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Case report

HEPATIC MULTIPLE HYPERINTENSE CYSTIC LESIONS: A RARE CAROLI DISEASE.

Alsharif M.H. [1]*, Bakhit N.M.[2], Alarifi A.[3,4], Nassir E.M.[5], Mahdi A.A.[4,6,7], Almasaad J.M.[8,9], Elamin A.Y.[7], Taha K.M.[10]

[1] Department of Basic Medical Science, College of Medicine, Prince Sattam Bin Abdulaziz University, Al Kharj, Saudi Arabia
[2] Department of Anatomy, Arabian Gulf University, Manama, Bahrain
[3] Department of Basic Sciences, College of Science and Health Professions, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
[4] King Abdullah International Medical Research Center, King Abdulaziz Medical City, Riyadh, Saudi Arabia
[5] Radiology Department, College of Medicine, Prince Sattam Bin Abdulaziz University, Al Kharj, Saudi Arabia
[6] Department of Basic medical Sciences, College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
[7] Department of Histology and Embryology, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Turkey
[8] Department of Basic Medical Sciences, College of Medicine, King Saud Bin Abdul Aziz University for Health Sciences, Jeddah, Saudi Arabia
[9] King Abdullah International Medical Research Centre, King Abdulaziz Medical City, Jeddah, Saudi Arabia
[10] Department of Anatomy, Faculty of Medicine, University of Garden City, Sudan

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Abstract

Caroli's disease is a rare malformation of the biliary tract with an incidence rate being one per million of people. Most cases of hepatic cystic lesions are asymptomatic and are discovered incidentally during abdominal ultrasonography. It is reported that Caroli's disease is an autosomal-recessive disorder with multifocal segmental non-obstructive dilation features of intrahepatic bile ducts that may involve a segment, a lobe, or the whole liver. Several complications might be developed in some cases, such as cholangiocarcinoma. Therefore, early diagnosis is vital for proper management. There is a lack of literature discussing Caroli's disease among Africans compared to Asians. Females are more affected than males. Moreover, most of Caroli's disease cases were about 22 years old of age.

This study describes the existing case's novelty in that we discuss a rare Caroli's disease case of an African male patient; moreover, the patient age in mid-adulthood. In addition, the severity of the current case is that both hepatic lobes showed severe multiple cystic lesions.

The embryonic justification of the case is the large cranial portion of the hepatic diverticulum gives rise to the cords of hepatocytes and intrahepatic biliary networks. On the other hand, the small caudal portion forms the extrahepatic biliary tract. The hepatocytes as well as cholangiocytes, are differentiated from the hepatoblasts under the influence of typical hepatic genes, α-fetoprotein, liver-specific transcription factors, and albumin.

Based on the above, Caroli disease is defined by biliary tract malformation, whereas Caroli syndrome is determined by the presence of associated congenital hepatic fibrosis.

Keywords: *Caroli disease, cystic lesions, biliary tract, hepatic lobes.*

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Address for Correspondence:

Dr. Mohammed H. Karrar Alsharif, PhD
Department of Basic Medical Science, College of Medicine Prince Sattam Bin Abdulaziz University
Al Kharj 11942, Saudi Arabia
Tel.: 00966552644088
E-Mail: dr.anatomy83@yahoo.com

INTRODUCTION

In 1958, the French gastroenterologist Dr. Jacques Caroli was the first who describe Caroli's disease (CD) as a rare congenital pathology in which the intrahepatic bile ducts become segmentally dilated [*Caroli J et al., 1958*]. When the small bile ducts are involved and associated with portal hypertension, congenital hepatic fibrosis, and polycystic kidney disease, it is known as Caroli's syndrome, complex CD [*Todani T et al., 1979*]. Caroli's disease is common in Asia, with ages about 22 years. However, the female-to-male ratio is 4:1. Moreover, it must be considered that the isolated CD is very rare compared to complex CD, as the CD incidence is as rare as one per million people [*Todani D, 2000*]. It is reported that CD is an autosomal-recessive disorder with multifocal segmental non-obstructive dilation features of intrahepatic bile ducts that may involve a segment, a lobe, or the whole liver [*Giovanardi R, 2003*], while complex CD is an autosomal recessive trait [*Alshaikhli A, Al-Hillan A, 2022*]. It is worth noting that based on Todani's classification, the CD is categorized as Type V choledochal cysts [*Kim B et al., 2022*]. It has been documented that most of the hepatic cysts are benign, although some are malignant. Cholangiocarcinoma has been found in 7% of CD cases; hence, early diagnosis is very important for appropriate management [*Raynaud P et al., 2011*].

