PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS

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ABSTRACT

A case of progressive familial intrahepatic cholestasis (PFIC) is described in a 7 years old girl who presented with pruritis and progressive jaundice alongwith failure to thrive. Laboratory indicated PFIC type 1or 2 along with cirrhosis. Patient is responding to supportive therapy while liver transplantation is being awaited.

Key words: Progressive familial intrahepatic cholestasis, failure to thrive, jaundice, cirrhosis.

INTRODUCTION

Cholestasis is either an alternative or concomitant response to injury caused by extrahepatic or intrahepatic obstruction to bile flow[1]. Progressive familial intrahepatic cholestasis (PFIC) is an important cause of cholestasis and biliary cirrhosis in pediatric age group[2]. A high index of suspicion is required in the diagnosis of PFIC as neonatal cases as well as older children are usually misdiagnosed and thus maltreated for a long time thus narrating a long history of suffering.

A case of Progressive Familial Intrahepatic Cholestasis is described in which the patient presented with pruiritis and progressive jaundice alongwith failure to thrive. PFIC 3 was ruled out due to normal gama GT. PFIC 1 or 2 could not be differentiated as histopathology was confounded due to fibrosis setting in.

CASE REPORT

A 7 year old girl presented with itching all over the body for 7 months, anorexia for 3 months and progressive jaundice with dark yellow urine for the last 1 month. There had been repeated self limited episodes of jaundice each lasting a few weeks since later infancy. An undocumented liver biopsy was done at 1 year of age. She had 2 healthy siblings out of a consanguineous parentage. There was no family history of jaundice.

Physical examination revealed a thin underweight girl who was deeply jaundiced with scratch marks all over her body. She was active alert, and well oriented. She had normal vital signs with weight of 17 kg. (< 5th percentile) and height of 110cm (< 5th percentile) indicating failure to thrive. Liver was 1 cm palpable with a span of 11 cm. Rest of the physical examination was unremarkable.

The working diagnosis was cholestatic jaundice. The hemoglobin was 10.4 gm%, MCV 82.8 fl, MCH 28.9 pg, MCHC 34.9 gm/dl, TLC 9.2x10 ^{3}/mm^3, platelets 374.00 x 10 3/mm^3, urea 28 mg%, creatinine 0.4 mg%, potassium 3 meq%, sodium 136 meq%, bicarbonates 19 meq%, serum calcium 9.5 mg%, bilirubin total 12 mg% with direct bilirubin of 10 mg%, alanine aminotransferase (ALT) of 33u/l, aspartate amino transferase 75u/l, alkaline phosphatase 1183 u/l, gamma glutamyltransferase (gGT) of 31 U/L with prothrombin time (PT) of 16/13 sec and serum cholesterol of 116 mg/dl. Liver biopsy revealed moderate periportal inflammation with extensive septal fibrosis focally and nodule formation. There was marked bile stasis, and bile ducts were reduced with no evidence of malignancy, i.e. moderate active inflammation with impending fibrosis stage III and IV and marked bile stasis.

She showed partial improvement on supportive therapy like cholestyramine, phenobarbitone, nutritional advice and vitamin/mineral supplements. She is a candidate for liver transplantation as cirrhosis has already started taking its roots in the liver.

DISCUSSION

Cholestasis may be due to infectious, genetic, metabolic or undefined abnormalities giving rise to either mechanical obstruction of bile flow or to functional impairment of hepatic biliary function and bile secretion[3]. PFIC is an

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Received: May 11, 2007; accepted: September 27, 2007

important cause of cholestasis and biliary cirrhosis in pediatric group[2]. Cholestasis is caused by impaired bile secretion associated with, and often secondary to, intracellular accumulation of bile acids in hepatocytes[2]. It represents a group of diseases affecting membrane transport proteins involved in bile formation and falls into the category of non-syndromic paucity of interlobular bile ducts. It presents as hepatocellular cholestasis; often in the neonatal period causing liver failure at variable age, ranging from infancy to adolescence and eventually may result in death[4].

This entity is often overlooked and labeled as biliary atresia or neonatal hepatitis. Misdiagnosis is the result of sub-optimal ultrasonography and non-visualization of gallbladder on Hepatic imminiodiacetic acid (HIDA) scan due to poor uptake by hepatocytes[5].

Adolscents with conjugated hyperbilirubinemia should be evaluated for acute and chronic hepatitis, alpha-1-antitrypsin deficiency, Wilsons disease, liver disease associated with IBD, autoimmune (AIH), syndromes of intrahepatic cholestasis, cholelithiasis, abdominal tumours, enlargd lymph nodes or hepatic inflammation from drug ingestion[6].

PFIC is an autosomal recessive condition and is classified as 3 types i.e. types 1, 2 and 3. The differentiation is on clinical grounds and laboratory findings. PFIC-1 is due to a defect of familial intrahepatic cholestasis-1 gene, (FIC-1{ATP8B1}) which is localized on chromosome 18[3]. FIC-1 activates the transcription of the FXR (Farsenoid X receptor), an important modifier of bile acid homeostasis gene[7]. In PFIC 2 the gene defect lies at chromosome 2 q24, the FIC-2 locus[6]. Gene ABCB 11 defect is in the canalicular ATP-dependent bile acid transporter BSEP (bile salt export promoter)[7]. PFIC-3 is characterized by elevated serum gGT. Early. PFIC-3 is associated with MDR-3 gene (ABCB4) deficiency[3].

This genetic mapping could not be conducted in the present case. The girl had presented in childhood with failure to thrive, progressive jaundice and cirrhosis. Due to the undocumentation of liver biopsy in the infancy, it could not be ascertained with surety as to whether it was type I or 2 PFIC. The present histopathology had such marked changes of cirrhosis that the distinction could not be made. This case emphasizes the importance of early diagnosis and documentation to retard irreversible changes in a potentially fatal condition.

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