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Caroli's Syndrome with Atypical Course in a 15 Year Old Girl : A Case Report.

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Abstract:
Caroli's syndrome is a rare autosomal recessive inherited disorder and it is the involvement of small biliary ducts and congenital hepatic fibrosis. Both Caroli disease and syndrome share similar clinical features include abdominal pain, hepatomegaly, steatorrhoea, portal hypertension and hematuria, renal stones, infection, azotemia, and hypertension if there is renal involvement. Diagnosis is made by ultrasonography, computed tomography, magnetic resonance cholangiopancreatography(MRCP), and treatment is medical and surgical in severe cases. Our case is a 15 years old girl with abdominal pain, fever, hematemesis, hepatomegaly, and splenomegaly, and imaging was suggestive of ***Caroli's syndrome****. Non-pediatric clinicians should not ignore this rare kind of congenital liver disorder when they encounter unexplained portal hypertension, abdominal pain, hepatomegaly.*

(Keywords: *Caroli disease, Caroli's syndrome, congenital hepatic fibrosis, Rare disease, childhood, polycystic disease, liver disease, recurrent bacterial infections, congenital bile duct dilatation)*

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I. Introduction

Caroli disease is described by Jacques Caroli in 1958 and Desmet[1,2] as an arrest in ductal plate formation at the level of large intrahepatic bile ductal system and Caroli syndrome is arrest in the whole pathway of bile duct differentiation like small interlobular ducts[3,4]. Common in females but more commonly symptoms produce in adulthood but it may present in the pediatric group too. This is an autosomal-recessive kind of disease and it has a relation with ARPKD and ADPKD and some reported that has a relation with choledochal cyst [5,6]. Signs and symptoms included in Caroli disease and syndrome are intermittent abdominal pain, hepatomegaly, steatorrhoea, portal hypertension. The pathophysiology is ductal ectasia causes bile stagnation, biliary sludge, the stone formation that leads to recurrent infection like cholangitis [5]. Diagnosis is made by ultrasonography, computed tomography, isotope scan, magnetic resonance cholangiopancreatography(MRCP). MRCP usually showed irregular cystic dilatation of the large intrahepatic ducts [6,7]. Complications of these diseases are cholangitis, biliary abscess, cholelithiasis, septicemia even cholangiocarcinoma that occurs due to long exposure of ductal epithelium to the high concentration of unconjugated bile acid [8,9,12]. Treatment of Caroli's syndrome includes medical and surgical therapy. For cholangitis and abscess, an antibiotic is suggested. For severe localized cases lobectomy is done and for diffuse form, liver transplantation may be necessary [9,10].

II. Case Report

A 15-years-old girl, the second issue of consanguineous parents, immunized according to the EPI schedule, presented to the Paediatric Gastroenterology and Nutrition Department, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh with diffuse dull intermittent pain in the right upper quadrant of the abdomen for 7 days, associated with high-grade intermittent fever and vomiting for several episodes. Vomiting was non-projectile, nonbilious, and not mixed with blood. She gave the history of nasal bleeding for two episodes in the last 2 days. On examination, She was conscious, oriented, co-operative, moderately pale, anicteric, febrile with stable vital signs, no stigmata of chronic liver disease, and anthropometrically thriving well. Systemic examination revealed a soft non-tender abdomen with

splenomegaly(6cm) and hepatomegaly(2cm) [Figure 1] and absence of ascites, skin rash, or venous dilatation of the abdominal wall. The physical examination of other systems was normal. She was admitted to the hospital at 10 years of age with complaints of fever and hematemesis for several episodes and was diagnosed with Biliary cirrhosis due to Biliary ascariasis with Portal Hypertension.

Laboratory investigations are shown in [Table 1]. There was anemia with a high erythrocyte sedimentation rate. The liver function tests were **normal**. Regarding viral markers HBsAg, Anti HAV IgM, Anti HCV were negative. In imaging findings, an Ultrasonogram of the abdomen showed Hepatomegaly with coarse hepatic parenchymal echotexture, Mild splenomegaly with moderate ascites, findings are in favor CLD, Suggestive of small calculus / fragmented calcified dead worm in Gall Bladder, Suggestive of bilateral nephropathy and Mild pleural effusion(rt). Magnetic resonance cholangiopancreatogram [Figure 2] revealed diffuse small (<2cm) cystic dilatation of intrahepatic biliary ducts of both lobes of liver giving beaded appearance having central dot signs represent portal radical & communication with biliary tree suggestive of Caroli's disease.

