

Partial internal biliary diversion for patients with
progressive familial intrahepatic cholestasis type 1

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Abstract

We herein report a case of progressive familial intrahepatic cholestasis with partial internal biliary diversion (PIBD). Although by using PIBD an external stoma can be avoided, exposure of the ileocecal junction to bile reflux as well as the effects of the direct bile flow on the colonic mucosa require further investigation.

Key words: progressive familial intrahepatic cholestasis, partial biliary diversion, enterohepatic cycle, children

Introduction

Progressive familial intrahepatic cholestasis type 1 (PFIC1), also known as Byler disease, is an inherited disorder of childhood. Cholestasis of hepatocellular origin often presents in the neonatal period, which leads to death from liver failure before adolescence [1].

Before the 1990s, liver transplantation (LT) was the only therapeutic option. However, during the last 15 years, two alternative methods of surgical treatment have been proposed: namely, partial external biliary diversion (PEBD) and ileal bypass [2,3]. The purpose of both procedures is to reduce the reabsorption of bile acids from the terminal ileum. This report describes a case of PFIC1 with partial internal biliary diversion (PIBD) and also reviews the relevant literature.

Case report

Our patient was a 1.6 year-old male who presented with jaundice, debilitating pruritus, restlessness, sleeping problems, and a normal serum GGT activity. He was diagnosed with PFIC1 at the age of 8 months based on mutations of the familial intrahepatic cholestasis-1 gene identified by an analysis of serum bile acid, and a histopathological examination of liver biopsy specimens. In the liver biopsy, cholestasis in hepatocytes and a bile plug in bile canaliculi were seen in the hepatic parenchyma, and interlobular bile ducts were diminished in some portal tracts and damaged bile ducts were seen in other portal tracts. A ductular reaction was also observed at the portal tract periphery. Portal fibrous expansions with bridging fibrosis were also found in some places. The patient was administered ursodeoxycholic acid, cholestyramine, phenobarbital, and rifampin. Despite performing appropriate treatment, the pruritus continued and worsened until the patient finally underwent PIBD.

According to previous studies [2,3], laparotomy was performed (Fig. 1a) on the ventral side of the gall bladder (Fig. 1b), which was distended. A 15-cm-long jejunal conduit was prepared 40 cm distal to the ligament of Treitz and was anastomosed between the

terminolateral side of the gall bladder (Fig. 1c) and the proximal portion of the transverse colon with antireflux suture fixation (Fig. 1d). Continuity of the jejunum was established by jejuno-jejunal anastomosis.

The postoperative course was uneventful. The consumption of normal food was resumed on the third postoperative day (POD), and the patient was discharged on the seventh POD. A relief of pruritus was achieved (on the third POD), and the sleeping patterns became normalized. He experienced no diarrhea after PIBD.

In the follow-up schedule, blood examinations and body measurements were performed monthly. The findings of hepatic laboratory tests (AST/ALT, Fig. 2a; T.Bil/D.Bil, Fig. 2b) improved. At seven months after PIBD, liver biopsy and colonoscopy were performed. A histopathological examination of the liver biopsy specimens showed a progression of fibrosis. The endoscopic findings of colonoscopy showed no gross abnormalities, but histopathological examinations of the colon biopsy specimens showed foam cell infiltration, which was similar to cholesterosis of the gall bladder.

Discussion

In recent years, it is hypothesized that interrupting the enterohepatic circulation would prevent reabsorption of excreted bile acids from the small intestine, thereby stopping their accumulation and reducing their toxic effects on the liver [3]. In 1972, Williams et al [4] performed cholecystostomy tube drainage for PFIC1 and observed a temporary relief of cutaneous pruritus and an improvement of the liver function. In 1988, Whittington and Whittington [5] introduced PEBD, in which the creation of an external biliary stoma to remove excess bile acids contributed to histopathologically evident diminished fibrosis in the liver, the relief of cutaneous pruritus, and an improvement of hepatic laboratory tests. Emond and Whittington [6] performed PEBD in eight children with PFIC1; six patients (excluding two with decompensated liver failure) showed an improvement of clinical manifestations and liver structure, confirmed by histopathological examinations.

Biliary diversion results in a decreased bile acid pool size and a possible reduction in preload for defective transport mechanisms [1]. The disadvantage of PEBD is the requirement of a permanent external stoma, which can be an issue, especially when concerning children.

Hollands et al [7] attempted to perform the ileal exclusion of bile without creating an external bile stoma; approximately 15% of the small bowel proximal to the ileocecal valve was bypassed with an ileocolonic anastomosis or ileoileal, side-to-side, functional end-to-end anastomosis, which is referred to as an ileoileal by-pass procedure. Although the patient experienced a short-term improvement in the clinical manifestations, a satisfactory result was not obtained long-term, according to follow-up observations from ileal exclusion methods, possibly due to gradual adaptation of the terminal ileum after exclusion [8].

