Benign Recurrent Intrahepatic Cholestasis (BRIC) Managed with Plasmapheresis

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Introduction

Benign recurrent intrahepatic cholestasis (BRIC) and Progressive Familial Intrahepatic Cholestasis (PFIC) are rare conditions of defective bile salt transport, each with an estimated prevalence of 1/50,000-100,000. Symptoms include episodic jaundice and severe pruritus. Pruritus management is difficult due to limited clinical experience and disease rarity. Treatment typically focuses on symptomatic relief of pruritus. We present a case of BRIC refractory to conventional medical treatment managed with plasmapheresis.

Case Description

A 32-year-old woman with a past medical history of BRIC type 1 diagnosed at age 14 with ATP8B1 mutation with clinical concern for overlapping PFIC type 1 presented with intractable pruritus and jaundice. She experienced seven episodes of similar presentation previously controlled with conventional medical therapy.

Physical exam was remarkable for jaundice and diffuse excoriations. Pertinent lab values are shown in Table 1. Liver ultrasound was unremarkable and negative for acute biliary pathology. Liver biopsy demonstrated panlobular hepatocanalicular cholestasis with mild perivenous, perisinusoidal, and periportal fibrosis (figure 1 and 2), compatible with chronically impaired biliary drainage.

This episode was refractory to conventional treatment with ursodiol, cholestyramine, diphenhydramine, sertraline, rifampin, naltrexone, and odevixibat. Five sessions of plasmapheresis with albumin were performed every other day with improvement in pruritus and jaundice.

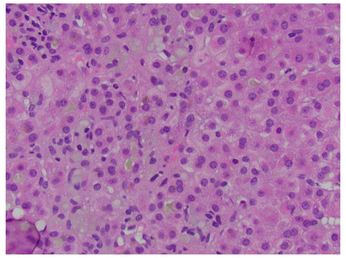

Figure 1 HE stain: canalicular cholestasis with pigmented macrophages

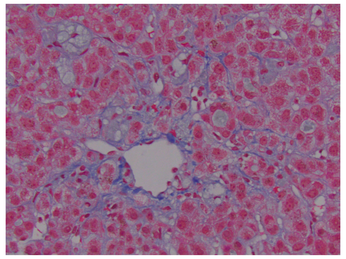

Figure 2 Trichrome stain: perisinusoidal fibrosis.

Credit: Lydia Du, MD Department of Pathology, AHN, PA

Table 1: Labs on admission versus post- plasmapheresis sessions

	Labs on admission	Labs post`- plasmapheresis
Total bilirubin (mg/dL)	30.6	15.1
Direct bilirubin (mg/dL)	25.6	11.6
AST (U/L)	39	28
ALT (U/L)	20	10
Alkaline phosphatase (U/L)	184	67
GGT (U/L)	18	__
Bile acids (umol/L)	388.5	432

Discussion

BRIC and PFIC are on opposite ends of a clinical spectrum and overlap can be present.
Subtype 1 is an autosomal recessive mutation within the ATP8B1 gene, encoding phospholipid flippase. The defect results in impaired bile salt transport.

Patients with PFIC may present in the neonatal or early childhood period and usually progress to end-stage liver disease, while the typical patient with BRIC presents later with episodic cholestasis without hepatic fibrosis.

In our case, the patient's symptoms were refractory to multiple lines of conventional therapy but responsive to plasmapheresis, which is presumed to remove circulating cholestatic pruritogens from the blood. Subjective assessment of symptom relief is recommended when evaluating treatment response, as serum bile acid levels may not correlate with cholestatic symptoms.

Our case highlights the potential usefulness of this promising modality in improving pruritus and shortening the duration of attacks in BRIC/PFIC patients.

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