Cholecysto-appendicostomy as partial internal biliary drainage in Progressive Familial Intrahepatic Cholestasis Type 1: A case report and review of literature

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A B S T R A C T

Intractable pruritus secondary to bile salts retention in Progressive Familial Intrahepatic Cholestasis (PFIC) can be relieved surgically by diverting bile drainage from ileum to reduce bile salts reabsorption into entero-hepatic circulation. We are reporting on the successful biliary diversion in a child with PFIC, with the use of the appendix as a conduit to drain bile from gallbladder to the colon (cholecysto-appendicostomy).

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Progressive Familial Intrahepatic Cholestasis (PFIC) is an autosomal recessive disorder, typically presented during infancy with jaundice, pruritus and failure to thrive [1]. It is characterized by impaired bile acid metabolism and excretion causing intrahepatic cholestasis [1,2]. The concentrated biliary compounds lead to disabling pruritus and hepatocellular damage, subsequently progresses to liver failure and death in early childhood or adolescence [2,3]. Mutation in the ATP8B1 gene, a regulator of intestinal bile acid absorption, has been identified in PFIC Type 1, also known as Byler disease [4]. Before 1990, liver transplant (LTX) was the only treatment option for PFIC [2]. However, in the past 2 decades, surgical intervention with biliary diversion (BD) had been considered for symptomatic relief and was found to curtail liver impairment, and delaying the need for LTX [2,3]. In this report, we share our experience of cholecysto-appendicostomy (CA, a partial internal biliary drainage, PIBD) in a child with PFIC and reviewed the literature of BD surgery.

1. Case report

A 7-year-old girl presented with jaundice and failure to thrive since the age of 10 months old. She was born at term with a birth weight of 2.25 kg. She had neonatal jaundice but did not require admission or phototherapy. Her parents were healthy and unrelated, and there was no family history of liver disease. She was admitted at the age of 10 months old for acute gastroenteritis but found to be jaundiced and her weight was 4.6 kg (below 3rd centile). Liver function test (LFT) showed raised levels of Aspartate Aminotransferase (AST) and Alkaline Phosphatase (ALP) but with normal level of Gamma-Glutamyl Transpeptidase (GGT, 5 U/L). She had conjugated hyperbilirubinemia (82 umol/L). Hepatobiliary ultrasound showed no evidence of biliary obstruction or focal liver disease. Additionally, screenings of her thyroid function, immunology and inborn error of metabolism were all normal. Percutaneous liver biopsy was reported with paucity of intrahepatic bile ducts. Subsequent assessments for Alagille syndrome included...
spine x-rays, echocardiogram and ophthalmology examination were normal. Importantly, genetic study found mutation in ATP8B1 gene, diagnostic for PFIC Type 1.

She is under close follow-ups by the paediatrics gastroenterology and hepatology team, together with the dietician. She has persistent hyperbilirubinaemia with deranged liver enzymes (raised ALT and ALP). During her disease course, she developed severe skin pruritus, disturbing her social activity and sleep, and her skin became lichenified due to persistent scratching. Despite treatment with antihistamines, ursodeoxycholic acid and cholestyramine, her pruritus persisted and surgical referral was made for consideration of BD at the age of 7 years old.

Laparotomy was performed via a right upper transverse muscle-cutting incision. Operative cholangiogram showed patent biliary tree with grossly distended and elongated gallbladder (Fig. 1). The appendix was identified, mobilized and brought up close to the gallbladder via a small mesenteric defect created medial to caecum/ascending colon to facilitate a tension-free, non-kinking anastomosis (Fig. 2). Liver biopsy was obtained. The surgery was uneventful and her postoperative recovery was excellent.

At recent follow-ups, she reported markedly reduced pruritus, with improved quality of life. Moreover, her parents observed less intense scratching at home and she had better quality of sleep. Clinically, she was less jaundice and her skin was less lichenified. Although her liver enzymes recorded minimal improvement but her bilirubin level has markedly reduced (Fig. 3). Her liver biopsy only showed evidence of chronic hepatitis with fibrosis. She remained well 8 months after surgery with no symptoms to suggest progression of liver impairment.

2. Discussion

Intractable pruritus is one of the most disturbing and disabling symptom of PFIC [2,5], with persistent scratching leading to social and sleep disturbances, and skin lichenification. Medical therapy with cholestyramine, phenobarbital, rifampin or ursodeoxycholic acid may relieve symptoms in 60% of patients [4,6]. LTX was the only surgical intervention until the late 1980s when surgery for BD was introduced and considered. BD involves diversion of biliary drainage, bypassing the ileum to reduce bile salts reabsorption into entero-hepatic circulation and thus increases the elimination of bile acids from the body [2].

