

Biliary Atresia Associated With Meconium Peritonitis Caused by Perforation of Small Bowel Atresia

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Background/Purpose: This report describes our experiences with 5 cases of biliary atresia associated with meconium peritonitis caused by perforation of small bowel atresia.

Methods: A review of medical records was undertaken in an effort to recognize cases of biliary atresia associated with meconium peritonitis.

Results: Five patients of 171 with biliary atresia (2.9%) were detected to have meconium peritonitis caused by perforation of small bowel atresia. The biliary atresia was not suspected during the initial operation for meconium peritonitis. Total parenteral nutrition (TPN) made it difficult to make an early differential diagnosis of biliary atresia because of the presence of TPN-associated cholestatic jaundice, and the Roux-en-Y limb used for hepatic portoenterostomy could not be made long enough to prevent cholangitis caused by preexisting short bowel. The main complications were severe, intractable cholangitis, short bowel syndrome with malnutri-

tion; TPN-associated liver injury; and wound problems. Two patients died of ascending cholangitis, 1 patient of liver failure that was exacerbated by TPN-associated liver injury, and 1 patient is awaiting a liver transplant. Only 1 patient is in good health, being anicteric and showing normal growth and development.

Conclusions: Biliary atresia is evidently closely associated with meconium peritonitis caused by perforation of small bowel atresia. The management of these patients is more difficult than that of patients with the usual form of biliary atresia, because of the necessity for a long period of TPN and the combined short bowel syndrome. The ideal management of these conditions has yet to be determined.

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INDEX WORDS: Biliary atresia, meconium peritonitis, intestinal atresia, short bowel syndrome.

THE ACTUAL CAUSES of biliary atresia remain unknown, although a number of associated factors, such as developmental malformation,¹ perinatal viremia,² toxicity of bile constituents,³ and anatomic abnormalities in the hepatobiliary system,⁴ have been implicated. Recently, biliary atresia has been proposed to be the result of a perinatal event, caused by some injurious agent, which results in the progressive fibrosis of normally formed extrahepatic bile ducts.^{5,6} Microscopic examination of bile ducts resected during hepatic portoenterostomy has shown ductal obstruction caused by inflammatory processes.⁷

Here we describe 5 cases of extrahepatic biliary atresia, which followed a well-defined perinatal inflammatory event, namely, meconium peritonitis, which was caused by the perforation of small bowel atresia.

MATERIALS AND METHODS

The medical records of infants with biliary atresia that were diagnosed at Yonsei Medical Center during the period between January 1990 and June 2000, were reviewed retrospectively to investigate the association between biliary atresia and meconium peritonitis.

RESULTS

Between January 1990 and June 2000, 171 cases of extrahepatic biliary atresia in infants were diagnosed at the Yonsei Medical Center, and among these, 5 infants (2.9%) were found to have meconium peritonitis (Table 1). In these 5 cases, the initial operation was for meconium peritonitis caused by perforated intestinal atresia (jejunal atresia in 2 and ileal atresia in 3). The presence of biliary atresia was not suspected during the first operation.

Parenteral hyperalimentation was necessary for nutritional support in all cases, which made it difficult to make an early differential diagnosis of biliary atresia in the presence of total parenteral nutrition (TPN) associated cholestatic jaundice. The final diagnosis of biliary atresia was made by relaparotomy at 24 to 66 days of age (mean, 45.4 days) in all cases. Four cases had type A biliary atresia, one had a portal cyst, and one had type B.⁸ All patients received hepatic portoenterostomy for biliary atresia, but case 2 received hepatic portocholecystostomy, which should have been switched to hepatic portoenterostomy because of a sudden cessation of bile flow.

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Table 1. Five Cases of Biliary Atresia That Were Associated With Meconium Peritonitis Caused by Perforation of Small Bowel Atresia

Case No.	Sex/Age (d)*	Type of Meconium Peritonitis	Location of Small Bowel Atresia	TPN	Type of Biliary Atresia ⁸	Length of Rouex-en-Y Limb (cm)	Length of Small Bowel for Digestive Tract (cm)	Major Problems After Kasai Operation	Long-Term Result
1	M/24	Unrecorded	Ileum	Done	Type A	50	40	Cholangitis, short bowel syndrome, wound dehiscence, pneumonia, sepsis	Died of cholangitis, sepsis
2	M/46	Meconium psuedocyst	Ileum	Done	Type B	40	40	Short bowel syndrome, cholangitis, wound infection, enterocutaenous fistula	Anicteric, normal growth
3	F/66	Meconium psuedocyst	Ileum	Done	Type A with cyst	25	30	No bile flow after Kasai operation (Failure of Kasai operation)	Waiting for a liver transplant
4	F/50	Meconium psuedocyst	Jejunum	Done	Type A	40	100	Short bowel syndrome, cholangitis, focal hepatic infarct, wound dehiscence, enterocutaenous fistula, TPN-associated cholestatic jaundice, liver failure	Died of liver failure
5	M/41	Meconium psuedocyst	Jejunal atresia	Done	Type A	40	80	Short bowel syndrome, cholangitis, recurrent enterocutaenous fistula	Died of cholangitis

*Age at diagnosis of biliary atresia.

