

## CAROLI'S DISEASE PRESENTING WITH HAEMATEMESIS AND MELAENA

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### Abstract

Caroli's disease is a rare congenital disorder of intrahepatic biliary tree characterized by multifocal communicating segmental saccular or cavernous dilatation of bile ducts. It involves the liver partially or diffusely. Common presentations are intermittent upper abdominal pain and fever due to recurrent cholangitis which may be complicated by liver abscess and intra ductal stone formation. Liver cirrhosis, cholangiocarcinoma and rarely amyloidosis are uncommon complications. Upper GI bleeding in the form of haematemesis and melaena is an uncommon presentation. A case of Caroli's disease with secondary biliary cirrhosis, who presented with haematemesis and melaena, is reported here.

**Key Words:** Caroli's disease; cholangitis; oesophageal varices; ductal stone; ductal plate; ductal plate malformation central dot sign; common bile duct.

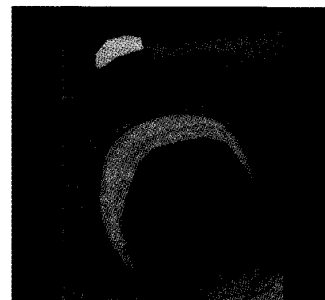
### Introduction

Caroli's disease is a rare inherited disorder of the liver characterized by saccular and cystic dilatation of intrahepatic bile ducts<sup>1</sup>. Though the first case of intrahepatic bile duct dilatation reported in 1906, Caroli's Disease clearly described by Jacques Caroli in 1958 in his classical paper<sup>2</sup>. Caroli described the disease as communicating non obstructive saccular or fusiform multifocal segmental dilatation of intrahepatic bile ducts<sup>2</sup>. The mode of inheritance is still unclear but in most cases it is transmitted in autosomal recessive fashion<sup>3</sup>. Autosomal dominant mode of inheritance was also reported in a family<sup>4</sup>. The disease results from the arrest of or a derangement in the normal embryologic remodeling of ducts, called ductal plate malformation and causes varying degrees of destructive inflammation and segmental dilatation<sup>7</sup>. Since his first report by Jacques Caroli there are many case reports and a number of small series reports of Caroli's disease at

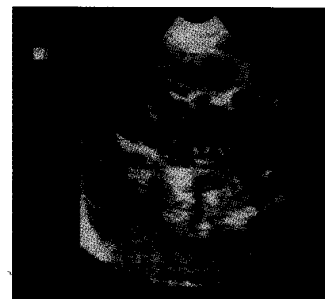
different age groups. The age of presentation varies widely. Most of the cases are diagnosed in children less than 10 years of age<sup>5</sup> and in a few detected in intrauterine life<sup>6</sup>. Review of literature reveals that the disease may remain asymptomatic or becomes symptomatic as late as the seventh decade<sup>2</sup>. The main clinical features are recurrent cholangitis and hepatomegaly<sup>2</sup>. Liver cirrhosis and portal hypertension complicated with haematemesis and melaena is an uncommon presentation.

### Case Report

A 42-years-old male admitted in the hospital with the complaints of haematemesis and melaena for 2 days, yellow discoloration of urine, upper abdominal pain and marked generalized weakness. He gave the history of a similar attack about one year back. Since then he noticed yellow discoloration of urine intermittently and progressive fatigue. He had intermittent mild to moderate right upper abdominal pain since his childhood and each episode of pain used to persist for several days. Those episodes were



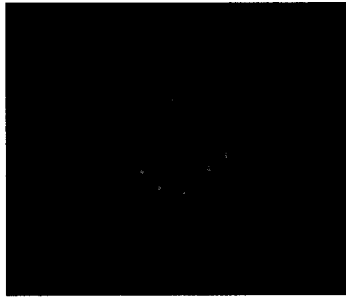
**Fig 1 :** Clinical photograph of the patient showing surgical scar mark



**Fig 2 :** USG showing cystic dilatation of intrahepatic bile ducts

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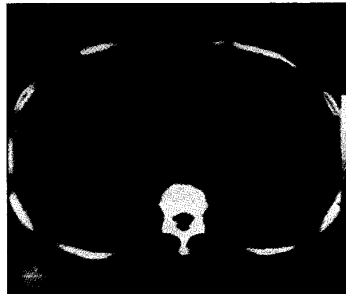
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**Fig 3 :** USG showing cystic dilatation of intrahepatic bile ducts containing stones

not associated with fever or jaundice but with occasional vomiting. Each time he was treated by local physicians and became asymptomatic.

