Monolobar Caroli's Disease: Report of Two Cases within a Family

Min-Chieh Shieh, Ching-Chung Chiang, Chi-Wen Tu, Chao-Ming Shih, Chi-Szu Liao, Chen-Hsien Su

Caroli's disease is a congenital disorder characterized by segmental communicating saccular dilatation of larger intrahepatic bile ducts. This malformation may occur in association with autosomal dominant or recessive polycystic kidney disease of varying severity. This study reports the successful management of two cases with monolobar Caroli's disease within a family by partial hepatic resection. Case one was a 74 year-old female, who had a known diagnosis of autosomal dominant polycystic kidney disease, and clinically manifested repeated episodes of bacterial cholangitis and septicemia. Abdominal computed tomography and magnetic resonance cholangiopancreatography confirmed the presence of saccular dilatation of intrahepatic bile ducts confined to the left lobe, hepatolithiasis and choledocholithiasis. Case two was a 43 year-old male, who was the son of case one, had autosomal dominant polycystic kidney disease, and clinically manifested acute bacterial cholangitis. Abdominal computed tomography demonstrated the presence of dilated left intrahepatic bile ducts, hepatolithiasis and choledocholithiasis. Both patients underwent cholecystectomy, choledocholithotomy and left lateral segmentectomy and the post-operative recovery was uneventful in both cases. There was no recurrence of cholangitis during a 14-month and a four-month follow-up, respectively. The diagnosis of Caroli's disease was established by imaging studies. Magnetic resonance cholangiopancreatography is preferred and it could provide a noninvasive, safe and accurate diagnosis of Caroli's disease. Partial hepatic resection may be curative in patients with Caroli's disease confined to a single lobe or segment of the liver.

Key words: Caroli's disease, autosomal dominant polycystic kidney disease, hepatic resection

Caroli's disease is a rare congenital disorder characterized by segmental communicating saccular dilatation of larger intrahepatic bile ducts. This malformation may occur in association with either renal cystic disease of varying severity or congenital hepatic fibrosis.[1,2] When it is associated with congenital hepatic fibrosis, it is named Caroli's syndrome. Both Caroli's disease and Caroli's syndrome have been described in the same family. In cases, Caroli's disease is transmitted in an autosomal recessive inheritance and is associated with autosomal recessive polycystic kidney disease (ARPKD).[1] Rare cases associated with autosomal dominant polycystic kidney disease (ADPKD) have been reported.[3] Caroli's disease may be multifocal and diffuse, or localized to a single lobe or segment of the liver. In the diffuse type, saccular dilatation of the segmental bile ducts affects the whole intrahepatic biliary tree, and in the localized type, they are often

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confined to the left lobe. This study reports the successful management of two cases with monolobar Caroli's disease within a family by partial hepatic resection.

Case Reports

Case 1

A 74 year-old female was hospitalized with symptoms of right upper quadrant abdominal pain and fever for three days. She had a known diagnosis of autosomal dominant bilateral polycystic kidney disease and underwent right nephrectomy, complicated by end-stage renal failure, hypertension and anemia. Tracing back her family history, familial clustering of autosomal dominant polycystic kidney disease was found in the kindred (Fig 1). In the past three years, three episodes of acute cholangitis and Escherichia coli septicemia occurred, clinically manifested with fever, chills and right upper quadrant abdominal pain without generalized jaundice. The physical examination was unremarkable except for mild right upper quadrant abdominal tenderness. Abdominal sonography showed gallstones, common bile duct (CBD) and left intrahepatic duct (IHD) dilatation. Contrast-enhanced abdominal computed tomography (CT) revealed CBD and left IHD dilatation with multiple stones in situ and multiple irregular cysts in the left kidney (Fig 2). Magnetic resonance cholangiopancreatography (MRCP) demonstrated saccular cystic dilatation of IHD mainly confined to the left lateral segment (Fig 3). Monolobar Caroli's disease was established from the above imaging studies.

The patient underwent elective cholecystectomy, choledocholithotomy with T-tube drainage and left lateral segmentectomy because of repeated episodes of acute bacterial cholangitis. The saccular dilated IHD was predominantly limited to the left lateral segment and in continuity with the rest of the biliary tract. Multiple bilirubinated stones were removed from the gallbladder, CBD and left IHD. The choledochoscopic examination did not reveal any residual stone. The post-operative recovery was uneventful and the patient was discharged on the 13th post-operative day. No recurrence of cholangitis was found during a four-month follow-up.

