

Diffuse Caroli's disease with atypical presentation: a case report

Maíra Lima Acioli, Lawrence Raizama Gonçalves Costa, Mônica Souza de Miranda Henriques

Faculdade de Medicina Nova Esperança and Universidade Federal da Paraíba, Brazil

Abstract

This paper describes a case of Caroli's disease in a female patient aged 32, who complained of nonspecific abdominal pain without cholestasis or cholangitis. Liver resonance shows segment saccular dilations closely connected to intrahepatic biliary ducts, that differ from the Caroli's syndrome, which is more common and consists of multiple intrahepatic cystic dilations, associated to congenital hepatic fibrosis. This patient has a congenital anomaly with an uncommon oligosymptomatic form of Caroli's disease that should be included in the differential diagnosis of patients with recurrent abdominal pain.

Keywords Cholangiopathy, Caroli's syndrome, Von Meyenburg complex, congenital bile duct dilatation

Ann Gastroenterol 2014; 27 (1): 79-81

Introduction

Caroli's disease (CD) is an uncommon congenital malformation, first described by Jacques Caroli in 1958 [1]. Its incidence is extremely low (1 in 1,000,000 population), and comprises two entities, namely CD and Caroli's syndrome [4].

Caroli's syndrome is more common than CD and consists of multiple cystic or saccular dilatation of intrahepatic biliary ducts (IHBD) associated with congenital hepatic fibrosis [4]. Caroli's syndrome is a genetic disorder with a probable autosomal recessive inheritance pattern. Many authors believe that the two conditions are different stages of the same disease characterized by ductal dilatation and periportal fibrosis [2].

Patients with Caroli's syndrome have signs and symptoms of portal hypertension and hepatocellular insufficiency, recurrent attacks of cholelithiasis and cholangitis, and occasionally biliary abscess [5]. Patients with CD present recurrent attacks of cholangitis (right upper quadrant pain, fever and jaundice rarely) [6].

This paper describes a case of a woman with CD with cystic formations randomly distributed by the hepatic parenchyma, diagnosed at adulthood, during the investigation of nonspecific abdominal pain framework.

Case report

A female patient, aged 32, Caucasian, appeared to the outpatient clinic complaining of abdominal pain, that started six months ago, it was mild to moderate, continuous, recurrent, located in the upper right quadrant, relieved with simple analgesics. The patient also reported intestinal constipation, making use of laxatives, but had no fever, chills, jaundice, weight loss, nausea and/or vomiting.

The patient had a history of transient ischemic attack, which was investigated and attributed to an inherited thrombophilia (mutations A1298C and C677T on the *methylene-tetrahydrofolate reductase -MTHFR*) which was treated with warfarin daily. She had a daughter with Turner syndrome (TS), but no history of abortion, liver disease or any thrombotic event in the relatives, and denied alcohol and tobacco consumption.

The clinical examination of respiratory, cardiovascular and gastrointestinal systems showed no significant findings. There were no jaundice, fever, no stigmata of chronic liver disease and no signs of portal hypertension.

Hematological and biochemical exams are shown in Table 1. Abdominal ultrasound showed sparse cystic anechoic formations in the liver parenchyma of about 1.1 cm. Magnetic resonance cholangiopancreatography (MRCP) (Fig. 1) demonstrated multiple small cystic formations, with intimate anatomical relation with biliary branches. An MRI of the upper abdomen showed that such formations were randomly distributed in hepatic parenchyma (Fig. 2 and 3).

The dilatation of intrahepatic biliary ducts with intimate anatomical relation with biliary branches, without cholangitis, chronic liver disease or signs of portal hypertension suggested an oligosymptomatic form of CD.

So far, the prognosis is favorable, since the patient has no

Gastroenterology Department at Faculdade de Medicina Nova Esperança-Famene, João Pessoa, Paraíba, Brazil

Correspondence to: Professor Mônica Souza de Miranda-Henriques, Rita Sabino de Andradre, 354, Zip code: 580366-610, João Pessoa, Paraíba, Brazil, Tel./Fax: +55 83 21064777, e-mail: mrsmonicca@gmail.com