While some authors believe that right hypochondrium pain, fever, and jaundice are signs and symptoms of most symptomatic cases of CD [Strazzabosco M et al., 2005], others believe that patients with complex CD present signs and symptoms of hepatocellular insufficiency, and/or portal hypertension other than recurrent attacks cholangitis and cholelithiasis along with biliary abscess in some cases [Vachha B et al., 2011]. This study describes a rare case that was discovered incidentally during abdominal ultrasonography of an asymptomatic African male in Middle adulthood with Multiple hyperintense cystic lesions.

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

CASE REPORT

A male patient, aged 42, African, asymptomatic, appeared at the outpatient clinic for a routine checkup at Prince Sattam bin Abdulaziz University Hospital in Alkharj, Saudi Arabia. There was no fever, weight loss, nausea, chills, or vomiting mentioned by the patient. Clinical examination showed hepatomegaly but no jaundice or ascites, splenomegaly or varicose veins of the anterior abdominal wall, and no evidence of portal hypertension or other symptoms. There were no notable results in clinical studies of the respiratory and cardiovascular systems. However, the hematological and biochemical results revealed typically elevated levels of gamma-glutamyl transferase and alkaline phosphatase. An abdominal ultrasound (US) showed multiple small rounded anechoic structures, corresponding to the biliary tree's saccular dilatations (Fig. 1). The magnetic resonance cholangiopancreatography (MRCP) reported Multiple hyperintense cystic lesions were seen in both lobes of the liver, demonstrating continuity between cystic lesion and the biliary tree (Fig. 2).

DISCUSSION

The embryonic development of the liver and biliary tract begins in the fourth week of gestation. The liver is endodermal, originating from the hepatic diverticulum of the foregut tube. The large cranial portion of the hepatic diverticulum gives rise to the cords of hepatocytes and intrahepatic biliary networks. On the other hand, the small caudal portion forms the extrahepatic biliary tract. The hepatocytes and cholangiocytes are differentiated from the hepatoblasts under the influence of typical hepatic genes, α-fetoprotein, liver-specific transcription factors, and albumin [*Raynaud P et al., 2011*]. Caroli disease is defined by biliary tract malformation, whereas Caroli syndrome is determined by the presence of associated congenital hepatic fibrosis [*Umar J et al., 2021*].

Furthermore, a type I choledochal cyst is a fusiform dilation of the common bile duct. In contrast, a type II choledochal cyst is defined as an isolated diverticulum that protrudes through the wall. Because it arises from the intraduodenal portion of the common bile duct, type III is also known as choledochocele. Multiple extrahepatic and intrahepatic origin

