

A Retrospective Study Between Type I Cystic Biliary Atresia and Infantile Choledochal Cyst at a Tertiary Centre

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Abstract

Purpose: Type I cystic biliary atresia (CBA) is an uncommon variant of biliary atresia (BA) which is liable to misdiagnosis as infantile choledochal cyst (ICC). We assessed our experience with type I CBA and compared with that of ICC. **Methods:** Seven patients (4 males and 3 females) with type I CBA, receiving liver function detection, radiological imaging studies, liver/cyst histological examinations and radical surgery, were compared with 23 ICC patients (14 males and 9 females) admitted in our division during a 6-year period. **Findings:** The mean levels of total bilirubin (T-Bil), direct bilirubin (D-Bil), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (AKP) in the type I CBA group were significantly higher than those in the ICC group ($p < 0.01$). The mean diameter of the cyst in the type I CBA group was significantly smaller than that in the ICC group ($p < 0.01$). All 7 patients in the type I CBA group were accurately diagnosed by magnetic resonance cholangiopancreatography (MRCP) preoperatively, being in accordance with the results of intraoperative cholangiography and liver/cyst histology. Six cysts (85.7%) in the type I CBA group had a fibroinflammatory wall with no biliary epithelial lining while all 23 (100%) cysts in the ICC group had normal biliary epithelial lining. Six infants (85.7%) with type I CBA cleared their jaundice (total bilirubin $\leq 20 \mu\text{mol/L}$) within 6 months after a Kasai portoenterostomy or hepaticojejunostomy procedure. All patients with ICC were in good condition with no jaundice and cholangitis after the operation. **Conclusions:** While elevated T-BIL/D-BIL and AST/ALT/AKP as well as smaller gallbladder/extrahepatic cyst imply type I CBA, MRCP can provide further effective assistance in making a relatively accurate diagnosis before operation. Either hepaticojejunostomy or Kasai portoenterostomy could be chosen as an optimal procedure in the treatment of type I CBA.

Key words

Choledochal cyst; Biliary atresia; Differential diagnosis; Type I cyst

Introduction

Biliary atresia (BA) is an obliterative condition of the immature extra and intrahepatic biliary tract, and is usually

classified into three types.¹ Type I, atresia of common bile duct; type II, atresia of hepatic duct; and type III, atresia of porta hepatis. When a cystic dilatation is accompanied with type I BA, it is called type I cystic biliary atresia (CBA).²

Type I CBA might be quite similar to infantile choledochal cyst (ICC), which is a lesion associated with an anomalous pancreaticobiliary union occurring in infants (age < 12 months).^{3,4} Clinically, it is necessary for the surgical treatment of ICC to wait for an appropriate time. However, patients with type I CBA have to be operated as early as possible, because delayed diagnosis and treatment will be associated with increased postoperative morbidity and mortality as results of liver failure and its sequel.^{5,6} Due to the similar presentations and radiological

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characteristics, it is difficult to differentiate type I CBA from ICC, and the optimal operative procedure for type I CBA is still controversial.²⁻⁴ In this study, we assessed our experience with type I CBA and compared with that of ICC.

Methods

During the period between August 2006 and July 2012, 7 infants with obstructed jaundice were diagnosed with type I CBA (based on intraoperative cholangiography and liver histology) out of 40 patients with BA, which was classified according to the Japanese Association of Pediatric Surgeons classification.¹ We retrospectively studied these cases with liver function, radiological imaging features, operation details, histological characteristics and outcomes after surgery. We compared these patients with another group of 23 patients with ICC who were diagnosed according to the Todani classification⁷ and have received hepaticojejunostomy (HJ) during the same period.

There were 4 males and 3 females with median age at operation of 58 days (ranging from 35 days to 108 days) in the type I CBA group, 14 males and 9 females with median age at operation of 82 days (ranging from 45 days to 127 days) in the ICC group. Liver function were examined in all patients and compared between the two groups. Ultrasonography (US), magnetic resonance cholangiopancreatography (MRCP) and intraoperative cholangiography were performed for all patients in both groups.