Conflict of Interest: None

Received 11 March 2013; accepted 27 May 2013

Table 1 Hematological and biochemical parameters

Hemoglobin	13 (g/dL)
Hematocrit	37 (%)
Leukocytes	5000 (/mm ³)
Lymphocytes	30 (%)
Platelets	320 (/mm ³)
Prothrombin activity	70 (%)
INR	1.21
Antinuclear factor	Negative
Anticardiolipin	IgG=0.6 IgM=78
C-reactiveprotein	147 (mg/L)
AST	24 (UI/mL)
ALT	13 (UI/mL)
GGT	16 (U/L)
CEA	0.12 (mcg/ L)
Alkaline phosphatase	62 (U/L)
Total bilirubin	0.59
Direct bilirubin	0.25
Indirect bilirubin	0.34
Albumin	4.3 (g/dL)
LDH	349 (U/L)
α-Fetoprotein	1.82 (mcg/mL)
Leiden factor	Negative
Homocysteine	7.7 (μmol/L)
Antithrombin	96%
Antiplatelet lupus	Negative
Protein S	57%

INR, international normalized ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyl transferase; CEA, carcinoembryonic antigen; LDH, lactate dehydrogenase

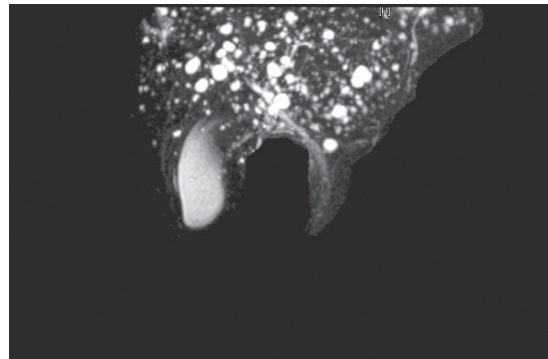


Figure 1 Magnetic resonance cholangiopancreatography showing diverticulum-like sacculi of intrahepatic bile ducts ectasias and communication with the biliary branches

cholangitis or no major clinical manifestations that modified her daily life.

Liver biopsy was not performed, once the patient was using warfarin, and the procedure would bring more risks than benefits, reasons that prevent the definitive diagnosis.

Currently, the patient continues under clinical follow-up, with no other complaints.

Discussion

The cause of CD is unknown, but occasional familial clustering suggests that some cases are inherited, especially if it occurs in association with polycystic kidney disease and genetic mutations. So far, no single gene responsible for the disease has been identified [3].

Proposed mechanisms for malformation of biliary duct include neonatal occlusion of hepatic artery, leading to ischemia of the biliary duct and cystic dilatation; abnormal growth rate of development of biliary epithelium and connective tissue, and the lack of normal involution of ductal plates that sur-

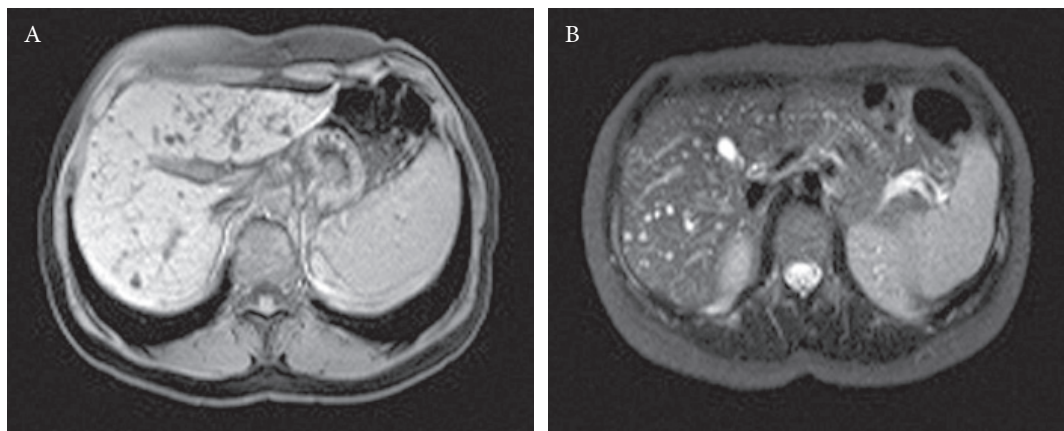


Figure 2 (A) Axial magnetic resonance imaging T1. (B) T2 showing cystic dilatation of biliary ducts distributed diffusely in the liver parenchyma

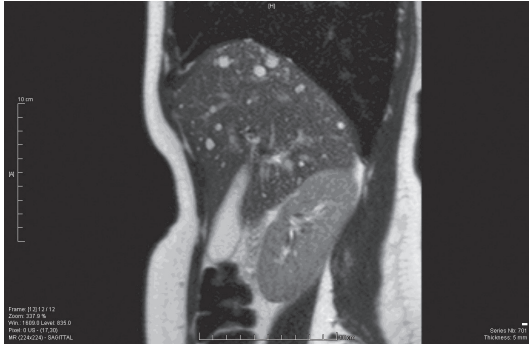


Figure 3 Sagittal MRI in T2 showing cystic dilatations of bile ducts

round the portal tracts, resulting in cysts surrounding the portal triads [9].