The Rouex-en-Y limbs were 25 to 50 cm long (mean, 39 cm), and the remaining small bowels for digestive tract were 30 to 100 cm in length (mean, 58 cm). Four cases showed active bile excretion after hepatic portoenterostomy, and one did not. In this case the surgeon did not reoperate because he believed that prognosis would have been poor. There were 4 cases of short bowel syndrome, 4 of severe postoperative cholangitis, 3 of wound problems, and 3 of enterocutaneous fistula. Two patients died of ascending cholangitis and 1 patient of liver failure that was aggravated by TPN-induced liver injury; 1 patient is waiting liver transplant. Only 1 patient (3.5 years old) has normal growth and development and an anicteric status.

Case Reports

Case 2. A boy weighing 3.39 kg was delivered after 34 weeks' gestation by cesarean section because of fetal distress at a branch hospital of Yonsei Medical Center. Meconium peritonitis had been diagnosed before birth, and a laparotomy was performed on the day of birth during which cystic meconium peritonitis was found. Irrigation and drainage were performed. A second laparotomy was then performed at 10 days of age, after the baby had been stabilized with parenteral antibiotics and TPN. After the diagnosis of perforated ileal atresia, a Santulli type enterostomy was performed. After the second operation, his stools were at first normally colored, but they became progressively paler, and jaundice deepened, essentially caused by conjugated bilirubin, and this remained high despite the cessation of parenteral alimentation. The patient was referred to the main hospital of Yonsei Medical Center with suspected biliary atresia. Abdominal ultrasonography showed no evidence of an extrahepatic bile duct, and a DISIDA scan showed no

evidence of bile excretion into the bowel. A third laparotomy was performed at 46 days of age. Operative cholangiography confirmed the diagnosis of biliary atresia (type B).⁸ Hepatic portocholecystostomy and repair of the enterostomy then were performed. The baby showed transient bile flow after hepatic portocholecystostomy, which stopped suddenly at 53 days of age. A fourth operation was performed at 57 days. Revision of the hepatic portocholecystostomy and hepatic portoenterostomy were conducted with a Rouex-en-Y limb about 40 cm in length and a 40-cm length of small bowel for the digestive tract. Parenteral alimentation was necessary because of the extended duration of the short bowel syndrome. The baby suffered from wound infection, enterocutaneous fistula, intraabdominal biloma, short bowel syndrome, and intermittent severe cholangitis. The symptoms related to short bowel syndrome and cholangitis progressively resolved, and for over 3 years he has maintained normal growth and development with no dietary restrictions. Recent tests indicated that his bilirubin level is normal but that his liver enzymes are mildly elevated.

Case 4. A girl weighing 2.44 kg was delivered by cesarean section in another hospital after 37 weeks' gestation. Polyhydroamnios, intestinal atresia and meconium peritonitis had been diagnosed before birth. The first laparotomy was performed at 3 days of age and showed perforated jejunal atresia and cystic meconium peritonitis. End-to-end jejunojejunostomy was performed. The baby was treated with TPN because of short bowel syndrome and small bowel stasis. The color of the stool initially was dark greenish but this changed to a whitish color as her jaundice deepened. TPN was stopped on the suspicion of TPN-associated cholestatic

jaundice, but the stool color did not return. Abdominal ultrasonography and DISIDA scan could not exclude biliary atresia. She was transferred to Yonsei Medical Center for further evaluation and treatment. Magnetic resonance cholangiography showed no evidence of extrahepatic bile duct. The second laparotomy at 58 days of age showed biliary atresia (type A).⁸ Hepatic portoenterostomy was performed with a Rouex-en-Y limb of about 40 cm in length and a 100-cm length of small bowel for the digestive tract. Even though focal infarction of the liver developed (anterior segment of the right lobe) as a postoperative complication, the baby recovered after the operation and passed green stools. However, the stool became intermittently acholic because of several attacks of severe cholangitis. TPN was maintained for an extended period because the short bowel syndrome and enterocolitis persisted for several months. However, TPN had to be stopped at the age of 5.5 months because of the aggravation of TPN-associated cholestatic jaundice and liver injury. At the age of 6 months, her body weight was only 3.6 kg. She also suffered from wound dehiscence, enterocutaneous fistula, sepsis, and malnutrition. The baby deteriorated progressively and died of liver failure at the age of 6 months.

