

Caroli's disease: An unusually early presentation

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Abstract

Caroli's disease is a rare congenital disorder characterized by cystic dilatation of large intra-hepatic bile ducts. The affected patient presents with recurrent episodes of cholangitis usually manifesting in adulthood. Imaging studies and liver biopsy help establish a diagnosis. We describe a case of Caroli's disease in an infant aged 5 months who presented with recurrent episodes of high grade fever, lethargy and refusal to feed since neonatal period necessitating hospitalisation and antibiotic therapy. A sibling aged 5 years had died due to polycystic kidney disease. In the current hospitalisation, laboratory parameters were suggestive of sepsis. USG abdomen was suggestive of central intra hepatic bile duct dilatation. Diagnosis was established on MRCP which revealed multifocal dilatation of main hepatic ducts with patent biliary confluence. However intrahepatic biliary radicles appeared normal. The liver biopsy showed mild proliferation of irregular ductal structures with normal appearing parenchyma. Thus the clinical, laboratory and imaging studies were pathognomic of Caroli's disease. The patient was provided IV antibiotics with supportive care and discharged home on nutritional supplements and ursodeoxycholic acid. The patient was advised subsequent liver transplantation. The uncommon feature of this case of Caroli's disease was its presentation in infancy as opposed to the hitherto reported cases which are in the second or third decade of life. This case highlights the need to nurse a high index of suspicion when dealing with an infant/child who has repeated hospitalisations with features of sepsis to look for an underlying anomaly.

Keywords: Caroli's Disease, Cholangitis, Intrahepatic Biliary Dilatation, Magnetic Resonance Cholangiopancreatography (MRCP)

Introduction

Caroli's disease (CD) is an uncommon congenital malformation, first described by Jacques Caroli.⁽¹⁾ The defective remodelling affecting the large intra hepatic biliary radicles results in Caroli's disease, while in Caroli syndrome the entire intra hepatic biliary tree is affected.⁽²⁾ The incidence of this rather uncommon disease is 1/10,00,000 and manifests in the third decade of life with features of recurrent cholangitis.^(3,4) The disease is essentially diagnosed by MRCP which shows presence of cystic liver lesions in continuity with the biliary tree and supported by liver biopsy which reveals the presence of dilatation and proliferation of bile ducts. We describe a case of Caroli's disease in a male baby aged 5 months, who presented with recurrent episodes of fever, lethargy and refusal to feed. Abdominal USG, MRCP and liver biopsy studies clinched the diagnosis. This case is unusual in its very early presentation in infancy as opposed to previous reports in third and fourth decade of life.

Case Report

A male infant aged 5 months weighing 3.5 kg was admitted with complaints of recurrent episodes of high grade fever, lethargy and refusal to feed since neonatal period. The baby was born out of a non-consanguineous marriage to a 28 year old third gravida mother with no adverse antenatal influences. The baby was treated in the neonatal period for jaundice and sepsis. There was a sibling death at 5 years of age due to complications of polycystic kidney disease.

On examination the infant was febrile (temperature 39.5 degree), lethargic and dehydrated.

The blood pressure and oxygen saturations were normal. Abdominal examination revealed enlarged, firm and non-tender hepatomegaly (liver span- 7.5 cm). Examination of other systems was normal.

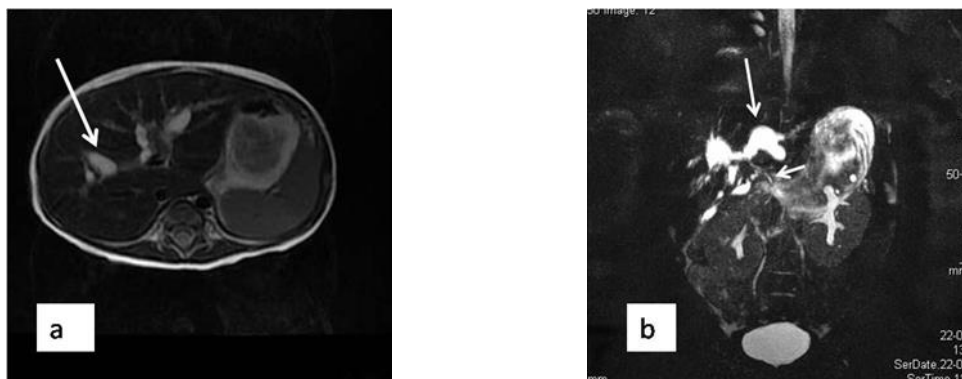


Fig. 1: MRCP Studies of patient revealing caroli's disease

- (a) Axial T2W HASTE (Half Fourier Acquisition Single Shot Turbo Spin Echo) image demonstrates the intrahepatic biliary tree with multifocal dilatation of central biliary radicles (arrow).
- (b) MRCP 3D sequence depicting the dilatation of main hepatic ducts (large arrow) and normal intrahepatic biliary radicles. Common bile duct is normal in calibre (small arrow).