We evaluated the grade of liver fibrosis from liver tissue and examined the epithelium of cysts in both groups obtained during operation. This retrospective review of histologic findings in liver was performed by a single pathologist blinded to outcome. Fibrosis on liver biopsy was graded as grade 1 (mild fibrosis localised to the portal area), grade 2 (moderate fibrosis with porto-portal bridging fibrosis), grade 3 (severe expansive fibrosis with porto-portal bridging) and grade 4 (liver cirrhosis), respectively, according to the new Inuyama classification.⁸

Two patients of the type I CBA group received Kasai portoenterostomy (KP), and the other 5 patients with dilated hepatic duct and all patients in the ICC group received HJ. Good outcome was assessed as clearance of jaundice (total bilirubin ≤ 20 $\mu\text{mol/L}$) within 6 months of age in type I CBA group.⁹ The mean follow-up period was 3 years 4 months (8 months to 6 years) in type I CBA group, and 4 years 8 months (14 months to 6 years) in ICC group, respectively. Data were quoted as median (range) and

mean \pm SD. Statistical significance was evaluated using the Student *t* test and P value less than 0.05 was regarded as significant.

Results

1. Liver Function and Radiological Imaging Characteristics

Table 1 shows that the mean levels of total bilirubin (T-Bil) and direct bilirubin (D-Bil) in the type I CBA group were significantly higher than those in the ICC group ($p < 0.01$). The mean levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (AKP) were also significantly higher than those in ICC group ($p < 0.01$).

The mean diameter of the cysts in the type I CBA group, assessed at preoperative US, was 14 ± 3.8 mm, which was significantly smaller than that (38 ± 6.7 mm) in the ICC group ($p < 0.01$).

All patients of both groups were examined by MRCP preoperatively. In the type I CBA group, MRCP showed that the intrahepatic bile ducts varied from being cloud-like pattern with no discernible structure beyond fine biliary ductless to any degree of intrahepatic duct opacification (Figures 1a-c), which is in contrast with that of ICC group (Figure 2). Before receiving MRCP, one patient with big cyst and dilated hepatic ducts was diagnosed as ICC by US. However, MRCP showed no clear intrahepatic bile ducts (Figure 3). Considering with remarkable, simultaneously increased T-Bil/D-Bil and ALT/AST/AKP, we re-diagnosed that patient with type I CBA before surgery. The following outcome of both intraoperative cholangiography and liver/cyst histology confirmed the diagnosis.

Table 1 Liver function comparison between two groups

	Type I CBA group (n=7, mean \pm SD)	ICC group (n=23, mean \pm SD)
Total bilirubin (T-Bil)	188 \pm 34	56 \pm 19
Direct bilirubin (D-Bil)	147 \pm 29	32 \pm 11
Alanine aminotransferase (ALT)	158 \pm 37	46 \pm 12
Aspartate aminotransferase (AST)	136 \pm 27	38 \pm 13
Alkaline phosphatase (AKP)	1034 \pm 298	546 \pm 121

P value for difference between the two groups is less than 0.01 (statistically significant)

CBA: cystic biliary atresia; ICC: infantile choledochal cyst

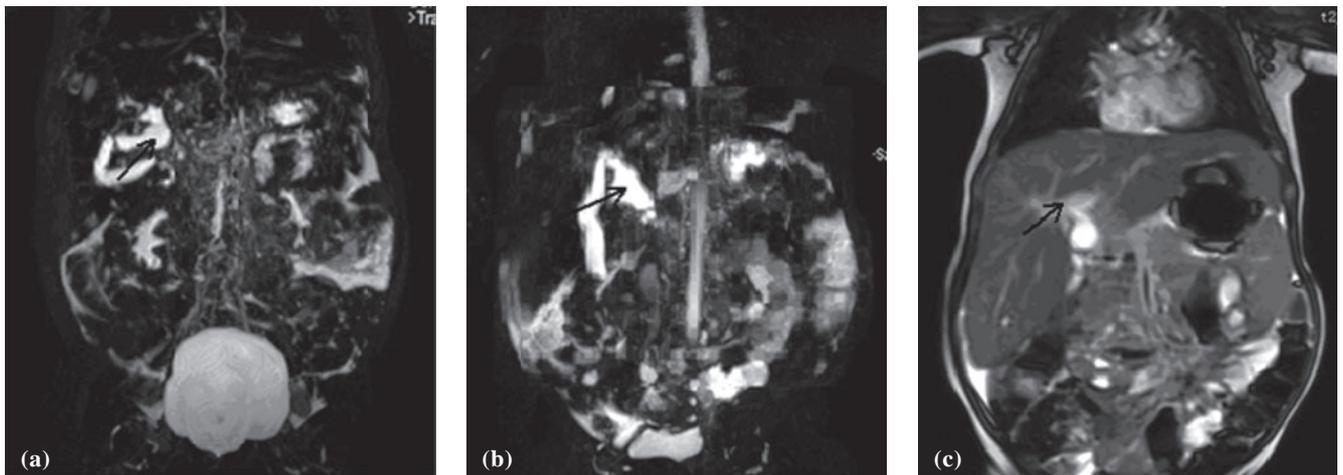


Figure 1 Preoperative magnetic resonance cholangiopancreatography of patients with type I cystic biliary atresia (CBA). (a) and (b) show the atretic gallbladder and mildly dilated common bile duct (arrow shows), (c) shows cloudy-like pattern of intrahepatic bile ducts (arrow shows) in a patient with type I CBA. Note that gallbladder cannot be seen in this image.



