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Early onset Caroli's disease with associated renal cystic disease presented with recurrent fever and epigastric pain: a case report

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Abstract

Background Caroli's disease is characterized by non-obstructive dilatation of intrahepatic biliary radicals with formation of calculi followed by recurrent episodes of cholangitis. It is a rare congenital malformation and often remains silent, diagnosed accidentally. But if kept unattended, and without any early intervention, it may lead to fatal residual complications. Hence, its early recognition is of utmost importance to prevent recurrent cholangitis, hepatic abscess, liver cirrhosis and cholangiocarcinoma. Hence, we feel that this case must be reported so as to increase awareness among physicians regarding this entity.

Case presentation We hereby report a case of 10-year-old boy who reported with complaints of recurrent episodes of fever, breathing difficulty and multiple episodes of epigastric abdominal pain with apparently healthy siblings. His routine investigation, laboratory parameters were within normal limits. Ultrasonography abdomen showed liver with normal echo-texture with varying sized multiple thin walled cysts involving both the lobes, right more than left with saccular dilatation of 2nd and 3rd order intra-hepatic biliary radicals without calcification without any colour flow on Doppler evaluation. The common hepatic and common bile ducts were normal in calibre and lumen. Magnetic resonance imaging abdomen had similar findings and upper GI endoscopy was also normal. He was finally diagnosed to be a case of Caroli's disease and was managed with broad spectrum antibiotics, ursodeoxycholic acid, multivitamins, and calcium supplements. He made an uneventful recovery thereafter. Parents were counselled about the risk of cholangitis and cholangiocarcinoma and was referred to tertiary care centre for genetic counselling and for future need of liver transplantation.

Conclusion Age presentation of Caroli's disease varies. Majority present during adolescence and early adulthood. This often poses a diagnostic challenge owing its rare entity and silent presentation. A strong index of suspicion and prompt diagnosis is warranted to prevent its fatal residual complications.

Keywords Caroli's disease, Caroli's syndrome, Autosomal recessive polycystic kidney disease, PKHD1

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Background

Caroli's disease was first described by a French physician Dr. Jacques Caroli in 1958. Caroli's disease and Caroli's syndrome are rare and have an incidence of less than one per 100,000 population. The incidence of autosomal recessive polycystic kidney disease (ARPKD)/congenital hepatic fibrosis is approximately 1:20,000 live births [1, 2]. Men are affected less as compared to females with an estimated male to female ratio of 1:1.8. These conditions are usually diagnosed in first two decades of life; however, individuals may remain asymptomatic [3, 4]. It is an autosomal recessive disease and is recognized in two forms: Simple form or Caroli's disease and Caroli's syndrome when associated with congenital hepatic fibrosis. These patients are at an increased risk for developing cirrhosis of liver with portal hypertension.

Caroli's disease is sporadic, whereas Caroli's syndrome is generally inherited in an autosomal recessive [5]. Caroli's disease may be diffuse or focal. The focal form may be segmental or lobar. Caroli's disease belongs to a group of hepatic fibro polycystic diseases [6, 7]. A genetic cause is postulated, due to its association with ARPKD. Mutations in *PKHD1* gene on chromosome 6p21, which is the gene linked to ARPKD, have been identified in patients with Caroli's syndrome also.

Cholangiociliopathies in a rat model appears to be associated with decreased intracellular calcium and increased cyclic AMP (cAMP) levels, causing hyperproliferation of cholangiocytes, abnormal cellular matrix interactions, and deranged fluid secretion, which result in biliary dilatation [7]. In Caroli's disease, hepatic impairment is restricted to formation of cysts and usually presents with right hypochondrium pain, obstructive jaundice, and cholangitis. However, Caroli's syndrome cystic disease coexists with congenital hepatic fibrosis. These patients clinically manifest features of hepatic insufficiency and portal hypertension and usually present with splenomegaly, ascites, edema, coagulation disorders, and esophageal varices [8, 9].

Case presentation

We are reporting a case of Caroli's disease in a 10-year-old boy who reported with complaints of recurrent episodes of fever, breathing difficulty, and multiple episodes of epigastric abdominal pain. There was no history of consanguinity. Their elder sibling was asymptomatic.