Table 1: Laboratory investigations

Investigation	**Results 1st admission**	**Results 2nd admission**	**Normal range**
Complete Blood Count			
Haemoglobin (g/dL)	8.6	6.2	11-16.5
Erythrocyte sedimentation rate (mm in 1st hr)	62	140	Upto 20
White blood cell count (/cu mm)			
Neutrophil (%)	6,000	3,200	4,500-11,000
Lymphocytes (%)	65	58	40-75
Platelet count (/cu mm)	26	33	20-50
	-	150,000	150,000-400,000
Liver function tests			
Total Bilirubin (mg/dl)	.9	1	0.3-1.0
Serum albumin (gm/L)	37	43	34-50
Prothrombin Time (sec)	11	15.30	12-16
International normalized ratio	1.18	1.28	<1.4
Alanine aminotransferase (U/L)	36	-	35-50
Alkaline phosphatase(U/L)	37	-	-
Serum Lipase(U/L)		184	12-53
Fecal Fat in stool (droplets/HPF)	8-10	Upto 60	
Renal Function Test			
Complete urine analysis:		Straw	
Colour		0-2/HPF	
Pus cell		Nil	
RBC		Not found	
Casts		1.005	
Specific gravity	.60		0.5-1.1
Serum creatinine(mg/dl)			

USG of whole Abdomen	Mildly coarse hepatic parenchyma, mild splenomegaly, mild pelvic collection	Hepatomegaly with coarse hepatic parenchymal echotexture, mild splenomegaly with moderate ascities, findings are in favour CLD, suggestive of small calculus / fragmented calcified dead worm in Gall Bladder, suggestive of bilateral nephropathy, mild pleural effusion(right).
MRCP		Diffuse small (<2cm) cystic dilatation of intrahepatic biliary ducts of both lobes of liver giving beaded appearance having central dot signs represent portal radical & communication with biliary tree suggestive of Caroli's disease, hepatosplenomegaly and features of CLD - caroli's syndrome, distended gallbladder with cholelithiasis.

Liver Biopsy	Biliary cirrhosis	
Endoscopy of upper GI	Grade II Oesophageal varices	

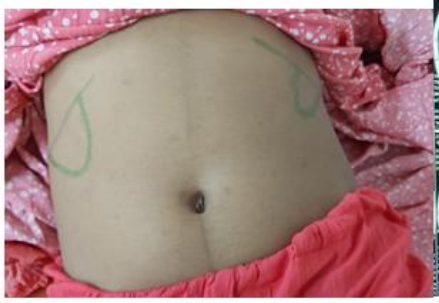

Figure 1: Shows there is presence of hepatosplenomegaly

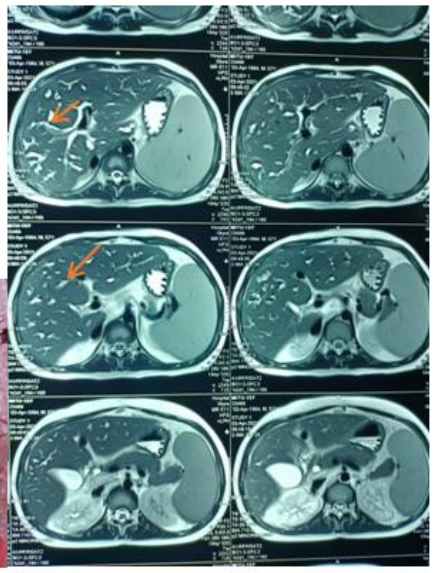

Figure 2: Diffuse small (<2cm) cystic dilatation of intrahepatic biliary ducts of both lobes of liver giving beaded appearance having central dot signs represent portal radical & communication with biliary tree suggestive of Caroli's disease, hepatosplenomegaly and features of CLD ,Caroli's syndrome, distended gallbladder with cholelithiasis.

III. Discussion

Caroli described the disease in 1958 and is congenital segmental dilatation of large intra-hepatic duct where Caroli syndrome is, which is more common, congenital segmental dilatation of small intra-hepatic biliary ducts and congenital hepatic fibrosis. This malformation may either segmental or diffuse and may be limited to one lobe of the liver [6]. It is a portal tract lesion of ductal plate malformation. If there is pure ductal ectasia then it is called Caroli disease but if involved small biliary ducts then it is called Caroli's syndrome that contains congenital hepatic fibrosis. It is usually associated with ARPKD and rarely ADPKD but some studies found its relation with a choledochal cyst, so then it is considered as a part of the choledochal cyst [6,8]. Caroli has two forms of congenital dilatation. One is congenital intrahepatic biliary dilatation that manifested as intermittent crampy abdominal pain, with or without jaundice, probably due to biliary stasis or stone formation [4,11]. There is repeated attack of intrahepatic stone formation and cholangitis with liver abscess, septicemia and death, hepatomegaly, steatorrhoea, portal hypertension and renal fibrocystic disease, renal tubular ectasia, part of the spectrum of renal fibropolycystic disease that manifests as hematuria, renal stones, infection, azotemia, and hypertension.[9,10].