Figure 2 Magnetic resonance cholangiopancreatography of a patient with choledochal cyst showing a normal gallbladder and distinct intrahepatic bile ducts.



Figure 3 Magnetic resonance cholangiopancreatography of a patient with type I cystic biliary atresia. Note that in this image, while the cyst and right and left hepatic ducts obviously dilate, the gallbladder is atrophic (arrow shows) and no clear intrahepatic bile ducts can be seen.

2. Liver and Cyst Histology

Only grade 3 and 4 of liver fibrosis were seen in all 7 patients (100%) in the type I CBA group. Among the 11 patients in the ICC group whose liver histology were available due to abnormal gross appearance of the liver, 4 of them (36.4%) had evidence of liver fibrosis of different grades except grade 4, as shown in Table 2. Although there is obvious difference in the grades of fibrosis between these two groups, statistical significance could not be drawn due to the small number of patients with type I CBA.

Histologically, 6 (85.7%) of the epithelium of the cyst wall in the type I CBA group were denuded; only one specimen showed that the lumen was covered by columnar epithelium, accompanied by fibrous tissue. In contrast, all (23) the epithelium of the cyst wall in the ICC group was normal, with a few specimens showed scattered inflammation cells in the epithelium.

3. Surgical Procedure and Outcome

Among the 7 patients with type I CBA, the common hepatic ducts of 5 patients were sufficient for anastomosis, and we performed HJ by interrupted sutures using 6-0 polydioxanone suture (PDS) on both the anterior and posterior wall. For other two patients, we performed KP due to tenuous extrahepatic ducts. All the patients in the ICC group received HJ.

In the type I CBA group, 6 patients (one with KP) had good postoperative bile drainage and were alive without jaundice but one (with KP), which was operated on at the age of 67 days, had refractory cholangitis and persistent hyperbilirubinemia, and died of hepatic failure at the age of 6 months. All patients in the ICC group were in good condition after operation with no jaundice and cholangitis.

Discussion

Type I (including type I cyst) BA is much less frequent than type III (approximately 85%). Type II is uncommon (<5%). Nio et al¹⁰ reported 38 cases of type I CBA from 50 type I BA, which was the largest report we found so far.

Due to the fact that type I CBA might be quite similar to ICC, the key clinical problem is to differentiate type I CBA from ICC, which has similar presentations such as earlier onset of jaundice, clay-colored stool, abdominal cyst found by ultrasonography before or after birth and early onset liver fibrosis.¹¹ The choledochal cyst in neonates or young infants less than 1 year of age is somewhat different from that in children and adults. It is characterised by large cysts,

Table 2 Liver histology: fibrosis

Liver Histology grades	Type I CBA group (n=7)	ICC group (n=23)
Normal	0	7
Grade 1	0	2
Grade 2	0	1
Grade 3	3	1
Grade 4	4	0

CBA: cystic biliary atresia; ICC: infantile choledochal cyst

a high incidence of jaundice, and the absence of pancreatitis. To differentiate it from type I CBA is usually difficult, especially in prenatally diagnosed patients due to the lack of clinical information.¹² Thus effective methods capable of making an accurate pre-operative diagnosis are still lacking.

In this six-year retrospective research, we found that in the type I CBA group, the mean levels of both T-BIL/D-BIL and ALT/AST/ALP were significantly higher than those in the ICC group (p<0.01), respectively, and therefore, the laboratory test of liver function will benefit the diagnosis of type I CBA before operation.

