explanted liver from patient 2. Several biliary dilatations are present in both hepatic lobes. Most of these cavities are filled with dark matter, consisting mainly of pigmentary lithiases

lowing surgery, the patient presented with recurrent episodes of cholangitis, despite treatment with various antibiotic regimes including amoxicillin-clavulanic acid, second- and third-generation cephalosporins, piperacillin, amikacin, and ciprofloxacin. The association of imipenem-cilastatin and aztreonam only obtained a slight, temporary improvement in the symptoms in the 3 months prior to OLT.

The patient underwent OLT on 23 February 1990 because of the recurrent and uncontrollable bacterial cholangitis. The explanted liver was enlarged, had an irregular surface, and showed several cystic biliary dilatations of up to 4 cm in diameter in the section. Most of these dilatations contained purulent material and lithiasis. The immunosuppressive regime after OLT consisted of steroids, azathioprine, and cyclosporin. The surgical procedure and early postoperative course were uncomplicated, and the patient was discharged 4 weeks after the operation. Biopsy-proven acute liver rejection was diagnosed 18 months after OLT. Pulse therapy with methylprednisolone was given, and rapid clinical improvement and normalization of the liver function tests followed. Five months later, an increase in serum transaminase levels was detected, and a second liver biopsy showed changes suggesting chronic hepatitis. A test for antibodies against hepatitis C virus was positive. At her last check-up in June 1995, the patient was still in excellent general condition. The laboratory tests showed only a slight increase in the serum aspartate and alanine aminotransferase levels. There has no been evidence of biliary infection since OLT.

Patient no. 2

A 21-year-old man underwent OLT for Caroli's disease and recurrent bacterial cholangitis on 13 January 1995. His medical history revealed that he had presented with intermittent abdominal pain since childhood. In 1981, an exploratory laparotomy showed nodular hepatomegaly with cysts on the liver surface. Polycystic liver disease was diagnosed, and symptomatic treatment was prescribed. The patient was admitted to another hospital in 1992 because of new episodes of abdominal pain. Abdominal ultrasonography and computerized tomography showed diffuse, cystic dilatation of the intrahepatic biliary tree with intracystic calcifications. This led to the diagnosis of Caroli's disease. In July 1994, the patient was readmitted due to an episode of acute bacterial cholangitis. In the following months, continued therapy with ursodeoxycholic acid and several antibiotic associations, including ofloxacin, cefixime, clindamycin, and piperacillin-tazobactam, were unable to control the recurrent cholangitic episodes until OLT was performed.

The explanted liver was enlarged, weighed 2550 g and had a nodular surface. The section showed multiple biliary dilatations forming cavities of various sizes in both lobes. Pigmentary lithiasis were observed in some of these cavities (Fig. 2). The patient received steroids, azathioprine, and cyclosporin as immunosuppressive drugs. On the 9th postoperative day, the patient developed a wound infection. *Enterococcus faecalis* and *Klebsiella pneumoniae* grew in the wound secretion cultures. He was treated with piperacillin-tazobactam for 10 days and responded well. Acute graft rejection developed in the 3rd postoperative week. There was a favorable response to methylprednisolone pulse therapy. The patient was discharged on day 26. Eight months after OLT, the patient remains asymptomatic with normal liver function.

Discussion

Bacterial cholangitis is the most frequent and life-threatening complication of Caroli's disease [2]. It is usually caused by Gram-negative bacilli and has a recurrent course [2, 13, 15, 21, 23]. Episodes of cholangitis may appear spontaneously in these patients, but have also been described following invasive diagnostic and therapeutic procedures involving the biliary tree, such as endoscopic or intraoperative cholangiography, cholecystectomy, choledocotomy, T-tube drainage, and biliointestinal anastomoses [2, 5, 7, 9]. Therefore, since the diagnosis of Caroli's disease can easily be established by confirming the presence of intrahepatic bile duct dilatations and lithiasis with computed tomography and ultrasonography [3, 8, 11], endoscopic retrograde cholangiography is superfluous and it should not be done for these patients to ensure that the risk of biliary sepsis is avoided.

Medical treatment of bacterial cholangitis in patients with Caroli's disease is extremely difficult because bile duct dilatations and lithiasis favor bacterial persistence after the initial biliary tree colonization. Wide spectrum antimicrobial agents, including modern beta-lactam antibiotics, aminoglycosides, and quinolones have been used in treatment of these patients, with improvement of the symptomatology. This improvement, however, is usually temporary and closely associated with a continuous administration of parenteral antibiotics. The recurrence of cholangitis is the rule after the suppression of this therapy and, consequently, these patients require frequent hospital readmissions for the treatment of recurrent cholangitis episodes. In the two cases presented here, intensive intravenous antibiotic therapy was given during the episodes of cholangitis, and was followed by oral quinolones as maintenance treatment. Despite this therapeutic approach, both patients presented recurrent cholangitis episodes during 6 and 18 months, respectively, with the necessity of frequent readmissions. This, of course seriously impaired the quality of their lives until OLT was performed.

External biliary drainage has been reported to be successful in some patients with Caroli's disease and recurrent cholangitis [19]. Internal biliary drainage, especially choledocojejunostomy, has been the most common surgical treatment for the diffuse forms of Caroli's disease, although these surgical procedures often result in incomplete drainage of the biliary tree and a very high morbidity [6, 21]. Hepatic resection has been successfully performed in localized or monolobar forms [10, 15–17]. According to the results obtained in the majority of studies, the surgical treatment of Caroli's disease should be restricted to selected patients. The risk of cholangitic episodes after surgery, which is specially high in patients with choledochal cysts, should be taken into account [26]. As an example of this risk, our case 1 developed her first cholangitis episode a few days after having undergone a Roux-en-Y hepaticojejunostomy.

Intracystic pigment stones are frequently found in patients with Caroli's disease, and abdominal pain, cholestasis, and acute pancreatitis associated with stone migration into the common bile duct have been described [3, 20]. Although surgical or endoscopic sphincterotomy may facilitate the extraction of these stones, these procedures may increase the frequency and severity of cholangitic episodes and, consequently, are not recommended for these patients [2, 7, 26].

Due to the poor results of both medical and surgical therapies for patients with diffuse forms of Caroli's disease and recurrent bacterial cholangitis, OLT has been suggested by several authors as a possible treatment [2, 9, 16, 21]. However, to the best of our knowledge, no specific cases have been reported yet. In fact, there are very few reports of OLT in patients with Caroli's disease in the literature in which OLT was performed because of the development of either cholangiocarcinoma [1] or severe portal hypertension secondary to congenital hepatic fibrosis, a condition frequently associated with Caroli's disease [25].

The good postoperative courses of the two cases reported here indicate that OLT is a feasible option in the treatment of patients with a diffuse form of Caroli's disease complicated by recurrent bacterial cholangitis when other medical treatment has been ineffective. Furthermore, OLT may also avoid the development of cholangiocarcinoma, a complication that has been reported in around 7 % of patients with Caroli's disease [6, 13, 22].

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