Various techniques of BD have been reported (Table 1). In 1988, Whitington and Whitington introduced partial external biliary drainage (PEBD): jejunum was used as a conduit to drain bile from gallbladder to an external stoma (cholecysto-jejuno-cutaneostomy), with very encouraging short-term outcomes [7]. Successful PEBDs were further reported but issues related to stoma or external biliary fistula, such as stoma prolapse and high output stoma losses were documented, respectively [5,9]. In 2005, Metzelder et al.
Fig. 3: Progression of bilirubin levels before and after surgery. Marked reduction in bilirubin level was recorded after surgery.

<table>
<thead>
<tr>
<th>Author &amp; Year</th>
<th>Procedure</th>
<th>Number of Patient ($n$)</th>
<th>Follow-up Duration</th>
<th>Complications</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Partial External Biliary Drainage (PEBD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whitington et al. [7] 1988</td>
<td>Cholecysto-jejunostomy (with a cutaneous end stoma)</td>
<td>6</td>
<td>3–8 years</td>
<td>Postoperative hemorrhage from ostomy ($n=1$), postoperative bowel obstruction and acquired acute cholangitis (in 1 patient with underlying arteriohepatic dysplasia)</td>
<td>The reported 6 cases include 4 patients with progressive intrahepatic cholestasis and 2 patients with arteriohepatic dysplasia. Faster recovery time and minimal abdominal scar</td>
</tr>
<tr>
<td>Metzelder et al. [8] 2005</td>
<td>Laparoscopic cholecysto-jejuno-colic anastomosis</td>
<td>4</td>
<td>1.5–2.5 months</td>
<td>None mentioned</td>
<td></td>
</tr>
<tr>
<td>Arnell et al. [9] 2008</td>
<td>Cholecysto-jejuno-colic anastomosis (with a cutaneous end stoma)</td>
<td>13</td>
<td>11–21 months</td>
<td>Stomal leakage and prolapse ($n=1$), hypotension due to excessive losses of bile fluid ($n=5$)</td>
<td></td>
</tr>
<tr>
<td>Halaweish &amp; Chwals [4] 2010</td>
<td>Hepatico-jejuno-colic anastomosis (with a cutaneous loop stoma)</td>
<td>7</td>
<td>6 months</td>
<td>4 patients had stoma related complications (3 prolapse &amp; 1 persistent efferent loop stoma reflux), 2 had high stoma output and died from gastroenteritis-related dehydration</td>
<td></td>
</tr>
<tr>
<td>Sharma et al. [10] 2010</td>
<td>Cholecysto-appendicostomy (with a cutaneous end stoma)</td>
<td>1</td>
<td>6 months</td>
<td>None mentioned</td>
<td>Less extensive bowel resection. Appendicular stoma had better cosmesis. On average 2–4 h drainage period per day. Avoided enteric anastomosis</td>
</tr>
<tr>
<td>Clifton et al. [11] 2011</td>
<td>Button cholecystostomy</td>
<td>3</td>
<td>1–2.5 years</td>
<td>Button dislodgement but easily replaced</td>
<td></td>
</tr>
<tr>
<td>Schukfeh et al. [12] 2014</td>
<td>Laparoscopic button cholecystostomy</td>
<td>2</td>
<td>6 months</td>
<td>None mentioned</td>
<td></td>
</tr>
<tr>
<td>Vicinal exclusion (IE) Hollands et al. [6] 1998</td>
<td>Ileo-colonic anastomosis</td>
<td>5</td>
<td>6–22 months</td>
<td>Bleeding from stapled anastomosis requiring re-operation ($n=1$)</td>
<td>Reported late recurrence of symptoms in up to 60% of patients probably secondary to gradual adaptation of the ileum to the 15% resection [13]</td>
</tr>
<tr>
<td>Ricca et al. [14] 2014</td>
<td>Ileo-ileostomy (100 cm of ileum bypassed)</td>
<td>1</td>
<td>7 months</td>
<td>Ileocolic intussusception of the excluded ileum causing symptoms recurrence within 7 days. Ischemic intussusception resected leaving 10 cm terminal ileum intact, ileocolostomy taken down and had ileo-ileostomy (no bypassed segment)</td>
<td></td>
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<tr>
<td><strong>Partial Internal Biliary Drainage (PIBD)</strong></td>
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<td></td>
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<tr>
<td>Bustorff-Silva et al. [2] 2007</td>
<td>Cholecysto-jejuno-colonic anastomosis</td>
<td>2</td>
<td>NA</td>
<td>Transient increase in number of bowel movement in 1 patient</td>
<td>1 patient had internalization of PEBD (cholecysto-jejuno-cutaneoustomy) to a cholecysto-jejuno-colonic anastomosis.</td>
</tr>
</tbody>
</table>