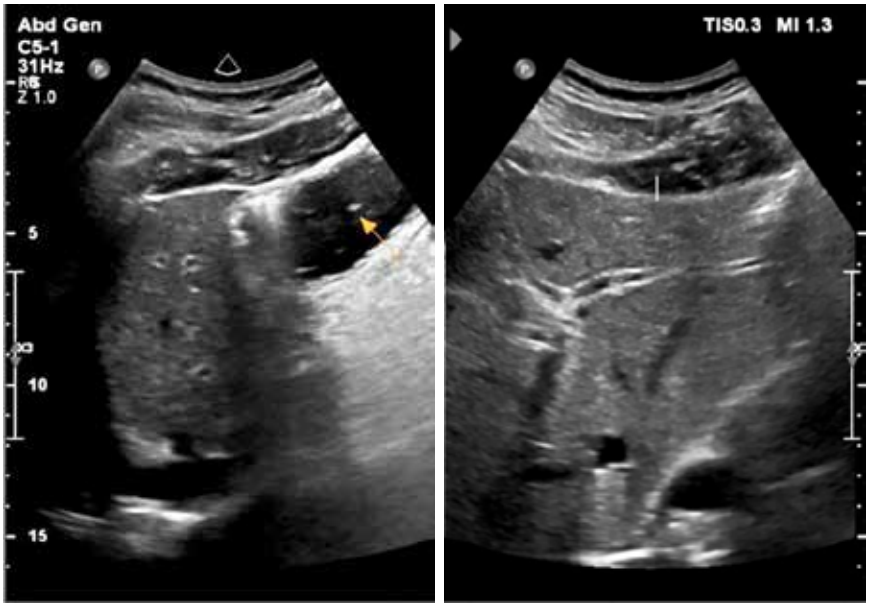

Figure 1. *US image of the liver shows violated branching structures, cystic changes, and peripheral dots noted at the right lobe suggestive of directed biliary ducts with the normal extrahepatic common bile duct.*

dilations are classified as type IVa, while extrahepatic bile ducts are classified as type IVb [*Sallahu F et al., 2013*]. The etiology of CD is believed to be linked to incomplete and defective remodeling of the embryonic ductal plate [*Lemfadli Y et al., 2020*]. Some researchers assume that the presence of an unbalanced translocation between chromosomes 3 and 8 is the underlying cause of CD, indicating the pathogenetic role of distal 3p and 8q loss or gain or both in CD. Alternately, structural changes to the genes at 3p23 and 8q13 could have a significant impact. These chromosomal breaks may also aid in identifying the genes causing Caroli disease in inherited variants unrelated to polycystic kidney disease [*Parada L et al., 1999*]. Some authors believe that the Etiology of this hereditary illness is the PKHD1 gene, which affects the fibrocystin protein known as polycystic kidney and hepatic disease [*Cao J et al., 2021*].

Caroli's disease is relatively challenging to diagnose because the condition typically manifests no symptoms during the early years of the patient's life [*Agustsson A, Cariglia N, 2007*]. In most cases, superinfections and the development of intrahepatic stones are associated with CD sequelae [*Orsoni P et al., 1994*]. Among 62 patients of CD reported in the Japanese literature, cholangitis, hepatolithiasis, esophageal varices, and cholangiocarcinoma were found to be complications in 43.5%, 30.6%, 17.7%, and 8.1% of the cases, respectively. Thereby, different techniques must be used to accurately diagnose the complication. CT scan can confirm the diagnosis of bacterial cholangitis. However, an X-ray and MRI can demarcate the enlargement of intra-hepatic bile ducts as a result of ectasia. The US is also a helpful tool in displaying the tubular dilation of the bile ducts. Nevertheless, MRCP is considered the favorable approach to demonstrate the enlarged bile ducts as a result of CD [*Chiba T et al., 2002; Fahrner R et al., 2020*]. The MRCP diagnostic technique has

