

Case Report

Caroli's disease misdiagnosed as intraductal papillary neoplasm of the bile duct

Dae Hoe Gu, Min Seon Park, Chang Ho Jung, Yang Jae Yoo, Jae Young Cho, Yun Ho Lee, Yeon Seok Seo, Hyung Joon Yim, Soon Ho Um, and Ho Sang Ryu

Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

Caroli's disease is a rare autosomal-recessive disorder caused by malformation of the ductal plate during embryonic development. Although it is present at birth, Caroli's disease is typically not diagnosed until between the second and fourth decades of life, as it was in the present patient. Here we report a rare case of Caroli's disease limited to one liver segment, which was initially misdiagnosed as an intraductal papillary neoplasm of the bile duct. The asymptomatic patient was treated with liver segmentectomy. (*Clin Mol Hepatol* 2015;21:175-179)

Keywords: Caroli's disease; Intraductal papillary neoplasm of the bile duct; Segmentectomy

INTRODUCTION

Caroli's disease belongs to a group of hepatic fibropolycystic diseases. It is characterized by multifocal congenital dilatations of the intrahepatic bile ducts, which may be diffuse or limited, presenting in a sack form that produces cystic structures, which communicate with the biliary tree. Two types have been described: a pure form or Caroli's disease (type 1) and a complex form associated with congenital hepatic fibrosis or Caroli's syndrome (type 2).^{1,2} Clinical symptoms of Caroli's disease include right upper quadrant abdominal pain, jaundice, and recurrent cholangitis.^{3,4} Bacterial cholangitis occurs frequently and may be complicated by hepatic abscess formation and sepsis. Recurrent cholangitis dominates the clinical course and is the principal cause of morbidity and mortality. Caroli's disease limited to 1 liver segment is extremely rare, and there have been only a few cases of segmentec-

tomy for Caroli's disease in Korea. In this report, we present a case of Caroli's disease that was misdiagnosed as an intraductal papillary neoplasm of the bile duct (IPNB) and was treated with segmentectomy.

CASES

A 30-year-old man with no underlying diseases visited our hospital for further evaluation and treatment of a liver mass discovered on abdominal computed tomography (CT) scan at another hospital. This patient was asymptomatic on transfer to our hospital. The physical examination showed no abnormality, and the initial vital signs were as follows: body temperature, 36.9°C; pulse rate, 70 beats/min; respiratory rate, 20 breaths/min; and blood pressure, 120/70 mmHg. His height and body weight were 179

Abbreviations:

CT, computed tomography; IPNB, intraductal papillary neoplasm of the bile duct; MRCP, magnetic resonance cholangiopancreatography; MRI, magnetic resonance imaging

Corresponding author : Yeon Seok Seo

Department of Internal Medicine, Korea University College of Medicine, 73 Incheon-ro, Seongbuk-gu, Seoul 136-705, Korea
Tel: +82-2-920-6608, Fax: +82-2-953-1943
E-mail: drseo@korea.ac.kr