Laboratory investigations revealed polymorpho leucocytosis, raised CRP and normal platelet counts. Blood Culture was sterile. Liver function tests were normal. There was hyponatremia (168meq/l) & normokalemia (3.8meq/l). Renal function tests revealed azotemia (BUN – 146mg/dl) and serum creatinine values of 2.06meq/l. TORCH studies were non-contributory. Ultrasound examination of the abdomen revealed grossly enlarged liver with normal echotexture. Central intra hepatic biliary radical dilatation was marked. Kidneys were enlarged bilaterally with increased echogenicity with loss of corticomedullary differentiation. MRCP studies showed multifocal dilatation of main hepatic ducts with patent biliary confluence normal in calibre. Kidneys were enlarged bilaterally with increased signal intensity on T2W images. Liver biopsy studies were suggestive of ductal plate malformation viz. predominantly maintained lobular architecture with portal tracts showing bile ductular proliferation and focal duct injury. No significant parenchymal inflammation was seen. (Fig. 2 & 3)

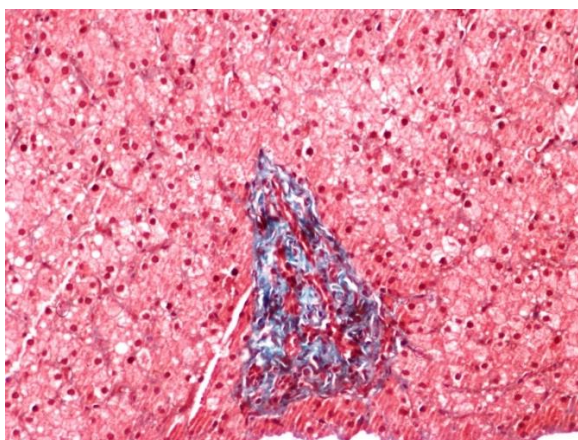


Fig. 2: Histopathology studies of liver (Masson's Trichrome)

Liver biopsy showing mild proliferation of irregular ductal structures with normal appearing parenchyma.

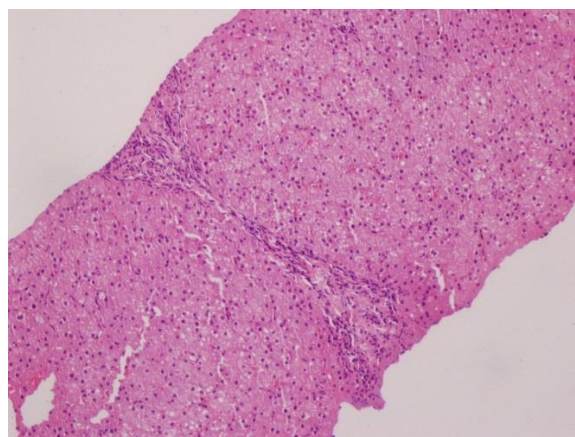


Fig. 3: Histopathology Study of Liver (Hematoxylin & Eosin Stain)

Liver biopsy showing mild ductular proliferation with normal appearing parenchyma.

Based on the clinical picture, laboratory findings of sepsis, imaging studies demonstrating intrahepatic central biliary radical dilatation and liver histopathology picture of bile duct proliferation, a diagnosis of Caroli's disease was made.

The infant was treated with intravenous fluids, antibiotics (Cefotaxime & Levofloxacin) and supportive therapy. He became afebrile, accepted orally and showed clinical & laboratory regression of infection. He was discharged with the diagnosis of Caroli's disease with the provision of nutritional supplementation and ursodeoxycholic acid (UCDA) therapy. The patient was advised liver transplant as a long term measure. Two months later the baby was hospitalised with features of septic shock to which he succumbed within a few hours.