On physical examination he was found icteric and moderately anaemic, afebrile and normotensive. Abdominal examination reveals a surgical scar mark of roof top incision (Fig.1), and it was soft and nontender. The liver was palpable but spleen was impalpable. There was no sign of ascites. Oedema and flapping tremour were absent. No other abnormalities were detected on systemic examination. Laboratory investigations showed that hemoglobin (Hb%) was 41%, total WBC count was



**Fig 4 :** Contrast enhanced CT showing echogenic septa in dilated bile ducts.



**Fig 5 :** CT shows cystic dilatation of intrahepatic bile ducts extensive involvement of both lobes of liver

7500/cmm, ESR was 120mm in 1st hour, ALT 73 unt/l and serum bilirubin was 4.5gm/dl, serum alkaline phosphatase was 198u/l, S. albumin was 3.3g/dl, prothrombin time was prolonged (16 Sec) HBs Ag was negative. Ultra Sonogram (USG) of abdomen showed hepatosplenomegaly with cystic dilatation of intrahepatic bile ducts involving both lobes of the liver (Fig. 2 & 3). There were multiple bright echogenic structures in dilated intrahepatic ducts of right lobe casting posterior acoustic shadow suggestive of stones. Computed tomography (CT) scan showed hepatomegaly with cystic dilatation of the intrahepatic bile ducts (Fig. 4 & 5). The cystic lesions involved both lobes of the liver. Some of the cystic lesions showed small hyperdense nodule like focus consistent with "Central Dot Sign". Others showed echogenic septa. The spleen was enlarged with uniform parenchymal density. The portal vein was dilated. No features of hepatic fibrosis were seen and both kidneys were normal in size, shape and position. CBD was not dilated. Liver biopsy was not done due to impaired liver function tests. Upper gastrointestinal endoscopy could not be done due to technical reasons. The episode of bleeding in this patient was probably due to ruptured esophageal varices caused by portal hypertension. A diagnosis of Caroli's disease with portal hypertension due to cirrhosis of liver was made in this patient. He was treated conservatively. By analyzing his previous medical records it reveals that he underwent medical and surgical treatment abroad two years back. Surgical interventions included open cholecystectomy, choledocolithotomy, T-tube drainage, CBD stenting, ERCP and sclerotherapy at different sessions. As his liver enzymes were persistently elevated he was advised for liver transplantation but was not possible due to poor socioeconomic condition. He was discharged with proper counseling and advised for regular follow up later.

#### Discussion

Two forms of Caroli's disease have been described in the literature. One is "Pure form" which shows only intrahepatic biliary tree dilatation called Caroli's disease; another is called Caroli's Syndrome in which intrahepatic bile duct abnormality is associated with congenital hepatic fibrosis and renal cystic disease<sup>8</sup>. Renal cystic diseases include modularly sponge kidney, corticalcyst and autosomal recessive kidney disease (ARKD)<sup>9</sup>. The former mainly affects the proximal or larger

intrahepatic bile ducts and the later affects distal or peripheral smaller bile ducts. Both the conditions result from malformation of embryonic ductal plate at different level of the biliary tree<sup>10</sup>.

Intrahepatic bile ducts develop from bipotential liver progenitor cells in contact with the mesenchyme of the portal vein and thus form "the ductal plate"<sup>11</sup>. The ductal plate is a double layered sleeve of cells (cholangiocytes) with a slit like lumen surrounding the portal vein at 8 weeks of gestation. Liver progenitor cells are bipotential cells capable of differentiation either into hepatoblasts or cholangiocytes. The ductal plates are remodeled and partially involuted to form mature tubular ducts. Lack of remodeling and insufficient resorption results in the persistence of periportal epithelial sleeves or "ductal plate malformation" (DPM)<sup>12</sup>.

