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Case Report

A Rare Case Report on Benign Recurrent Intrahepatic Cholestasis

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Abstract:

Benign recurrent intrahepatic cholestasis is an inherited and occasionally sporadic disease presents as recurrent episodes of obstructive jaundice without any obstruction in billiary channel with intervening symptom free periods. Here we are presenting a case of 20-year-old male with a recurrent jaundice and pruritus who later diagnose as BRIC.

Key words: BRIC, Pruritus, Jaundice.

Introduction:

Benign recurrent intrahepatic choleastasis (BRIC) is a form of rare inherited disorder characterized by recurrent episode of jaundice and pruritus which resolve spontaneously without any liver damage. In between the episodes, patient lives completely symptom free. The diagnosis is usually by exclusion of other cause of intrahepatic cholestasis along with a liver biopsy and the treatment is usually symptomatic.

Case Report:

A 20-year-old male presented with recurrent episode of jaundice, pruritus, pale stool and dark urine for last 3 years. There has been 6 episodes each persisting 3 months. Each episode is also associated with generalized skin pigmentation, intermittent dull epigastric pain without any radiation, aggravating or relieving factor and average weight loss of 6 kg. In between the episodes he remains completely symptom free and even

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gains his lost weight. There is no history of abdominal distention blood transfusion or bloody diarrhoea. There is no history of taking any medication prior to the illness. There is no history of fever during or prior to the illness. There is also no history consanguinity between his parents or no such illness in his family.

On examination he had an average body built with a BMI 20 kg/M^2. He was icteric with generalized skin pigmentation, there were multiple scratch marks all over the body and shiny nail. There was no lymphadenopathy, no signs of chronic liver disease or any vitamin deficiency feature. His vital signs were normal.

Abdominal examination showed hepatomegaly of 6 cm which was nontender smooth surface and has sharp margin. There was no other organomegaly or ascities. Rest of the systemic examination was normal. Investigation (table-1) revealed his total as well as both direct and indirect billirubin was raised there was also raise in alkaline phosphatase but normal GGT. His ultrasonogram of abdomen and MRCP was normal. Viral markers and auto antibodies for liver disease was also normal. Based on above findings a diagnosis benign recurrent intrahepatic cholestasis (BRIC) was made and DNA analysis was not done due to lack of facilities.

Table-1: Investigation

Hameglobin	13.7gm/dl
ESR	25mm in 1sthour
Total count of WBC	8500/mm^3
Platelet count	450000/mm^3
Serrum total billirubin	9.2mg/dl
Conjugated billirubin	4.56 mg/dl
Unconjugated billirubin	4.67
ALT	23 IU/L
AST	45IU/L
ALP	950IU/L
GGT	23 U/L
PT	Patient 12 second Cntrol 11.8
Haemoglobin electrophoresis	Normal study
Ultrasonogram of abdomen	Normal
MRCP	Normal Distended Galblader
ANA	Negative
p-ANCA	Negative
Anti mitochondrial anti body	Negative
Anti smooth muscle antibody	Negative
Urinar 24 hour copper	< 20 mg (normal)
Ceruloplasmin	42mg/dl
Serrum ferretin	290mg/ml
HBsAg	Negative
AntiHCV	Negative
Anti HEV	Negative
Liver biopsy	Not done

Disscussion:

In 1959 Summerskill and Walshe first Describe BRIC. After that a few has been reported. Correct diagnosis of BRIC is very essential for management as well as for preventing over-investigation of the patient.

It occurs due to defect in cannalicular excretion of bile acids and phospholipids. There are 3 types. BRIC 1 and 2 are both autosomal recessive disorders while BRIC 3 is autosomal dominant. BRIC 1 is due to mutation in ATP8B1 gene on chromosome 18q21. BRIC 2 is due to mutation in bile salt export pump (ABCB11) on chromosome 2q24. Defects in ABCB4 encoding the multidrug resistant protein 3 resulting in impaired biliary phospholipid secretion results in BRIC 3. All the 3 subtypes are phenotypically similar. This disease is distributed worldwide with both sexes being equally affected.

