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RESEARCH ARTICLE

A RARE CONGENITAL LIVER DISORDER WITH VARIED CLINICAL PRESENTATIONS –REPORT OF TWO CASES

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ABSTRACT

Caroli's disease and Caroli's syndrome are rare congenital cystic disorders of intrahepatic biliary radicals. It is still unclear whether they represent distinct entities or, are different stages of the same disease distinguished by hepatic fibrosis. Here we are reporting two cases-a three-year-old boy presenting with portal hypertension, cholestatic jaundice and rickets, and a ten-year-old girl with recurrent episodes of cholangitis. They were diagnosed as Caroli's syndrome and Caroli's disease respectively. A renal calculus with medullary sponge kidney was detected on abdominal imaging in second case. We concluded that they are probably the different stages of the same disorder and ongoing search should be continued to quantify accurately the disease spectrum, and its associations.

INTRODUCTION

Caroli's disease (CD) is a rare congenital condition (estimated incidence, 1/1,000,000 populations) characterized by multifocal segmental dilatation of the intra-hepatic biliary channels (Miller *et al,* 1995). It is mainly inherited in an autosomal recessive manner, although other modes of inheritance (autosomal dominant) were also described (Tsuchida *et al,* 1995). But the exact mode of inheritance is still unknown. Two forms of CD have been identified - the pure form and the complex form (Caroli's syndrome, CS) in which congenital hepatic fibrosis accompanies the bile duct abnormalities. The pure form is frequently accompanied by stone formation, recurrent cholangitis and hepatic abscesses. CS, more common form, might present with portal hypertension and is usually associated with autosomal recessive (ARPKD) or dominant polycystic kidney disease (ADPKD), renal tubular ectasia, or others cystic diseases of the kidneys and possibly the pancreas (Borges Pinto *et al,* 1998). But the presentation of CS with cholestatic jaundice and rickets or association of the pure form with medullary sponge kidney and renal calculus, have rarely been described earlier in literature. Here we are reporting two such unique presentations and/or association of this rare disorder.

Case Presentations

First case, a 3-year-old boy, born of non-consanguineous parentage with uncomplicated antenatal and perinatal period, presented with gradual swelling of upper abdomen for last one year, progressive cholestatic jaundice and two episodes hematemesis and melena in last one month. There was no history of fever, abdominal pain, vomiting or other bleeding manifestations. Past and family histories were unremarkable. His development was normal and immunization was complete. On examination, the child was moderately pale, deeply icteric without any edema or clubbing. His vitals including blood pressure (94/60 mmHg) and skin condition were normal. His weight (12.6 kg) and height (95 cm) were at 15th and 50th percentile of WHO growth charts, respectively. Systemic examination revealed bulging upper abdomen with downward displacement of umbilicus without superficial venous engorgement. There was moderate firm, non-tender hepatomegaly (liver span 12.5) with smooth surface and well-defined margins. He also had moderate splenomegaly without any palpable abdominal masses or ascites. Musculoskeletal system examination showed bilateral genu valgum and other features of rickets (hypotonia, widened wrist) (Fig. 1). Other system examinations revealed no abnormalities. Blood reports showed Hb – 8.2gm%, TLC – 6200/µL, Neutrophils 68, Lymphocytes 25, Monocytes 2, Eosinophil 4, Basophil1, ESR 36mm. LFT showed total serum bilirubin (TSB) 4.8mg%, conjugated (CB) 2.8 mg%, AST 89 U/L, ALT 68 U/L, γ-glutamyl transferase (GGT) was 982 IU/L (reference, 5–50), alkaline phosphatase (ALP) 386 IU/L (reference, 30–150), total protein 5.6gm%, serum albumin – 3.4gm%; serum calcium – 6.8mg%, serum phosphate - 2.9mg%. The serum parathormone level was 256 pg/ml, (reference, 2-72). The 25-hydroxy-cholecalciferol level was 12 ng/mL, (reference, 20-100). Prothrombin time was 19sec (control 13sec) and activated