PIBD avoids an external biliary stoma, and lacks the potential for malabsorption that may result from partially excluding the terminal ileum from the intestinal transit [3]. However, there remain some concerns associated with exposure of the ileocecal junction to bile reflux and the effects of a direct bile flow on the colonic mucosa. In order to prevent exposure of the ileocecal junction to bile reflux, we used the transverse colon and antireflux suture fixation, although the jejunal conduit was anastomosed between the gall bladder and the ascending colon in the literature [2,3]. As previously done [3], the conduit was made at least

15-cm-long to create resistance to the bile flow and allow a certain amount of it to flow to the duodenum. This served to prevent the entry of large amounts of bile salts to the colon and avoid choleric diarrhea. Although the effect of the direct bile flow on the colonic mucosa remains unclear, foam cell infiltration of the colonic mucosa, similar to that observed in cholesterosis of the gall bladder, was observed in the short-term follow-up in our patient.

In this report, we reviewed seven cases [2,3], including our own case, of PFIC1 with PIBD (Table 1). Bustorff-Silva et al [3] previously reported that both of their patients (n=2) experienced a complete resolution of their pruritus and a normalization of the hepatic laboratory test findings. In one case, a previous PEBD had been converted to PIBD because the patient complained regarding the stoma. Gün et al [2] reported significant improvement in the biochemical parameters, regained growth, controlled pruritus, and normalization of sleeping patterns in four patients. Two of seven patients developed mild choleric diarrhea which could be successfully controlled with the use of cholestyramine.

In conclusion, PIBD appears to be a very attractive surgical option for the treatment of PFIC1 in

children with a normal gall bladder. Compared to PEBD, this procedure avoids the disadvantages of a permanent stoma. Long-term follow-up, as well as repeat liver biopsy and colonoscopy, is necessary to evaluate the long-term results and eventual complications.

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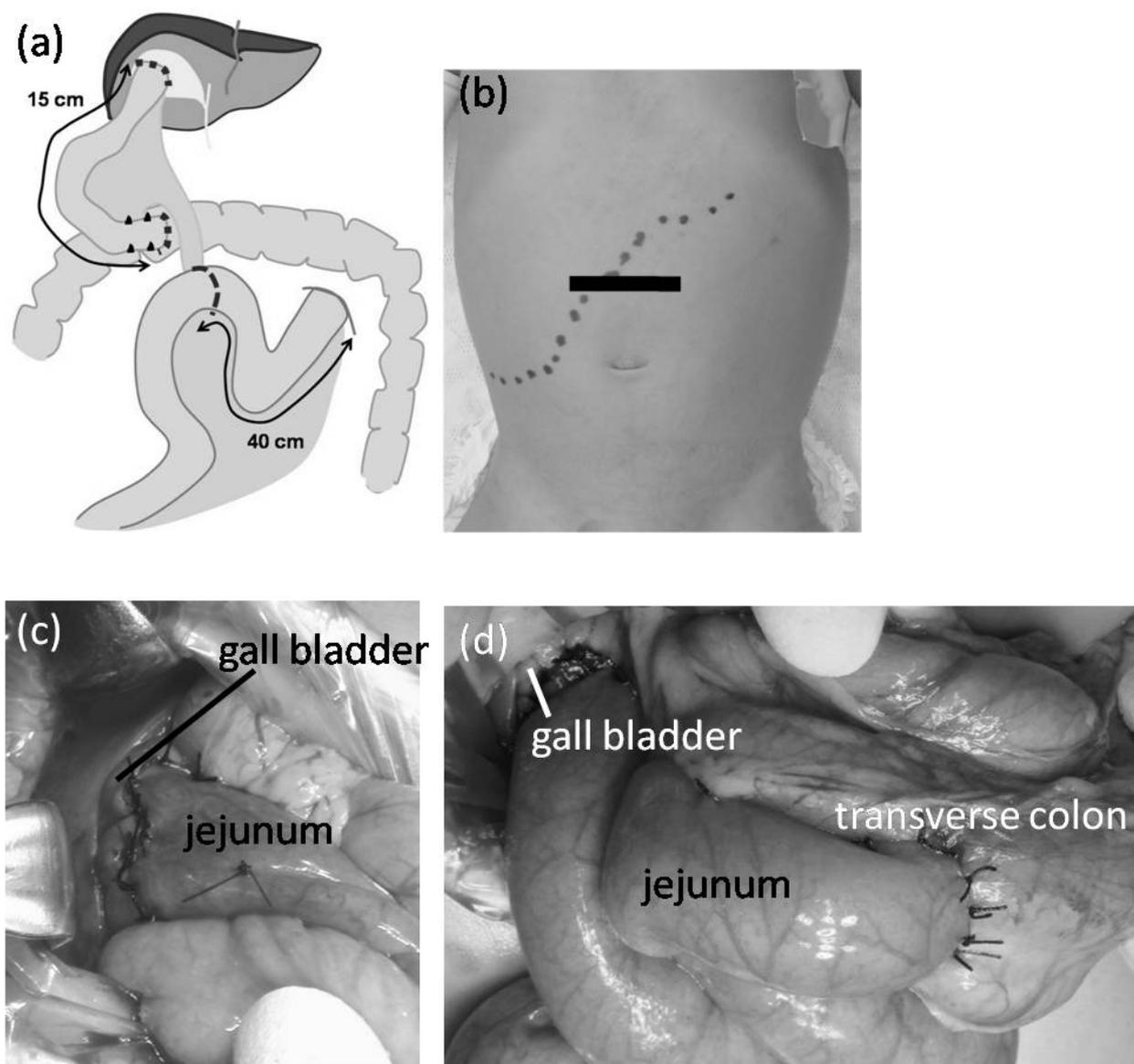
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Figure Legends**Fig. 1.**

