CASE REPORT
J Rehman Med Inst. Vol. 2, No. 3, 2016

ASYMPTOMATIC ADOLESCENT MALE WITH CONGENITAL HEPATIC FIBROSIS WITHOUT ANY ASSOCIATED SYNDROME

Sanum Gandapur, Muhammad Naveed Anwar, Muhammad Rizwan Bashir

Submitted: July 18, 2016
Accepted: August 23, 2016

Author Information

Dr. Sanum Gandapur, Trainee Medical Officer, Department of Gastroenterology, Rehman Medical Institute, Peshawar, Khyber Pakhtunkhwa, Pakistan.

Dr. Muhammad Naveed Anwar, Consultant Gastroenterologist, Department of Gastroenterology, Rehman Medical Institute, Peshawar, Khyber Pakhtunkhwa, Pakistan. (Corresponding Author) Email: naveed.anwar@rmi.edu.pk

Dr. Muhammad Bashir Rizwan, Senior Registrar, Department of Pathology (Histopathology), Rehman Medical Institute, Peshawar, Khyber Pakhtunkhwa, Pakistan.

ABSTRACT

Congenital hepatic fibrosis is an autosomal recessive fibro-polycystic disorder with variable degree of hepatic fibrosis, portal hypertension and renal cystic disease. It is often diagnosed incidentally and patients have well preserved liver functions.

The patient presented was a 14 years old male, referred from Department of Pediatrics, Rehman Medical Institute (RMI), with ultrasound findings of chronic liver parenchymal disease and splenomegaly associated with moderate derangement of liver function. On examination, no specific findings of chronic liver disease were present. CT-Scan followed by liver biopsy confirmed distorted normal lobular architecture. Upper GI endoscopy showed grade-1 esophageal varices. Hepatitis B & C serology were negative, serum auto-antibodies, serum IgG and alpha-1 antitrypsin were within normal limits. A final diagnosis of congenital hepatic fibrosis was reached after review of the case with multi-disciplinary team.

This case illustrates that congenital hepatic fibrosis, though rare, can be considered as a precursor of liver cirrhosis and it is important for physicians to be aware of this diagnosis, as early detection would allow regular follow up for signs of deteriorations or complications like hepatocellular carcinoma.

The authors declare no conflict of interest. All authors contributed substantially to the planning of research (SG, MNA), questionnaire design (SG, MNA, MBR), data collection (SG, MNA, MBR), data analysis (SG, MNA) and write-up of the article (SG, MNA, MBR) and agreed to be accountable for all aspects of the work.

Citation: Gandapur S, Anwar MN, Bashir MR. Asymptomatic adolescent male with congenital hepatic fibrosis without any associated syndrome. J Rehman Med Inst. 2016 Jul-Sep;2(3):68-71.

INTRODUCTION

Congenital hepatic fibrosis is an autosomal recessive fibro-polycystic disorder with variable degrees of hepatic fibrosis, portal hypertension and renal cystic disease accounting for the different clinical presentations.[1] The latent form is usually diagnosed incidentally.[2] Clinically, the first manifestations of congenital hepatic fibrosis in most patients are characterized by signs and symptoms related to portal hypertension, especially splenomegaly and varices, often with gastrointestinal bleeding with well-preserved liver function.[3] Onset of the symptoms and signs is highly variable and ranges from early childhood to the fifth or sixth decade of life, although this disorder is diagnosed in most patients during adolescence or young adulthood.[4] Hepatocellular and renal functions are usually well preserved even in the presence of portal hypertension.[5] Hepatic fibrosis is a dynamic disorder that shows progression in the extent of liver fibrosis over time.[6]

A diagnosis of congenital hepatic fibrosis is suggested when normal hepatocellular function is associated with hypersplenism and increased levels of Alkaline Phosphatase and Gamma Glutamyl Transferase.[7] Definite diagnosis is by liver biopsy.[7] The hepatic stellate cell is at the centre of the hepatic fibrotic process associated with liver disease and has also been shown to play a role in the progression of disease in congenital hepatic fibrosis.[3] A liver biopsy is essential in the diagnosis and differential diagnosis of congenital hepatic fibrosis as the presence of small bile duct dilatation and proliferation would rule out other metabolic disorders of the liver.[3]