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partial thromboplastin time was 59 sec (control 39sec). All other blood reports were normal and serological markers for viral hepatitis were negative. Skeletal x-ray showed features of rickets (Fig. 2). We treated the patient with injections vitamin K injection cholecalciferol (600000 IU) and other fat soluble vitamin supplementation, along with oral calcium supplementation and endoscopic band ligation of the esophageal varices. Abdominal USG showed hepato-splenomegaly, dilated intrahepatic biliary radicals without any gall stones, and normal kidneys. Upper gastrointestinal endoscopy revealed Grade III esophageal varices. CT scan (Fig. 3) and magnetic resonance cholangiopancreatography (MRCP) showed hugely dilated intrahepatic biliary radicles suggestive of Caroli's disease. So, our diagnosis was a case of CS complicated by cholestatic jaundice and rickets.

Second case, a ten-year-old girl presented with high grade fever with chill and rigor, right upper abdominal pain and non-bilious vomiting for last five days. There was no history of jaundice, abdominal distension, bleeding manifestations or chronic medications. There was history of two similar episodes, eight months and three months back; for which she required hospitalization and improved with conservative managements (intravenous fluids and antibiotics). The patient was born of non-consanguineous parentage with normal birth history and insignificant family history. On examination, the child was toxic, slightly pale, highly febrile (103˚F), tachycardic and tachypnic with normal BP. General survey was otherwise unremarkable. Abdominal examination was normal except for local tenderness and rigidity over right hypochondrium. We also started conservative management, with which she responded. Blood reports showed Hb – 9gm%, TLC – 15200/µL, Neutrophils 76, Lymphocytes 20, Monocytes 1, Eosinophil 3, Basophil 0, ESR – 46mm, LFT showed TSB – 1.8mg%, CB – 0.8 mg%, ALP – 580 IU/L, ALT - 38 U/L, AST – 46 U/L, total protein and albumin were 6.2 and 3.8 gm% respectively. Other investigation reports (Typhi dot, Dengue serology, urine culture) were normal. USG abdomen showed dilated intrahepatic biliary channels without any hepatic infiltration (? hepatic cysts). Contrast enhanced CT scan revealed Type V choledochal cyst and a tiny calculus in the pyramid of the left kidney and early nephrocalcinosis due to medullary sponge kidney (Fig. 4). MRCP showed Caroli's Disease (Fig. 5). So our diagnosis was a case of pure form of CD with medullary sponge kidney complicated with renal calculus.

DISCUSSION

Although structural changes in CD are already present at birth, in most of the cases, the disease is diagnosed around the age of 20, with onset of abdominal pain, fever, hyperbilirrubinemia, hepatomegaly or symptoms of portal hypertension (Millwala *et al,* 2008). CD is rarely present in childhood although its occurrences in pediatric age group even in neonates have been reported (Keanea *et al,* 1997). Patients with CD may experience symptoms of intermittent abdominal pain owing mainly to cholestasis and choledocholithiasis or recurrent cholangitis with severe danger of bacteremia and sepsis. Biliary abscess, liver cirrhosis and Cholangiocarcinoma (approximately 7% of cases) are the other potential complications (Gupta *et al,* 2006).

Associated cystic dilatation of kidneys is seen in 60-80% of the cases (renal tubular ectasia, medullary sponge kidney, cortical cyst, ARPKD or rarely ADPKD) (Gupta *et al,* 2006, Bavikar and Kulkarni, 2011).