Irregular saccular dilatation of the IHD was disclosed on gross examination of the left lateral segment of the liver (Fig 4). Microscopically, the bile ducts showed neutrophil infiltration, periductal fibrosis and were compatible with the typical features of acute cholangitis. No hepatic fibrosis or malignant cells were found.

Case 2

A 43-year-old male, the only son of case one, was admitted because of high fever (body temperature 39 °C) and persistent right upper quadrant abdominal pain for two days. He had a known diagnosis of autosomal

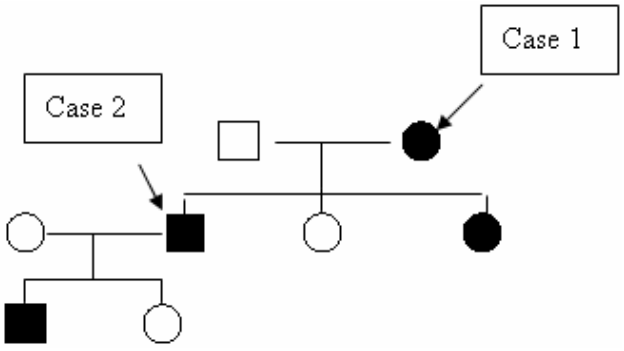

Fig 1. Pedigree showing familial clustering of autosomal dominant polycystic kidney disease in the kindred.

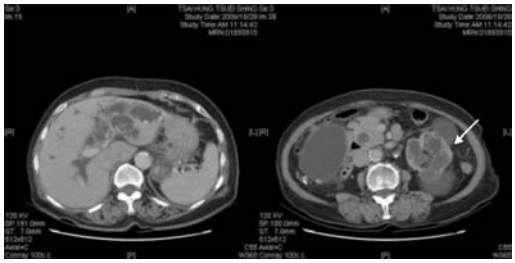

Fig 2. Contrast-enhanced abdominal CT showing left IHD dilatation with multiple stones in situ and multiple irregular cysts in the left kidney (arrow).

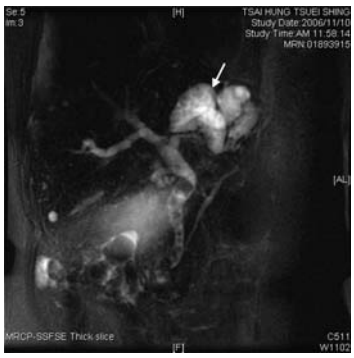

Fig 3. MRCP showing the saccular cystic dilatation of IHD limited to the left lateral segment (arrow) and multiple CBD and IHD stones in situ.

dominant bilateral polycystic kidney disease two years previously. Abdominal examination was unremarkable except for mild right upper quadrant tenderness and yellowish scleras. Laboratory data showed leukocytosis (17,260 cells/mm^3) with left shift (band form neutrophils 1%, segmented neutrophils 95%). Biochemical tests revealed hyperbilirubinemia (total bilirubin 3.15 mg/dl, direct bilirubin 2.1 mg/dl). Abdominal sonography demonstrated gallstones, and a dilated CBD and left IHD. Abdominal CT confirmed the presence of multiple stones in the CBD and left IHD and multiple irregular cysts in both kidneys (Fig 5).

The patient underwent emergent cholecystectomy, choledocholithotomy with T-tube drainage and left lateral segmentectomy because of acute cholangitis. The saccular segmental dilated IHD was limited to the left lateral segment and in continuity with the rest of the biliary tract. Multiple bilirubinated stones were removed from the CBD and left IHD. Intra-operative choledochoscopy demonstrated no residual stones. The post-operative recovery was smooth and he was discharged on the 12th post-operative day. There was no recurrence of cholangitis during a 14-month follow-up.

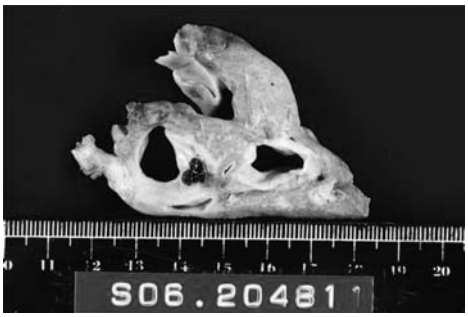

Fig 4. Gross examination of the resected liver showing the presence of cystic segmental dilatation of left intrahepatic bile ducts.