Discussion

Caroli's disease and syndrome represent the varied spectrum of ductal plate malformation at different biliary levels. Caroli's disease occurs when there is ductal plate remodelling at the level of large intra hepatic biliary ducts. Caroli's syndrome however denotes involvement of the smaller ducts with congenital hepatic fibrosis. These two entities are seen in association with various renal disorders including autosomal recessive polycystic kidney disease, medullary sponge kidney and medullary cystic disease.⁽⁵⁾ Caroli's disease is sporadic in occurrence while Caroli's syndrome is inherited as autosomal recessive trait.^(6,7) The two conditions represent different stages of the disease which manifests as ductal dilatation and periportal fibrosis.⁽⁸⁾

Clinically the affected patients present with recurrent episodes of cholangitis with the risk of sepsis and bacteremia usually in the third decade and may sometimes even remain asymptomatic throughout life. The patients present with clinical features of cholangitis, intra hepatic calculi, abscess and sepsis.⁽⁹⁾ However the disease may also remain asymptomatic throughout life.⁽¹⁰⁾ There is approximately 7% risk of malignancy in Caroli's disease.⁽¹¹⁾ Our index case presented with recurrent episodes of sepsis in the first year of life which is unusually early as compared to previous reports.

Characteristic imaging findings include dilated sacculi or cystic spaces communicating with the biliary tree which can be seen either on USG, CT or MRI abdomen. Other findings which can be seen are saccular or tubular dilatation of biliary radicles, intraluminal bulbar protrusion, septation within the biliary radicles and portal radicles surrounded by the dilated ducts which give the appearance of central dot sign on axial scan viz. portal radicles appear as echogenic or hyperdense centrally surrounded by the dilated bile duct.⁽¹²⁾ Sludge or calculi can be seen within the dilated ducts. In the present case, the dilatation of main hepatic biliary ducts was prominent.

MRCP is the modality of choice as it is non-invasive and the entire biliary tree and hepatic parenchyma can be evaluated in a single study. In Caroli's disease there is either multifocal dilatation or diverticular outpouching of intra hepatic biliary ducts giving lollypop tree appearance which means cystic structures of varying size and shapes communicating with biliary tree. In our case there was multifocal dilatation of large intrahepatic biliary ducts while the smaller ducts and common bile duct was normal.

Differential diagnosis includes polycystic liver disease, obstructive biliary dilatation, primary sclerosing cholangitis, biliary papillomatosis and choledochal cyst. In polycystic liver disease multiple cysts are seen in liver which are not seen in continuity with the biliary tree with multiple renal cysts. Clinically these patients will have abdominal pain with normal liver function with deranged kidney function and hypertension. In obstructive biliary disease the cause of obstruction is either a calculi, mass

or stricture. Sclerosing cholangitis can be primary or secondary and on imaging there will be alternate areas of dilatation and narrowing of biliary radicles. Choledochal cyst depending on the type, would be seen as fusiform, focal or saccular dilatation of entire CBD or multifocal dilatation of intrahepatic biliary radicles.

The goal of management rests upon the spectrum of clinical findings which include recurrent attacks of cholangitis with cholelithiasis or recurrence of sepsis which is treated with antibiotic therapy and ursodeoxycholic acid (UCDA). Emergence of drug resistant polymicrobial flora may result subsequently leading to severe sepsis and adding on to the mortality in such patients. In patients with Caroli's disease confined to one lobe, hemi-hepatectomy is the choice. In contrast diffuse Caroli's disease needs an extended resection (multi-section ectomy). For patients with diffuse involvement of both lobes in association with cirrhosis or associated hepatic fibrosis, liver transplantation is the option. Septicaemia and cholangitis is treated with appropriate antibiotics. Litholysis and UDCA is indicated for intra hepatic cholelithiasis.⁽¹³⁾ In our case baby was managed for sepsis and discharged with supportive therapy viz. mineral & vitamin supplementation, UCDA and nutritional rehabilitation. The option of liver transplantation was provided to the parents.

Conclusion

Caroli's disease is a rare congenital disorder usually presenting in the third decade of life. The disease presents with recurrent attacks of cholangitis and septicaemia along with cholelithiasis and hepatic abscess. Our case is unusual in that it manifest all the classical features of Caroli's disease at a very early age i.e. infancy. This case reiterates the need to entertain a high index of suspicion when dealing with a baby getting recurrent episodes of sepsis. This case emphasises the need to investigate recurrent sepsis in infancy for an underlying congenital abnormality. An early diagnosis and management will ensure better survival and improved quality of life and also enable appropriate genetic counselling for parents.

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