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CLINICAL OBSERVATIONS

Caroli's disease in children: Is it commonly misdiagnosed?

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Abstract

Aim: Caroli's disease is a simple form of intrahepatic bile duct ectasia. It can be complicated with the involvement of liver parenchyma and portal hypertension. Herein, the difficult management of delayed presentation of Caroli's disease is reported. *Methods and results:* We report on four different forms of clinical presentation of Caroli's disease: an infant with fulminant liver failure, a teenager with persistent biliary fistula, a boy with hypersplenism in the face of portal hypertension and a girl with variceal bleeding.

Conclusions: Caroli's disease must be included in the differential diagnosis of cystic lesions in the liver. Delayed diagnosis of Caroli's disease is difficult to manage and appropriate investigations are warranted before planning a surgical approac!..

Key Words: *Caroli's disease, Caroli's syndrome, hepatic fibrosis, portal hypertension, recurrent cholangitis*

Caroli's disease is defined as the congenital dilatation and ectasia of the intrahepatic segmental bile ducts. It can be complicated with the presence of diffuse parenchymatous liver disease in addition to cystic lesions [1]. Most of the patients present early in life with the signs and symptoms of recurrent cholangitis or portal hypertension. The aim of the study is to draw attention to the difficult management of delayed presentations of Caroli's disease in the paediatric population.

Case reports

Four cases, each of whom was diagnosed to have pathologies other than Caroli, were referred to our department with complications. Table I documents the clinical properties, biochemical tests at admission and progress of these patients. None of the parents of the cases had consanguinity, and they were not investigated for cystic lesions of either liver or kidney, as they had no complaints.

Case 1

She was referred with multi-organ failure 1 y after an operation, in which the patent extrahepatic biliary system and cirrhotic liver were determined. She was in Child-Pugh C liver cirrhosis, and magnetic resonance (MR) imaging demonstrated multiple cystic dilatations in both lobes of the liver (Figure 1). The child was included in the liver transplant waiting list but died soon after her referral due to repeated episodes of severe cholangitis and liver failure.

Case 2

External drainage was performed after laparotomy, as the cyst detected by ultrasonography contained bile not a germinative membrane. She was admitted to us 8 mo after operation because of persistent biliary fistula. The serologic analysis for hydatid disease was negative. The computed tomography (Figure 2) and MR imaging revealed the presence of multiple cysts in dilated bile ducts in the vicinity of the cystic lesions in both liver lobes. She also had medullary spongious cysts in both kidneys. The drainage tube was gradually removed. The free bile drainage through the fistulous tract easily ceased by the application of a nipple to the skin level. No derangement in liver and kidney function tests was detected in her follow-up. Blood pressure was in normal ranges for her age.

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Table I. Clinical properties, biochemical tests at admission and progress of the patients are documented.

	Case 1	Case 2	Case 3	Case 4
Age, sex	2 mo, female	9 y, female	9 y, male	10 y, female
Complaint	prolonged jaundice	abdominal pain	abdominal pain	abdominal pain
Diagnosis	biliary atresia	hydatid disease	cryptogenic cirrhosis	simple cyst
Approach	laparotomy, biopsy	laparotomy, external drainage	follow-up	follow-up
Reason for reference	multi-organ failure	persistent biliary fistula	cholangitis, hypersplenism	variceal bleeding
Haematocrit	11	40	14	38
Leukocyte	1300	9800	1100	6700
Platelet	15 000	337 000	27 000	175 000
Albumin	1.2	4.3	2.5	3.9
Total bilirubin	6	0.63	5	0.75
SGOT/SGPT	430/380	120/221	70/100	30/20
Liver biopsy	cirrhosis	minimal fibrosis	moderate fibrosis ductulary proliferation bile plugging leukocyte infiltration	moderate fibrosis ductulary proliferation bile plugging leukocyte infiltration
Diagnosis	Caroli's syndrome	Caroli's disease	Caroli's syndrome	Caroli's syndrome
Cyst location in MRI	right–left lobes	right–left lobes and kidneys	right lobe	right lobe
Approach	transplantation list	nipple	splenectomy, sclerotherapy	sclerotherapy
Follow-up period	exitus	7 y	3 y	2 years

Normal ranges and units for biochemical tests: haematocrit: 35–46%; leukocyte: 3.8–10.8 × 10^3 μ/l; platelet: 150–400 × 10^3 μ/l; albumin: 3.5–5 g/dl; total bilirubin: ⩽1 mg/dl; SGOT: ⩽42 U/l; SGPT: ⩽48 U/l.