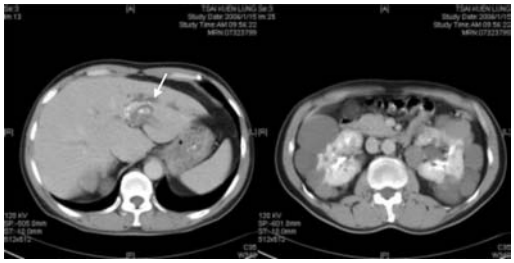

Fig 5. Abdominal CT showing left IHD dilatation with stones in situ (arrow) and multiple irregular cysts.

Discussion

Caroli's disease was first described in 1958 by Jacques Caroli, who identified the "pure form," or isolated congenital dilatation of the intrahepatic ducts (Type I or Caroli's disease), and a second form, associated with congenital hepatic fibrosis (Type II or Caroli's syndrome). Since then, most information regarding Caroli's disease has been derived from case reports and small series, and about 200 cases were reported in the English literature up to 2004.[4] The pathogenesis of Caroli's disease is incompletely understood, but it appears to be related to an arrest or derangement in remodeling of the ductal plate of the larger intrahepatic bile ducts during embryogenesis with resultant destructive inflammation and segmental dilatation.[5] Occasional familial clustering suggests that some cases are inherited, especially when occurring together with polycystic kidney disease.[6] Both cases in this study have a past history of ADPKD. Two mutated genes identified in ADPKD are called polycystic kidney disease 1 (PKD1) and polycystic kidney disease 2 (PKD2), which have been mapped to chromosome 16p13.3 and chromosome 4q21-22.[7] PKD1 gene mutations account for 85% of the cases and most of the remainder are due to change of the PKD2 gene. Proteins encoded by the PKD1 and PKD2 genes are named polycystin-1 and polycystin-2. To date, it is known that they interact as part of a multiprotein membrane-spanning complex involved in cell-cell or cell-matrix interactions, intracellular signal reception and transduction in processes such as proliferation or apoptosis.[7, 8] Mutations of PKD1 or PKD2 genes give rise to functionally deficient proteins that alert the above-mentioned processes. This leads to uncontrolled cell proliferation, enhanced transepithelial fluid secretion and interstitial fibrosis. Polycystin-1 is highly expressed in the fetal kidney and liver including the biliary system and is likely involved in the embryogenesis of these organs.[8] It is strongly speculative to postulate that overexpression of polycystin may account for the abnormal overgrowth of biliary epithelium and segmental dilatation of the intrahepatic bile ducts which are characteristic in Caroli's disease.[3, 8]

The clinical manifestations of Caroli's disease or Caroli's syndrome are related to the biliary abnormalities and portal hypertension or poor hepatic reserve from congenital hepatic fibrosis. In both Caroli's disease and Caroli's syndrome, the saccular dilatation of the bile

ducts predisposes to stagnation of bile leading to the formation of biliary sludge, hepatolithiasis, choledocholithiasis and gallstones. Bacterial cholangitis occurs frequently and may be complicated by repeated bouts of septicemia and hepatic abscess formation.[9] Patients with Caroli's syndrome can present with portal hypertension and its sequelae, such as ascites or esophageal variceal hemorrhage and may progress to end-stage hepatic failure. The symptoms of Caroli's disease may occur at any age, and the disease can be discovered even as late as in the forth to seventh decades of life.[10] Both cases in this study presented their symptoms as acute bacterial cholangitis because of intraductal lithiasis at the ages of 74 and 43, respectively.