Received : Aug. 22, 2013 / Revised : Oct. 9, 2013 / Accepted : Oct. 15, 2013

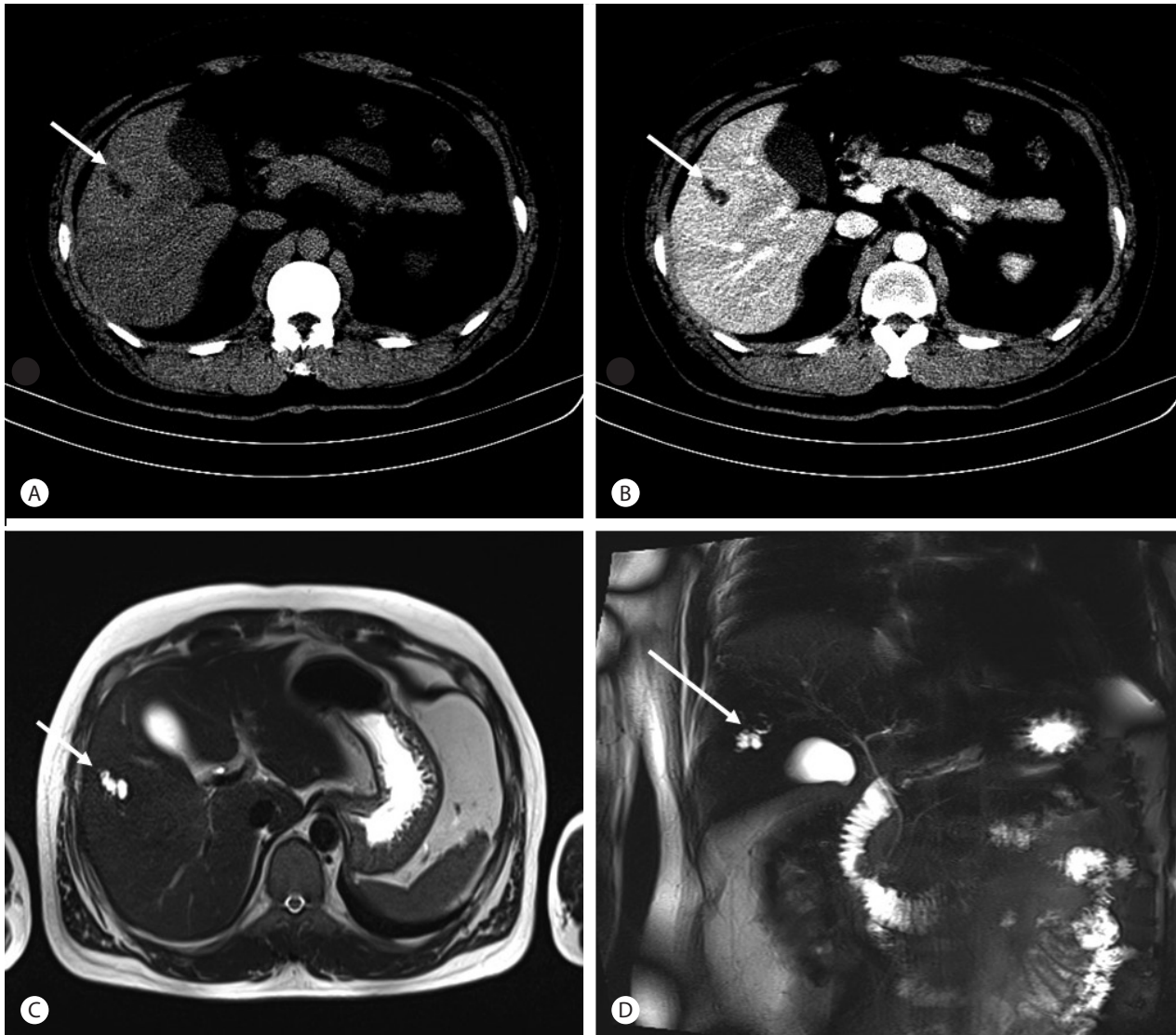


Figure 1. Abdominal computed tomography (CT), magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP) findings. Localized bile duct dilatation in segment 5 (arrow) presented as a high signal intensity in T2-weighted MRI but without a demonstrable intraductal mass lesion evident in the images. There was no evidence of liver cirrhosis (A: pre-enhancement phase of CT, B: portal phase of CT, C: T2-weighted MRI, D: MRCP).

cm and 93.4 kg, respectively. He consumed 120-180 g of alcohol per week, and his medical history and familial history were unremarkable. Laboratory examinations showed a white blood cell count of 5,800/ μ L, hemoglobin level of 15.9 g/L, and platelet count of 272,000/ μ L. The only abnormal finding on the liver function test was mildly elevated alanine transaminase levels, and the results were as follows: serum aspartate transaminase, 42 IU/L; alanine transaminase, 76 IU/L; alkaline phosphatase, 58 IU/L; gamma-glutamyl transferase, 82 IU/L; total bilirubin, 0.69 mg/dL; albumin, 5.3 g/dL; and international normalized ratio, 0.98. CA 19-9 and α -fetoprotein for malignancy work-up was carried out;

