**Scholars Journal of Applied Medical Sciences (SJAMS)**
***Abbreviated Key Title: Sch. J. App. Med. Sci.***
**ISSN 2320-6691 (Online)**
**ISSN 2347-954X (Print)**

A Unit of Scholars Academic and Scientific Society, India
www.saspublisher.com

Internal Medicine

# Adulthood Benign Recurrent Intrahepatic Cholestasis: An Intriguing Entity

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**Case Report**

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**Article History**
*Received: 20.05.2018*
*Accepted: 27.05.2018*
*Published: 30.05.2018*

**DOI:**
10.21276/sjams.2018.6.5.72

**Abstract:** Benign Recurrent Intrahepatic Cholestasis (BRIC) is a rare disorder characterized by recurrent episodes of cholestasis without causing any permanent liver damage. The first attack of jaundice in patients of BRIC is usually seen before the second decade of life. Here we report an interesting case of recurrent cholestatic jaundice who was diagnosed to have acute viral hepatitis on all the previous occasions before the final diagnosis of BRIC was made.
**Keywords**: Benign recurrent intrahepatic cholestasis (BRIC), Cholestatic jaundice, Ursodeoxycholic acid (UDCA).

## INTRODUCTION

Benign recurrent intrahepatic cholestasis (BRIC) is a rare familial liver disorder characterized by intermittent episodes of intrahepatic cholestasis without progression to chronic liver damage. BRIC belongs to a phenotype of intrahepatic cholestatic disorders that range from mild intermittent attacks in BRIC to a severe, chronic and progressive cholestasis seen in progressive familial intrahepatic cholestasis (PFIC). Both BRIC and PFIC are a consequence of mutation in the ATP8B1 and ABCB11 genes, respectively, encoding bile acid transport proteins. Age at first presentation ranges from infancy to late adulthood, but the first attack is usually seen before the second decade of life. We report a case of a 27-yr-old male patient with BRIC who presented with recurrent cholestatic jaundice with negative work up for all other possible etiologies. He was diagnosed as a case of viral hepatitis during the previous episodes. Histopathological examination confirmed a diagnosis of BRIC.

## CASE REPORT

27 years old male presented with recurrent jaundice since 2012. He had a total of 3 episodes previously and the last episode was in July 2014. His maximum Serum Bilirubin was 30.8 mg/dl with a direct fraction of 24 mg/dl in 2012 and 28 mg/dl in 2013.

His ALP was increased 397 IU/L which became normal (47 IU/L) over 5 weeks. He was managed as a case of acute viral hepatitis on all these occasions. His elder brother also had history of recurrent jaundice. He presented with symptoms of jaundice, pruritus, low grade fever and clay coloured stools of 20 days duration. On physical examination he had icterus and diffuses excoriations all around over his body caused by severe itching. There were no stigmata of chronic liver disease. Liver was palpable 3 cm below right sub costal margin with a span of 12 cm.

Laboratory examination revealed total bilirubin of 19.9 mg/dL with a direct component of 13.7 mg/dL. Liver enzymes were within normal range: alanine aminotransferase (ALT) was 18 IU/L (5-40), and aspartate aminotransferase (AST) was 35 IU/L (5-40). Alkaline phosphatase (ALP) was 220 IU/L (35 - 125), gamma glutamyltranspeptidase (GGT) was normal: 38 IU/L (10-45).

Prothrombin time and activated partial thromboplastin time were normal (PT: 12.8 s; aPTT: 33.1 s). His blood urea nitrogen, creatinine. serum electrolytes, cholesterol, calcium, phosphorus, uric acid, thyroid stimulating hormone, free thyroxine and free triio-dothyronine were all normal. Serologic tests for viral hepatitis (HAV, HEV, HBV, and HCV) were all negative. He was also negative for anti-nuclear antibody (ANA), antimitochondrial antibody (AMA), anti-smooth muscle antibody (ASMA) and anti-liver kidney microsome-1 antibody (anti LKM 1). He had normal 24-hr urinary copper, serum ceruloplasmin and negative KF ring. The liver was mildly enlarged (15.6 cm) with normal echotexture. Gall bladder, CBD and IHBR were normal. Spleen was normal sized (10.4 cm)

and there was no ascites. Bile ducts were also normal on magnetic resonance imaging. Since his bilirubin levels were persistently high, a liver biopsy was performed for further investigation. Biopsy of the liver showed preserved lobular architecture with 10 portal tracts. Hepatocytes showed areas of ballooning degeneration with intracanalicular and intercellular bile accumulation (Fig1). There was no evidence of ductopenia. Mild lymphomononuclear infiltrate was seen in the lobules. Reticulin stain did not show any fibrosis. He fulfilled all the criteria for diagnosis of BRIC[1].