DISCUSSION

The association between biliary atresia and meconium peritonitis from perforation of small bowel atresia has been reported by several investigators.⁹⁻¹¹ Oh et al⁹ reported that 1 patient (0.5%) in 214 with biliary atresia was operated on because of meconium peritonitis from a perforation associated with jejunal atresia. According to the Japanese Biliary Atresia Registry between 1989 and 1999, 6 patients (0.5%) in 1,198 with biliary atresia were associated with meconium peritonitis (Ohi, personal communication). Kishida et al¹¹ also reported 2 cases of meconium peritonitis (2.4%) in 84 cases of biliary atresia, which is in close agreement with the incidence of meconium peritonitis in biliary atresia (2.9%) found in the current study. These incidences of meconium peritonitis in biliary atresia, including ours, are substantially higher than the reported incidence of meconium peritonitis, approximately 1 in every 35,000 live births,¹² which includes cases of cystic fibrosis. Neonatal biliary atresia generally was believed to be an early developmental malformation. However, there are both clinical and morphologic arguments that seemingly contradict this early maldevelopment hypothesis. More recently, the consensus opinion is that small bowel atresia is caused by an ischemic lesion that occurs during the later stage of pregnancy.¹³ We suggest that biliary atresia may be related to a dynamic, acquired inflammatory process associated with meconium peritonitis that starts late in utero, and progresses postnatally. The meconium perito-

nititis-induced inflammation of adjacent periductal tissue could lead to a severe and protracted inflammatory reactions, with accompanying fibrosis, causing secondary obliteration of the extrahepatic biliary system.

The diagnosis of meconium peritonitis and perforation of small bowel atresia was apparent in all cases at the first operation, but the presence of biliary atresia was not suspected. Unfortunately, the gallbladder was not examined in all cases during the first operation, and, in particular, the records of the preoperative ultrasonography did not include details of the gallbladder. Because of the high incidence of biliary atresia in cases of meconium peritonitis, we recommended that the gallbladder be examined by preoperative ultrasonography and during the operation for meconium peritonitis. The etiology of persistent jaundice and acholic stool after the first operation for meconium peritonitis also was difficult to establish because of the duration of hyperalimentation. Central hyperalimentation usually is required for nutritional support in most cases of meconium peritonitis with intestinal atresia because of the combined effects of short bowel syndrome and the delayed return of adequate motility and absorptive capacity.¹³ Jaundice in small bowel atresia is not unusual because 20% to 30% of small bowel atresia cases also are associated with nonhemolytic jaundice.¹³ All our patients were treated using parenteral hyperalimentation over an extended period in which transitory obstructive jaundice may be complicated.

Another difficulty experienced with these patients involved the prevention of ascending cholangitis during and after hepatic portoenterostomy. This developed in 4 patients and persisted for a long time despite aggressive treatment and resulted in the deaths of 2 patients. The patient in case 3 did not have cholangitis because there was no active bile flow after hepatic portoenterostomy. During the hepatic portoenterostomy the decision whether to save the small bowel for the digestive tract to prevent short bowel syndrome or to make a Rouex-en-Y loop long enough to prevent ascending cholangitis is difficult. To decrease the risk of cholangitis, we made a long Rouex-en-Y limb, of more than 60 cm in length, without any other modification for ordinary biliary atresia cases. However, the Rouex-en-Y loop could not be made long enough in our cases because of a preexisting short bowel. Numerous modifications of intestinal conduits have been reported to prevent reflux in biliary reconstruction, but none has proven entirely satisfactory in terms of eliminating cholangitis.¹⁴⁻²¹ Appendico-duodenostomy²² was used to prevent reflux cholangitis and save the entire small bowel. Despite a lack of experience with this procedure, we think that it can be used in this special association.

We believe that bacterial overgrowth in the small

bowel, a well-recognized problem in children with short bowel syndrome,²⁴ may be another risk factor of ascending cholangitis in our cases. Another area of concern involves the management of short bowel syndrome in biliary atresia, which requires extended TPN, and also has been shown to increase the risk of cholestasis leading to liver cirrhosis, sepsis, and increased risk of mortality. We believe that TPN-associated liver injury was the cause of death in case 4.

We believe that our investigation shows that there is a

close relationship between biliary atresia and meconium peritonitis caused by small bowel atresia perforation, and that the combination of these major problems is associated with poor outcome. Moreover, it proved difficult to manage the nutritional requirements of patients and to prevent ascending cholangitis. Although we are not able to detail the ideal management of this rare condition, we believe that hepatic portoenterostomy should still be considered as the primary surgery, because we achieved 1 good result (case 2).

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