Before reach in any diagnosis Wilson's disease, alpha-1 antitrypsin deficiency, autoimmune Liver disease and chronic viral hepatitis are to be considered.

In 1999, Luketic and Schiffman proposed a diagnostic criteria for BRIC which includes (a) At least two episodes of jaundice separated by an asymptomatic interval of months to years, (b) laboratory values consistent with intrahepatic cholestasis, (c) severe pruritus secondary to cholestasis, (d) liver histology demonstrating centrilobular cholestasis, (e) normal intrahepatic and extra-hepatic bile ducts confirmed by cholangiography, (f) absence of factors associated with cholestasis[1]. Our patient fulfilled all the above-mentioned criteria except liver biopsy.

The severity and duration of episodes or intervening periods are unpredictable[2]. BRIC is a benign disease that does not progress to cirrhosis[3] or end stage liver disease, but a few cases as reported by Ooteghem et al., the disease has been progressive[4].

Treatment:

The main treatment for BRIC is reassurance and till now no specific treatment is available. However, pruritis which is the major disturbing symptom can be reduce with several medications that include: UDCA (13-15 mg/kg body weight/day), cholestyramine (12-16 g/day), rifampicin (300-600 mg/day), Phenobarbital[5, 6,7] and antihistamines (hydroxyzine and difenhydramine) especially for nocturnal pruritus[8].

The mechanism of UDCA in experimental evidence suggests three major mechanisms of action: (1) protection of cholangiocytes against cytotoxicity of hydrophobic bile acids, resulting from modulation of

the composition of mixed phospholipid-rich micelles, reduction of bile acid cytotoxicity of bile and, possibly, decrease of the concentration of hydrophobic bile acids in the cholangiocytes; (2) stimulation of hepatobiliary secretion, putatively via Ca(2+)- and protein kinase C-alpha-dependent mechanisms and/or activation of p38 (MAPK) and extracellular signal-regulated kinases (Erk) resulting in insertion of transporter molecules (e.g., bile salt export pump, BSEP, and conjugate export pump, MRP2) into the canalicular membrane of the hepatocyte and, possibly, activation of inserted carriers; (3) protection of hepatocytes against bile acid-induced apoptosis, involving inhibition of mitochondrial membrane permeability transition (MMPT), and possibly, stimulation of a survival pathway[9].

Rifampicin partly interferes with hepatic uptake of bile acids and decreases hepatocyte bile concentration[10]. Rifampicin also induces 6-hydroxylation of secondary bile salts which facilitates their elimination[11].

Corticosteroid therapy has been used to reduce cholestasis. Bile secretion and intrahepatic cholestasis also involves cellular mechanisms such as cellular immunity and it is suppressed by corticosteroids and explains their mechanism of action[12].

Simvastatin has also been proposed as an alternative medical therapy in one study[13].

Extracorporal albumin dialysis (MARS: Molecular Adsorbent Recycling System), has recently shown to be effective in resistant cases[14] MARS treatment shifts parts of the highly concentrated intracellular contents towards the extracellular compartments which results in decreased plasma concentrations of bile acids and bilirubin[15] MARS also improves transcription of apo A-1 gene which is suppressed in BRIC and therefore increases the plasma levels of apo A-1[13].

Nasobiliary drainage via ERCP has also been used in a study from Holland for long-lasting relief from pruritis and jaundice[16].

If there is any known trigger for BRIC, the patient is advised to avoid it. For example, if patient is taking OCP then patient should be advised to use other methods of contraception, such as IUD or sterilization[17].

Conclusion:

BRIC by its name says it has a benign course. But as some case has been reported to its progression to Cirrhosis[4] it should now keep under surveillance and any cholestatic symptom without any definite pathology in initial investigation BRIC should be kept in mind.

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