ACG CASE REPORTS JOURNAL

CASE REPORT | BILIARY

Preoperative Nasobiliary Drainage as a Predictor of Response Before Surgical Fistula Creation in Joubert Syndrome With Refractory Cholestatic Pruritis

Maya Biermann, MD[1], Preeyanka Rubiana Sundar, MD[2], Hima Veeramachaneni, MD[2], and Field Willingham, MD[2]

[1]*Department of Medicine, Emory University School of Medicine, Atlanta, GA*
[2]*Division of Digestive Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, GA*

ABSTRACT

Cholestatic pruritus is a debilitating symptom associated with many liver diseases and is often refractory to medical management. Nasobiliary drainage is a relatively safe and effective method for treating intractable cholestatic pruritus. It should be considered for patients with refractory cholestatic pruritus who have failed or have contraindications to medical therapy as a predictor of response before surgical fistula creation.

KEYWORDS: Joubert syndrome; pruritus; nasobiliary drainage

INTRODUCTION

Pruritus is a debilitating symptom that affects up to 80% of patients with acute and chronic cholestatic liver disease.[1] It is caused by an increase in enterohepatic circulation of pruritogens including bile acids, which activate a complex neural network.[2] Cholestatic pruritus is typically treated with 4 classes of medications that target different components of this neural pathway: anion exchange resins (cholestyramine), enzyme inducers (rifampin), opioid antagonists (naltrexone), and sertraline.[1] However, medications are often ineffective and many patients trial other therapeutic modalities including ultraviolet therapy, plasmapheresis, extracorporeal albumin dialysis, ileal bile acid transporter inhibitors, and biliary removal via nasobiliary drainage (NBD) or external biliary diversion. Liver transplant is the last resort for severe symptoms.[2,3]

NBD via endoscopic retrograde cholangiopancreatography (ERCP) is a method of relieving pruritus by reducing circulating pruritogens through trans-nasal drainage of bile.[4] We present refractory cholestatic pruritus secondary to congenital hepatic fibrosis in a patient with Joubert syndrome (JS) that used preoperative NBD as a predictor of success before surgical fistula creation.

CASE REPORT

A 19-year-old woman with JS, polycystic kidney disease status post nephrectomy and renal transplant, and congenital hepatic fibrosis with profound cholestatic pruritus presented to interventional gastroenterology for evaluation. The patient's symptoms had been ongoing for more than 10 years but had acutely worsened in the last 2. Her symptoms were refractory to first-line medications (ursodiol, cholestyramine, colesevelam, and sertraline, naltrexone) and experimental therapy (gabapentin, lidocaine, and ultraviolet radiation). Rifampin was not trialed because of interactions with her other medications.

On presentation, her vital signs were normal. Her physical examination was notable for alopecia. Laboratory test results were significant for alanine aminotransferase 65 IU/L, aspartate aminotransferase 59 IU/L, total bilirubin 0.6 mg/dL, creatinine 2.0 mg/dL, and platelets 156 $10E^3/\mu L$, all of which were at her baseline. Her total bile acid level, previously stable around 25 μmol/L (ref 2–5 μmol/L), was 87 μmol/L and had peaked at 221 μmol/L 2 months earlier (Figure 1). Magnetic resonance imaging of the abdomen

ACG Case Rep J 2023;10:e01171. doi:10.14309/crj.0000000000001171. Published online: October 3, 2023

Correspondence: Maya Biermann, MD (maya.biermann@emory.edu).

