Original Research Paper

Volume - 11 | Issue - 01 | January - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Internal Medicine

AN UNUSUAL CASE OF BENIGN RECURRENT INTRAHEPATIC CHOLESTASIS

Dr Divya Shanagonda*	Final Year Post-Graduate, Department Of Internal Medicine, Sriher, Porur, Chennai, Tamilnadu, India. *Corresponding Author
Dr Srinivasan Ramadurai	Associate Professor, Department Of Internal Medicine, Sriher, Porur, Chennai, Tamilnadu, India.
Dr G Sowmya	Professor, Department Of Internal Medicine, Sriher, Porur, Chennai, Tamilnadu, India.
Dr Preetam Arthur	Professor, Department Of Internal Medicine, Sriher, Porur, Chennai, Tamilnadu, India.

ABSTRACT Benign intrahepatic cholestasis (BRIC) is a rare genetic disorder characterized by episodic cholestasis. Each episode is characterized by repeated episodes of jaundice, intense pruritis last for weeks to months with complete remission. Although each episode is associated with significant morbidity, progressive liver injury and cirrhosis do not occur. In recent studies, few patients progressed to Progressive familial intrahepatic cholestasis. Here we report a case of 19 years boy with benign intrahepatic cholestasis due to an undulant course terminated by plasma exchange.

KEYWORDS :

INTRODUCTION:

Benign recurrent intrahepatic cholestasis is a rare genetic autosomal recessive disorder characterized by self-limited episodic cholestasis with index episode in the first two decades of life. Usually, episodes of cholestasis are either spontaneous or triggered by infections, pregnancy, and are manifested by pruritus, anorexia, fatigue, steatorrhea, and jaundice and last for weeks to months. BRIC had diagnosed by classical clinical presentation, laboratory parameters, histology, and by excluding the other causes. As it is self-limiting and non-progressive, there is no specific treatment for BRIC. If treated, it is aimed at relief of symptoms, shortening of episodes, and prevention of complications.

CASE REPORT

19 years male from Madurai presented to our institution with jaundice and intense pruritis all over the body for two months with pale stools and high colored urine. Weight loss of thirteen kgs was present within a span of two months. He had three similar episodes in the past, approximately one year apart which resolves spontaneously within a month with symptoms free interval. The first episode occurred at the age of 16 years and resolved in a month. No history of precipitating factors like food, infection. No history of fever, rash, abdominal pain, abdominal distension, vomiting, altered bowel habits, drug exposure, alcohol intake, abdominal surgeries, blood transfusions or arthralgia or bleeding manifestations, melena. No history of neonatal jaundice, hemolytic anemias or diabetes, hyperlipidemia. All other family members are doing well. No addictions, normal bowel, and bladder habits. Sleep pattern disturbed during the episodes due to intense itching. Non-vegetarian by diet. On examination, he is conscious and coherent, poorly built, and nourished with a Body mass index of 18.6. Pulse rate- 72/min, Blood pressure is 110/80 mm of hg in the right upper limb in the supine position. Icterus present, the skin was yellowish and scratch marks are present all over the body. No Kayser-Fleischer ring, cyanosis, clubbing, pedal edema, or lymphadenopathy. No signs of liver cell failure. No organomegaly or ascites on palpation of abdomen and bowel sounds heard. The Respiratory and cardiovascular system was unremarkable.

INVESTIGATIONS:

- He was found to have a hemoglobin of 12.4gm/dl, total counts-9300/cmm, platelets-3.57lakhs/cmm, and ESR of 20mm. Renal function tests and electrolytes were normal. Liver functions tests showed alkaline phosphatase-281U/L(normal-32-120), total bilirubin-20.69mg/dl(0.3-1.2) with direct -14.84mg/dl(1 in 5 dilution) (<0.2), alanine transaminase-16 U/L(<50), aspartate transaminase-40 U/L (<50), total protein-6.4gm.dl(6.6-8.3) with albumin – 3.3gm/dl(3.5-5.2), globulin-3.2gm/dl (2-3.5), Gamma - GT 36U/L(0-55), PTT-31.9sec (27-40) with control 26.3and PT-11.9 sec(11-16) and INR-1.09. HIV P24 Ag, HIV I & II Ab, HCV Ab, HBsAg are negative. Antinuclear, anti-smooth muscle, anti-mitochondrial, anti-LKM1 antibodies are negative and serum ceruloplasmin was found to be normal. Ultrasonography one year back showed- the liver span of 11.5 cm with uniform echo-pattern with no evidence of local or diffuse pathology and normal intra and extrahepatic biliary radicles and on present admission showed mild hepatomegaly with cholelithiasis. Upper gastrointestinal scopy showed normal mucosa without varices and Magnetic resonance cholangiopancreatography showed normal intrahepatic and extrahepatic biliary radicles with no evidence of stone in the common bile duct. Liver Biopsy showed a maintained lobular architecture comprised of hepatocytes showing scattered intra-hepatocytic cholestasis and focal lobular inflammation, bile canaliculi showing prominent intracanalicular cholestasis comprised of dark brown coarse bile pigments, Portal tracts show minimal lymphocytic infiltrates and No portal fibrosis, significant inflammation, or nodule formation. After exclusion of all other etiologies, with clinical features and investigations, patient was diagnosed as Benign intrahepatic cholestasis.

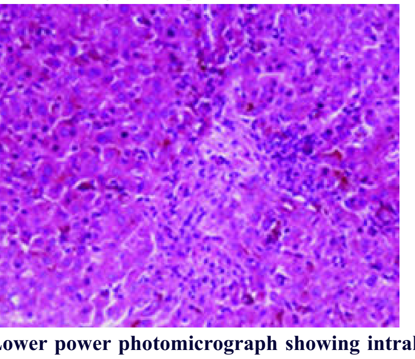

Fig 1: Lower power photomicrograph showing intrahepatic as well as canalicular cholestasis in zone 3

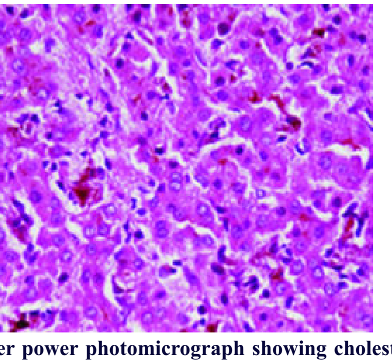

Fig-2: Higher power photomicrograph showing cholestasis with sinusoids showing pigment laden kupffer cells.

After treating with ursodeoxycholic acid 300mg thrice daily, cholestyramine 4grams daily, and the antihistamines, the patient had persistent jaundice and pruritis. Hepatology opinion obtained and advised for plasma exchange. Four cycles of Plasma Exchange had done. The Patient was improved symptomatically and advised to take a low-fat diet and fat-soluble vitamin supplements. At discharge, total bilirubin was 7.53, direct bilirubin 4.36. and alkaline phosphatase 141.

DISCUSSION

- Benign intrahepatic cholestasis (BRIC) also known as Summerskill-Walshe-Tygstrup syndrome as first described by Summerskill and Walshe in 1959. [1] Only 156 cases have been reported to date. It is a rare genetic autosomal recessive disorder characterized by intermittent cholestatic episodes with yellowish discoloration of sclerae, pruritis, pale color stools, high colored urine which last from weeks to months with a varying intensity and symptom-free interval. Presents at infancy to late adulthood usually index event occurs before the 2nd decade. There can be Several episodes per year to once in a decade. Triggered by Stress, pregnancy, airway, and gastrointestinal infections [2,3,4,5] and one case by cutaneous infection [6]. Laboratory tests reveal biochemical evidence of cholestasis without severe hepatocellular injury. Liver histology reveals non-inflammatory intrahepatic cholestasis without fibrosis, regardless of the number of attacks or severity of attacks. Liver histology returns to normal during remission. This BRIC is inherited in an autosomal recessive pattern and found to be associated with mutations of ATP8B1 and ABCB11 genes which are termed as BRIC-1 and BRIC-2 respectively. These BRIC-1 and BRIC-2 are distinct disorders as there are clinical differences between these two subtypes.