Mutations in genes that encode the structural formation of the kidneys and biliary tree are responsible to embryonic malformation of the ductal plate. According to cytogenetic studies, mutations are found on the chromosome 6p21, *PKHD-1* gene, involved in the synthesis of fibrocystin protein responsible for major structural abnormalities of the liver and kidneys [8]. There are also mutated genes PKD-1 and PKD-2, at locations 16p13.3 and 3q13.23 respectively [3], which synthesize polycystin and also relate to structural abnormalities of kidneys and liver [8].

Magnetic resonance is the most specific and non-invasive method to depict the multiple ductal dilatation seen in CD, called the “lollipop tree”, were cystic structures of different sizes, shapes and distribution freely communicate with the biliary tree [7,9]. Unlike, in Caroli's syndrome, cystic structures are smaller (<2cm) and periportal fibrosis is present [6].

Clinicians must also be aware of the differential diagnosis of CD, such as the Von Meyenburg complex, a rare condition that usually does not cause symptoms or disturbances in liver function, diagnosed by chance in MRCP, showing multiple small-size cystic nodules (<1.5 cm) that do not communicate with the biliary tree [10].

The treatment of CD depends on the clinical findings and the extent of biliary abnormalities. Cholangitis must be handled with antibiotics and the cholestasis can be treated with ursodeoxycholic acid. In case of abnormalities located

in one lobe, lobectomy may be the best option, in addition to promoting reduced risk of malignancy, once cholangiocarcinoma may develop in up to 7% of cases due to longtime inflammatory processes [4]. However, in cases in which there is diffuse involvement of both lobes, conservative with endoscopic treatment for extracting the gallstones, or even bypass to the digestive tract can be done. In select cases, liver transplantation has to be indicated [5].

In conclusion, this case reports an oligosymptomatic and sporadic form of CD, without evidence of cholangitis or portal fibrosis. Although this is a rare congenital anomaly, it must be recognized and included in the differential diagnosis of patients with non specific abdominal pain. Therefore, the presence of C677T and A1298C mutations represent risk factors for thrombotic events that might cause embryonary biliary ischemia and predispose to development of ectasias. This hypothesis has to be confirmed.

References

1. Pimentel F. Enfermedad de Caroli. *Rev Chil Cir* 2004;**56**:426-433.
2. Yonem O, Bayraktar Y. Clinical characteristics of Caroli's syndrome. *World J Gastroenterol* 2007;**13**:1934-1937.
3. Parada LA, Hallén M, Hagerstrand, I, Tranberg KG, Johansson B. Clonal chromosomal abnormalities in congenital bile duct dilatation (Caroli's disease). *Gut* 1999;**45**:80-782.
4. Gupta AK, Gupta A, Bhardwaj VK, Chansoria M. Caroli's disease. *Indian J Pediatr* 2006;**73**:233-235.
5. Vachha B, Sun MRM, Siewert B, Eisenberg RL. Cystic lesions of the liver. *Am J Roentgenol* 2011;**196**:355-366.
6. Strazzabosco M, Fabris L, Spirli C. Pathophysiology of cholangiopathies. *J Clin Gastroenterol* 2005;**39**:S90-S102.
7. Miller WJ, Sechtin AG, Campbell WL, Pieters PC. Imaging findings in Caroli's disease. *Am J Roentgenol* 1995;**165**:333-337.
8. Levy AD, Rohrmann, JR, Murakat LA, Lonergan GL. Caroli's disease: Radiological spectrum with pathologic correlation. *Am J Roentgenol* 2002;**179**:1053-1057.
9. Guy F, Cognet F, Dransart M, Cercueil JP, Conciatori L, Krause D. Caroli's disease: magnetic resonance imaging features. *Eur Radiol* 2002;**12**:2730-2736.
10. Sinakos E, Papalavrentios L, Chourmouzi D, Dimopoulou D, Drevelegas A, Akriviadis E. The clinical presentation of Von Meyenburg complexes. *Hippokratia* 2011;**15**:170-173.