Case 3

He was referred with cholangitis and hypersplenism after 4 y of follow-up because of cirrhosis and portal hypertension. MR imaging detected multiple cysts with varying sizes communicating with each other in the right liver lobe (Figure 3). Splenectomy and wedge liver biopsy were performed after regression of the cholangitis attack with antibiotherapy. Oesophageal varices were detected in endoscopy at the same session. He is being followed-up in the endoscopic sclerotherapy programme for 3 y. He is well with no abdominal collection and variceal bleeding.

Case 4

She was admitted with variceal bleeding, which was controlled with endoscopic sclerotherapy. The MR imaging determined the increase in size of the cyst located in the right liver lobe, which had been assumed to be a simple cyst for 2 y, and documented its communication with biliary system (Figure 4). She was

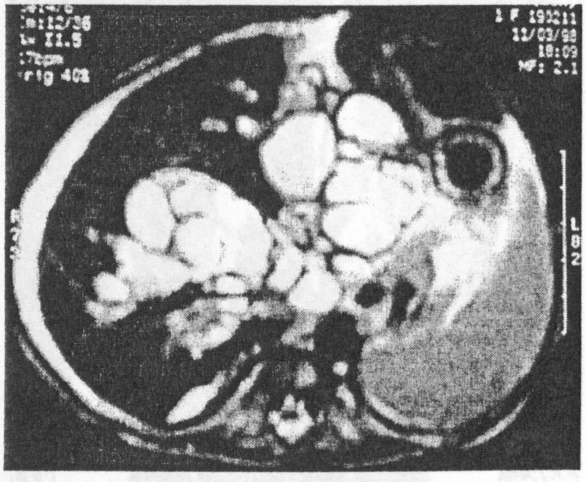

Figure 1. T2-weighted MR image showing multiple cysts connecting with the biliary system in both lobes of the liver with ascites. The outer contour of the liver is irregular.

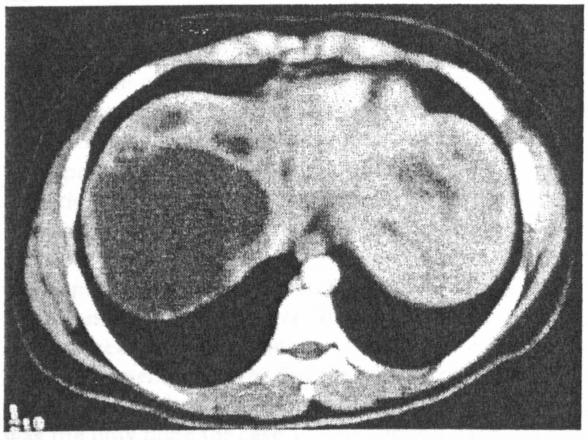

Figure 2. Abdominal computed tomography demonstrating cysts in both liver lobes. A dilated bile duct around the portal vein, central dot sign, which is typical for Caroli's disease, is seen at the periphery of the cysts in the right liver lobe.

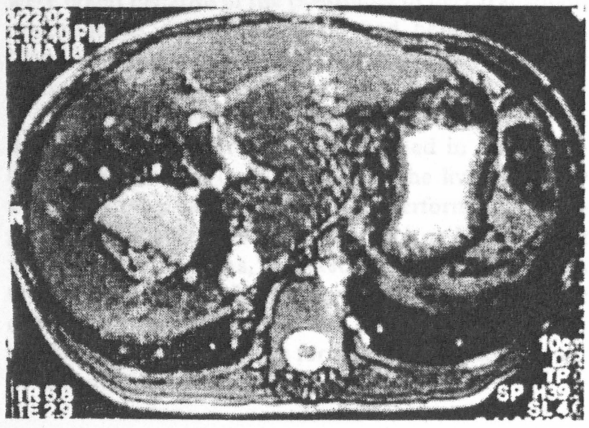

Figure 3. The connection of the cysts in the right liver lobe with the bile ducts is demonstrated in this fat-saturated T2-weighted axial MR image.

included in the sclerotherapy programme. No bleeding attacks have occurred since then and liver functions have been preserved.