Partial internal biliary diversion (PIBD). a, Schema of PIBD; b, laparotomy above the gall bladder; c, the jejunal conduit anastomosed between the gall bladder; d, the jejunal conduit anastomosed to the transverse colon with antireflux suture fixation.

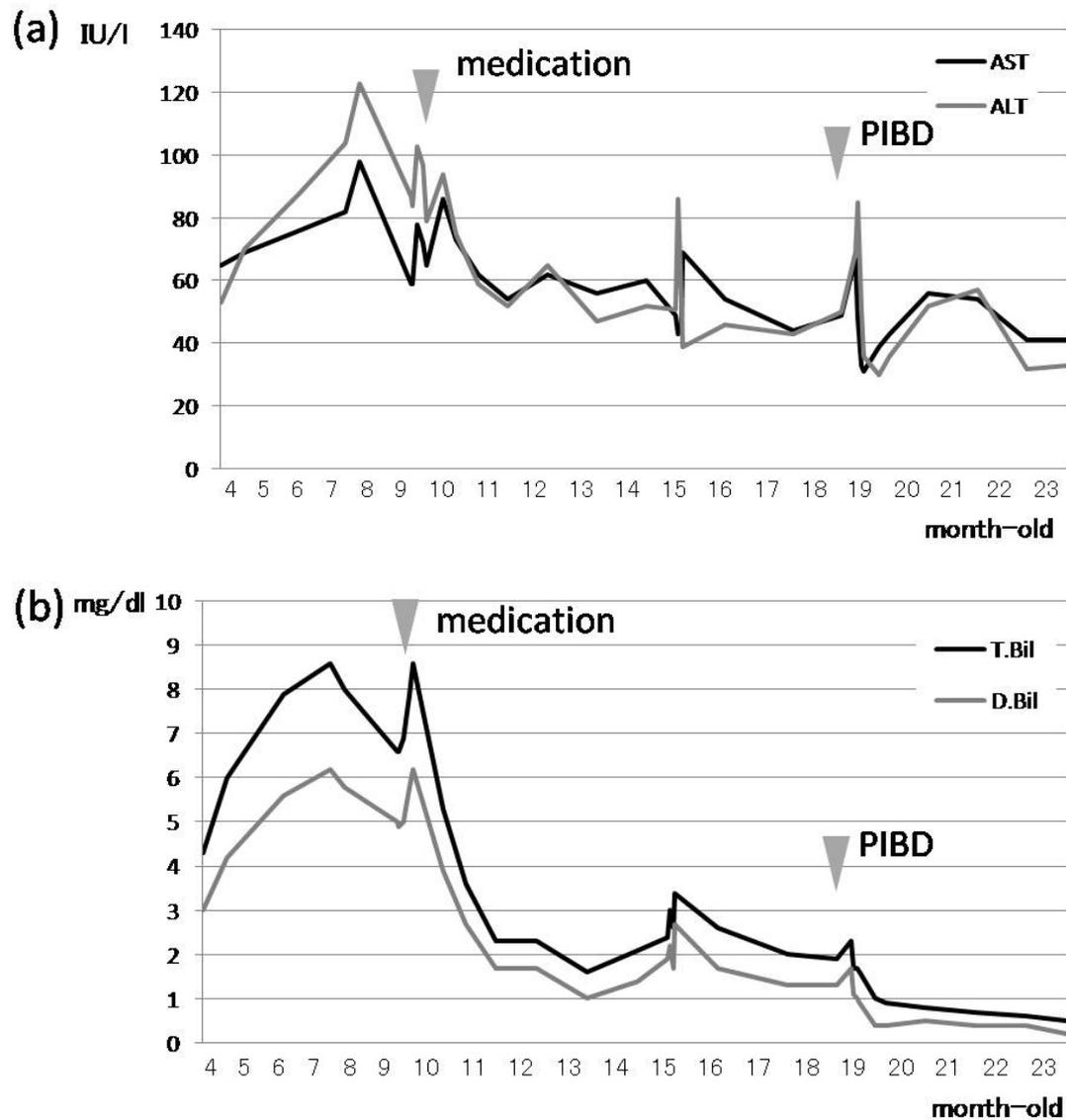


Fig. 2.

The preoperative and postoperative transition in data. a, AST/ALT declined gradually after medication and reduced further after PIBD; b, T.bil/D.bil also declined gradually after medication and then further decreased after PIBD.