Original Article
Caroli’s disease in two siblings

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Abstract: We report two cases of Caroli’s disease in a pair of siblings. The first patient, a seven year-old female child, presented with right upper quadrant abdominal pain for one year. Physical examination showed abdominal bulging and hepatosplenomegaly. Laboratory investigations revealed liver function damage. Abdominal ultrasonography and computer tomography showed intrahepatic bile duct dilatation and increased wall thickness. Liver biopsy demonstrated intrahepatic bile duct distension and proliferation, severe portal tracts fibrosis and inflammatory cell infiltration. She was diagnosed with Caroli’s disease. The patient’s 3 year-old brother also presented with similar symptoms, and his laboratory tests, imaging studies and pathological findings were also consistent with the diagnosis of Caroli’s disease. The parents of the siblings showed no abnormalities.

Keywords: Caroli disease, siblings

Introduction

Caroli’s disease (CD) is a rare autosomal recessive congenital disorder first described in 1958 and is characterized by abnormal dilatation of the intrahepatic bile duct [1]. The clinical course can be asymptomatic in the first two decades from birth, in fact, typical symptoms may scarcely arise throughout the patients’ life [2]. However, disease progression may lead to recurrent cholangitis, hepatolithiasis, secondary biliary cirrhosis and portal hypertension [3]. Most cases of CD have been reported in individual patients, but CD could also occur in siblings, as noted in a few reports in the English and Chinese literatures [2, 4-11]. Here, we reported Caroli’s disease presented in two siblings.

Case report

Clinical findings and imaging

Case 1: This 7 years and 6 months old female child presented with right upper quadrant abdominal pain one year ago. She was brought to another hospital where abdominal ultrasoundography showed hepatosplenomegaly. The patient received transfusion and medication for pain control. Subsequent ultrasonography imaging showed that her liver and spleen was of similar size. After one year, she was referred to our hospital for treatment of recurrent pain with fever. Her physical examination showed abdominal bulging, both her liver and spleen were palpable and 4 cm and 5 cm below the costal margins, respectively. She also had bilateral lower limb edema. Laboratory tests showed a white blood cell count of 5.60×10^9/L, hemoglobin level of 70.00 g/L, and platelet count of 83.00×10^9/L. Her serum aspartate transaminase was also slightly elevated. Her total protein was 46.60 g/L and albumin 19.80 g/L. Electrolytes, creatinine, glucose, serum copper and ceruloplasmin were all within normal limits. Serological tests for hepatitis B and hepatitis C virus were negative. Abdominal ultrasonography showed dilations of intrahepatic bile ducts with increased echogenicity over the duct wall and hepatosplenomegaly (Figure 1). Computerized tomography scans of the abdomen revealed hepatocirrhosis, splenomegaly, cavernous transformation of portal vein with portal hypertension, ascites, dilated intrahepatic ducts in the right posterior section of the liver and gallstones (Figure 2).

Case 2: This 3 years and 6 months old boy, also the brother of the patient described in Case 1, had abdominal distention from birth. His clinical examinations, laboratory investigations,
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Image findings and histological examination were very similar to that of Case 1. He had abdominal bulging and hepatosplenomegaly. The only abnormal indexes on the initial laboratory tests included a platelet count of 81.10×10^9/L, total protein of 58.90 g/L, serum albumin of 38.60 g/L, glutamic-pyruvic transaminase of 105.00 U/L, and aspartate aminotransferase of 53.00 U/L. Abdominal sonography and computed tomography displayed dilatation of hepatic bile duct (Figures 3 and 4).

Pathology

The liver biopsy specimen was composed of 2 pieces of tissue measuring 1.5×0.2×0.1 cm. The specimen was fixed in neutral-buffered 4% formaldehyde and embedded in paraffin. The sections were stained with hematoxylin-eosin, masson’s trichrome and reticulin.

Under microscope examination, the tissue of case 1 showed disorganized liver issue, marked liver cell edema, intrahepatic bile duct distension and proliferation, severe portal tracts fibrosis and inflammatory cell infiltration (Figure 5). The tissue of case 2 showed: bile ducts were dilated and proliferation with fibrosis (Figure 6).

