

Case Report

Unusual Presentation of a Young Child with Cirrhosis: A Case Report

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- Tyrosinemia
- Cystic fibrosis

Abstract

Cirrhosis (Greek word) by definition is a hard, nodular regenerating disease of liver in which the hepatocytes are constantly injured (by insulting agent) with fibrosis due to increase in connective tissues that ultimately lead to destruction in structure and function of liver. Cirrhosis in paediatric population occur due to acute/chronic liver damage which may be due to viral hepatitis (HBV, HBV and HDV co infection, HCV, CMV or NANB hepatitis), autoimmune disorders, toxins (drug induced), certain inborn errors of metabolism (Wilson's disease, alpha-1 antitrypsin deficiency, tyrosinemia etc.), glycogen storage disease or cryptogenic. We report a case of a 2 year 6 month old baby boy who presented with bleeding from nose, abdominal distension and hepatomegaly; investigation revealed a cirrhotic liver disease pattern.

INTRODUCTION

Liver damages that occur in paediatric population are due to different types of infection, metabolic and neoplastic disorders that lead to jaundice, deranged liver function test and hepatomegaly. Liver also develops cholestatic syndromes of infancy and childhood, which could be due to biliary atresia or neonatal hepatitis [1].

In some patients cirrhosis is completely asymptomatic and they have a reasonably normal life expectancy. Some individuals also develop severe symptoms of end-stage liver disease and a limited chance for survival. Common signs and symptoms of liver damage are decreased hepatic synthetic function i.e. coagulopathy, portal hypertension i.e. variceal bleeding, or decreased detoxification capabilities of the liver i.e. hepatic encephalopathy [2].

Early interventions and preventions are required to stabilize disease progression and to avoid or delay clinical decompensation and the need for liver transplantation. In the 21st century, the challenges in the management of patient with cirrhosis need to be dealt with to prevent the need for liver transplantation [3].

CASE REPORT

A 2 year 6 month old baby boy was brought to the paediatric emergency. The family belonged to a low socioeconomic status. The baby came with the presenting complaint of

intermittent nasal bleeding since one year, abdominal distension since one year and fresh nasal bleed in the last one-week. Patient has three siblings, none of whom had a congenital or similar illness. His parents had a consanguineous marriage. He was delivered at full term via spontaneous vaginal delivery. No history of maternal illness or drug exposure or premature rupture of membranes. The child was fully immunized. There was no developmental delay of milestones to this date. In the first few months of life the child did not have any clay or black colored stools. Physical examination revealed an active and responsive baby boy with Occipito Frontal Circumference (OFC) of 47 cm at 95th percentile. According to Center of Disease Control and Prevention (CDC), weight and height were found to be at 50th percentile (CDC). The child was afebrile.

On abdominal examination, there was marked hepatomegaly with a total span of 14 cm and palpable 4 cm below the right costal margin. It was firm in consistency. On palpation, left lobes of liver were found to be coarse and notches were felt. Spleen was not palpable. There was no ascites. Chest was found to be clear on auscultation. On CVS examination, flow murmurs (Haemic Murmur) were found.

Laboratory investigations included a stool D/R which did not show any abnormal finding. In urine D/R: albumin (protein) was found with RBC 2-4/High power field, WBC 8-10/High power field. Post transfusion, complete blood count showed haemoglobin (Hb) of 10 g/dl. Liver function tests were done which showed alanine

transaminase (ALT) =56 IU/L, alkaline phosphatase (Alk PO₄) =122IU/L, gammaGT: 167IU/L, Total bilirubin (TB) =0.6mg/dl, Direct bilirubin (DB) =0.1mg/dl, Indirect bilirubin (IB) =0.5mg/dl, Prothrombin time (PT)=18.9/12.0, International normalized ratio (INR) =1.7, Activated partial thromboplastin time (APTT) =42/30.

The child was managed in line with a deranged coagulation profile and received FFP and packed cell during the admission. Further treatment included fat soluble vitamins in recommended doses according to age.

Ultrasound revealed a nodular echo texture of the liver characteristic of cirrhosis. C.T scan showed moderate hepatomegaly, no lesion was seen in gallbladder, seminal vesicles and prostate, no evidence of abdominal or pelvic lymphadenopathy. Liver biopsy (trucut biopsy) was done in which liver consisting of single tan white linear core measuring 2×0.1cm was obtained. Sections reveal a single liver parenchyma showing severe chronic non-specific inflammation and extensive fibrosis with focal nodular formation. Crushed artifact was also seen. Bile ductular proliferation was noted (Figure 1a, b & c).

