Journal of Pediatric Surgery 50 (2015) 507–510

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Original Articles

Postnatal management of prenatally diagnosed biliary cystic malformation

Hiromu Tanaka, Hideyuki Sasaki, Motoshi Wada, Tomoyuki Sato, Takuro Kazama, Kotaro Nishi, Hironori Kudo, Megumi Nakamura, Masaki Nio *

Department of Pediatric Surgery, Graduate School of Medicine, Tohoku University, Sendai, Japan

ARTICLE INFO

Article history:
Received 16 May 2014
Received in revised form 3 August 2014
Accepted 6 August 2014

Key words:
Prenatal diagnosis
Biliary atresia
Choledochal cyst
Biliary cystic malformation

ABSTRACT

Purpose: Recent advances in ultrasonography have increased prenatal diagnosis of biliary atresia (BA) and choledochal cyst (CC). These conditions are not easy to distinguish before or just after birth. This study investigated diagnostic and therapeutic problems in prenatal diagnosis of BA and CC.
Methods: We retrospectively studied clinical characteristics and progression of hepatobiliary cysts in 10 patients (4 cases of BA, 6 cases of CC) from the time of diagnosis. Chronological changes in cyst size and gallbladder morphology were assessed and measured sequentially by ultrasonography.
Results: Three cases of BA were type I cyst and 1 case was type III-d. All cases of CC were type Ia. Cyst size decreased between birth and surgery in BA but increased in CC. The gallbladder appeared atrophic in BA. There was no significant difference in gestational age or cyst size at prenatal diagnosis, changes in cyst size between birth and surgery, and degree of liver fibrosis.
Conclusions: BA should be suspected if cyst size decreases before and after birth and the gallbladder atrophies after birth. Cholangiography is the only reliable method to differentiate BA from CC. Neonatal surgery is indicated for CC with icterus and liver dysfunction.

Recent advances in ultrasonography have increased prenatal diagnoses of biliary atresia (BA) and choledochal cyst (CC). The Japanese Biliary Atresia Society classifies biliary cystic malformations in BA as either type I cyst (correctable) or type III-d [1]. In type I cysts, atresia of the distal common bile duct accompanies cystic dilatation. Type III-d BA shows atresia of the bile duct at the porta hepatis, with a solitary cyst in the fibrous remnant. Patients with untreated BA progress to irreversible cirrhosis and death. In contrast, the optimal time for prenatal diagnosis and treatment of CC has not been established. A previous study reported that delayed surgery results in liver fibrosis [2–4]. It is important to distinguish between prenatally diagnosed BA and CC as soon as possible and to institute appropriate treatment in response to each pathological condition, after birth. In this study, we analyzed prenatally diagnosed biliary cystic malformations and investigated the postnatal management and points of differential diagnosis.

1. Materials and methods

Hepatobiliary cysts were prenatally detected in 10 cases with biliary cystic malformation (4 cases of BA and 6 cases of CC) from 1991 to 2012. All patients were female. BA and CC were eventually distinguished and the type of BA was determined based on surgical findings and intraoperative cholangiography. We retrospectively investigated and analyzed gestational age (GA) at prenatal diagnosis, cyst size at prenatal diagnosis, chronological change in cyst size, GA and body weight at birth, gallbladder morphology, direct bilirubin (D-bil), γ-glutamyltransferase (G-GTP) level, stool color, disease type, age at surgery, degree of liver fibrosis, progression of disease, and outcome.

Cyst size was assessed and sequentially measured by ultrasonography (US). Patients were classified into 3 groups according to the degree of change in cyst size from baseline (at diagnosis or birth) to assessment (at birth or operation): reduction group (<90% of baseline cyst size, D group), the no change group (<110% but >90% of baseline cyst size, NC group), and the expansion group (>110% of the baseline cyst size, U group).

Gallbladder findings were classified into 2 groups: atrophic, where the gallbladder was either absent or small, and normal, where the lumen of gallbladder was detectable by postnatal sonography.

We measured D-bil (mg/dl) and G-GTP (U/l) from birth to operation. G-GTP levels vary with age, sex, and assay methods. In this study, we defined a normal G-GTP level as 100 U/l, which is twice the upper range for adults.

Intraoperative cholangiography was performed, via the gallbladder and common bile duct, to distinguish BA from CC. Patients diagnosed with BA were classified according to the classification of the

* Corresponding author at: Department of Pediatric Surgery, Graduate School of Medicine, Tohoku University, 1–1 Seiryo-machi, Aoba-ku, Sendai 980–8574, Japan. Tel.: +81 22 717 7237; fax: +81 22 717 7240.
E-mail address: mnio@ped-surg.med.tohoku.ac.jp (M. Nio).

http://dx.doi.org/10.1016/j.jpedsurg.2014.08.002
0022-3468/

Japanese Biliary Atresia Society [1]. Patients with CC were classified according to the classification reported by Todani et al. [5].

Liver biopsies were performed intraoperatively. Specimens were fixed in formalin and stained with hematoxylin-eosin and elastica-Goldner stains, and the degree of liver fibrosis was assessed. We scored the degree of liver fibrosis according to the new Inuyama classification as F0 (no fibrosis), F1 (fibrous portal expansion), F2 (bridging fibrosis), F3 (bridging fibrosis with architectural distortion), and F4 (liver cirrhosis) [6]. This classification is used to define the underlying liver status and can separately assess the degree of fibrosis and the grade of necroinflammatory activity [6,7].