5.7 IU/mL and 3.6 ng/mL, respectively. Results for viral markers including hepatitis B surface antigen and anti-hepatitis C virus were negative. Abdominal CT (Fig. 1A, B) performed at the other hospital and abdominal magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) (Fig. 1C, D) performed at our hospital revealed a localized bile duct dilatation measuring 2.0 \times 0.8 cm in liver segment 5 without a demonstrable intraductal mass lesion and underlying steatosis of the liver. Although an obstructing lesion was not found on the images, we considered the duct obstructed with a mass or parasite proximal to the dilated ductal area because size of the dilated ductal

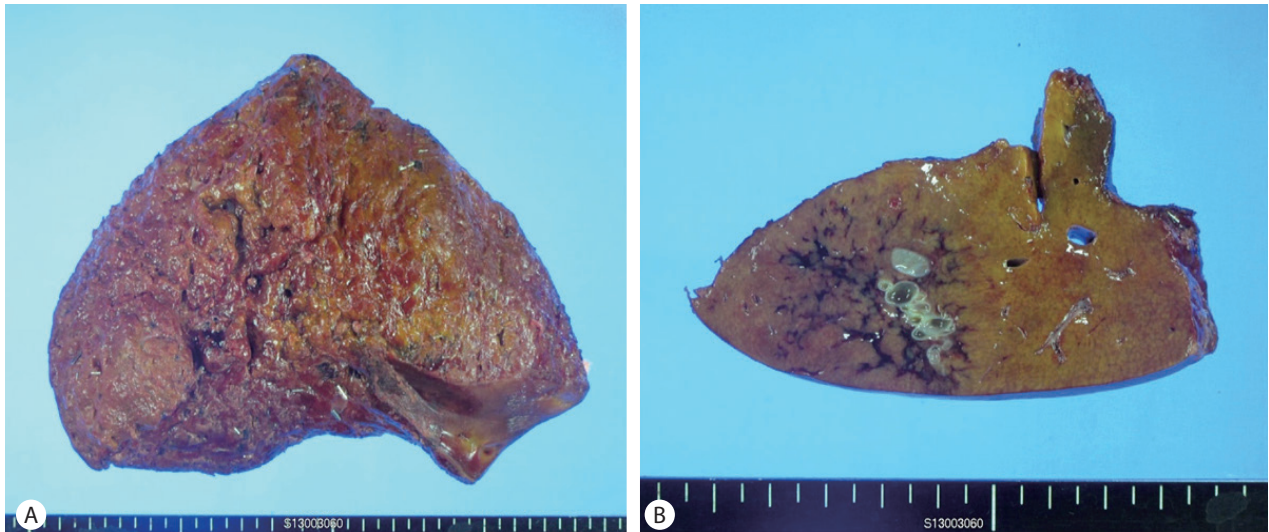


Figure 2. Gross findings of the resected liver. (A) There were no grossly remarkable findings on the surface of the resected liver. (B) No stones or mass was found in the cut surface of the serial section, and a diffuse parenchymal hemorrhagic soft dilated lesion was noted. The dilatation of the intrahepatic duct appeared in clusters. Hemorrhagic peliosis was seen in the periductal area, and the liver parenchyma had a slight greenish color that was suggestive of cholestasis.