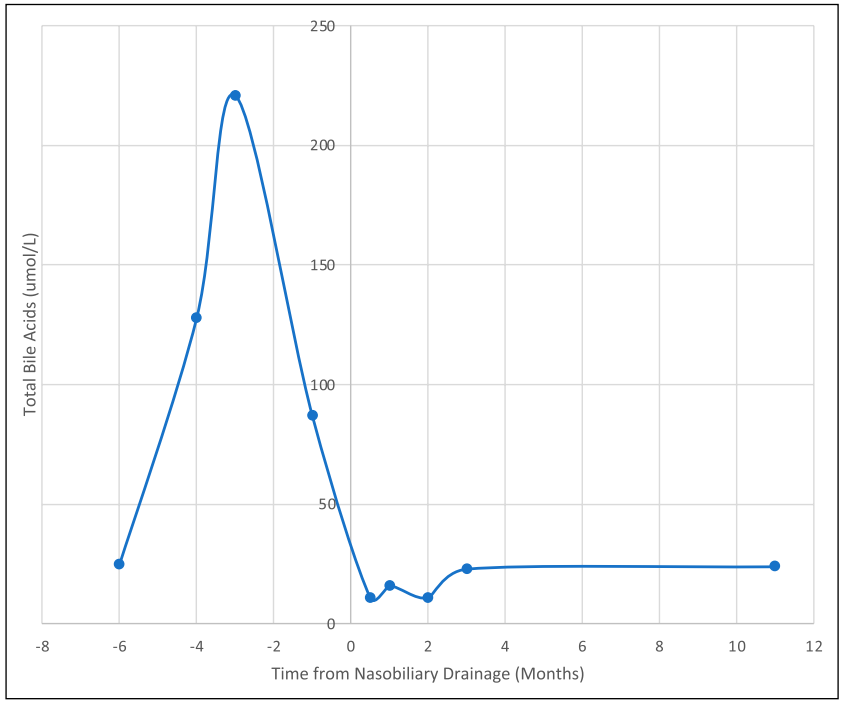

Figure 1. Total bile acid levels before and after nasobiliary drainage.

and pelvis revealed early radiographic findings of portal hypertension with evidence of an enlarged portal vein and splenomegaly and without any overt paraesophageal or perisplenic varices.

NBD with interventional gastroenterology was pursued with immediate improvement in her pruritus (Figure 2). Owing to success of the NBD, she underwent a placement of an external biliary drain with a jejunal conduit 1 week later. Her postoperative course was unremarkable with bile output of approximately 100–300 mL/day. She was discharged 3 days later. Her bile acid levels down-trended and stabilized approximately 20 μmol/L (Figure 1). Three months after the procedure, she was successfully weaned off medications with complete resolution of her pruritus 2 years later.

DISCUSSION

We present the case of a patient with JS and congenital hepatic fibrosis with chronic cholestatic pruritus refractory to medication management whose symptoms dramatically improved after NBD.

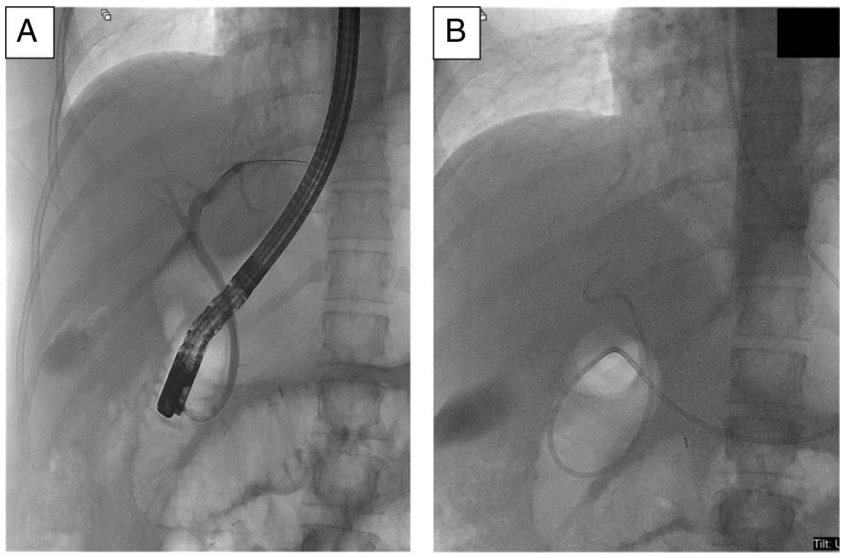

Figure 2. (A) Endoscopic retrograde cholangiopancreatography is used to guide placement of the nasobiliary drainage tube. (B) The nasobiliary drainage tube inserted into the gallbladder.

JS is a rare, autosomal-recessive ciliopathy characterized by cerebellar and brainstem malformations with a characteristic "molar tooth sign" on neuroimaging, and polycystic kidneys and congenital hepatic fibrosis. Liver involvement is found in up to 43% of patients with JS.[5,6] Although the patient had no evidence of biliary obstruction on imaging, the etiology of her pruritus was likely functional because of histological abnormalities of the small branches of her biliary tree that is typical in congenital hepatic fibrosis seen in JS.

Many patients with this condition remain symptomatic despite medical therapy.[1] In patients refractory to medications, NBD and surgical management through partial external biliary diversion may be considered.

