Liver Transplantation for Caroli Disease

M. Zahmatkeshan*[1], A. Bahador[2], B. Geramizade[3], V. Emadmarvasti[1], S. A. Malekhosseini[2]

[1]*Department of pediatrics, school of medicine, Shiraz University of Medical Sciences, Shiraz, Iran.*
[2]*Department of organ transplantation, school of medicine, Shiraz University of Medical Sciences, Shiraz, Iran.*
[3]*Department of pathology, school of medicine, Shiraz University of Medical Sciences, Shiraz, Iran*

ABSTRACT

Caroli disease is a rare congenital disorder characterized by multifocal, segmental dilatation of intrahepatic bile ducts. Patients with Caroli disease who have recurrent bouts of biliary infection, particularly those who also have complications related to portal hypertension may require liver transplantation. In liver transplant ward of Shiraz University of Medical Science we had 4 patients with Caroli disease who were transplanted. Herein, we describe the demographic characteristics and post-transplant course of the patients.

These patients presented with liver failure, recurrent cholangitis and portal hypertension sequelae unresponsive to medical treatment. The mean age of patients was 24.5 (range: 18–36) years, the mean MELD score was 17.5 (range: 11–23), three patients were female; one was male. All of the patients had good post-transplantation course except for one patient who developed post-operative biliary stricture for whom biliary reconstruction was done.

KEYWORDS: Caroli Disease; Transplantation; Bile Ducts, Intrahepatic; Hypertension, Portal; liver failure; Cholangitis

INTRODUCTION

First described by Jacques Caroli in 1958, Caroli disease is a rare congenital condition characterized by non-obstructive saccular or multifocal segmental dilatation of the intrahepatic bile ducts [1]. The complex form of Caroli disease, the so-called "Caroli syndrome," is associated with congenital hepatic fibrosis and is less common than Caroli disease [2].

The clinical features of Caroli syndrome include bouts of cholangitis, hepatolithiasis, gallbladder stone and portal hypertension [3]. Caroli syndrome can be complicated by hepatic abscess and cholangiocarcinoma. Medical treatment of Caroli syndrome is antibiotic therapy for attacks of acute cholangitis. If the process of Caroli disease is confined to one lobe, lobectomy completely relieves the symptoms, but in diffuse forms of the disease, liver transplantation represents the only curative treatment. In case of current cholangitis, malignancy should be prevented by early liver transplantation [4,5]. Caroli disease is not a common cause of liver transplantation in many liver transplantation centers. UNOS data showed 104 patients with Caroli disease transplanted between 1987 and 2006.

*Correspondence: Mozhgan Zahmatkeshan, Department of pediatrics, school of medicine, Shiraz University of Medical Sciences, Shiraz, Iran.
Tel: +98-711-647-4298
Fax: +98-711-647-4298
E-mail: zahmatm@sums.ac.ir

Table 1: Caroli disease patients history and hospital course

Case	Description
1	An 18-y/o female who presented with pruritus and jaundice from 2 years before. Her LFT showed high alkaline phosphatase, direct hyperbilirubinemia and high gamma glutamyl transpeptidase (GGT). Patient had 2 episodes of cholangitis. Abdominal sonography showed intrahepatic cystic anechoic areas. CT of hepatobiliary system localized intrahepatic cysts. Pruritus was intractable to medical treatments. Patients scheduled for living donor liver transplantation with MELD score of 19. Patient had good post-operative course without any complications.
2	A 36-y/o female presented with repeated attacks of fever, jaundice and clay color stool, was treated as cholangitis. Her abdominal CT was in favor of Caroli disease with multiple hepatic cystic lesions. The patient had a MELD score of 11 and underwent liver transplantation from cadaver. The patient developed high grade fever, abdominal pain and jaundice 3 weeks after transplantation. Abdominal sonography and CT showed hepatic abscess which was treated with percutaneous drainage and iv antibiotics.
3	A 24-y/o male referred because repeated GI bleeding, pruritus and gall stone. Patient's liver sonography and CT was inconclusive so MRCP was done which was in favor of Caroli,s disease. Patient had MELD score of 17 and underwent liver transplantation from cadaver.
4	A 20-y/o female presented with pruritus, jaundice, and repeated attacks of GI bleeding. Her sonography showed increase in liver parenchymal echogenesity and multiple cystic lesions, hepatobiliary CT was in favor of Caroli disease. Patient had evidence of chronic liver disease and a MELD score of 23. The patient underwent liver transplantation from cadaver liver. Explanted liver from all of these patients showed diagnosis of Caroli disease due to multiple biliary ductular dilatations.

