Cystic Fibrosis-Associated Liver Disease: A Rare Etiology of Cirrhosis

Darian Fard, MD[1]; Muhammad Nadeem Yousaf, MD[2]; Mahmoud Mansour, MD[1]; Isma Perveze, MD[3]; Ahmad Ali, MD[2]
1*Department of Internal Medicine, 2*Department of Gastroenterology and Hepatology, 3*Department of Pathology
*University Hospital, University of Missouri-Columbia, MO, 65201

INTRODUCTION

- Cystic fibrosis (CF) is a rare etiology of cirrhosis. Cystic fibrosis-associated liver disease (CFLD) results from bile duct injury due to alteration in bile hydration and alkalinity
- Factors associated with rapid progression of CFLD include:
  - Class I-III mutations in CF transmembrane conductance regulator (CFTR)
  - Male sex
  - History of pancreatic insufficiency
  - Meconium ileus
- Approach to prevention and management of CFLD is unclear in current guidelines.
- We present a patient with CFLD who progressed to cirrhosis.

CASE DESCRIPTION

- A 24-year-old man with CF (diagnosed at age 14 years, with c.489+1G >T/c.579+1G >T mutations) and pancreatic exocrine insufficiency was evaluated for chronic liver disease
- Two years later, he developed cholestatic pattern of elevated liver enzymes that progressively worsened.
- At time of evaluation, the patient was asymptomatic with unremarkable examination.
- Laboratory workup (reference ranges):
  - Total bilirubin 1.62 mg/dL (0.2-1.6 mg/dL)
  - Alkaline phosphatase 259 IU/L (40-129 IU/L)
  - AST 88 IU/L (<40 IU/L)
  - ALT 246 IU/L (4-51 IU/L)

IMAGES

- Abdominal ultrasound showed coarse hepatic echotexture and splenomegaly.
- MRI/MRCP revealed markedly nodular hepatic contour, splenomegaly, caudate lobe hypertrophy, diffuse hepatic steatosis with morphological changes of cirrhosis
- Liver biopsy demonstrated regenerative nodules, prominent ductular reaction and thick biliary secretions in the lumen consistent with cirrhosis due to CFLD

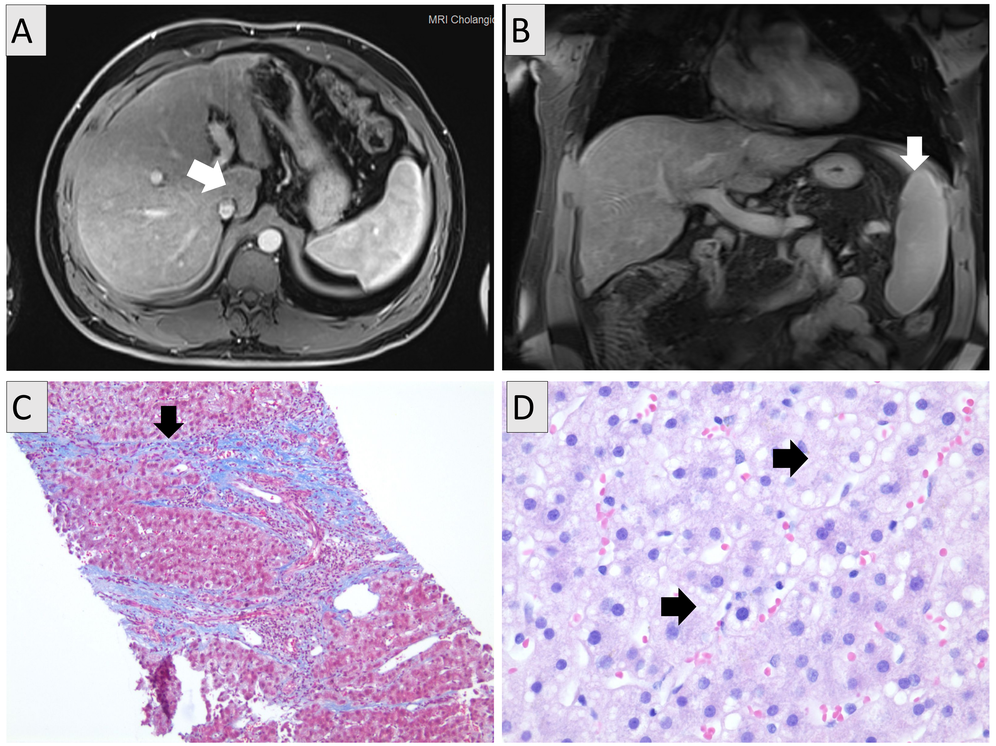

Figure 1.
Magnetic resonance cholangiopancreatography (MRCP); transverse (A) and coronal (B) view shows hypertrophic caudate lobe (arrow) with nodular contour of liver, splenomegaly. Liver histology; trichrome stain (C) shows cirrhotic nodule at 100x (arrow) and hepatic steatosis (D) at 400x (arrow).

CASE DESCRIPTION

- Laboratory evaluation continued:
  - Coagulopathy; INR 2.1 (1.0-1.4)
  - Thrombocytopenia, platelet count 126 x10^9/L (150-450 x 10^9/L)
- He was managed with ursodeoxycholic acid (UDCA), multivitamin, pancreatic enzyme, dornase alfa and follow up in 6 months for hepatocellular cancer screening

DISCUSSION

- CFLD is an uncommon extrapulmonary manifestations of CF. This case demonstrates insidious nature of CFLD. His initial symptoms were only related to fat soluble deficiencies, followed by cholestatic transaminitis that over the course of eight years developed into fulminant cirrhosis and ultimately referral for liver transplantation.
- A high index of clinical suspicion is required for early identification of CFLD in patients with cholestatic pattern of elevated liver enzymes, male sex, class I-III mutation of CFTR, and history of pancreatic insufficiency.
- There is no effective treatment of CFLD. Efficacy of UDCA is controversial as it improves biochemical parameters but its effects on outcomes of CFLD remain unknown.
- Further, while steatosis has been described in patients with CFLD, its impact on CFLD outcomes need to be addressed in large cohorts.
- Primary goals in managing CFLD is close monitoring of liver function, early identification of cirrhosis, its complications and liver transplant in progressively liver failure.

Author Contact: Darian Fard: dsfc22@umsystem.edu; (8572053080)