Markers were sero negative for infection with hepatitis A, B or C virus, Iron profile was found to be normal, sero-positivity for ANA/SNA antibody titre was < 1: 80, sero negative for ANA, AATD (alpha-1 antitrypsin antibody) was found to be negative, plasma tyrosine and phenylalanine levels were not found to be elevated, autoimmune hepatitis profile was negative and no fatty changes were seen on ultrasound or on C.T scan.

All the clinical labs were done to determine the causes leading to cirrhosis in this patient. However, it can be appreciated in (Figure 2), that cirrhosis in our case was suggestive of acryptogenic cause.

Liver transplant was advised. However, follow up of this child was not possible because the parents were reluctant to bring the child to hospital again despite repeated counseling.

DISCUSSION

The repercussion of all chronic liver disease is cirrhosis,

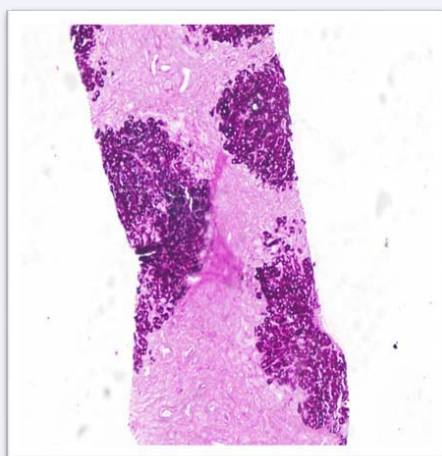


Figure 1a Liver biopsy showing loss of lobular architecture with regeneration nodules surrounded by fibrous septae. (PAS stain x 10).

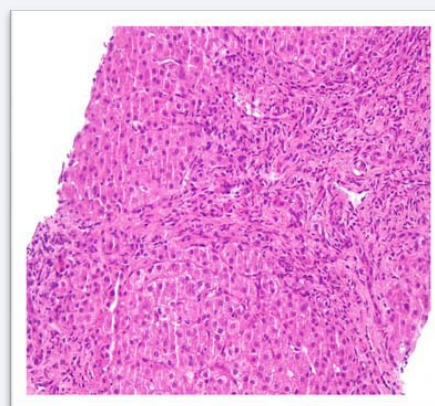


Figure 1b Liver biopsy showing inflammations in the fibrous septae with interphase inflammation. No vacuoles are found in it. (H & E stain x 10).

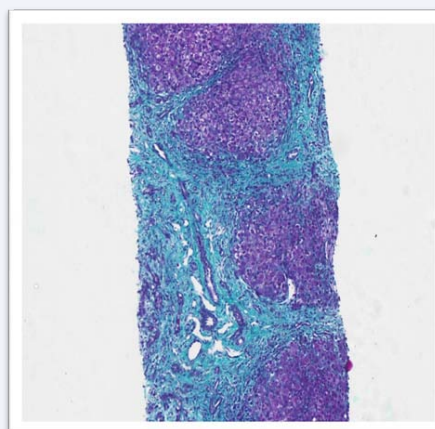


Figure 1c Liver biopsy high power view showing regeneration nodules, fibrous septae with bile duct proliferation. (Trichrome stain x 10).

which is characterized by tissue fibrosis with conversion of normal liver parenchyma into abnormal regenerating nodules [4]. According to studies the determinant in children with cirrhosis were found to be viral hepatitis (10%), biliary disease (5%), primary haemochromatosis (5%), idiopathic (5%) and most commonly seen was nonalcoholic steatohepatitis (NASH)(33%). Autoimmune liver disease(22%) and the rare determinants included Wilson's disease, alpha-1 anti-trypsin deficiency, galactosemia, tyrosinosis, cancer or drugs [5].