The objective of the present study was to assess the demographic characteristics and post-operative course of patients with Caroli disease who underwent liver transplantation in Shiraz University of Medical Sciences transplantation ward.

MATERIALS AND METHODS

During a period of 15 years from 1995 to 2010, 943 liver transplantation were done in our center. A retrospective study was performed on all liver transplantation patients who had undergone operation from 1995 to 2010 to find the cases of Caroli disease. Among the patients we found four who had Caroli disease; they were evaluated for the complications of Caroli disease. After routine laboratory investigations, abdominal sonography and abdominal computed tomography were performed to assess the evidence of hepatobiliary anatomic abnormalities. In cases that the final diagnosis of Caroli disease was not approved by the above investigations, magnetic resonance cholangiopancreatography (MRCP) was performed. All patients were followed two to four years after liver transplantation.

RESULTS

The prevalence of Caroli disease in our liver transplant recipients was 0.44% (4/900 patients). Among these four patients, three were female.

The patients had a mean±SD age of 24.5±4.3 (range: 16–36) years. Clinical findings are summarized in Table 1. The clinical manifestations were different including pruritus, jaundice, recurrent cholangitis, repeated gastrointestinal bleeding and gall stone.

Three patients had radiologic evidence of Caroli disease in sonography and computed tomography of liver; in the 4th patient the diagnosis was confirmed by MRCP. The sever-

ity of liver disease among these patients were assessed by MELD score; the score varied from 11 to 23 (mean = 17.5). All patients had diffuse form of Caroli disease with portal hypertension (Caroli syndrome). All patients received intravenous methylprednisolone for the first three post-operative days that changed to prednisolone (0.5 mg/kg/d), tacrolimus (0.15 mg/kg/d) and mycophenolate mofetil (20 mg/kg/d) from the fourth post-operative day. Prednisolone was tapered and discontinued during the first six months of transplantation.

During post-operative course, one patient developed liver abscess which was treated with percutaneous drainage and antibiotics (imipenem 500 mg iv, q6h for 2 weeks followed by oral therapy for a total of 6 weeks and vancomycin 1 g iv, q6h for 2 weeks).

Explanted liver pathology documented the diagnosis of Caroli disease with no evidence of malignant transformation. After four years of follow-up, all patients were alive and healthy.

DISCUSSION

Caroli disease is a rare congenital condition. It is an autosomal recessive disease, although autosomal dominant mode of inheritance has been reported [6,7]. Although drainage procedures with ERCP or PTC and sphincterotomy can aid biliary drainage and stone removal, radiological, endoscopical and surgical biliary drainage techniques are palliative treatments leading to temporarily bile drainage. It is necessary to consider that repeated palliative treatments could result in persistence of the symptoms and increase the risk of malignant transformation (cholangiocarcinoma) and should reasonably be avoided [4,8,9]. Liver transplantation represents the only curative treatment for the symptomatic Caroli disease. However, when cholangitis occurs, a large number of patients die within 5–10 years [8].

In our study, all patients with Caroli disease were selected and scheduled for liver transplantation early after the attack of cholangitis, so the patients tolerated the surgical intervention well and their post-transplantation course was uneventful. In three patients liver were cirrhotic; the high MELD score recorded were indicative of need for transplantation. However, in the fourth patient who had a low MELD score, repeated attacks of cholangitis was the indication for transplantation.

In conclusion, according to our experience, although Caroli disease is rare, since there is no cure for the disease, liver transplantation must be done early in the course of cholangitis [10,11] to reduce the risk of malignancy. All four patients reported were diagnosed as Caroli disease during recent years which may be due to possible misdiagnosis of former cases.

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