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Partial internal biliary diversion for Alagille syndrome: case report and review of the literature

Shari Sheflin-Findling[a,b,*], Ronen Arnon[b,c], Samantha Lee[c], Jaime Chu[b,c], Fiona Henderling[c], Nanda Kerkar[b,c], Kishore Iyer[c,d]

[a]*Division of Pediatric Gastroenterology, Mount Sinai Medical Center, New York, NY 10029, USA*
[b]*Division of Pediatric Hepatology, Mount Sinai Medical Center, New York, NY 10029, USA*
[c]*Recanati/Miller Transplantation Institute, Mount Sinai Medical Center, New York, NY 10029, USA*
[d]*Department of Surgery, Mount Sinai Medical Center, New York, NY 10029, USA*

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Abstract This is a case report of the first patient with Alagille syndrome (AGS) to undergo a partial internal biliary diversion (PIBD) for the treatment of symptoms refractory to medical therapy. Alagille syndrome is a hereditary disease resulting in chronic cholestasis and hypercholesterolemia that can lead to severe and intractable pruritus and disfiguring and debilitating xanthomas. PIBD has proven to be an effective treatment option for other causes of cholestatic liver disease. This report reviews the immediate and 2-year follow-up of a patient after this surgical procedure. The results suggest that PIBD has potential to provide relief of intractable symptoms and improve the quality of life in patients with AGS while avoiding an external stoma. It does not, however, appear to prevent the progression of liver disease. Long-term follow-up is still needed.

Alagille syndrome (AGS) is an autosomal dominant disorder characterized by paucity of intrahepatic bile ducts, typical facies, congenital cardiac defects, posterior embryotoxon of the eye, and butterfly vertebrae. Renal disease, growth retardation, and neurovascular accidents can also be seen [1]. The paucity of bile ducts in AGS results in inefficient bile excretion and leads to intrahepatic cholestasis, hyperbilirubinemia, and hypercholesterolemia. These manifest in patients as pruritus and xanthomas [2].

Most patients with AGS can be treated conservatively with optimization of nutrition, supplementation of fat-soluble vitamins, and medications to relieve the severe pruritus. Although liver transplantation is curative of the cholestatic liver disease, the associated complications and morbidity make this a less desirable option. Surgical techniques aimed at reducing the symptoms associated with the disease have been used for the last 20 years. Partial external biliary diversion (PEBD) allows for external drainage of bile by creating a conduit between the gallbladder and the skin using a segment of jejunum, resulting in a permanent ostomy [3]. Ileal exclusion (IE) creates an end to side ileocolostomy by bringing the proximal ileum to the right colon and, therefore, excluding the terminal ileum [4].

* Corresponding author. Pediatric Gastroenterology and Hepatology, Mount Sinai Medical Center, One Gustave L Levy Place, New York, NY 10029. Tel.: +1 212 659 8060; fax: +1 212 241 2064.
E-mail address: shari.sheflin-findling@mssm.edu (S. Sheflin-Findling).

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Recently, a surgical technique has been described in patients with progressive familial intrahepatic cholestasis (PFIC) to decrease cholestasis and itching, namely, partial internal biliary diversion (PIBD) [5]. Herein, we describe the use of PIBD for a child with AGS. To our knowledge, this is the first such reported use in the literature.

1. Case report

A 6-month-old boy born full term after a normal pregnancy was referred for evaluation of jaundice since birth and itching over the last month. The patient was noted to be icteric with hepatomegaly, mild splenomegaly, and an otherwise normal examination.

Initial laboratory evaluation included direct bilirubin, 7 mg/dL; aspartate aminotransferase, 486 IU/L; alanine aminotransferase, 492 IU/L; gamma-glutamyl transferase, 271 U/L; and cholesterol, 463 mg/dL. The remaining laboratory tests and evaluation as well as an abdominal ultrasound were normal. Liver biopsy showed neonatal hepatitis without evidence of biliary obstruction. The cytokeratin 19 stain was inconclusive but raised the question of paucity of bile ducts. An echocardiogram revealed mild stenosis of the left pulmonary artery. A spinal x-ray and ophthalmological examination were normal. The patient was started on ursodeoxycholic acid and supplementation of vitamins A, D, E, and K.