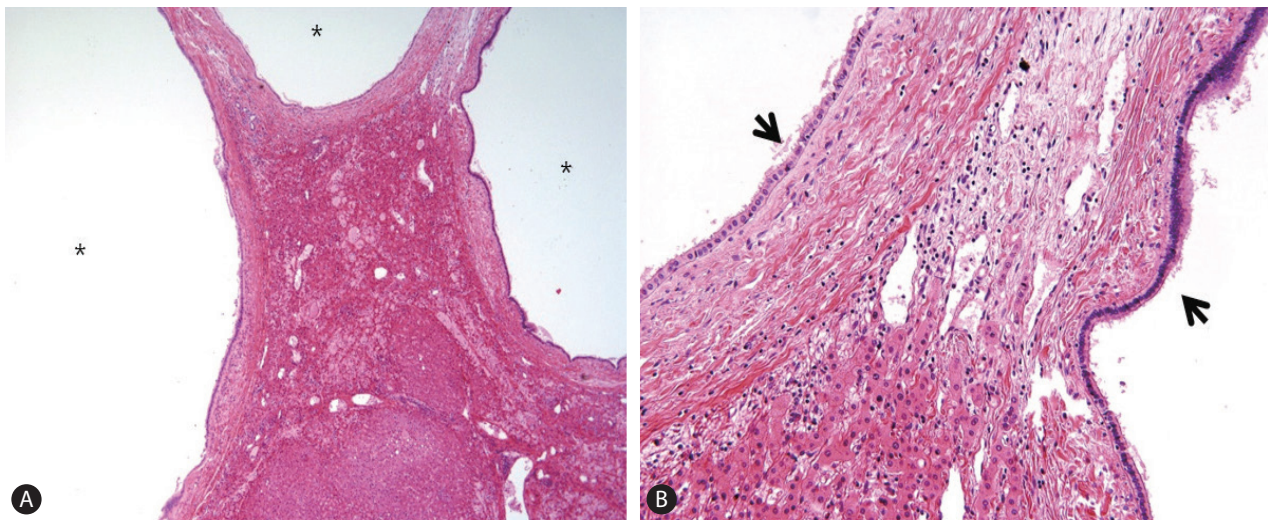


Figure 3. Microscopy findings of the resected specimen. Bile ducts were dilated and had thickened walls (asterisks). Ectasias result in a predisposition to repeated attacks of cholangitis with complications such as intrahepatic lithiasis, amyloidosis, and cholangiocarcinoma, but they were not present in this case. The lining epithelium (arrows) comprised columnar and cuboidal cells (hematoxylin and eosin stain, A: $\times 40$, B: $\times 200$).

site was very limited and could not find any evidence of other bile duct disease. Assuming that the lesion of the localized bile duct dilatation in liver segment 5 was due to an IPNB, we decided to perform surgery after consultation with the general surgery department because the possibility of malignancy with IPNB could not be excluded. He was transferred to the general surgery department and underwent segmentectomy of liver segment 5. Although the 16 \times 7 \times 16 cm resected liver specimen showed grossly unremarkable

findings on the surface or inner surface (Fig. 2A), a diffuse parenchymal hemorrhagic soft dilated lesion was noted in the 4.5 \times 3.5 cm cut surface, 0.5 cm from the resection margins in a serial section of the specimen (Fig. 2B). Histopathologic findings showed congenital dilatation of the intrahepatic bile ducts (Caroli's disease) with approximately 50% centrilobular macrovesicular type fatty change (Fig. 3). This patient is seen regularly at the outpatient department and has no complications 5 months after surgery.

DISCUSSION

Caroli's disease, a congenital cystic dilatation of the hepatic ducts, has been reported steadily worldwide since the first report in 1958 by Caroli et al.⁵ The incidence worldwide is 1 case per million, and most patients are diagnosed before the age of 30 years.⁶ It is clinically complicated with recurrent cholangitis, intrahepatic cholelithiasis, or liver abscess; cancer also can be found in 7–24% of cases.^{7,8} Caroli's disease can be divided into the diffuse type, which involves both lobes, and the localized type, which occurs in a single lobe. Most cases are the diffuse type in which the intrahepatic bile ducts are dilated in both lobes. Liver fibrosis is found more frequently in the diffuse type than in the localized type, and such fibrosis is accompanied by portal hypertension, which is known as Caroli's syndrome. Caroli's syndrome is mostly comorbid with cystic kidney diseases such as polycystic kidney disease and medullary cystic kidney disease.^{9–11} The primary treatment of Caroli's disease is surgery such as segmentectomy, lobectomy, or hepaticojejunostomy, determined by the range of cystic formation. Because the diffuse type is mostly inoperable, these patients are usually treated conservatively with antimicrobial and ursodeoxycholic acid administration and stone removal or bile duct drainage with endoscopic retrograde cholangiopancreatography if there is intrahepatic cholelithiasis.¹² In contrast, in localized Caroli's disease, cure is possible with lobectomy; therefore, many domestic and foreign reports exist.^{13,14}