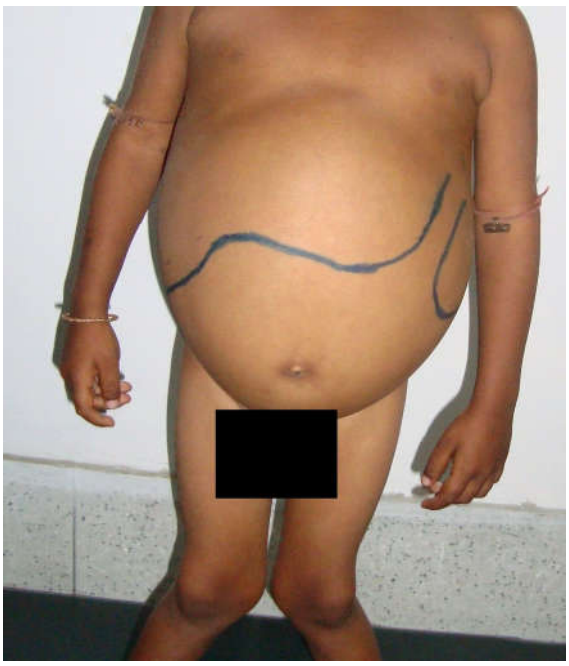

Fig. 1. Image of the patient showing widened wrist, genu valgum, protruded abdomen with hepatosplenomegaly

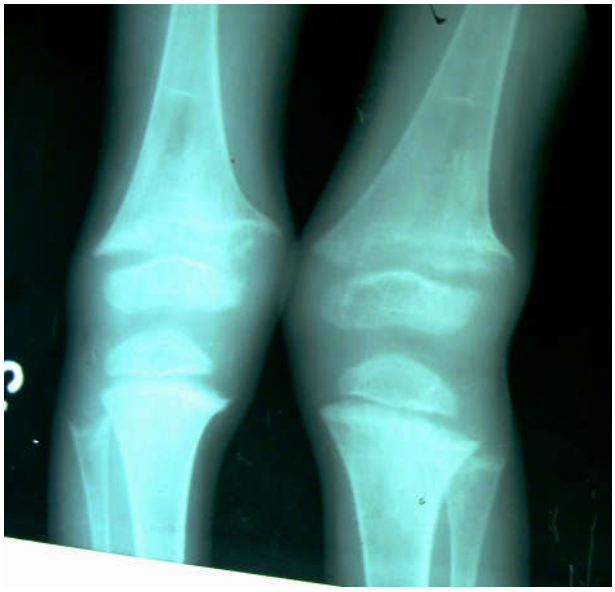

Fig. 2. X-ray right knee joint showing cupping, fraying and splaying suggestive of rickets

These patients are usually asymptomatic (as far as renal disease is concerned) but may develop renal stone disease and infections (Bavikar and Kulkarni, 2011). These conditions are commonly associated with CS. But association of renal stone and medullary sponge kidney with CD had not been described earlier as seen in our second case. Patients may rarely present with acute pancreatitis, uterovesicle calculi etc; or CD may rarely be associated with a sickle-cell disease, amyloidosis, the Laurence-Moon-Biedl syndrome, and some other rare disorders (Gupta *et al,* 2006).

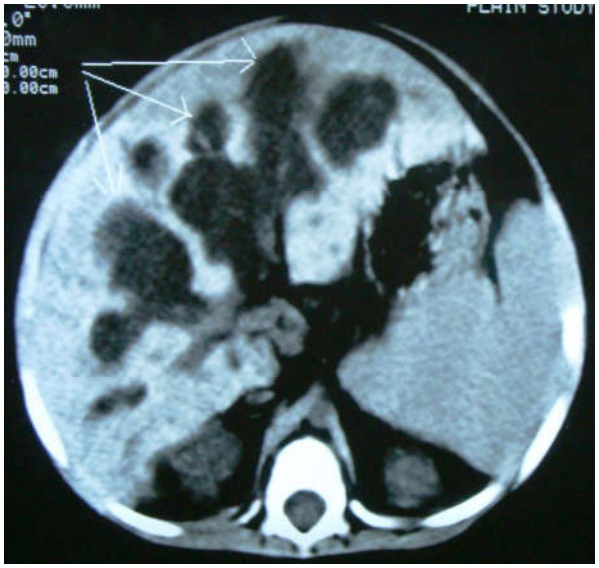

Fig. 3. CT Scan showing multiple cystic spaces with dilated intra-hepatic biliary radicles