The definitive diagnosis of Caroli's disease is based on the confirmation of the communications between the irregular saccular dilatation of IHD and the rest of biliary tract by imaging studies.[11] Several imaging modalities have been used, including ultrasound, CT, percutaneous transhepatic cholangiography (PTC), endoscopic retrograde cholangiopancreatography (ERCP) and MRCP. Ultrasound and CT provide information regarding the severity, location and extent of liver involvement of Caroli's disease and may disclose accompanying abnormalities, such as cirrhosis, hepatic abscess or polycystic kidney disease. However, ultrasound and CT can not provide the critical image of communications between the dilated cystic structures and the bililary tract. Cholangiography is definitive and considered as the method of choice for an accurate diagnosis of Caroli's disease.[12] However, serious complications such as sepsis, bile leakage and bleeding, and even death may occur with both ERCP and PTC, especially during the acute episode of bacterial cholangitis.[13] MRCP could be a noninvasive, safe and accurate alternative to diagnose Caroli's disease.[14] The MRCP in case one demonstrates the typical finding of saccular cystic dilatation of IHD complicated with hepatolithiasis. The principal differential diagnosis of Caroli's disease includes recurrent pyogenic cholangitis and choledochal cyst. Obstructive biliary dilatation may initially mimic Caroli's disease; however, the biliary dilatation in mechanical obstruction is generally diffuse and tubular and lacks focal stricture formation.[15] Although the Todani classification of choledochal cysts includes Caroli's disease as a type V choledochal cyst (multiple intrahepatic cysts),[16] the current understanding of the pathogenesis of Caroli's disease (autosomal dominant or recessive inheritance and often associated with polycystic kidney disease) and choledochal cysts (congenital, noninheritable and not associated with polycystic kidney disease) makes it unlikely that these entities are related.[9] A liver biopsy is rarely required to make a diagnosis. Histologically, there is only ectasis of the larger intrahepatic ducts in Caroli's disease. An acute and chronic inflammatory cell infiltrate may be seen around the dilated bile ducts. Liver biopsy may show features of cholangitis.

The major aim of treatment is to obtain sufficient biliary drainage and relieve the symptoms. Repeated episodes of stone formation, cholangitis, and localized areas of biliary obstruction may lead to hepatic abscess and overwhelming sepsis. The saccular dilated intrahepatic bile ducts are diffuse in 60~80% of case, but may be localized in one lobe or segment of the liver, of which the left lobe is more common. Partial hepatic resection may be curative in rare patients with disease confined to a single lobe or segment.[17] Patients with diffuse disease may temporarily benefit from intraoperative removal of biliary stones and debris, surgical biliary diversion, or the placement of irrigation catheters and drains.[18] Orthotopic liver transplantation appears to be a promising treatment option in the presence of decompensated liver disease and its related severe complications in Caroli's disease.[19]

The prognosis is variable depending on the severity of disease and the presence of coexisting renal dysfunction. Recurrent infections and other complications related to biliary lithiasis can be associated with significant morbidity and mortality. Cholangiocarcinoma is a well-known late complication and its reported incidence is 7% in Caroli's disease.[20] Patients with Caroli's disease have a 100-fold greater risk of developing cholangiocarcinoma by comparison with the general population.

In summary, we report two cases of monolobar Caroli's disease within a family, and both patients were treated successfully by partial hepatic resection. Long-term follow-up is required to detect the possible development of cholangiocarcinoma.

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單葉性卡羅里氏病：同一家族兩病例報告

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卡羅里氏病是肝臟的先天性疾病，肝內膽管會出現多發性囊狀異常擴張。此種疾病常與體細胞顯性遺傳或隱性遺傳的多發性腎臟囊腫疾病合併出現。我們提出同一家族內出現兩個肝臟單葉性卡羅里氏病的案例，在接受部分肝臟切除手術後得到滿意的成果。

案例1是一位74歲女性病患，已診斷罹患體細胞顯性遺傳多發性腎臟囊腫疾病十年並已進展至慢性腎衰竭。她以反覆發生急性膽管炎及菌血症作爲臨床表現。腹部電腦斷層及核磁共振檢查都證實左葉肝內膽管出現囊狀異常擴張、肝內結石及總膽管結石。案例2是一位43歲男性病患，同時是案例1的兒子，在兩年前也診斷罹患體細胞顯性遺傳多發性腎臟囊腫疾病。他以阻塞性黃膽合併急性膽管炎作爲臨床表現。腹部電腦斷層發現左側肝內膽管異常擴張、肝內結石及總膽管結石。兩位案例在接受膽囊切除、總膽管截石及左外側肝臟接除手術後，術後恢復都相當順利。病患術後分別追蹤4個月及14個月，臨床上都無膽管炎復發的症狀出現。卡羅里氏病的確切診斷需要依賴影像學檢查。經內試鏡逆行性胰膽管攝影是最好的診斷方法，它能提供非侵入性、安全及準確的診斷。對侷限於單葉或單節肝臟的卡羅里氏病患者，進行部份肝臟切除可以提供治癒的機會。

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