To our knowledge, there are 6 cases of localized Caroli's disease, including our case in Korea (Table 1),^{14–18} and among them, this is the second case that was treated with segmentectomy. In addition, considering the location, 5 cases including our case involved the right lobe and only 1 of 6 total cases of localized Caroli's disease reported in Korea involved the left lobe. The foreign case reports of localized Caroli's disease differ. In one study, the

disease affected the left lobe in 75–89% of cases,¹⁹ and another study presented similar rates between right and left lobes.²⁰ However, most cases in domestic studies involved the right lobe.

In this case, segmentectomy alone was effective treatment because the lesion size of the bile duct dilatation was small. Although abdominal CT and abdominal MRI were performed before resection, Caroli's disease was not suspected because the lesion of the localized bile duct dilatation was smaller than the lesions in other reported cases, and the incidence of localized Caroli's disease is low. Irregular tubular structure and presence of tiny dots with strong contrast enhancement within the dilated intrahepatic bile ducts (the "central dot" sign) shown in CT scan or localized tubular cystic lesion seen in brightly high signal intensity in MRI T2-weighted image accompanied with communication between biliary tree in MRCP is considered very suggestive finding of Caroli's disease. However, in present case we could not find those evidences of Caroli's disease. Although mass lesion suggesting IPNB or obstruction of bile duct with stone or parasite was not found, surgery was performed because it was possible that malignancy could not be visualized between image cuts. We incidentally diagnosed Caroli's disease by a histopathological examination performed after resection for suspected IPNB or parasite infestation and thus, treated the asymptomatic Caroli's disease. Optimal management of patients with Caroli's disease is debatable,¹² especially in the localized pure form of Caroli's disease, as in the present case. Some may argue that if localized Caroli's disease was suspected, the surgery should not have been performed, as our patient was asymptomatic and had no complications such as hepatic fibrosis, biliary lithiasis, cholangitis, or liver abscesses. However, considering that IPNB, which is potentially malignant, cannot be ruled out with imaging studies, and liver biopsy was unnecessary since only focal dilatation of the bile duct with no mass lesion was noted, liver segmentectomy was considered the

Table 1. Clinical characteristics of patients diagnosed as localized Caroli's disease in Korea

Sex	Age (yrs)	Symptom	Symptom duration	Initial impression	Location	Management	Prognosis	Reference NO.
F	43	Dyspepsia, RUQ pain, fever	11 years	Cholelithiasis	Right lobe	Open T-tube drainage	Unknown	18
F	2	Jaundice, abdominal pain, vomiting	4 months	Hepatitis	Left lobe	Hepaticojejunostomy	OPD f/up	17
F	22	Abdominal pain	Several months	Caroli's disease	Right lobe	Segmentectomy	OPD f/up	16
M	22	RUQ pain	1 month	Caroli's disease	Right lobe	Lobectomy	OPD f/up	15
M	40	No symptom	-	Cholelithiasis	Right lobe	Lobectomy	OPD f/up	14
M	30	No symptom	-	IPNB	Right lobe	Segmentectomy	OPD f/up	Present case

RUQ, right upper quadrant; OPD, outpatient department; f/up, follow-up; IPNB, intraductal papillary neoplasm of the bile duct.

best choice in our situation.

Conflicts of Interest

The authors have no conflicts to disclose.