Although liver biopsy is highly specific for the diagnosis of congenital hepatic fibrosis, it has been shown to have low sensitivity.[8] Because of the difficulty in the clinical and pathologic diagnosis of congenital hepatic fibrosis, imaging studies could play a crucial role in the diagnosis of this disorder if accurate and reliable signs can be determined but unfortunately little is known about the radiologic diagnosis of congenital hepatic fibrosis with no specific imaging feature known.[9] Some distinct CT features were frequent in congenital hepatic fibrosis such as hepatomegaly, varices, splenomegaly, associated ductal malformations and renal abnormalities. The combination of these CT signs is very important for the diagnosis of congenital hepatic fibrosis.[1] Prognosis is dependent on the degree of portal hypertension, the signs and symptoms of which can be decreased by surgical shunts.[7]

CASE PRESENTATION

We present the case of an asymptomatic 14 years old male referred to the medical unit by the Pediatric Department after incidentally being found to have abnormalities on the ultrasound and liver function tests. He had mildly enlarged liver with coarse heterogenous parenchymal echo pattern suggestive of chronic liver parenchymal disease and splenomegaly on ultrasound and a raised Gamma Glutamyl Transferase of 625 IU/L (normal is <55), Alkaline Phosphatase 530 IU/L (normal is 54-369) and ALT 123 IU/L (normal is <45), Total bilirubin 2.3 mg/dl (normal is 0.1-1.2), and Direct Bilirubin 1.3 mg/dl (normal is 0-0.2). Complete Blood Count (Hb 11.8 g/dl, Total leucocyte count 8.68 x 10^9/mm^3, Platelets 192 x10^9/mm^3), Renal function tests (Urea 31 mg/dl, Creatinine 0.55 mg/dl), Serum Ferritin 234 ng/ml (normal is 28- 365) and serum Amylase (32 U/L) were all normal. Urine R/E showed positive nitrites, + bilirubin, 1-2 WBCs/ HPF, + proteins, - ketones, +++ urobil inogen, negative for RBCs and crystals. Growth and development were normal for his age. No hepatomegaly, splenomegaly or other stigmata of chronic liver disease were noted on examination.

CT scan abdomen with contrast showed hepatomegaly with heterogenous hepatic parenchyma without any focal mass lesion, bulky spleen, multiple enlarged discrete lymph nodes at porta hepatis and celiac axis level with multiple prominent mesenteric lymph nodes, multiple tortuous peri-gastric, peri-splenic and peri-oesophageal vessels. Correlation with liver biopsy findings was advised.

Liver biopsy revealed markedly distorted normal lobular architecture with micronodule formation (Figure 1). Significant expansion of portal tracts with Porto-portal and Porto-central thick fibrous band formation were seen. Bile ductile proliferation with irregular and anastomosing biliary channels were also identified. Mild infiltration of lymphocytes and neutrophils with interface hepatitis were noted. There was no evidence of malignancy seen.

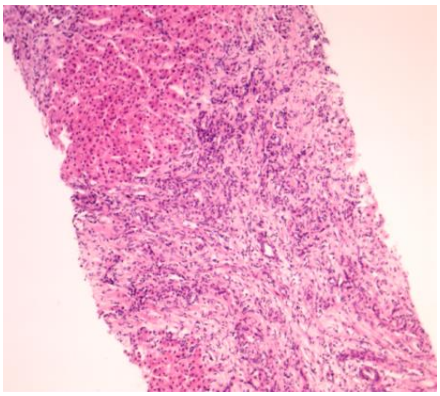

Figure 1: Liver Trucut biopsy. The lower portion of the image shows portal area with extensive fibrosis and bile ducts proliferation arrested at different stages of the maturation process. At upper left, lobules of normal hepatocytes can be appreciated (x10 Low power magnification).

Masson Trichrome for fibrosis and Reticulin stain highlighted the nodule formation as seen in Figure 2.

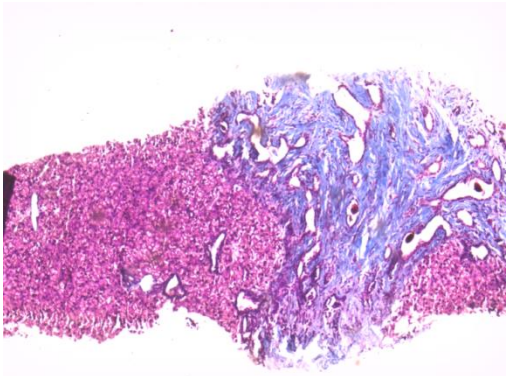

Figure 2: Liver biopsy. The center of the image depicts a portal area with extensive fibrosis and the proliferation of several bile ducts containing bile plugs and showing fibrosis (in blue color) highlighted on Trichrome stain. (x10 Low power magnification).