By 15 months old, the patient started to display the typical facies associated with AGS (including a triangular-shaped face and deep set eyes). He had also developed multiple xanthomas, and the pruritus was intensifying. Rifampin was started, followed shortly by cholestyramine; however, his symptoms continued to progress.

At 18 months old, genetic analysis revealed that the patient had a mutation in JAG1, and the diagnosis of AGS was confirmed. Surgical options were discussed, and a liver biopsy was performed as part of his presurgical evaluation. The biopsy showed cholestasis with stage 1-2 fibrosis. All portal tracts in the biopsy lacked biliary ducts. The absence of cirrhosis at that time supported the consideration of a nontransplant surgical intervention.

Partial external biliary diversion was offered to the family for progressive xanthomas and intractable pruritus. The family was opposed to a permanent ostomy and refused this option. Ileal exclusion was discussed as well, but the poor success rates in long-term follow-up made this a less suitable option. A decision was made to go ahead with PIBD as this option eliminated the need for an ostomy despite the possibility of bile acid–induced diarrhea.

At 2 years old, the patient underwent a PIBD. His growth at that time was profoundly affected, and he had fallen off his own curve. His presurgical laboratory evaluation included aspartate aminotransferase, 177 IU/L; alanine aminotransferase, 171 IU/L; gamma-glutamyl transferase, 464 U/L; direct bilirubin, 14.7 mg/dL; cholesterol, 1164 mg/dL; international normalized ratio, 1; albumin, 3.8 g/dL; hemoglobin level, 9 g/dL; platelets, 244 000/mL; and total bile acids, 341 μmol/L.

2. Surgical procedure

The patient underwent a limited laparotomy, and the PIBD was performed as per the original report by Bustorff-Silva et al [5]. Initial evaluation showed a markedly cholestatic liver,

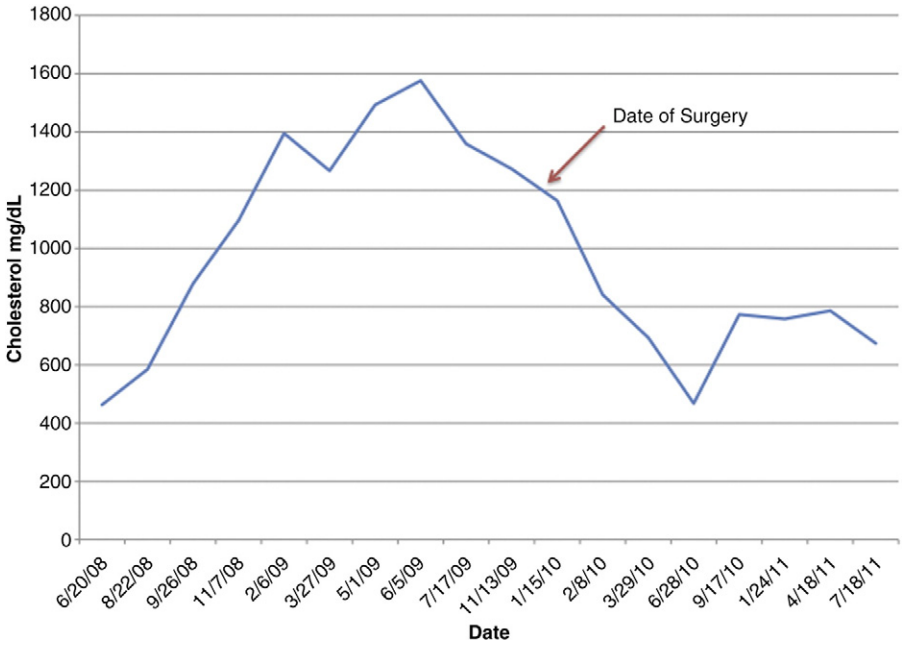

Fig. 1 Total cholesterol level.