REFERENCES

1. Tallón Aguilar L, Sánchez Moreno L, Barrera Pulido L, Pareja Ciuró F, Suárez Artacho G, Alamo Matinez JM, et al. Liver transplantation consequential to Caroli's syndrome: a case report. *Transplant Proc* 2008;40:3121-3122.
2. Lendoire JC, Raffin G, Grondona J, Bracco R, Russi R, Ardiles V, et al. Caroli's disease: report of surgical options and long-term outcome of patients treated in Argentina. Multicenter study. *J Gastrointest Surg* 2011;15:1814-1819.
3. Sato Y, Ren XS, Nakanuma Y. Caroli's Disease: Current Knowledge of Its Biliary Pathogenesis Obtained from an Orthologous Rat Model. *Int J Hepatol* 2012;2012:107945.
4. Zhang DY, Ji ZF, Shen XZ, Liu HY, Pan BJ, Dong L. Caroli's disease: a report of 14 patients and review of the literature. *J Dig Dis* 2012;13:491-495.
5. Caroli J, Couinaud C, Soupault R, Porcher P, Eteve J. [A new disease, undoubtedly congenital, of the bile ducts: unilobar cystic dilation of the hepatic ducts]. *Sem Hop* 1958;34:496-502/SP.
6. Giovanardi RO. Monolobar Caroli's disease in an adult. Case report. *Hepatogastroenterology* 2003;50:2185-2187.
7. Dayton MT, Longmire WP, Tompkins RK. Caroli's disease: a pre-malignant condition? *Am J Surg* 1983;145:41-48.
8. Levy AD, Rohrmann CA, Murakata LA, Lonergan GJ. Caroli's disease: radiologic spectrum with pathologic correlation. *AJR Am J Roentgenol* 2002;179:1053-1057.
9. Kerkar N, Norton K, Suchy FJ. The hepatic fibrocystic diseases. *Clin Liver Dis* 2006;10:55-71.
10. Srinath A, Shneider BL. Congenital hepatic fibrosis and autosomal recessive polycystic kidney disease. *J Pediatr Gastroenterol Nutr* 2012;54:580-587.
11. Wen J. Congenital hepatic fibrosis in autosomal recessive polycystic kidney disease. *Clin Transl Sci* 2011;4:460-465.
12. Bockhorn M, Malagó M, Lang H, Nadalin S, Paul A, Saner F, et al. The role of surgery in Caroli's disease. *J Am Coll Surg* 2006;202:928-932.
13. Yilmaz S, Kirimlioglu H, Kirimlioglu V, Isik B, Coban S, Yildirim B, et al. Partial hepatectomy is curative for the localized type of Caroli's disease: a case report and review of the literature. *Surgeon* 2006;4:101-105.
14. Cha BH, Lee SH, Hwang JH, Kim SY, Kim HY. [A case of caroli disease with biliary stones]. *Korean J Gastroenterol* 2009;54:201-204.
15. Kil H, Choi EY, Jeong JI, Park CS, Park SM, Kim SH, et al. [A case of simple type Caroli's disease confined to right lobe of the liver]. *Korean J Gastroenterol* 2007;50:271-276.
16. Yoo SJ, Moon YS, Lee SW, Yang JH, Park SJ, Park JW, et al. Case Reports : A case of simple type Caroli's disease confined to one segment of the Liver. *Korean J Med* 2005;68:448-453.
17. Chung HJ, Seo JK, Ko KW, Park KW, Kim WK. A case report of Caroli's disease. *Korean J Pediatrics* 1985;28:731-735.
18. Kim WC, Bahk YW, Kim HK. Caroli's disease. *J Korean Med Assoc* 1974;17:73-77.
19. Boyle MJ, Doyle GD, McNulty JG. Monolobar Caroli's disease. *Am J Gastroenterol* 1989;84:1437-1444.
20. Kassahun WT, Kahn T, Wittekind C, Mössner J, Caca K, Hauss J, et al. Caroli's disease: liver resection and liver transplantation. Experience in 33 patients. *Surgery* 2005;138:888-898.