Some reports showed sonographic features may permit an accurate differential diagnosis, with the smaller, static, anechoic cysts likely to represent CBA.^{13,14} Kim et al¹⁵ showed that US findings of a large cyst and dilated intrahepatic ducts are more indicative of choledochal cyst (CC) than BA in neonates and young infants. In our research, the mean diameter of the cyst in the type I CBA group, assessed at preoperative US, was 14 mm, which was significantly smaller than that of cysts (38 mm) in the ICC group (p<0.01). The sonographic appearance of the gallbladder has also been suggested as useful, with an atretic or irregularly elongated structure indicating CBA.¹⁵⁻¹⁷

Biliary atresia is an obliterative disease of the extrahepatic as well as the intrahepatic biliary systems, and type I CBA has a dilated common bile duct which communicates with intrahepatic ducts. Many authors thought that intraoperative cholangiography should be done with care at the time of surgery to evaluate the pattern of bile duct in order to make a definitive diagnosis of BA.^{9,18} Intraoperative cholangiography may exhibit a spectrum of intrahepatic biliary tree abnormalities. According to the cholangiography at the corrective operation, Nio et al² classified type I CBA into 3 types: cloudy (48%), treelike (13%), and mixed (39%). However, the aforementioned procedure must be done during operation, and therefore is

helpless in making a preoperative diagnosis which is important for the surgeon to determine an appropriate operation time. In recent years, MRCP has been advocated as an ideal and non-invasive diagnostic modality for CC as it ensures accurate visualisation of the entire pancreatobiliary system.^{19,20} The use of MRCP can obviate the necessity of performing intraoperative cholangiography.

In this research, we performed MRCPs in all patients in both groups before operation. In the type I CBA group, the intrahepatic bile ducts varied from being cloud-like pattern to any degree of intrahepatic duct opacification, comparing that with clear and distinct intrahepatic bile ducts in the ICC group. Although one patient with significantly dilated common bile duct was initially diagnosed with ICC by US, his MRCP couldn't show the intrahepatic bile duct, which was different from the characteristic of ICC. This patient was finally diagnosed as type I CBA by intraoperative cholangiography and liver/cyst histology. This provides a convincing proof that MRCP is very useful in making a relatively accurate diagnosis before operation. Although MRCP appears non invasive when compared to cholangiogram, performing MRCP in an infant is not easy and many motion artifact can disturb the image. Also the cost of MRCP remains high in many countries. Occasionally it may overestimate extrahepatic bile duct luminal integrity and thus wrongly favour choledochal cyst. In case of suspicion, exploration should never be delayed.

Compared with the ICC group, the type I CBA group had severe liver fibrosis, although we did not draw a conclusion that there is a significant difference between them. Six cysts (85.7%) in the type I CBA group had a fibroinflammatory wall with no biliary epithelial lining while all 23 (100%) cysts in the ICC group had normal biliary epithelial lining, which maybe an important point in distinction, albeit postoperatively.

The prognosis of type I CBA is usually much better than that of the other types.^{2,3} So far, there are limited numbers of reports of long-term outcome of type I CBA. In addition, the operative procedure for this type of BA is still controversial. Although this type of BA has a patent lumen of the duct, some physicians still recommend the Kasai portoenterostomy rather than a hepaticojejunostomy. Caponcelli et al⁹ reported that all 29 patients of type I cyst underwent Kasai portoenterostomy at a median age of 46 days. Of these 29 patients, 18 (62%) patients were alive with their native liver, but 11 (38%) patients had undergone liver transplantation at a median age of 1 year. Nio et al² reported that 323 patients with BA were operated on at their

institute between 1953 and 2004, and 50 were type I. Of these patients, 31 underwent KP and 19 underwent HJ. The overall survival rate of nontransplant type I patients was better than that of type II/III patients (52% vs 33%, $p=0.009$). The average age of nontransplant type I survivors was 23.7 years. Komuro et al⁶ suggested the long-term results after either a hepaticoenterostomy or a portoenterostomy in patients with type I BA to be satisfactory because follow-up periods extended to 20 years.

In this series, HJ were performed in 5 patients with type I CBA. Six patients (one with KP) had good postoperative bile drainage and were alive without jaundice but one (with KP), died of hepatic failure at the age of 6 months. Our outcomes suggested that a short-term result after either HJ or KP in patients with type I BA was satisfactory. We believe that both the KP and the HJ are acceptable in treating type I CBA, in which KP is the preferable choice of surgery for a patient whose common hepatic duct is tenuous.

Conclusions

In conclusion, our findings support the contention that while elevated T-BIL/D-BIL and AST/ALT/ALP as well as smaller gallbladder/extrahepatic cyst imply type I CBA, MRCP is useful in making a relatively accurate diagnosis before operation, which may lead to an early explorative laparotomy. Intraoperative cholangiography and liver/cyst histology is still the golden standard for differential diagnosis between type I cystic biliary atresia and infantile choledochal cyst. Either a hepaticoenterostomy or Kasai portoenterostomy could be chosen as optimal procedure in the treatment of type I CBA.

Conflicts of Interest

There are no conflicts of interest.

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