Biliary Atresia Associated with Meconium Peritonitis

Mei-Yung Chung, MD; Tan-Yung Ko, MD; Chung-Bin Huang[1], MD;
Chiang-Hsuan Lee[2], MD; Chih-Sung Hsieh[3], MD

Biliary atresia, malrotation, meconium peritonitis and transient hypothyroidism are occasionally seen in neonatal infants. Biliary atresia associated with malrotation has been reported in some patients with polysplenia syndrome, but biliary atresia associated with meconium peritonitis has only been described by a few investigators. Here we present a case of meconium peritonitis due to malrotation with volvulus, followed by biliary atresia and transient hypothyroidism during early infancy. *(Chang Gung Med J 2006;29:203-6)*

Key words: biliary atresia, malrotation, meconium peritonitis, transient hypothyroidism.

Biliary atresia (BA) is detected in 1 of 10000 to 15000 live births.(1) The etiology of BA is still unclear. Infants with BA have an increased incidence of other abnormalities, such as polysplenia syndrome with abdominal heterotaxia, malrotation, levocardia, and intra-abdominal vascular anomalies. The polysplenia syndrome constitutes 10% to 25% of cases of BA.(2) Tanano et al.(3) described seven (8%) of 87 patients with BA who had multiple congenital structural anomalies including situs inversus, polysplenia, preduodenal portal vein, absent portal vein, absent inferior vena cava, malrotation and congenital heart disease. The etiology of BA with structural anomalies may be a part of defective organogenesis during the early fetal period. Recently, BA has been proposed to be the result of an inflammatory process involving the extrahepatic bile ducts during the late intrauterine or early neonatal period. However, few researchers reporting BA associated with meconium peritonitis have supported the hypothesis.(4) We present a case of BA associated with malrotation and meconium peritonitis and discussed the possible pathologic mechanism.

CASE REPORT

A female baby with birth weight of 2.9 kg was born via cesarean section to a gravida 2, para 2 mother. The gestational age was 37 weeks. Apgar scores were 5 and 7 at 1 minute and 5 minutes, respectively. Ascites was first detected in the fetus at the 34th week of gestation using antenatal ultrasonography. There was no skin thickness, pleural effusion or pericardial effusion detected on a follow-up antenatal ultrasonography. Emergency cesarean section was performed due to fetal distress. The weight of the placenta is around 500 g. Cardiac ultrasonography revealed an atrial septal defect (2.9 mm). After birth, only a little ascites was found using abdominal ultrasonography. The gallbladder was visible at that time. The abdomen was soft. No abdominal distension or peritoneal sign was noted by the physician. There was only a little fluid drained out using nasogastric tube during the first 24 hours. Meconium had passed. Feeding with half-strength formula was tried on the second day but poor digestion was noted. Unfortunately, abdominal distension

Department of Pediatrics, Chang Gung Memorial Hospital, Kaohsiung; [1]Department of Pediatrics, Chang Gung Memorial Hospital, Chiayi; Department of [2]Nuclear Medicine, and [3]Pediatric Surgery, Chang Gung Memorial Hospital, Kaohsiung.
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Correspondence to: Dr. Chih-Sung Hsieh, Department of Pediatric Surgery, Chang Gung Memorial Hospital. 123, Dabi Road, Niaosung Shiang, Kaohsiung, Taiwan 833, R.O.C. Tel.: 886-7-7317123 ext. 8715; Fax: 886-7-7338009; Email: sm7583@adm.cgmh.org.tw

was found on the third day and plain abdominal film showed obvious dilatation of bowel. Pneumoperitonium was suggested. Exploratory laparotomy was done by the pediatric surgeon immediately. Povidone iodine was used during surgery. The finding during the operation was meconium peritonitis due to malrotation with volvulus. Lysis of adhesions and Ladd's procedure were performed. A normal-sized gallbladder was found. Ascites grew *Pseudomonas aeruginosa* on culture media. The patient recovered gradually under antibiotic treatment but feeding was still not smooth. No stool passage was found during the days following the procedure. Thyrotropin was checked and abnormal elevated level was noted. We rechecked the thyroid function and confirmed the diagnosis of hypothyroidism (Thyroid stimulating hormone: 288 μIU/ml, T4: less than 1.0 μg/dl, and Free-T4: 0.12 ng/dl). We traced the history of the pregnancy and no abnormal thyroid function was found and no medication was used. No autoantibodies were detected in mother's blood, either. The thyroid scintigraphy revealed that the thyroid was a normal size with diffusely increased distribution of the agent. Dyshormonegenesis or transient hypothyroidism was considered. However, the results might be due to the iodine-contained antiseptic used on the patient during surgery, malnutrition, or illness. After thyroxin replacement therapy, the feeding was smooth 2 weeks after the treatment and approached full feeding status 3 weeks after the treatment. At that time, we found clay-colored stool and jaundice. Phenobarbital was prescribed. The clay-colored stool and direct hyperbilirubinemia persisted. Abdominal ultrasonography revealed a visible gallbladder during fasting but poor contraction of the gallbladder after feeding. The blood biochemistry revealed bilirubin: (total/direct) 5.3/3.73 mg%, serum glutamic-oxaloacetic transaminase: 101 U/L, serum glutamic-pyruvic transaminase: 23 U/L, albumin: 2.6 g%, alkaline phosphatase: 125 U/L, and gamma-glutamyl transpeptidase: 272 U/L. The hepatobiliary scintigraphy revealed a fair liver uptake and no visualization of gallbladder or bowel activity throughout the examination course up to 24 hours after injection of the isotope. The second operation confirmed the diagnosis of biliary atresia and the Kasai procedure was performed at 49 days of age. The gallbladder was measured $2.8 \times 0.7 \times 0.7$ cm. The microscopic examination revealed inflammation of the gallbladder and bile ducts, as well as atretic bile ducts. After a second operation, the clay-colored stool and jaundice disappeared. No post-operative cholangitis was found. The girl is 3 years old. She is healthy with normal liver function. Re-evaluation of thyroid function after withdrawal of thyroxine for 1 month at the age of 2 years revealed normal thyroid function. Transient hypothyroidism was diagnosed and the girl successfully discontinued thyroxine replacement therapy.