The patient was admitted with a clinical suspicion for lower respiratory tract infection. There was no pallor, cyanosis, clubbing, icterus or pedal edema, or venous engorgement of neck. The abdomen was soft and non-tender without organomegaly. Hemoglobin was 11 gm%, total leucocyte count was 11,700 cells/mm^3 with neutrophils and lymphocytes counts being 43% and 48% respectively. Total serum bilirubin was 0.2 mg/dL. Serum liver enzyme levels were normal. Serum gamma glutamyl transferase (GGT) level was 25 IU/L, blood urea and serum creatinine levels were 23 mg/dl and 0.7 mg/dL respectively. Serum electrolytes were normal. Urine routine and microscopic examination of was normal and culture grew no organisms. Chest radiography was reported as normal. Ultrasonography abdomen showed normal liver size with normal echo texture of hepatic parenchyma with multiple thin walled cysts of varying sized involving both the lobes, right more than left with saccular dilatation of 2nd and 3rd order intra-hepatic biliary radicals (Fig. 1). A well-defined thick walled cystic lesion measuring 6×3 cm was seen in segment VII e showing an intra-lesional solitary thick septa and dependent debris in the lumen. No calcification or any solid component is seen within the lesion. No color flow on Doppler was seen. The common hepatic and common bile ducts were normal in caliber and lumen. Main portal vein and its right and left branches were normal in calibre with echo-free lumen and revealed normal Doppler characteristics. The gall bladder, pancreas, and spleen were normal. Interestingly kidneys showed diffusely raised cortical echotexture with preserved corticomedullary differentiation. However, kidneys were normal in size and outline. No calculus or dilatation of collecting system was seen. A single simple cortical cyst in left kidney measuring 15×9 mm was also reported. Thus depending upon the ultrasonographic findings, a diagnosis of Type V Choledochal cyst was made with a possibility of secondary infection or abscess formation in one of

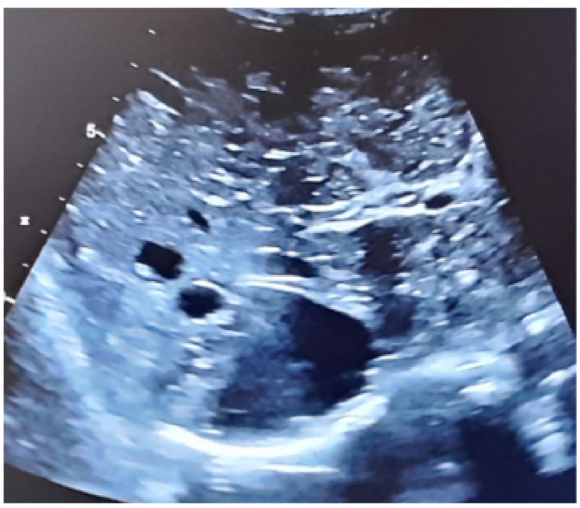

Fig. 1 USG abdomen showing multiple dilated intrahepatic biliary radicals with a large dilated biliary radical in seg VII of right lobe of liver

the dilated biliary radical in segment VII. A suspicion of renal medical disease was also raised. The patient underwent a magnetic resonance imaging (MRI) of abdomen which confirmed the ultrasonographic findings (Fig. 2). The upper GI endoscopy was normal with no evidence of portal hypertension. Further evaluations ruled out any evidence of hepatic synthetic dysfunction or cholestasis at present. The boy was managed with broad spectrum antibiotics and ursodeoxycholic acid, multivitamins, and calcium supplements. He responded well thereafter. Parents were counselled about the risk of cholangitis and cholangiocarcinoma associated with the condition and were advised for genetic counselling for Caroli's disease and autosomal recessive polycystic kidney disease spectrum. With the future possibility of liver transplantation. Presently the boy is under follow-up.

