CASE REPORT

Cholecystoappendicostomy for Progressive Familial Intrahepatic Cholestasis

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We report a rare case of progressive familial intrahepatic cholestasis type 2 from India. The diagnosis was confirmed on the basis of gene mutation analysis. The child had intense pruritus refractory to conventional medical management. As liver biopsy did not reveal any cirrhosis, partial external biliary diversion was considered as an alternative to liver transplant. We performed cholecystoappendicostomy rather than the conventional method of using an ileal loop as a conduit between the gall bladder and abdominal wall. Child recovered completely.

Key words: *Cholecystoappendicostomy, Progressive familial intrahepatic cholestasis.*

This is the first report of progressive familial intrahepatic cholestasis type 2 from India. The treatment options in this condition are dictated by the stage of the disease. Early diagnosis of this condition allowed us to use a novel surgical approach to treat this condition and prevent or delay the evolution of secondary cirrhosis, and possible need for liver transplantation.

CASE REPORT

A one month old girl presented to our hospital with jaundice and passage of clay colored stools. She was a product of non consanguineous marriage, born at term by normal delivery. She was icteric, and liver and spleen were just palpable below the subcostal margin. Investigations revealed direct hyperbilirubinemia with serum bilirubin 7.4 mg/dL with a conjugated fraction of 5 mg/dL; serum albumin was 4.3 mg/dL, AST was 413 IU/dL, ALT 629IU/dL, GGT 27I U/dL and prothrombin time was 18 seconds (control 14s). Ultrasound abdomen revealed coarse echotexture of liver with a normal gall bladder and common bile duct. Hepatobiliary immunodiacetic acid (HIDA) scan demonstrated good concentration of dye in liver with prompt excretion into small bowel. Her TORCH screen, alfa 1 antitrypsin levels, and thyroid function tests were within normal limits. Liver biopsy was postponed to a later date, on the request of parents. She was discharged on ursodeoxycholic acid, phenobarbitone and multivitamins. She did not return for follow-up after discharge. At 2 years of age, the girl was readmitted with intense pruritus, skin excoriation and mild fever. Severe itching had resulted in alopecia accreta and lichenification of skin of hands and feet. Her liver function tests had, however, improved (serum bilirubin total 0.3 mg/dL, conjugated 0.1mg/dL, AST 201 and ALT 532), while GGT remained normal.

A diagnosis of progressive familial intrahepatic cholestasis was considered in view of intense pruritus due to cholestasis and normal GGT. The liver biopsy demonstrated disruption of lobular architecture with cholestasis and portal to portal bridging fibrosis which was compatible with this diagnosis. To further categorize the type of PFIC, the family sought a gene mutation analysis overseas which confirmed it to be bile salt export pump (BSEP) defect with gene mutation ABCB 11, confirming it to be PFIC type 2.

Despite medical therapy with ursodeoxycholic acid and phenobarbitone, the itching persisted leading to multiple skin lesions. Since her symptoms were refractory to medical management for more than twenty months, surgical intervention was considered. As the liver biopsy did not demonstrate any features of cirrhosis, it was decided to give a trial of partial external biliary diversion (PEBD). Rather than using the conventional method of using a jejunal loop as a conduit between the gall bladder and abdominal wall, an appendicular graft based on Mitrofanoff principle was used to create a cholecystoappendicostomy, and appendicular stoma was matured in the right iliac fossa.

She had an early recovery after surgery and went on to oral feeding on day two. The post operative recovery was satisfactory other than a wound infection. The appendix was intubated for three weeks after surgery as an outpatient to drain bile from gall bladder. On removal of the tube, she was left with a 5mm size stoma in the right iliac fossa through which she drains about 150 ml of bile every day into a stoma bag. All oral medications have been gradually tapered. Six months following surgery she is completely asymptomatic and her latest liver function tests are completely within normal limit.

DISCUSSION

PFIC, also known as Bylers disease presents in early childhood with pruritus, jaundice, hepatomegaly and growth failure and can progress to liver failure before adolescence due to secondary cirrhosis(1). The diagnosis of PFIC needs a high index of suspicion. The laboratory parameters which can aid in diagnosis are low to normal GGT, low cholesterol and high levels of bile acids in blood(2). PFIC results from mutations in various genes encoding hepatobiliary transport proteins. Mutations in the FIC1 gene causes PFIC type 1. PFIC type 2 results from mutations in the bile salt export pump (BSEP) gene. PFIC type 3 is caused by mutations in the MDR3 gene(3). Accumulation of bile acids causes intrahepatic cholestasis which leads to progressive fibrosis and cirrhosis by the end of first decade of life.

Medical management is ineffective in interrupting the progression of disease and in alleviating the pruritus in a majority of the patients(4). For children with decompensated cirrhosis the only treatment is liver transplantation(5).

Early institution of biliary drainage can delay progression of this disease to end stage liver failure and need for liver transplantation. Prior to 1990, liver transplantation was the only effective therapy for these children, as in the vast majority, the disease was detected at a more advanced stage of the disease with end stage liver failure. A better understanding of the disease and earlier recognition has lead to development of biliary drainage as a surgical option(6).

Pruritus can be alleviated by interrupting the enterohepatic circulation and reducing the bile acid pool. Various surgical techniques have been used for this. In 1998, Whitington, *et al*.(7) introduced cholecystojejunocutaneostomy for partial external biliary diversion. Though, it leads to significant clinical improvement, a stoma care was not considered an acceptable solution for this problem. Therefore, an attempt was made to use internal ileal bypass procedure, so that the bile salts could bypass the terminal small bowel where they get absorbed(8). Although initial results were encouraging but late recurrence of symptoms and choleretic diarrhea led to revision in surgery in some cases; this procedure is therefore not a popular option .

We performed an external drainage as the family was willing for a stoma. Instead of jejunum we used the appendix as our choice of conduit. This was based on the availability of a normal appendix, preventing the need for a resection and anastomosis of small bowel and thus reducing the stay in hospital significantly. The cosmetic appearance of an appendicular stoma, the position below the waist line and possibility of intubating the stoma for drainage were other obvious advantages(9,10).

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