Biliary drainage diverts pruritogenic substances such as bile and bile salts away from the ileum where they are reabsorbed and circulated back to the liver.[2] NBD is a procedure in which a 6 or 7 French transnasal catheter is placed endoscopically into the common bile duct during ERCP to allow continuous drainage of bile out through the nose (Figure 2).[3] Biliary drainage can also be accomplished surgically through partial external biliary diversion.[7] Notably, symptomatic relief of pruritus has not been shown to correlate with a decrease in total bile acid levels.[1]

Although robust data on the use of NBD in the treatment of cholestatic pruritus is limited, several studies have shown encouraging results in primary biliary cholangitis and benign recurrent intrahepatic cholestasis with minimal adverse events.[1,2,8] Potential complications of NBD include post-ERCP pancreatitis, cholangitis, and dislodgement.[9] Compared with external biliary diversion, NBD is less invasive and can be used repeatedly and/or continuously for several months.[10]

Owing to its safety and convenience, NBD can be used preoperatively as a predictor of response before more definitive management with invasive procedures such as partial external biliary diversion. Patients who experience symptomatic relief from NBD are likely to also benefit from surgical biliary drainage interventions. NBD should be considered for patients with refractory cholestatic pruritus to direct potential future surgical interventions.

DISCLOSURES

Author contributions: M. Biermann: drafting of the article, critical revision of the article for important intellectual content, and is the article guarantor. PR Sundar: participation in case, drafting of the article, and critical revision of the article for important intellectual content. H. Veeramachaneni: drafting of the article and critical revision of the article for important intellectual content. F. Willingham: participation in case and critical revision of the article for important intellectual content.

Financial disclosure: F. Willingham received research funding for clinical trials from Cook Medical, PCI Biotech, CSA Medical/Steris, and Boston Scientific.

Informed consent was obtained for this case report.

Received July 7, 2023; Accepted September 5, 2023

REFERENCES

1. Hegade VS, Krawczyk M, Kremer AE, et al. The safety and efficacy of nasobiliary drainage in the treatment of refractory cholestatic pruritus: A multicentre European study. *Aliment Pharmacol Ther*. 2016;43(2):294–302.
2. Beuers U, Wolters F, Oude Elferink RPJ. Mechanisms of pruritus in cholestasis: Understanding and treating the itch. *Nat Rev Gastroenterol Hepatol*. 2023;20:26–36.
3. Hegade VS, Kendrick SFW, Dobbins RL, et al. BAT117213: Ileal bile acid transporter (IBAT) inhibition as a treatment for pruritus in primary biliary cirrhosis: Study protocol for a randomised controlled trial. *BMC Gastroenterol*. 2016;16(1):71.
4. Cotton PB, Burney PG, Mason RR. Transnasal bile duct catheterization after endoscopic sphincterotomy: A method of biliary drainage, perfusion, and sequential cholangiography. *Gut*. 1979;20:285–7.
5. Strongin A, Heller T, Doherty D et al. Characteristics of liver disease in 100 individuals with Joubert syndrome prospectively evaluated at a single center. *J Pediatr Gastroenterol Nutr*. 2018;66(3):428–35.
6. Sattar S, Gleeson JG. The ciliopathies in neuronal development: A clinical approach to investigation of Joubert syndrome and Joubert syndrome-related disorders. *Dev Med Child Neurol*. 2011;53(9):793–8.
7. Kalicinski PJ, Ismail H, Jankowska I, et al. Surgical treatment of progressive familial intrahepatic cholestasis: Comparison of partial external biliary diversion and ileal bypass. *Eur J Pediatr Surg*. 2003;13:307–11.
8. Stapelbroek JM, van Erpecum KJ, Klomp LW, et al. Nasobiliary drainage induces long-lasting remission in benign recurrent intrahepatic cholestasis. *Hepatology*. 2006(43):51–3.
9. Lin H, Li S, Liu X. The safety and efficacy of nasobiliary drainage versus biliary stenting in malignant biliary obstruction. *Medicine (Baltimore)*. 2016;95(46):e5253.
10. Appleby VJ, Hutchinson JM, Davies MH. Safety and efficacy of long-term nasobiliary drainage to treat intractable pruritus in cholestatic liver disease. *Frontline Gastroenterol*. 2015;6(4):252–4.