DISCUSSION

Controversy continues over the pathogenesis of BA. The presence of an inflammatory process involving the extrahepatic bile duct during the late intrauterine or early neonatal period has been proposed.[5] In addition, viral infection,[6] teratogenic insult, vascular insufficiency,[7,8] autoimmune obliteration of the bile ducts and pancreatic reflux leading to destruction of the biliary duct system were also reported in patients with BA. Although there have been many possible mechanisms suggested, the actual etiology of BA remains unclear.

Coexistence of BA with other anomalies has been widely reported and involves both single and multiple organ systems.[9] In general, 29% to 40% of BA cases had part or most of laterality sequence. Other frequently involved organs and systems included the heart, kidney, and gastrointestinal tract. Miyamoto and Kajimoto[10] reported that ventricular septal defect was commonly associated with BA. In addition, renal and gastrointestinal anomalies were found in 16% and 23% of BA patients, respectively. We know that situs inversus, polysplenia, portal vein anomaly, absent inferior vena cava or cardiac defect result from defective organogenesis at around 5 to 6 weeks of gestation. Extrahepatic bile ducts begin to grow from the primordial bud of the intestine at 5 weeks of gestation, followed by normal canalization at 6 weeks. Normal rotation and fixation of the gut occur at around the 10th to 12th week of intrauterine life. Therefore, the etiology of BA with laterality sequence or cardiac defects may be defective organogenesis during the early fetal life, but BA with isolated malrotation and no other obvious laterality sequence as in our case would be difficult to be explained as simultaneous defective organogenesis.

The association between BA and meconium

peritonitis has been reported by a few investigators. The incidence of meconium peritonitis in BA patients is 0.5% to 2.9%.[4,7,8,11] Han et al.[4] recommended that the gallbladder should be examined using preoperative ultrasonography as well as during the operation for meconium peritonitis. However, in our case, the gallbladder was visible during the initial abdominal ultrasonography before the first operation for meconium peritonitis and even during the follow-up abdominal ultrasonography before the second operation for BA. A previous report in the literature stated that none of 49 patients with BA had visible gallbladders in hepatobiliary scintigraphy, but nine patients with BA had normal-sized gallbladders (length > 1.5 cm) on abdominal ultrasonography.[12] This supports that a visible gallbladder on an abdominal ultrasonography cannot exclude the diagnosis of BA. Although some types of BA have been found to preserve the gallbladder, intraoperative observation and operative cholangiography have proven these gallbladders to be either shrunken or fibrotic. With our experience in this case, the normal shape of a gallbladder and the contraction of a gallbladder after feeding on abdominal ultrasonography and gallbladder visualization on hepatobiliary scintigraphy are important clues for ruling out BA. If possible, intraoperative observation of the gallbladder and operative cholagiography during the operation for meconium peritonitis may be more valuable than preoperative ultrasonography. The results of microscopic examination of the bile ducts and gallbladder revealing inflammation in our case supported the hypothesis suggested by Han et al. that BA may be a dynamic, acquired inflammatory process associated with meconium peritonitis that starts late in utero, and progresses postnatally.[4] The prognoses in previous cases of BA associated with meconium peritonitis were poor because of the difficulties in diagnosis and recurrent cholangitis, however, we found that early diagnosis, early operation and no association with major anomalies may improve the outcomes. In addition, our case had hypothyroidism with feeding intolerance after the first operation. The feeding intolerance and hyperalimentation over an extended period can be complicated with hyperbilirubinemia. This may confuse the diagnosis of BA; therefore, it is important to check thyroid function of all sick or postoperative newborn infants with feeding intolerance.

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合併胎糞性腹膜炎之膽道閉鎖

鍾美勇 高丹榕 黃崇濱[1] 李將瑄[2] 謝志松[3]

膽道閉鎖、腸管旋轉不良、胎糞性腹膜炎及暫時性甲狀腺功能不良皆偶而可見於新生兒。膽道閉鎖合併腸管旋轉不良常發生於多脾症候群病人身上，但膽道閉鎖發生在胎糞性腹膜炎之後就只有零星個案報告。本篇探討一腸管旋轉不良暨胎糞性腹膜炎的新生兒之後發生膽道閉鎖及暫時性甲狀腺功能不良的情況，並探究其原因。(長庚醫誌 2006;29:203-6)

關鍵字：膽道閉鎖，腸管旋轉不良，胎糞性腹膜炎，暫時性甲狀腺功能低下。

長庚紀念醫院 高雄院區 兒童內科；[1]嘉義院區 兒童內科；高雄院區 [2]核子醫學科，[3]小兒外科
受文日期：民國93年5月11日；接受刊載：民國94年3月31日
通訊作者：謝志松醫師，高雄長庚醫院 小兒外科。高雄縣833鳥松鄉大埤路123號。Tel.: (07)7317123 轉 8715; Fax: (07)7338009; E-mail: sm7583@cgmh.org.tw