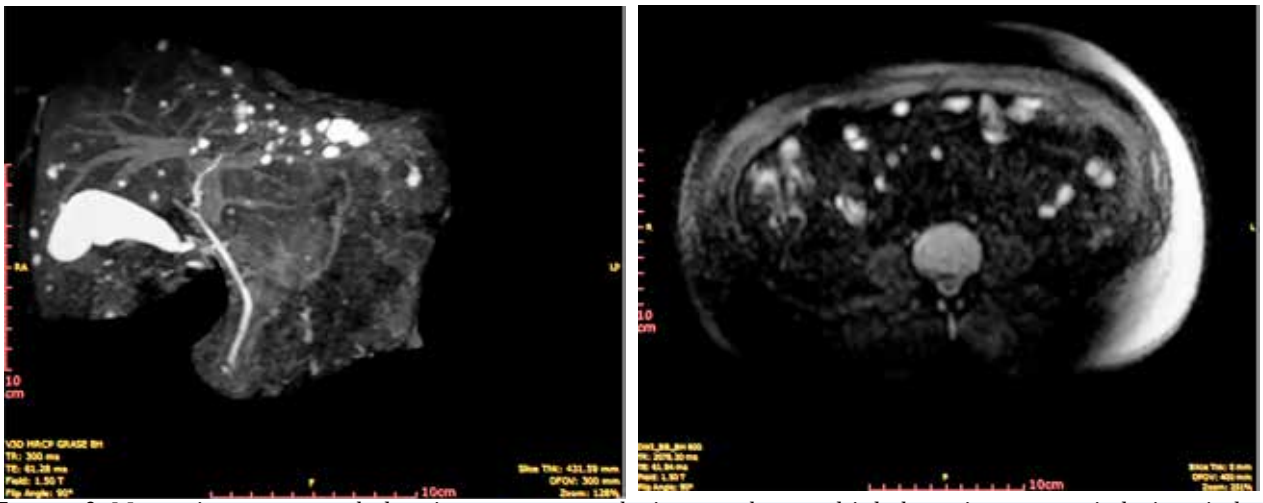

Figure 2. *Magnetic resonance cholangiopancreatography images show multiple hyperintense cystic lesions in both lobes of the liver, demonstrating continuity between the cystic lesion and the biliary tree.*

been demonstrated to be equivalent to endoscopic retrograde cholangiopancreatography in detecting the morphological features of congenital cyst lesions of the biliary ducts (at sensitivity and specificity equal to 82% and 100%, respectively) [*Zhong L et al., 2004*].

In cases of prenatal diagnosis, researchers concur that autosomal recessive polycystic kidney disease is related to Caroli syndrome, as they have a similar autosomal recessive pattern of inheritance. They noted that Approximately 50% of infants with autosomal recessive pattern of inheritance have clinical evidence of liver involvement, including Caroli syndrome, the dilatation of the common bile duct, which may lead to recurrent or persistent bacterial ascending cholangitis [*Sweeney W, Avner E, 2019*]. CD is generally asymptomatic and goes undiagnosed for years in a patient's life. According to some researchers, the incidence of CD is one per million, and the majority of these cases are identified at the age of about 20 years, making the diagnosis difficult for this case because our patient is 42 years old [*Giovanardi R, 2003, Gu D et al., 2015, Leblan H, Ramirez S, 2020*]. In the current case report, the patient is an African male individual, making the diagnosis even more difficult. There are currently no academic articles discussing CD or Caroli Syndrome among Africans, as there have been in Asia, where the incidence rate is higher [*Wang B et al., 2020*]. In the present case, multiple small, rounded anechoic entities corresponding to the saccular dilatations of the biliary tree were visible on the abdominal US. The liver displays cystic changes with violated branching structures (Fig. 1). Collectively, using MRCP, the Fast spin-echo T2-weighted showed multiple hyperintense cystic lesions (noticed at both lobes of the liver). A continuity pattern between the reported cystic lesions and the biliary tree was observed (Fig. 2). Organomegaly was absent in the spleen and kidneys. In addition, no signs of portal hypertension or polycystic kidney disease were noted. Treatment depends primarily on the clinical manifestation and location of the CD.

The clinical presentation depends on whether the dominant feature is intrahepatic biliary ductal ectasia or hepatic fibrosis. If fibrosis is predominant, the clinical manifestations are related to portal hypertension, with hematemesis from varices being the most significant symptom. When a sole lobe is affected, lobectomy can not only alleviate the associated symptoms but also limit the future risk of malignancy [*Karim A, 2004*]. Evidently, an association between CD and cancer was reported. Cholangiocarcinoma can develop in 7% of CD [*Karim A, 2004*]. Considering the emergence of carcinoma, patients who are unable to have radical surgery should undergo routine clinical follow-ups, which may include US and biopsies if necessary [*Johnsen F et al., 1996*]. Patients with end-stage liver disease or Caroli's syndrome are typically treated conservatively with the administration of antibiotics and ursodeoxycholic acid, stone removal, bile duct drainage using endoscopic retrograde cholangiopancreatography, or liver transplantation [*Ulrich F et al., 2002; Bockhorn M et al., 2006*].

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Yerevan State Medical
University after M. Heratsi.

Address for correspondence:

Yerevan State Medical University
2 Koryun Street, Yerevan 0025,
Republic of Armenia

Phones:

(+37410) 582532 YSMU
(+37493 588697 Editor-in-Chief
Fax: (+37410) 582532
E-mail: namj.ysmu@gmail.com, ysmiu@mail.ru
URL: http//www.ysmu.am

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Armenia, 0023,Yerevan,
Acharyan St. 44 Bulding,
Phone: (+374 10) 62 76 12,
E-mail: las.print@yahoo.com