Figure 3 shows Immunohistochemistry for CK 7 highlighting the proliferating ductules. Opinion was of a ductal plate malformation consistent with congenital hepatic fibrosis.

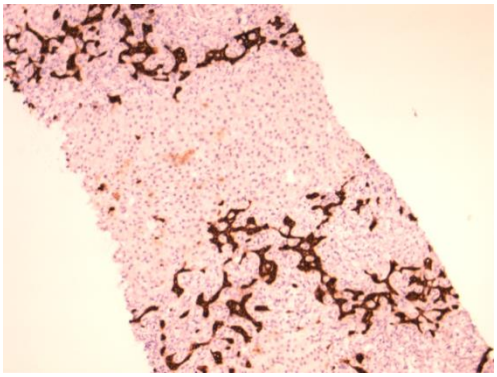

Figure 3: Liver biopsy. Bile ductules proliferation is strongly highlighted as darkly brown stained for immunohistochemical marker Cytokeratin (CK7). (x10 Low power magnification).

Our patient had no history of hematemesis or melena but grade I esophageal varices were noted on upper GI endoscopy. No history of previous hepatitis or alcohol abuse could be elicited. Markers for hepatitis B and C were negative. There was no family history of liver or kidney disease or any other significant illness. Serum ceruloplasmin levels were normal at 0.412 g/L (0.20-0.6g/l). Serum autoantibodies (ANA Anti-nuclear antibody, ASMA anti smooth muscle antibody and AMA Anti mitochondrial antibody) were negative. Serum IgG 15.76G/L (5.7- 17.1) and serum Alpha 1 anti-trypsin 1.90 (0.9-2.0) were also normal. Except for the deranged liver function tests, radiological and histopathological abnormalities, patient was well clinically.

The case was discussed with a multi-disciplinary team comprising of gastroenterologists, radiologists and histopathologists and it was concluded that our patient had congenital hepatic fibrosis based on liver biopsy results, radiological appearance and liver function tests with no other associated disease or syndrome. He was started on beta blockers and advised family screening.

DISCUSSION

Clinically, congenital hepatic fibrosis is characterized by portal hypertension with well-preserved liver function.[5] In adults, the disease is associated with two major risks; gastrointestinal hemorrhage caused by portal hypertension and cholangitis due to bacterial infection of dilated intra hepatic bile ducts.[3] The highest prevalence of cholangitis is reported in the adolescent group. Our patient was in the adolescent group but no episodes of cholangitis were found. However, he developed cirrhosis in the absence of recurrent cholangitis.

Congenital hepatic fibrosis is closely associated with polycystic kidney disease and Caroli's disease (dilatation of the intrahepatic biliary tree). Other associated disorders include medullary sponge kidney, Meckel syndrome, Ivemark familial dysplasia and Tuberous Sclerosis.[1] All these conditions had been ruled out in our patient.

A diagnosis of congenital hepatic fibrosis is suggested when normal hepatocellular function

is associated with hypersplenism and increased levels of Alkaline Phosphatase and Gamma Glutamy Transferase.[7] Definite diagnosis is by liver biopsy.[7] As mentioned, congenital hepatic fibrosis distorts the hepatic structure without any effect on the hepatocellular function, so the levels of liver enzymes are generally within normal ranges.[7] In cirrhosis, in contrast to congenital hepatic fibrosis, hepatocellular injury occurs and the abnormal level of liver enzymes is a distinctive feature.[10] The question is whether congenital hepatic fibrosis could be a precursor to liver cirrhosis?[11] In the search for diverse causes of liver cirrhosis, congenital hepatic fibrosis, though very rare, has not been considered previously despite a few cases reporting an association between congenital hepatic fibrosis and cirrhosis.

CONCLUSION

It is important for physicians who care for adult patients to be aware of this diagnosis, as the disease can remain clinically silent for many years. It is proposed that latent asymptomatic cases of congenital hepatic fibrosis without any associated disorder may be detected on imaging (with ultrasound as first line), and liver function tests. Early detection would allow a regular follow up for signs of deterioration or complications like hepatocellular carcinoma with liver function tests, alpha fetoprotein measurement and imaging.

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