In our part of the world, cirrhosis is seen to develop secondary due to hepatitis B infection and diagnosis is by a positive HBsAg. World Health Organization (WHO) has proposed that all children should be immunized for HBV (hepatitis B virus) and blood donations should be scrutinized for hepatitis B to reduce the chances of transmission of HBV and other blood borne infections. A positive HBeAg test suggests that the blood and body fluids are highly infectious [6]. In this patient HBsAg and HBeAg were found to be negative and the liver biopsy did not show ground

glass hepatocytes [Figure 1a], hence HBV infection as a cause of cirrhosis in this patient was excluded.

Clinical signs and symptoms suggested that in our patient cirrhosis might have developed due to inborn error of metabolism i.e. Glycogen storage diseases (GSD) in which histologically collection of glycogen occurs in various tissues. Clinical presentations of GSD type Ia, Ib and III are hepatomegaly, hypoglycaemia, elevated lactate and urate with or without neutrophil dysfunction [7]. However in our case there was hepatomegaly and no glycogen deposition or fat vacuoles were

found in liver biopsy as [Figure 1b]. Also, there was no growth retardation or related hypoglycemia, so GSD was excluded.

For the diagnosis of cystic fibrosis (CF), clinical evaluation, laboratory investigations, ultrasonography and liver biopsy is required. Clinically patient with cystic fibrosis (CF) presents repeated respiratory infections, elevation of serum liver enzymes, hepatic steatosis, focal biliary cirrhosis, multilobular biliary cirrhosis, neonatal cholestasis, cholelithiasis and cholecystitis [8]. None of these findings were present in this case.