Ductal ectasia predisposes to bile stangnation and formation of biliary calculi, cholangitis, biliary abscess, septicemia, liver cirrhosis and cholangiocarcinoma. Cholangiocarcinoma (7%) due to prolonged exposure of the ductal epithelium to high concentration of unconjugated secondary bile acids<sup>6</sup>. Amyloidosis is also described as a complication of Caroli's disease<sup>20</sup>. Choledochal cyst was found to be associated with Caroli's disease Todani et al described Caroli's disease as type IV A choledochal cyst<sup>14</sup>.

The diagnosis of Caroli's disease requires recognition of symptoms of liver dysfunction and characteristic features of imaging studies. Imaging studies will demonstrate the cystic dilatation of intrahepatic bile ducts are in continuity with the biliary tree. Ultra sonogram (USG) of abdomen, computed tomography (CT) scan, Endoscopic retrograde cholangio pancreatography (ERCP), Percutaneous Transhepatic cholangiography (PTC) and magnetic resonance cholangiography (MRC) all can demonstrate the lesions are in continuity with biliary tree<sup>7</sup>. Of these PTC and ERCP are invasive may predispose to bacterial cholangitis USG and CT scan are noninvasive and may show the cystic lesions in the liver with central dense dot like opacities, called "central dot sign" and linear band like opacities called intraductal bridging<sup>16</sup>. These features are diagnostic of Caroli's disease<sup>21</sup>.

"Central dot sign" corresponds to a portal vein branch protruding into the lumen of a dilated bile duct. Awareness of this sign allows an accurate diagnosis without resorting to more invasive and

expensive investigations. Intra ductal bridging are echogenic septa on USG and CT that completely or incompletely traversed the dilated lumen of the bile ducts. These are fibrovascular bundles containing portal vein and a branch of hepatic artery<sup>15</sup>. The cystic spaces often contain amorphous debris and calculi, as seen in this patient. Associated cystic lesions in kidney can be detected by USG and CT scan of abdomen. MRC is increasingly used to diagnose Caroli's disease as it provides excellent images of the extra hepatic and intrahepatic biliary trees<sup>13</sup>. This procedure is expensive and not available everywhere.

Differential diagnoses of Caroli's disease are polycystic liver disease, hydatid cysts, biliary hamartoma, primary sclerosing cholangitis, recurrent pyogenic cholangitis and obstructive bile duct dilatation. The first three are not in continuity with intrahepatic bile ducts. In the last one obstructive bile duct dilatation, the dilatation is most marked centrally tapers towards periphery and lacks focal areas of cystic dilatation. In primary sclerosing cholangitis and recurrent pyogenic cholangitis the ductal dilatation are not saccular in nature which is characteristic of Caroli's disease<sup>7</sup>.

Treatment depends on the clinical presentations and location of the biliary abnormalities. Cholangitis is treated with appropriated antibiotics. Recurrent cholangitis with cholelithiasis requires surgical drainage in addition. In case of intrahepatic cholelithiasis, litholytic therapy with ursodeoxycholic acid (UDCA) is indicated<sup>17</sup>. When ductal abnormalities localize to one lobe or segment lobectomy or partial hepatectomy relieves symptoms and appears to remove the disease and the risk of malignancy<sup>18</sup>. Diffuse involvement of both lobes of the liver can be treated with conservative management. Endoscopic procedures like sphinterotomy for clearance of intra hepatic stones and internal biliary bypass procedures (e.g. biliary/hepaticoenterostomy)<sup>19</sup>. In carefully selected cases with diffuse liver disease causing frequent cholangitis or secondary biliary cirrhosis liver transplantation is the treatment of choice<sup>15</sup>.

The patient discussed in this report developed hepatic failure and portal hypertension with haematemesis and melaena despite surgical interventions. At this moment no option remained for him except liver transplantation. Although Caroli's disease is a rare congenital anomaly it should be included in the differential diagnosis in patients presenting with upper abdominal pain,

hepatomegaly with cystic lesions and intrahepatic stones on USG. "Central dot sign" in cystic lesions on USG and CT of liver almost confirm the diagnosis. In fact more and more cases are being diagnosed due to the availability of non-invasive diagnostic procedures and awareness of diagnostic imaging criteria.

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