Discussion

Caroli's disease is described as congenital cystic dilatations of the intrahepatic bile ducts that communicate with the biliary system. An arrested re-modelling process of the ductal plate of the intrahepatic bile ducts is the probable pathogenetic factor of the disease [2–4]. Desmet et al. suggested that abnormal biliary structures are the result of improper ductal plate remodelling and the loss of balance with the surrounding mesenchymal tissue. Caroli's syndrome, a more

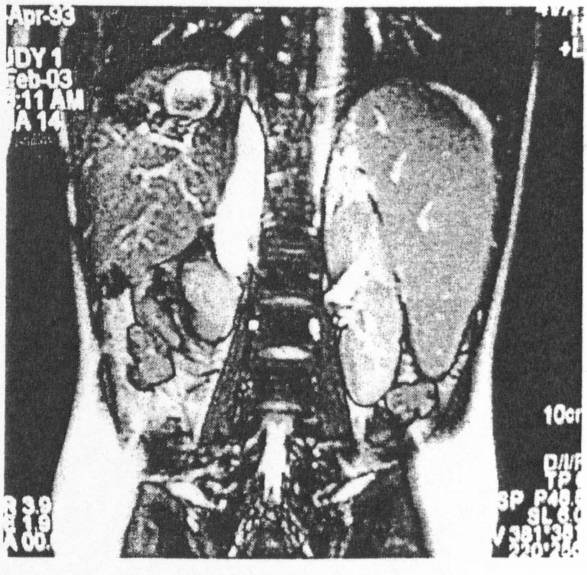

Figure 4. The cyst in the right liver lobe communicating with the biliary system is documented in this coronal T2-weighted MR image.

frequent variety, combines the lesions of ductal plate malformation and congenital hepatic fibrosis [2,5]. It seems that this theory was compatible in three patients with liver parenchymal involvement in this series. However, it is difficult to adapt this concept to the second case, who was diagnosed to have Caroli's disease.

The onset of symptoms can occur as early as the neonatal period, or the clinical course may be asymptomatic for the first 5–20 y; and, infrequently, the entire life of an individual [1,2,6]. The clinical setting varies from the neonatal period to early childhood as presented in our cases.

Repeated episodes of cholangitis and intrahepatic biliary lithiasis due to bile stagnation and sludge formation can lead to secondary biliary cirrhosis. Biliary epithelial dysplasia and cholangiocarcinoma have been associated with Caroli's syndrome, indicating a pre-malignant nature of this disease [1,2,7].

The condition typically causes recurrent cholangitis, which may present with any combination of fever, jaundice or abdominal pain. Portal hypertension complications could be the reason for admittance, also as in case 4. The disease might be associated with autosomal recessive polycystic kidney disease [12]. In the presented series, case 2 was found to have medullary spongious cysts in both kidneys in association with intrahepatic cystic dilations.

Diagnosis not only relies on detection of the cysts on ultrasound examination or computed tomography scanning but also on showing the communication of the cysts with the biliary tree [2,8]. Hepatobiliary hydroxyiminodiacetic acid scanning, endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography differentiate Caroli's disease from polycystic liver disease, simple liver cysts, lymphangioma or multiple liver abscesses, which do not communicate with the biliary tree. In this regard, MR imaging is a new and non-invasive method available to demonstrate the biliary system [2,9–11].

The aim of the treatment is to obtain sufficient biliary drainage and relieve the symptoms. It includes ursodeoxycholic acid, endoscopic retrograde cholangiopancreatography for hepatolithiasis and surgical resection when one lobe of the liver is primarily involved [1,8]. The cystic changes are diffuse in 60–80% of cases, but may be located in one lobe or segment of the liver, of which the left side is more common. Orthotopic liver transplantation appears to be a reasonable treatment option in the presence of a decompensated liver disease and its related severe complications [1,2]. Orthotopic liver transplantation was the only hope for case 1. The second case did not have any cholangitis attacks for 7 y and is being conservatively followed up. Splenectomy was performed in case 3 because of hypersplenism, but no further steps involving the right-sided monolobar Caroli's syndrome

were taken because of the possibility of liver transplant operation in the future as he had hepatic fibrosis. Complications related with portal hypertension are treated in case 4.

Caroli's syndrome can present in various forms during childhood. It must be included in the differential diagnosis of cystic lesions in the liver. Surgery should not be carried out before performing appropriate radiological investigations, such as MR imaging in the suspected cases, to detect communication with the biliary system. The suspected cases should be directed to referral centres for better evaluation and treatment strategy, in both forms of the disease, should be individualized for each case.

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