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DISTINCT CLINICOPATHOLOGICAL PHENOTYPES IN PEDIATRIC CHOLESTATIC LIVER DISEASE: A FOUR-CASE SERIES

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ABSTRACT
Pediatric cholestatic liver diseases show considerable heterogeneity in presentation and progression. We describe four children illustrating distinct clinicopathological phenotypes. A 6-year-old child with congenital hepatic fibrosis presented with massive splenomegaly, thrombocytopenia, and large esophageal varices requiring endoscopic ligation. An 11-year-old girl had biopsy-confirmed cirrhosis, severe fibrosis, and hypersplenism despite absence of gastroesophageal varices at initial endoscopy. A 3-year-old child with neonatal-onset conjugated hyperbilirubinemia had surgically and histologically confirmed extrahepatic biliary atresia with advanced biliary cirrhosis. A 15-month-old child presented with early hepatic decompensation, refractory ascites, intrahepatic ductal abnormalities, and culture-proven spontaneous bacterial peritonitis due to Klebsiella pneumoniae. These cases demonstrate that different cholestatic disorders may converge toward fibrosis, portal hypertension, and hepatic decompensation while retaining distinct phenotypic features. Multimodal assessment and longitudinal surveillance are important because individual manifestations may not reliably indicate overall disease severity.

KEYWORDS: Cholestasis; Portal hypertension; Congenital hepatic fibrosis; Biliary atresia; Cirrhosis; Children

INTRODUCTION
Pediatric cholestatic liver disease encompasses heterogeneous developmental, structural, metabolic, inflammatory, and inherited disorders. Persistent cholestatic injury may progress to fibrosis, portal hypertension, cirrhosis, and hepatic decompensation [1,2]. Clinical manifestations, however, may not parallel histological severity. We describe four children illustrating clinically distinct phenotypes and emphasize the importance of integrated assessment.

Case Series
Case 1: A 6-year-2-month-old child presented with progressive splenomegaly and thrombocytopenia. Splenomegaly measured 17 cm and the platelet nadir was 55,000/mm³. Endoscopy demonstrated large esophageal varices with gastroesophageal varices type 1. Liver biopsy showed broad fibrous portal tracts, dilated portal veins, and bile duct proliferation consistent with congenital hepatic fibrosis. Polycystic kidney involvement was present. Endoscopic variceal ligation was performed successfully.
Case 2: An 11-year-2-month-old girl had gross splenomegaly (16.9 cm), cytopenias, and a platelet nadir of 40,000/mm³. Transient elastography showed F4 fibrosis and liver biopsy confirmed cirrhosis with nodular regenerative architecture. Evaluation for Wilson disease, autoimmune hepatitis, chronic viral infections, and hemolytic anemia was non-contributory. Despite advanced fibrosis and hypersplenism, initial upper gastrointestinal endoscopy demonstrated no gastroesophageal varices.
Case 3: A 3-year-old child had neonatal-onset conjugated hyperbilirubinemia. Surgical exploration demonstrated a hypoplastic atretic gallbladder and cord-like extrahepatic biliary remnant. Histopathology demonstrated bile duct proliferation, portal fibrosis, and cirrhosis, confirming extrahepatic biliary atresia with advanced biliary cirrhosis.
Case 4: A 15-month-old child presented with jaundice, failure to thrive, tense ascites, and respiratory distress. INR was 1.96. MRCP demonstrated intrahepatic ductal abnormalities with nonvisualization of the right and left hepatic ducts. Liver biopsy showed portal fibrosis, cholestasis, and ductular abnormalities without features of biliary atresia. Ascitic fluid contained up to 2000 leukocytes/mm³ with 60–70% neutrophils and grew Klebsiella pneumoniae, confirming spontaneous bacterial peritonitis. The child improved with antibiotics, albumin, diuretics, and therapeutic paracentesis but was referred for transplant evaluation because of early hepatic decompensation.

Table 1. Clinicopathological Spectrum of the Four Children

Case	Age	Predominant Phenotype	Key Finding/Complication
1	6 y 2 mo	Congenital hepatic fibrosis	Massive splenomegaly, thrombocytopenia, large esophageal/GOV-1 varices requiring EVL
2	11 y 2 mo	Advanced cirrhosis with hypersplenism	F4 fibrosis and biopsy-proven cirrhosis; no varices at initial endoscopy
3	3 y	Extrahepatic biliary atresia	Neonatal cholestasis with advanced biliary cirrhosis
4	15 mo	Early decompensated cholestatic liver disease	Refractory ascites and Klebsiella pneumoniae spontaneous bacterial peritonitis, advised transplant.

EVL: Endoscopic variceal ligation; GOV-1: Gastroesophageal varices type 1.

DISCUSSION

The cases demonstrate that pediatric cholestatic liver disease may reach advanced stages through different clinicopathological pathways. Congenital hepatic fibrosis is associated with ductal plate abnormalities and renal cystic disease and may manifest predominantly through portal hypertension while hepatocellular function remains relatively preserved [3,4].

The second child highlights an important clinical observation: severe fibrosis and hypersplenism may exist despite absence of gastroesophageal varices at a single endoscopic examination. Development of varices depends on several hemodynamic factors and may evolve over time, supporting continued surveillance rather than reliance on a single negative endoscopy [5,6].

Transient elastography provides useful noninvasive assessment of hepatic fibrosis but cannot independently predict all manifestations of portal hypertension [7].

Biliary atresia remains an important cause of progressive pediatric liver disease; delayed recognition of neonatal cholestasis is associated with advanced fibrosis and poorer native-liver outcomes [8,9]. The third child illustrates advanced structural biliary disease, whereas the fourth demonstrates early decompensation with ascites and spontaneous bacterial peritonitis, a serious complication requiring prompt antimicrobial therapy and consideration of advanced hepatology care [10].

These cases emphasize that no single clinical, endoscopic, imaging, or histological parameter adequately defines disease severity. Integration of clinical examination, biochemical assessment, imaging, endoscopy, and histopathology with longitudinal surveillance is therefore essential.

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