Patients with unrecognized liver disease are also investigated

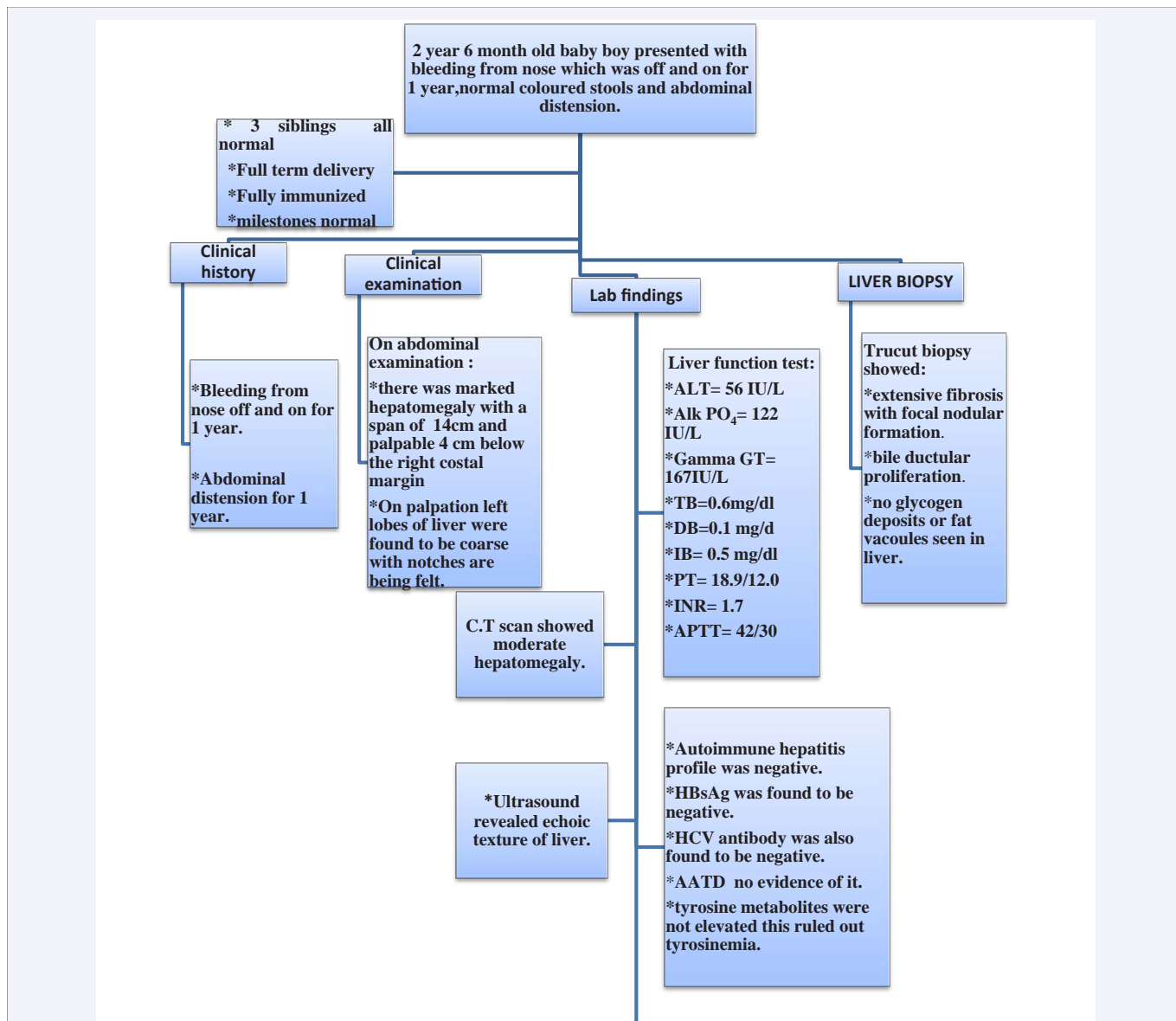


Figure 2: Flow chart showing history, examination and investigations done in the patient.

ALT: Alanine Transaminase; Alk PO₄: Alkaline phosphatase; TB: Total Bilirubin; DB: Direct Bilirubin; IB: Indirect Bilirubin; PT: Prothrombin Time; INR: International Normalized Ratio; APTT: Partial Thromboplastin Time; CT: Computerized Tomography; HBsAg: Hepatitis Surface Antigen; HCV antibody: Hepatitis C antibody; GSD: Glycogen Storage Disease; AATD: Alpha-1antitrypsin Deficiency

Figure 2

for alpha 1 antitrypsin deficiency (AATD) in which sign and symptoms of CLD (chronic liver disease), may be present. There is hepatomegaly. However, for the diagnosis of alpha 1 antitrypsin deficiency (AATD) there must be a low level of serum alpha-1 antitrypsin and in this case it was found to be negative [9].

A rare entity biliary atresia, affects about one out of every 18,000 infants. First symptom of biliary atresia is jaundice and other symptoms include dark urine, gray or white stools, slow weight gain and growth [10]. As we did not find jaundice and clay coloured stools and in liver biopsy [Figure 1c] there was no edema of the portal tracts and related clinical features, We suggested that our patient was not suffering from biliary atresia.

In the differentials of this case tyrosinemia possess importance and its clinical features conjecture that patient might have it. In acute form, sign and symptoms appear in neonatal life i.e. poor weight gain, an enlarged liver and spleen, distended abdomen, swelling of legs and an increased tendency to bleed more specifically nose bleed. Jaundice may or may not be present. In chronic form, there is a gradual onset with enlargement of liver, prominent spleen, abdominal distension, vomiting and diarrhoea may occur. In complicated patients, cirrhosis may develop. In this case, plasma tyrosine and phenylalanine levels were not found to be elevated and there was negative evidence of rickets on radiographs suggesting that patient was not suffering from tyrosinemia [11,12].

Cryptogenic cirrhosis is characterized by the development of cirrhosis due to unknown cause. Studies showed that cryptogenic cirrhosis may represent about 10% of all causes. Diagnosis is usually confirmed after the omission of all possible causes [13]. In late stages functioning capabilities of liver are markedly reduce. In such a case, liver transplant is the only remaining option [12].

Latest studies have shown a higher frequency such as Wilson's disease (20.7%), biliary atresia (17.9%), viral hepatitis [B, C] (7.4% and 1.38% respectively), alpha-1 antitrypsin deficiency (20%) and cystic fibrosis (10-30%) as a cause of cirrhosis [14]. However data suggests that the underlying factors which may frequently develop cryptogenic cirrhosis include autoimmune hepatitis (11.3%), idiopathic neonatal hepatitis (9.4%) [15] and non-alcoholic fatty liver disease [NAFLD] (44%) [16]. In some studies it has been shown that there is a high incidence of parental consanguinity (42.8%) which causes cirrhosis because of Wilson's disease, familial cirrhosis, chronic hepatitis B and biliary atresia [17]. In our patient the cause of cirrhosis was not determined despite appropriate investigations, hence the baby was labelled to have cryptogenic cirrhosis.

CONCLUSION

Cirrhosis in children is rare, but not so rare as has been supposed. In our case cirrhosis was cryptogenic.

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