CASE REPORTS

BENIGN RECURRENT INTRAHEPATIC CHOLESTASIS

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SUMMARY : Benign recurrent intrahepatic cholestasis (BRIC) is an autosomal recessive liver disease characterized by recurrent episodes of cholestasis without progression to chronic liver disease. This paper presents a 14-year-old boy with two episodes of cholestasis. After exclusion of the other causes of cholestasis, BRIC was diagnosed.

Key Words: *Intrahepatic Cholestasis, Rewrrence, Case Report.*

INTRODUCTION

Benign recurrent intrahepatic cholestasis (BRIC) is a rare autosomal recessive liver disease, characterized by recurrent episodes of pruritus and jaundice without evidence of duct obstruction. BRIC may occur in sporadic or familial form, and the latter has recently been attributed to a genetic abnormality on chromosome 18 (1, 2). Criteria for the diagnosis of this syndrome are several episodes of jaundice with pruritus and biochemical signs of cholestasis, bile plugs in liver biopsy, normal intrahepatic and extrahepatic bile ducts, absence of factors known to produce intrahepatic cholestasis, and symptom free intervals (3, 4).

CASE REPORT

A 14 year-old boy was referred to our hospital for the evaluation of pruritis and jaundice of 2 weeks duration. The patient's symptoms developed after an episode of upper respiratory tract infection. When he was 3 and 7 years old, he had had two more jaundice attacks. He had been taking no medications at that time. The jaundice had been resolved in a few weeks without sequelae. There was no family history of liver disease. Physical examination revealed only jaundice. He had normal complete blood count, prothrombin time, partial tromboplastin time, serum electrolytes, creatine, phosphate and blood urea nitrogen. The liver profile showed direct hyperbilirubinaemia, moderate elevations of serum aminotransferases, gamma glutamyl transpeptidase and bile acids. The level of alkaline phosphatase was within the normal range (Table 1).

The diagnosis of viral hepatitis, Wilson's disease, $\alpha 1$ - antitrypsin deficiency and autoimmune hepatitis were excluded by negativity of viral markers (HBsAg, IgM anti- HBc, IgM anti - HAV, anti HCV, IgM anti- Cytomegalovirus and Ig M EBV) by normal plasma levels of copper, ceruloplasmin and $\alpha 1$ - antitrypsin and by the auto antibody negativity (anti-smooth muscle, anti-nuclear, anti-liver kidney microsomal type 1). The liver appeared normal on ultrasonography with nondilated intrahepatic and extrahepatic bile ducts.

Table - 1 : Laboratory values of the patient on admission.

Parameter	Patient Value	Range
Biluribin	23 mg/dl	(0.2 - 1.6 mg/dl)
Direct Biluribin	6 mg/dl	(0.0-0.4 mg/dl)
AST	40 IU/L	(0-46 U/L)
ALT	181 IU/L	(0-46 U/L)
ALP	217 U/L	(30-110 U/L)
GGT	167 U/L	(0-50 U/L)
Cholesterol	261 mg/dl	(120-200 mg/dl)
Triglyceride	173 mg/dl	(50-170 mg/dl)

Bile ducts were also normal on MRI cholongiography. A percutaneous liver biopsy revealed cholestasis and hydropic degeneration. Bile ducts and blood vessels were normal (Fig 1a-1b).

After exclusion of congenital or acquired causes of intrahepatic cholestasis, BRIC was diagnosed.

The biluribin level decreased progressively ; by day 21, it was decreased to 1.74 g/dl. Pruritis had resolved completely, whereas the aminotransferases remained slightly elevated. Three weeks later, amino transferases returned to normal.

DISCUSSION

The patient's presentation and clinical course were consistent with the diagnosis of sporadic BRIC and the pathologic findings in his liver biopsy were typical of this entity. BRIC is characterized by multiple episodes of cholestasis without progression to chronic liver disease. In susceptible individuals, acute attacks are triggered by unknown factors that impair bile acid transport at the canalicular level. Triggers include acute gastroenteritis, upper respiratory tract infections, which occurred in our patient, and otitis media (5).

The attacks vary in duration (weeks to months) and resolve spontaneously. No biochemical abnormalities are found in patients between attacks. The initial episode can occur at any age from infancy to adulthood. The frequency of attacks varies from several times a year to less than once per decade (6).

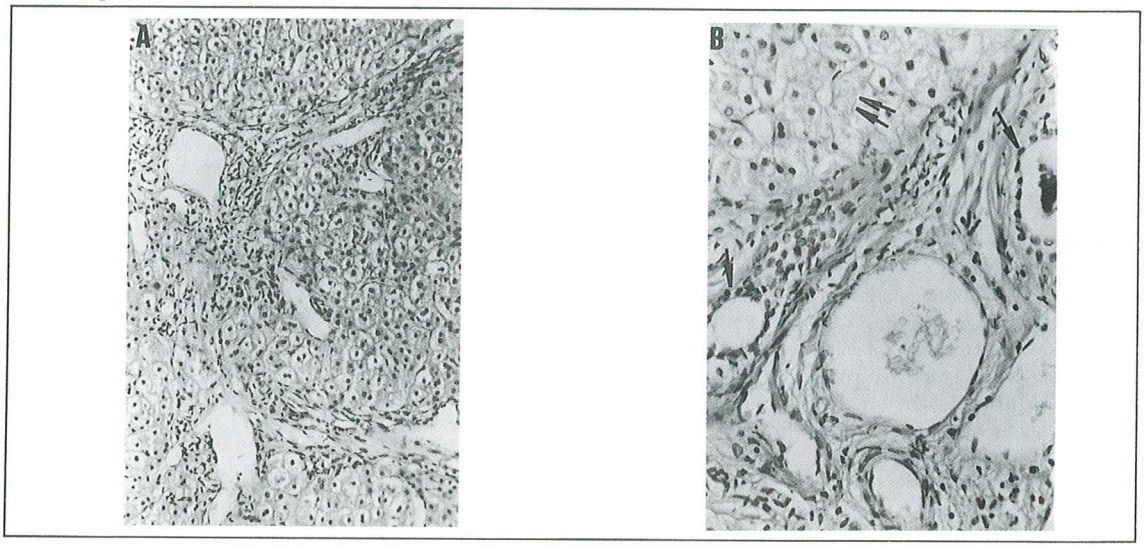

Fig. 1 : (A) Ballooaning degeneration and focal necrosis in hepatic parenchyma.There is mild inflammatory infiltrate within the portal tract (x 200). (B) Normal portal tract. There is no abnormality in bile ducts (arrowheads). Rosett formation is seen on periportal hepatocyte (double arrows) (x 400).

To date, no effective treatment has been identified to prevent attacks or to alleviate symptoms during an attack. Cholestyramine may alleviate symptoms in some patients. Rifampin was used in some patients to reduce the severity of pruritus. Rifampin competes with bile acids for hepatic uptake, thereby lowering hepatocyte bile salt concentration and possibly reducing pruritogen release (7).

As a result; BRIC should be kept in mind in patients with recurrent cholestatic attacks with symptom free intervals after main bile duct obstruction and other causes known to produce cholestasis are excluded.

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