Diagnostic criteria proposed by Luketic and Shiffman [2]

- At least 2 episodes of jaundice with an asymptomatic interval of months to years
- Laboratory investigations suggestive of intrahepatic cholestasis
- Cholestasis induced severe pruritis
- Cholangiography showing normal intra and extrahepatic bile ducts
- Liver histology – Centrilobular cholestasis
- Absence of other causes of cholestasis

BRIC had no definitive treatment. Treat conservatively with a low-fat diet, use of short-chain fatty acids, high dose fat-soluble vitamin supplementation, and for pruritis with bile acid sequestrants, antihistamines, Rifampicin, and Cholestyramine. ERCP mediated naso-biliary drainage for long term relief from jaundice and pruritis has been reported. [7] Extracorporeal albumin dialysis in a molecular adsorbent recycling system (MARS) can terminate cholestatic episodes rapidly. [8] Colestimide, an anion exchange resin that inhibits intestinal bile acid absorption also resulted in rapid remission of a cholestatic episode in another patient. [9] Liver transplantation is indicated when BRIC progresses to PFIC. On long-term follow-up, a benign course was observed but a recent report suggested that few patients progress to PFIC. In a study out of 63 BRIC patients, only four developed permanent cholestasis. [10]

CONCLUSION

Extracorporeal albumin dialysis in a molecular absorbent recycling system and Plasma exchange could be a newer modality for severe illness. BRIC can progress to permanent cholestasis rarely.

REFERENCES

[1]. Summerskill WHJ, Walshe JM. Benign recurrent intrahepatic "obstructive" jaundice. Lancet 1959;2:686 – 90.

[2]. V. A. Luketic and M. L. Shiffman, "Benign recurrent intrahepatic cholestasis," Clinics in Liver Disease, vol. 8, no. 1, pp. 133–149, 2004.

[3]. G. Folvik, O. Hilde, and G. O. Helge, "Benign recurrent intrahepatic cholestasis: review and long-term follow-up of five cases," Scandinavian Journal of Gastroenterology, vol. 47, no. 4, pp. 482–488, 2012.

[4]. F. Ermis, K. Oncu, M. Ozel et al., "Benign recurrent intrahepatic cholestasis: late initial diagnosis in adulthood," Annals of Hepatology, vol. 9, no. 2, pp. 207–210, 2010.

[5]. A. Norouzi, S. Ghajarieh Sepanlou, S. Tavassoli, and R. Malekzadeh, "Clinical challenge in hepatology," Middle East Journal of Digestive Diseases, vol. 3, no. 3, pp. 138–148, 2011.

[6]. Adil Salyani, Linda Barasa, Allan Rajula, Sayed K. Ali, "Benign Recurrent Intrahepatic Cholestasis (BRIC): An African Case Report", *Case Reports in Gastrointestinal Medicine*, vol. 2020, Article ID 2894293, 5 pages, 2020.

[7]. Stapelbroek JM, van Erpecum KJ, Klomp LW, et al. Nasobiliary drainage induces long-lasting remission in benign recurrent intrahepatic cholestasis. Hepatology 2006; 43:51.

[8]. Saich R, Collins P, Ala A, et al. Benign recurrent intrahepatic cholestasis with secondary renal impairment treated with extracorporeal albumin dialysis. Eur J Gastroenterol Hepatol 2005; 17:585.

[9]. Uegaki S, Tanaka A, Mori Y, et al. Successful treatment with colestimide for a bout of cholestasis in a Japanese patient with benign recurrent intrahepatic cholestasis caused by ATP8B1 mutation. Intern Med 2008; 47:599.

[10]. van Ooteghem NA, Klomp LW, van Berge-Henegouwen GP, Houwen RH. Benign recurrent intrahepatic cholestasis progressing to progressive familial intrahepatic cholestasis: low GGT cholestasis is a clinical continuum. J Hepatol. 2002 Mar;36(3):439-43. doi: 10.1016/s0168-8278(01)00299-9. PMID: 11867191.