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Case Report

The flickering jaundice

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ABSTRACT

Benign Recurrent Intrahepatic Cholestasis (BRIC) is a rare autosomal recessive disorder characterized by intermittent episodes of jaundice and pruritus. It is a benign disease with no progression to end stage liver disease. However, this condition remains under-diagnosed and patients of recurrent jaundice are usually subjected to several investigations and procedures to elucidate the etiology of the cholestatic jaundice. This case report presents a young male who presented with severe pruritus and acute onset jaundice at a tertiary care hospital in South India. He had his first episode of jaundice at the age of twelve and had several intermittent episodes since then. Diagnosis was made by the unique clinical presentation with exclusion of other causes of cholestatic jaundice.

Keywords: Benign jaundice, Benign Recurrent Intrahepatic cholestasis, Cholestatic jaundice, Recurrent jaundice

INTRODUCTION

Benign Recurrent Intrahepatic Cholestasis (BRIC) is a rare autosomal recessive disorder characterized by intermittent episodes of jaundice and pruritus. It is also known as Summerskill-Walshe-Tygstrup syndrome. BRIC was first described by Summerskill and Walshe in 1959.[1] Tygsrup and Jensen described the condition in five young males in 1969.[2]

It is a benign disease with no progression to end stage liver disease. The first episode of cholestatic jaundice occurs early in life and there are asymptomatic periods between attacks lasting weeks to years.

Despite cholestatic jaundice being a common presentation, BRIC is largely underdiagnosed. Recent literature also shows only sparse reports. This case report highlights the importance of detecting such cases of rarity and preventing unnecessary invasive diagnostic procedures on such patients.

CASE REPORT

A 21 year old unmarried male presented with complaints of jaundice since one month associated with pruritus and dark colored urine. He also gave history of several similar episodes in the past. However, there was no history of blood transfusion, rash, drug or alcohol intake. The first episode of jaundice occurred at the age of 16yrs and he has had seven episodes of jaundice since then. Each episode lasted for almost a month with intervening asymptomatic periods.

There was no history of similar complaints among other family members. The present episode of jaundice was preceded by fever and diffuse pain abdomen. Patient consulted a local hospital and was diagnosed to have a possible infective cause of hepatitis and received ayurvedic medication over the past month. As there was no symptomatic relief, patient visited a tertiary care hospital. On physical examination, he had deep icterus with scratch marks all over his body. There were also no signs of liver cell failure. A summary of the laboratory investigations done is shown in (Table 1).

Table 1: Summary of the laboratory investigations.

Laboratory investigation	Results
Total leucocyte counts	16,100/cumm
Total bilirubin	13.39mg/dl
Direct bilirubin	11.25mg/dl
Alanine aminotransferase	48 IU/L
Aspartate aminotransferase	79 IU/L
Alkaline phosphatase	292 U/L
PT/INR	15.2 seconds/ 1.42
Serum urea/ serum creatinine	20mg/dl /0.9 mg/dl
Serum sodium/potassium	135/ 4
Blood culture	Sterile
Urine culture	Sterile
Serology for Scrub typhus	Negative
Serology for leptospirosis	Negative
Malarial parasite	Negative
Hepatitis B surface antigen (HBsAg)	Negative
antibodies to hepatitis C virus (Anti HCV)	Negative
IgM antibodies to hepatitis A virus (IgM anti HAV)	Negative
IgM antibodies to hepatitis E virus (IgM anti HEV)	Negative

Ultrasound of abdomen and pelvis showed distended gall bladder with calculus and mild wall thickening. There was no evidence of intrahepatic biliary radicle dilatation.

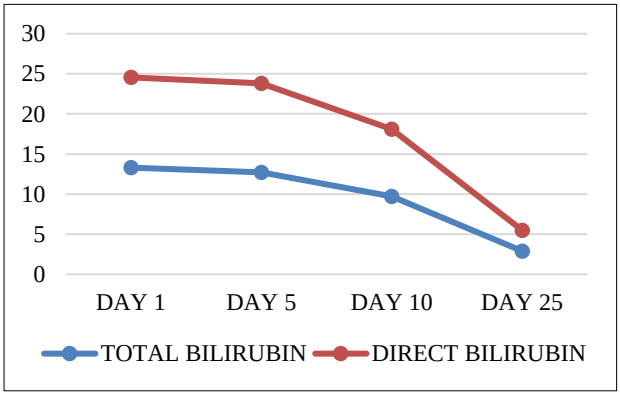

Figure 1: The trend of the hyperbilirubinemia from admission to follow-up.

The patient was diagnosed to have acute cholangitis as he presented with fever and pain abdomen during this episode of jaundice. But, in view of the past history of recurrent episodes of jaundice, absence of liver cell failure and recurrent direct hyperbilirubinemia , the patient was suspected to have Benign recurrent intrahepatic cholestasis(BRIC). He was given symptomatic treatment for pruritus with ursodeoxycholic acid and cholestyramine. His jaundice and pruritus improved over the following week and the patient was symptom free at discharge as shown in (Figure 1). His total bilirubin improved to 2.9mg/dl with direct bilirubin at 2.6mg/dl. As this condition has an autosomal recessive pattern, he also underwent genetic counselling and was explained the possibility of this disease manifesting in future generations.

DISCUSSION

Benign Recurrent Intrahepatic cholestasis (BRIC) is a rare genetic disorder that presents with by intermittent episodes of jaundice and pruritus. This condition was long suspected to be genetic and this was finally confirmed in 1998, when a mutation in the ATP8B1 gene on chromosome 18q21 was localized.[3]

Forms of familial intrahepatic cholestasis (FIC), include Progressive familial intrahepatic cholestasis (PFIC), BRIC, and intrahepatic cholestasis of pregnancy (ICP). All these three conditions have an autosomal recessive inheritance pattern and they are differentiated based on their clinical presentation. While PFIC starts in infancy or early childhood and often leads to liver cirrhosis, BRIC usually appears later in life and has a more benign recurrent pattern. There are two known genotypes of the recessive inherited forms of both BRIC and PFIC. BRIC1 and PFIC1 have a mutation in the ATP8B1 gene, while BRIC2 and PFIC2 have a mutation in the ABCB11 gene on chromosome 2q24.[4]

Prodromal symptoms are fatigue, loss of appetite, and nausea. Patients typically present with at least two episodes of cholestasis jaundice separated by an intervening asymptomatic period. Pruritus may precede other clinical manifestations and may impair quality of life. Subsequently, jaundice appears. Due to fatigue and loss of appetite, weight loss is common.[1]

Laboratory studies show a rise in the serum alkaline phosphatase (ALP) level suggesting cholestasis following the onset of pruritus. It is subsequently followed by conjugated hyperbilirubinemia, while serum gamma-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels remain normal or only mildly elevated.[5]

Usually the diagnosis is delayed, and the patients experience physical and mental challenges during the period of illness. There may also be several invasive procedures done for diagnosis that are unnecessary. However, prognosis is good as the disease does not progress toward cirrhosis. BRICS is managed only by supportive treatment during the period of illness. Following each episode, the symptoms of pruritus and jaundice subside followed by a remarkable recovery in the lab parameters as well. Also, patients may remain symptom free for months to years between episodes.[6]

CONCLUSION

As BRIC is a sparsely known and rarely diagnosed condition, this case report seeks to highlight the spectrum

of clinical symptoms, signs and lab diagnosis that consolidate this diagnosis. Also, awareness of this condition can eliminate unnecessary invasive and expensive diagnostic procedures to isolate the etiology of cholestatic jaundice.

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