(continued on next page)
introduced laparoscopic PEBD and documented shorter recovery time with minimal abdominal scar [8]. Sharma et al., in 2010 reported a modification of PEBD using appendix as a successful conduit (cholecysto-appendicocutaneostomy), with less extensive bowel resection and anastomosis, and with better cosmesis [10]. Button cholecystostomy as PEBD was reported by Clifton et al., in 2011 [11] and its laparoscopic approach was later introduced by Schukfeh et al., in 2013 [12]. Both authors considered their techniques as a much simpler approach with adequate bile drainage to relieve symptoms.

An alternative approach described by Hollands et al. for BD called ileal Exclusion (IE) or Ileal Bypass [6]. In this technique, there was no external stoma, with an ileo-colonic anastomosis bypassing approximately 15% of the ileum proximal to the ileocecal valve. Short-term outcome was promising but it failed to show long-term improvement, likely due to ileal adaptation and accommodation to re-absorb bile salts [13]. The bypassed ileum can lead to intussusception, as reported by Ricca et al. [14].

PIBD was considered an attractive surgical option with post-diversion outcome as good as PEBD without an external biliary fistula [2]. In 2007, Bustorff-Silva et al. reported a new PIBD technique by the creation of an intestinal conduit between gallbladder and ascending colon [2], with the use of 15–20 cm of mid-jejunum, and it involved 3 anastomoses, which was a major disadvantage of this technique [2,3]. In 2013, Diao et al. described their technique of laparoscopic cholecysto-colostomy, whereby the gallbladder was anastomosed to descending colon with an antireflux Y-loop; the success rate recorded was 85% with minimal morbidity [17] (Table 1). Mousavi and Karami in 2014 reported on the use of appendix as a successful conduit (cholecysto-appendicostomy), contrary to the end-to-side anastomosis. The appendix was brought through a surgically created mesenteric defect, affixed with sutures before anastomosed to the gallbladder in a tension-free, non-kinking manner. Continuous bile drainage was evidenced by clinical improvement of her symptoms (less intense pruritus and better quality of sleep), further supported by the biochemical improvement of her LFT, with marked reduction of bilirubin (by 8 folds).

| Table 1 (continued) |
| Author Year Procedure Number of patient (n) Follow-up duration | Complications | Remarks |
|---------------------|----------------|----------------|--------|
| Ganesh et al. [15] 2010 Cholecysto-jejuno-colonic anastomosis 1 | 2 years | Intermittent diarrhea | |
| Gun et al. [5] 2010 Cholecysto-jejuno-colonic anastomosis 4 | NA | Diarrhea in 1 patient (responded to cholestyramine) | |
| Mochizuki et al. [16] 2012 Cholecysto-jejuno-colonic anastomosis 1 | 7 months | HPE of colon mucosa at 7 months post-surgery showed foam cell infiltration similar to cholesterosis of gallbladder | |
| Diao et al. [17] 2013 Laparoscopic cholecysto-colostomy (with antireflux Y-loop) 20 | 12–104 months | None reported to have anastomotic stricture, cholangitis, diarrhea or intrahepatic reflux | 85% success rate, younger age group compared to other PIBD or PEBD series (median 1.47 years) |
| Mousavi & Karami [3] 2014 Cholecysto-appendicostomy (then convert to cholecysto-jejuno-colonic anastomosis) 1 | 9 months | Stricture post cholecysto-appendicostomy (symptoms recurred after 15 days post-surgery). Redo surgery done after a month, then asymptomatic | |
| Our case 2015 Cholecysto-appendicostomy 1 | 8 months | None (so far) | Single anastomosis Less extensive dissection No external biliary fistula |

NA = not available.

3. Conclusion

In our case, cholecysto-appendicostomy shows good medium-term outcome for intractable pruritus in PFIC. It avoids external biliary fistula (as in PEBD) and involves only a single anastomosis of appendix to the gallbladder. It is a promising surgical option for BD. Long-term follow-up is required to determine the successful outcome of this procedure.

Conflicts of interest

All authors agreed and declared that no potential financial and non-financial conflicts of interest.

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References


