A Rare Case of Benign Recurrent Intrahepatic Cholestasis (BRIC) Presenting as an Unexplained Cholestatic Jaundice

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Introduction

Benign Recurrent Intrahepatic Cholestasis (BRIC) is a very rare autosomal recessive disorder characterized by episodes of recurrent cholestatic jaundice manifested as pruritus, anorexia, fatigue, steatorrhea followed by complete resolution[1]. BRIC is associated with a mutation in both alleles of ATP8B1 (BRIC 1) or ABCB11 (BRIC2)[2]. It causes cholestasis by impairing the function of the bile salt export pump. Recognition of BRIC is important as it can lead to delayed or no diagnosis, also it is underrecognized and challenging. Diagnosis is based on a compatible clinical presentation, laboratory parameters and histology with exclusion of other causes of cholestasis and confirmed by genetic testing.[1,3,4] Treatment is supportive often aimed at relief of symptoms and shortening of episode. Despite being recurrent, BRIC does not progress to advanced liver disease.

Case

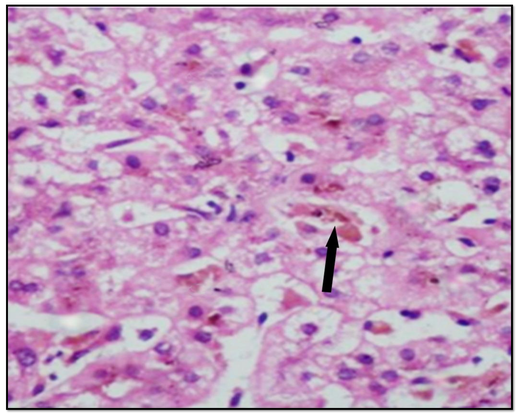
A 19-year-old South Asian male presented with nausea, vomiting, deep jaundice and pruritus of 10 days duration. Family history was negative for jaundice. He was not consuming alcohol or any drugs. Past medical records revealed three past episodes of undiagnosed cholestatic jaundice lasting for three to four weeks with complete recovery at the age of 8, 11 and 14 years respectively. Physical examination revealed stable vitals, deep icterus, cutaneous scratch marks and mild tender hepatomegaly. No stigmata of acute or chronic liver disease were identified. PT was prolonged with an INR of 1.8. AST and ALT were initially raised on admission which gradually trended down while serum total bilirubin, direct bilirubin and alkaline phosphatase continued to raise over 8 weeks. GGT remained within normal limits (Table 1). Viral markers for hepatitis A, B, C, E; HIV 1&2; EBV and CMV were negative.

Workups for autoimmune hepatitis and Wilson's disease were negative. Ultrasound of the abdomen and MRCP were unremarkable. A liver biopsy was performed which showed intrahepatic canalicular cholestasis predominantly involving zone 3 with preserved liver architecture suggestive of BRIC (Figure A). He was treated with intravenous fluids, antiemetics, cholestyramine and antihistamines for symptomatic relief. Because of severe pruritus, Rifampicin was added later on for 14 days resulting in significant improvement. Liver function tests returned to baseline after 3 months. The patient was followed up for 6 months and remained asymptomatic.

Table 1. Laboratory results.

	Total Bilirubin (mg/dl)	Direct Bilirubin (mg/dl)	ALP (U/L)	GGT (U/L)	ALT (U/L)	AST (U/L)
Day – 1	8.2	6.1	388	15.2	415	205
Day – 7	12.4	9.8	421	15.4	354	106
Day – 14	14.6	12.2	510	14.8	156	88
Day – 21	18.0	16.5	615	14.5	80	60
Day – 31	21.5	18.3	830	12	48	32
Day – 45	24.32	22.45	950	11.3	38	22
Day – 60	26.82	24.13	1152	10.1	36	20
Day – 75	11.24	9.12	353	9.2	32	18
Day – 90	1.6	0.8	86	9	28	15

Figure A. Liver Histology (H&E × 400): Intrahepatic cholestasis (black arrow) with preserved liver architecture.



Diagnostic Criteria for BRIC[1]

- At least two attacks of jaundice separated by a symptom-free interval lasting several months to years
- Laboratory values consistent with intrahepatic cholestasis
- GGT either normal or only minimally elevated
- Severe pruritus secondary to cholestasis
- Liver histology demonstrating centrilobular cholestasis
- Normal intra- and extrahepatic bile ducts by cholangiography
- Absence of factors known to be associated with cholestasis (i.e., drugs and pregnancy)

Discussion

BRIC (Benign Recurrent Intrahepatic Cholestasis), first described in 1959 has since been reported to occur worldwide.[1] Till date very few cases of BRIC have been reported, which may be due to the rarity of the condition compounded by under-recognition by clinicians.

Inheritance follows an autosomal recessive pattern with mutations in both alleles of ATP8B1 (BRIC1) or ABCB11 (BRIC2).[2] Both mutations cause cholestasis by impairing the function of the bile salt export pump (BSEP), which actively transports bile into canaliculi.[2] Despite being a genetic disease, most cases are sporadic. The first episode usually occurs in the first two decades of life. Episodes can last from weeks to months and can be of varying severity.[1-2] In between episodes, patients remain totally devoid of symptoms for periods ranging from months to years. Triggers include stress, pregnancy, respiratory and gastrointestinal infections.[3]

Diagnosis in our case was based on the past episodes of jaundice, present clinical features, laboratory parameters and liver biopsy findings as proposed by Luketic and Shiffman for the diagnosis of BRIC.[1] This is a self-limiting disease with no residual damage and treatment is aimed at relieving symptoms and shortening of episodes. High dose fat-soluble vitamins should be supplemented to prevent deficiency during prolonged episodes.[6] Bile acid sequestrants such as cholestyramine and ursodeoxycholic acid may reduce pruritus but not the duration of episodes. Rifampicin, plasmapheresis have shown to relieve symptoms and shorten episodes.[4] The effectiveness of Rifampicin is related to its enzyme-inducing effects.[7] Endoscopic nasobiliary drainage is an effective treatment option in patients refractory to standard therapy.[8]

Contact

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