In laboratory and radiological investigation of Caroli disease, the level of alkaline phosphatase and direct bilirubin maybe increase. The level of transaminases may normal but can be high when there is progressive hepatic fibrosis in the case of Caroli syndrome[6,7]. Leukopenia and thrombocytopenia on complete blood count in case of hypersplenism[5.6]. The final diagnosis is confirmed by histopathology, but current noninvasive imaging tools, such as ultrasonography (USG) in expert hand, computed tomography (CT), and magnetic resonance imaging (MRI) are considered to be the first-line diagnostic modalities. The ultrasound shows, saccular or spindle-shaped cystic dilations predominant around the hepatic hilum without any underlying obstacle, which communicate with the rest of the biliary tree[9,10]. It is also a very good technique for intrahepatic stone. Also, the liver shows the change of portal hypertension with splenomegaly. The characteristics findings in CT are saccular or tubular dilatation of intrahepatic bile ducts, intraluminal bulbular protrusions, bridge formation across dilated bile ducts resembling internal septa, within the dilated bile ducts and portal radicles-if seen in axial projection- appear as tiny, hyperechogenic structure, centrally there is dilated bile ducts named as "central dot"[5,6,7]. Occasionally it shows nonspecific presentation like oral or intravenous cholangiography may show intrahepatic stones. Although a mixed form is seen predominant fibrosis is congenital hepatic fibrosis and predominant cystic dilatation is Caroli disease.

In our case, a 15-years-old girl presented with diffuse dull intermittent pain in the right upper quadrant of the abdomen for 7 days, associated with high-grade intermittent fever and vomiting for several episodes. . She gave a history of nasal bleeding for two episodes in the last 2 days. On examination a soft non-tender

abdomen with splenomegaly(6cm) and hepatomegaly(2cm) and absence of ascites, skin rash, or venous dilatation of abdominal wall. The physical examination of other systems was normal.

She was admitted to the hospital at 10 years of age with complaints of fever and hematemesis for several episodes and was diagnosed with Biliary cirrhosis due to Biliary ascariasis with Portal Hypertension. Laboratory investigations were shown there was anemia. The liver function tests were abnormal. In imaging findings, an Ultrasonogram of the abdomen showed Hepatomegaly with coarse hepatic parenchymal echotexture, mild splenomegaly with moderate ascites and findings are in favor of chronic liver disease, small calculus / fragmented calcified dead worm in gall Bladder, there is bilateral nephropathy. Magnetic resonance cholangiopancreatogram revealed diffuse small (<2cm) cystic dilatation of intrahepatic biliary ducts of both lobes of liver giving beaded appearance having central dot signs represent portal radical & communication with biliary tree suggestive of Caroli's disease.

Congenital hepatic fibrosis(CHF) is an autosomal recessive disease. Male and female are equally affected. CHF varies a lot in clinical manifestation. Extrahepatic organ involvement and unusual progression of liver disease can provide clues of diagnosis. A systematic evaluation is favorable to diagnose CHF-associated syndromes and necessary to manage the disease thoroughly, including but not limited to renal, ophthalmic, pulmonary, genital, and neuromuscular involvement. Hepatic decompensation with subsequent portal hypertension is consistent with congenital hepatic fibrosis[13,14].

Therapy for Caroli's syndrome and congenital hepatic fibrosis(CHF) is a similar treatment of Caroli's syndrome include medical and surgical therapy. For cholangitis and abscess, an antibiotic is suggested. For severe localized cases lobectomy is done and for diffuse form, liver transplantation may be necessary. One study showed if the biliary lesion is confined to a discrete area predominantly, partial hepatectomy is then shown to be effective[15]. In case of biliary obstruction, and endoscopic sphincterotomy, radiological or surgical drainage may be applied[12]

IV. Conclusion

Though Caroli's syndrome is a rare disease and better diagnosis in resource-rich hospitals like in developing countries, therefore, non pediatric clinicians should not ignore this rare kind of congenital liver disorder when they encounter unexplained portal hypertension or isolated injured liver function. If available, it is essential to perform a liver biopsy for early diagnosis.

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