Diagnosise and treatment

Combining the clinical symptoms, physical examinations, laboratory indices, image and pathological findings, a diagnosis of Carolí’s disease was confirmed in these children. The patient received conservative treatment to relieve her symptoms and liver transplantation was suggested.

Discussion

Carolí’s disease is uncommon, and usually to be present at childhood and young adults [12]. The cause of Carolí’s disease is unknown. The inheritance of Carolí’s disease seems to be autosomally recessive [13]. An unbalanced switch between chromosomes 3 and 8 sug-
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Proposed mechanisms for dilatations of the intrahepatic bile duct are in direct communication with the rest of the biliary system. This bile duct ectasia that may be usually with accompanying bile stones, this condition advantages the formation of cholangitis. It is the common clinical presentation in half of the patients with CD [15]. Caroli described two types: the simple type, the characterized which ectasias of the intrahepatic bile ducts without other histologic abnormalities; the combined type in which associated with periportal fibrosis [16]. Most common symptoms of CD are: fever, right upper quadrant pain and, more rarely, jaundice and so on [15]. Abdominal pain and distention were the primary reasons for our patients to seek treatment.

Laboratory tests in CD are non-specific and liver function test are usually normal or slightly increased in the early stages of the disease [17]. Definitive diagnosis of Caroli’s disease is made with imaging studies such as ultrasonography, endoscopic retrograde cholangiopancreatography, computed tomography, radionuclide hepatobiliary imaging, intraoperative cholangiography and percutaneous transhepatic cholangiography [2]. The characteristic findings of the disease is intrahepatic cystic anechoic areas visible under ultrasonography and computed tomography, which represent fibrovascular bundles composed of portal veins, hepatic arteries and linear bridges or septa [18]. Sonography can demonstrate liver cysts, intrahepatic lithiasis and common bile duct structure, but it is difficult to differentiate between cysts originating from Caroli’s disease and those from other diseases, namely polycystic liver disease [1]. Computed tomography scans may show bile duct ectasia and irregular cystic dilatation of the large proximal intrahepatic bile ducts with a normal common bile duct. Compared with ultrasonography and computed tomography, endoscopic retrograde (ERCP) has greatly enhanced sensitivity in diagnosing CD. However, ERCP is an invasive investigation and may lead to complications [19]. This disease have been identified in two forms, the simple type (type I) and the periporal fibrosis type (type II). Histopathologic examination is required to differentiate the two types. Both our patients had type II CD.

Figure 5. Liver biopsy of Case 1 shows hepatic cell edema, portal tracts fibrosis, and dilated bile ducts.

Figure 6. Liver biopsy of Case 2 shows dilated bile ducts with prominent fibrosis.
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The main differential diagnosis of CD is primary sclerosing cholangitis (PSC) and Von Meyenburg complex. Segmental and saccular dilation of intrahepatic bile ducts in CD is different from isolated and fusiform dilation of intrahepatic bile ducts in PSC. On imaging, the cystic nodules of the Von Meyenburg complex are lesser in diameter compared to the dilated ducts in CD, and do not communicate with the biliary tree.

The treatment of patients with CD depends on the clinical features of the disease and the extent of biliary abnormalities. Cholangitis should be treated with appropriate antibiotics. Ursodeoxycholic acid is a useful treatment for cholestasis. Surgical treatment options include segmental or lobar hepatic resection and liver transplantation [17]. Hepatic resection should be considered for patients with localized disease, and do not have fibrosis or associated liver cirrhosis, biliary cirrhosis, or associated malignancy [1, 20]. Malignancy is a complication of long-term CD and some patients are presented with cholangiocarcinoma, surgery was considered the best choice [18]. In the diffuse form of the Caroli’s disease which had complicated with liver fibrosis or cirrhosis, liver transplantation is recommended, always this is the best treatment in patient [21]. In our case, two patients had Caroli’s disease with severe liver function damage and episodes of cholangitis, so orthotropic liver transplantation is the best option for curative therapy.

In the majority of literatures demonstrated that the mode of inheritance in Caroli’s disease is an autosomal recessive fashion. But a few cases about the occurrence of CD appeared in family aggregation were reported. Here we provide two cases of Caroli’s disease in two siblings, which is rare in the literature.

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Disclosure of conflict of interest

None.

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