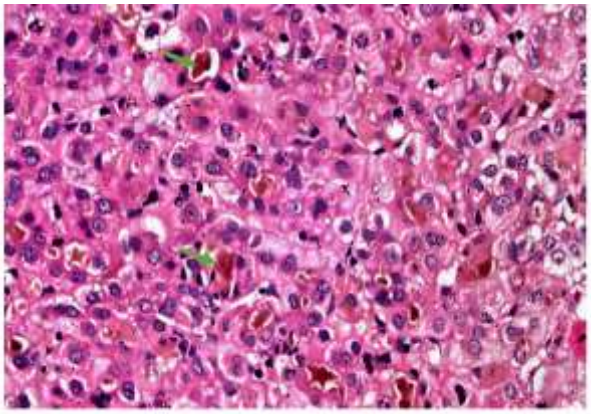

Fig 1- Photomicrograph showing intrahepatic bile stasis. Arrows. (H&Ex400)

He was treated with tab Ursodeoxycholic acid 300 mg t.d.s. He responded well to the treatment. His bilirubin came down to 3.2 mg/dl with a direct fraction on 2.3 mg/dl over next 6 weeks of treatment. Ten weeks later, the patient was free of symptoms with all normal laboratory findings. There has been no recurrence ever since.

## DISCUSSION

BRIC is a rare autosomal recessively inherited or sporadic disorder that is characterized by intermittent attacks of cholestasis. It was first described by Summerskill and Walshe in 1959[2]. Cholestatic attacks can last for several weeks to months. Symptom-free intervals also can range from several months to years. Liver biopsy is characterized by centrizonal cholestasis with preservation of normal liver architecture. There is no progression to liver cirrhosis[3].) Although attacks may be associated with a viral prodrome, an inciting viral agent or toxin has not been defined [4]. Mutations in a single gene, FIC1 (recently renamed ATP8B1) were found to be responsible for this disease in most families described till date, although genetic heterogeneity is present[5]. Recently BRIC type 2 (BRIC 2) caused by another mutational change in ABCB11 gene has been demonstrated[6]. In comparison to patients with ATP8B1 mutations, patients with ABCB11 mutations lack extrahepatic symptoms such as pancreatitis and are more likely to exhibit cholestasis[7].

The attacks can start at any age, but the first episode is usually seen before the second decade of life. In a large series of patients the age of presentation varied from 1 to 59 years and duration of icteric phase was also variable lasting from weeks to months[8].

In our patient, the first attack was seen at age of twenty-three. Each episode lasted approximately for eight weeks. Initial presentations are usually misdiagnosed as acute viral hepatitis. The diagnosis of BRIC is based on at least two episodes of jaundice separated by a

symptom free interval lasting several months to years, lab findings of cholestasis with normal GGT, imaging evidence of normal intra and extra hepatic bile ducts and liver histology demonstrating intra hepatic cholestasis in centrilobular distribution[1].

Treatment of BRIC is symptomatic to relieve pruritus. Several drugs have been used,such as cholestyramine, ursodeoxycholic acid (UDCA) and rifampicin[9]. UDCA is a hydrophilic bile acid, non-toxic to hepatocytes which replaces toxic hydrophobic bile salts. It is causes increased biliary secretion of bile acids and phospholipids leading to shortened duration of cholestasis in BRIC[10].

## CONCLUSION

We report a case of adulthood BRIC who was previously being repeatedly diagnosed as acute viral hepatitis. Although a rare disease and even rarer in adulthood, the diagnosis of BRIC should be kept in mind in patients with recurrent cholestatic jaundice with symptom free intervals after extrahepatic biliary obstruction and other congenital or acquired causes of intrahepatic cholestasis excluded. Histopathological examination of liver confirms the diagnosis.

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