Discussion

Caroli's disease is a rare entity and diagnosed with strong clinical suspicion and supportive diagnostic imaging [1, 3]. Clinically, it may be suspected in patients presenting with pain in right hypochondrium or epigastrium with fever, jaundice or a palpable mass in right upper abdomen. However, all these features may not be seen altogether leading to a diagnostic dilemma. During radiological evaluation, the disease may be suspected based on the characteristic pattern of dilatations involving intrahepatic biliary radicals [4]. A contrast computerised tomography (CT) of abdomen reveals intrahepatic dilatation of biliary radicals with a central dot sign which represents abnormally dilated biliary ducts with a cross-section of enhancing portal vein visualized as a dot in center, best appreciated in axial sections [2, 6]. This sign is useful to differentiate this condition from primary sclerosing cholangitis [3, 5, 7]. A magnetic resonance cholangio-pancreatography is highly useful in diagnosing this condition and has a high sensitivity and specificity. It provides necessary information about the severity and extent of hepatic involvement. The anticipated complications in a long-standing Caroli's disease such as cholangitis or cholangiocarcinoma can also be diagnosed with CT or MRI [9]. The treatment of this condition depends on the distribution of lesions. In cases with monosegmental or monolobar Caroli's disease, hepatic lobectomy may be a satisfactory treatment option since it prevents the future likelihood of malignancy [5, 7, 8]. However, in cases with diffuse dilatation of biliary radicals in both lobes, hepatic transplantation is the only feasible option [7]. The incidence of cholangiocarcinoma is estimated to be about 7% in overall cases of Caroli's disease. Thus, a regular follow-up by contrast-enhanced CT or MRI is suggested in these patients along with a high index of clinical suspicion [7, 9].

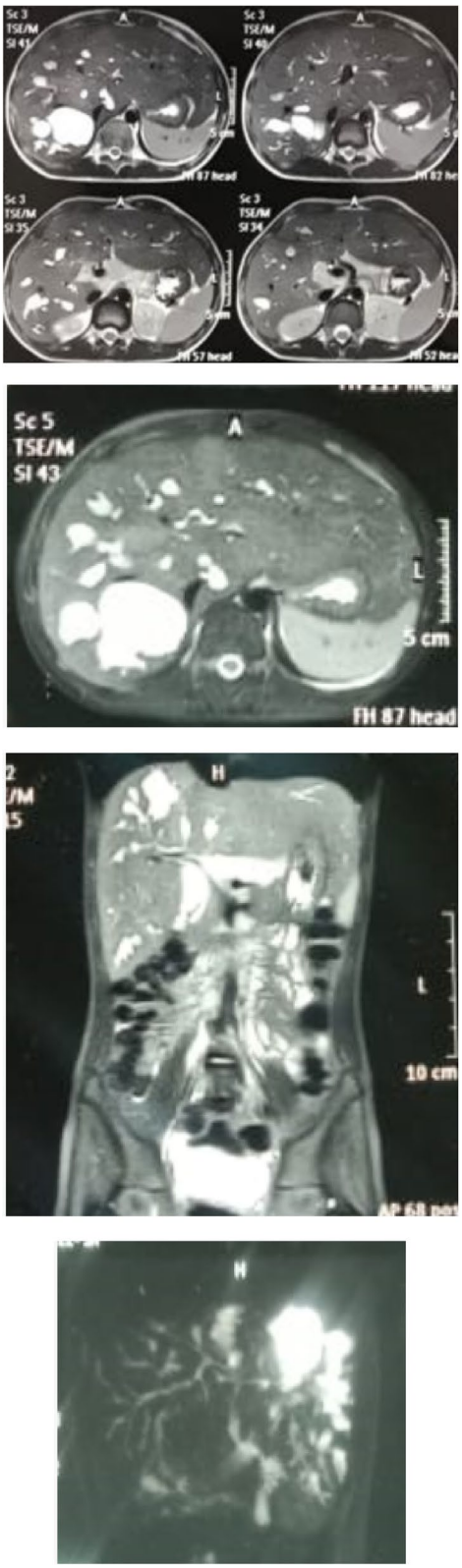

Fig. 2 MRCP abdomen shows multiple dilated intrahepatic biliary radicals appearing hyperintense in T2W axial section

Conclusions

Caroli's disease and Caroli's syndrome are congenital disorders characterized by multifocal dilatation of intrahepatic biliary radicals. The age at presentation varies, however majority of cases present in early adulthood. The disease poses a diagnostic challenge owing to its rare nature thus to ensure early diagnosis a strong clinical suspicion with supportive radiological imaging is strongly recommended. An early diagnosis is desired since it may predispose such patients to fatal complications like cholangitis or cholangiocarcinoma.

Abbreviations

ARPKD	Autosomal recessive polycystic kidney disease
cAMP	Cyclic adenosine monophosphate
GGT	Gamma glutamyl transferase

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Authors' contributions

AbM and AKM conceptualized and drafted the initial manuscript, and reviewed and revised the manuscript. AnM revised and did final editing of the manuscript. AKS critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Verbal and written informed consents were given by the patient's parents for the publication of this case.

Competing interests

The authors declare that they have no competing interests.

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