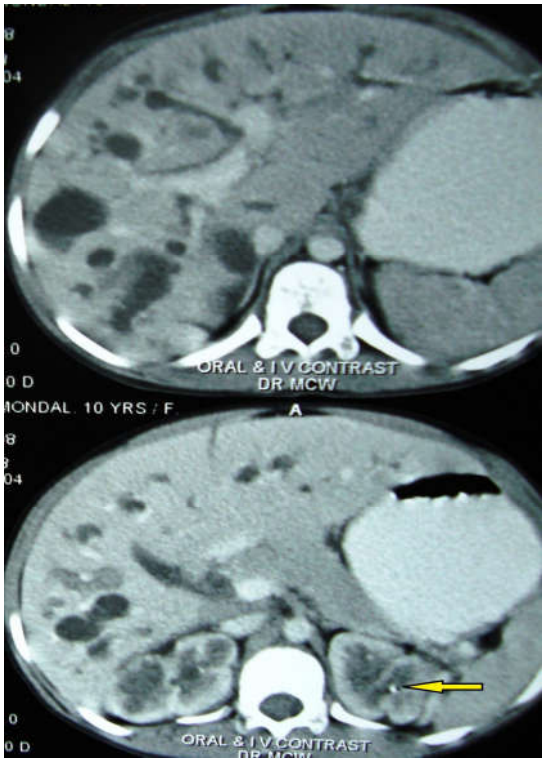

Fig. 4. CECT Scan of abdomen showing dilated intra-hepatic biliary channels with a tiny calculus in the pyramid of right kidney with evidences of early nephrocalcinosis suggestive of medullary sponge kidney

There is report of one case of CS from India where a nine year old boy presented with stage III chronic kidney disease with rickets (Shenoy *et al,* 2014). There are no reports of cases of CS complicated by cholestatic jaundice and rickets like ours. Endoscopic retrograde cholangiopancreatography (ERCP) and, especially in children, MRCP is the most specific and non invasive examination (Yonem and Bayraktar, 2007) to depict the multiple ductal dilatation seen in CD. It is still unclear whether these two types represent distinct entities or a single disorder distinguished by hepatic fibrosis. Many authors believe that the two conditions are different stages of the same disease (Bavikar and Kulkarni, 2011; Yonem O and Bayraktar, 2007). Liver biopsy was not done in our patient as the diagnosis was obvious and study reports showed that the correct diagnosis of congenital hepatic fibrosis may be determined in children using clinical, biologic, and noninvasive radiologic data without biopsy (Ernst *et al,* 1997). We conclude that CD and CS are, possibly the different stages of the same disorder. Still, ongoing search should be continued to quantify accurately the disease spectrum, its severity and associations.

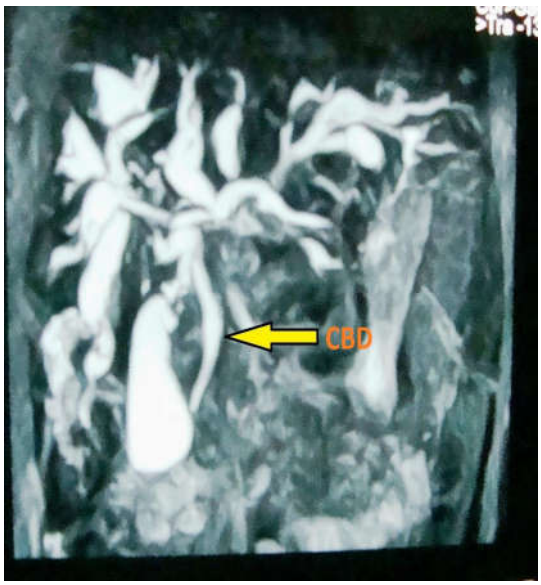

Fig. 5. MRCP showing dilated intrahepatic biliary radicals (type V choledochal cyst)

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