Change in cyst size, GA, body weight at birth, and age at surgery were expressed as means ± SD. The Mann–Whitney *U* test was used for statistical analysis of continuous data, and the chi-square test was used for categorical data. A value of $P < 0.05$ was considered statistically significant.

The institutional review committee approved this study. Informed consent was obtained in all cases.

2. Results

2.1. GA at prenatal diagnosis

The 4 cases of BA were diagnosed between 21 and 28 weeks (median, 25 weeks), and the 6 cases of CC were diagnosed between 20 and 37 weeks (median, 32 weeks). The mean GA, at the time of prenatal diagnosis, was less in the BA patients than in the CC patients, but the difference was not statistically significant (Table 1).

2.2. Sonographic cyst morphology

2.2.1. Prenatal cyst morphology

Mean cyst size at prenatal diagnosis was 19.5 ± 7.9 mm (median, 20 mm) in the BA group and 13.0 ± 5.4 mm (median, 12 mm) in the CC group. This difference was not statistically significant.

In 7 cases (4 BA and 3 CC), the chronological change in prenatal cyst size was examined at birth and the prenatal stage. In the BA group, 2 cases were NC, 2 cases were D, and none were U (Table 2). In contrast, in the CC group, 2 cases were U and 1 case was NC (Table 2). Cyst size appeared to decrease or remain unchanged between prenatal diagnosis and birth in BA patients, but expanded in CC patients. However, this difference was not statistically significant.

2.2.2. Postnatal cyst morphology

Mean cyst size at birth was 18.8 ± 10.1 mm (median, 17.5 mm) in the BA group and 26.0 ± 6.3 mm (median, 24 mm) in the CC group. The difference was not statistically significant.

In 9 cases (4 BA and 5 CC), the chronological change in prenatal cyst size was examined both at surgery and at birth. In the BA group, 2 cases were D, 2 cases were NC, and none were U (Table 2). In contrast, in the CC group, 4 cases were U and 1 case was NC (Table 2). Cyst size between birth and surgery decreased in BA patients and expanded in CC patients, a statistically significant difference ($P = 0.043$).

Table 1
Patient characteristics.

Case	Type	Gestational age at prenatal diagnosis (weeks)	Cyst size at prenatal diagnosis (mm)	Gestational age at birth (weeks)	Birth weight (g)
BA 1	I cyst	26	18	37	2610
BA 2	I cyst	24	22	37	2900
BA 3	III-d	21	8	39	3243
BA 4	I cyst	28	30	38	3194
CC 1	Ia	34	NA	39	2942
CC 2	Ia	30	12	41	2760
CC 3	Ia	29	NA	40	2754
CC 4	Ia	35	NA	37	2276
CC 5	Ia	37	20	39	2890
CC 6	Ia	20	7	38	2666

NA, not available.

Table 2
Preoperative findings.

Case	Change in cyst size (%)		Stool color	Gallbladder
	At birth*	At surgery**		
BA 1	79.4	93.3	Yellow	Atrophic
BA 2	90.9	105.0	Yellow	Atrophic
BA 3	75.0	1.6	Yellow → gray	Atrophic
BA 4	100.0	76.5	Yellow → gray	Normal
CC 1	NA	137.1	Yellow	Normal
CC 2	150.0	145.0	Yellow	Normal
CC 3	NA	129.6	Yellow → gray	Normal
CC 4	NA	NA	Yellow	Normal
CC 5	100.0	100.0	Yellow	NA
CC 6	175.2	170.8	Yellow	Normal

NA: not available.
* Size % compared to the size at prenatal diagnosis.
** Size % compared to the size at birth.

2.3. GA and body weight at birth

Mean GA at birth was 37.8 ± 0.8 weeks (median, 37.5 weeks) in the BA group and 39.0 ± 1.3 weeks (median, 39.0 weeks) in the CC group. The mean GA at birth was less in the BA patients than in the CC patients, but the difference was not statistically significant. Mean body weight at birth was 2986 ± 254 g (median, 3047 g) in the BA group and 2714 ± 216 g (median, 2757 g) for the CC group (Table 1), but the difference was not statistically significant.

2.4. Postnatal gallbladder morphology

Among BA patients, the gallbladder was atrophic in 3 cases (absent in 1 and no lumen detected in 2) and normal in 1 case. In contrast, the gallbladder morphology was normal in 5 cases of CC (Table 2). The difference between groups was statistically significant ($P = 0.018$).

2.5. Change in stool color

Stool color at birth was yellow in all cases. In 2 BA cases (50%) and 1 CC case (16.6%), the stool turned gray before surgery (Table 2). This difference was not statistically significant. Stool color gradually became gray in 2 cases of BA. One CC patient developed acholic stool and icterus suddenly at the age of 47 days and underwent surgery at 63 days of age.

2.6. Laboratory data

Mean value of D-bil was measured from birth until the fifth week. Mean value of D-bil was persistently increased in BA but not in CC (Fig. 1). Of the 4 BA patients, cases 3 and 4 showed preoperative elevation of D-bil, whereas cases 1 and 2 showed no elevation (Fig. 2).

Chronological changes in G-GTP levels were measured in 9 cases (4 BA and 5 CC) between birth and surgery. All BA cases had elevated G-GTP at birth, but the level of G-GTP decreased until surgery ($P = 0.034$) (Fig. 3). In contrast, case 3 in the CC group was icteric during follow-up, with G-GTP exceeding 1700 U/l, whereas other CC cases showed various inconsistent patterns (Fig. 3).