Cholangiographic characteristics of common bile duct dilatation in children

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Abstract

AIM: To investigate whether children with congenital common bile duct dilatation (CBDD) differ from children with obstructive CBDD in cholangiographic characteristics.

METHODS: In this retrospective cohort study, the baseline data and the results of imaging analyses were reviewed among children who had endoscopic retrograde cholangiopancreatography (ERCP) due to CBDD. ERCP was performed on all pediatric patients by experienced pediatric endoscopists. The maximal transverse diameter of the common bile duct (CBD) was measured on ERCP. To assess whether age-adjusted CBDD could be used for differential diagnosis, a CBDD severity index (SI) was calculated by dividing the measured CBD diameter by the age-corrected maximal diameter of a normal CBD.

RESULTS: A retrospective medical chart review revealed that 85 consecutive children under 16 years of age with hepatobiliary disease and CBDD were referred to Seoul Asan Medical Center. Fifty-five (64.7%) children had congenital CBDD and 30 (35.3%) had obstructive CBDD. The two groups did not differ significantly in terms of clinical characteristics except for sex. The congenital and obstructive CBDD groups did not differ significantly in terms of mean CBD diameter (19.3 ± 9.6 mm vs 12.2 ± 4.1 mm, P > 0.05). However, congenital CBDD cases had a significantly higher mean SI than obstructive CBDD cases (3.62 ± 1.64 vs 1.98 ± 0.71, P = 0.01). In multivariate analysis, an SI value ≥ 2.32 and comorbidity with anomalous union of pancreaticobiliary duct (APBDU) in ERCP independently predicted congenital CBDD.

CONCLUSION: Measuring the CBD may aid the differential diagnosis of both CBDD and APBDU in...
INTRODUCTION

The causes of common bile duct dilatation (CBD) may differ according to age and geography. In adults, CBD is generally caused by intrinsic luminal obstruction and thus investigative methods focus mainly on the causes of obstruction, such as biliary tract stones and pancreaticobiliary malignancies[1,2]. In children, congenital CBD (i.e., choledochal cyst) must be considered when investigating the causes of CBD[1,2]. However, in Western countries, pediatric choledochal cyst is rare, accounting for only 1.2%-8.6% of pediatric patients who undergo endoscopic retrograde cholangiopancreatography (ERCP) for pancreatic and biliary disease; by contrast, pancreatitis and cholelithiasis are diagnosed much more commonly in this pediatric population[3-5]. However, in East Asia, the most frequent diagnosis in children who are investigated by ERCP for pancreatic and biliary disease is choledochal cyst[6-8]. Moreover, the frequency of choledochal cyst differs depending on the patient's country of origin: one-third of the patients who are reported to have this condition in the world are from Japan[6-9].

The clinical manifestations of choledochal cyst also differ depending on patient age[9]. In Japan, cholelithiasis has been reported in 18%-70% of adults with choledochal cyst. By contrast, only 9% of pediatric patients with choledochal cyst were reported to have cholelithiasis[9,10], although recent findings suggest that this prevalence may be higher than was previously believed (17%-29%)[9-12]. Such relatively high cholelithiasis co-morbidity may initially complicate the differential diagnosis of CBD from cholelithiasis alone. Cholelithiasis can lead to CBD that can be initially misdiagnosed as choledochal cyst in both children and adults[13-15]. Thus, choledochal cyst should be diagnosed on the basis of both the clinical features and the results of various diagnostic modalities[6,9,16].

In adults with CBD, the diameter of the common bile duct (CBD) is considered to be of no clinical significance[17-19]. This is because the studies in adults aimed to differentially diagnose stones from mitotic lesions in the biliary tree. To our knowledge, studies of pediatric CBD that examine whether bile duct size can help to differentiate between obstructive and congenital causes of CBD have not yet been performed. Therefore, the aim of this study was to determine whether children with congenital CBD differ from children with other CBD causes in terms of cholangiographic characteristics.

MATERIALS AND METHODS

A retrospective medical chart review revealed that 85 consecutive children under 16 years of age with hepatobiliary disease and CBD were referred to Seoul Asan Medical Center, a tertiary referral center in Seoul, South Korea between January, 2000 and January, 2012[6,16]. The baseline data and the results of imaging analyses were documented. All children were screened by trans-abdominal ultrasonography (TUS) and more than one imaging modality, such as computed tomography and magnetic resonance cholangiopancreatography (MRCP). They underwent a total of 123 ERCP procedures. The study protocol was approved by the institutional review board of Asan Medical Center, Seoul.

ERCP was performed on all pediatric patients by experienced pediatric endoscopists[6]. The maximal transverse diameter of the CBD between the insertion of the cystic duct and the head of the pancreas was measured along its longitudinal axis via a cholangiogram[20,21]. Measurements were not taken within 5 mm of the origin of the CBD. The reference cut-off value for the normal maximum diameter of the CBD relative to age was obtained from the intravenous cholangiographic data of Witcombe et al[20]. To assess whether age-adjusted CBD could be used for differential diagnosis, a CBD severity index (SI) was calculated by dividing the measured CBD diameter by the age-corrected maximal diameter of a normal CBD. To avoid variation due to other causes, patients with a previous history of cholecystectomy, obstructive cholestasis, and premedication such as with opioids were excluded. Moreover, measurements were made on unmagnified cholangiograms by using electronic calipers. Neonatal cases were also excluded due to technical difficulties in ERCP. Although contrast dye
CBDD: Common bile duct dilatation.

Table 1  Etiological classification of common bile duct dilatation in children

| Causes                   | n = 85 | Descriptions                                      |
|--------------------------|--------|---------------------------------------------------|
| Congenital CBDD n = 55  | (64.7%)| Type 1 (n = 26)                                   |
|                          |        | Type II (n = 29)                                  |
| Obstructive CBDD n = 30 | (35.3%)| Idiopathic (n = 10)                               |
|                          |        | Chronic pancreatitis (n = 6)                      |
|                          |        | Leukemia (n = 2)                                  |
|                          |        | G6PD deficiency (n = 2)                           |
|                          |        | Spherocytosis (n = 2)                             |
|                          |        | Trauma (n = 1)                                   |
| Miscellaneous n = 7     |        | Chronic pancreatitis (n = 3)                      |
|                          |        | Lymphoma/pancreatic cancer (n = 3)                |
|                          |        | Trauma (n = 1)                                   |

Statistical analysis

For univariate analysis, continuous variables were assessed by using independent sample t-tests and categorical variables were assessed by using χ^2 tests. For multivariate analysis, a logistic regression model was used to generate odds ratios (ORs), the corresponding 95% confidence intervals (95%CIs), and the P values. The optimal cut-off of CBD that allowed congenital CBDD to be differentiated from obstructive CBDD was determined by using a receiver operating characteristic (ROC) curve. All statistical calculations were performed by using SPSS software (SPSS for Windows, version 14.0; SPSS Inc., Chicago, IL). A P value less than 0.05 was considered to indicate statistical significance.

RESULTS

In total, 33 boys (38.8%) and 52 girls (61.2%) were diagnosed with CBDD according to our study criteria. The mean patient age was 6.3 ± 3.6 years. The indications for ERCP are summarized in Table 1. Fifty-five (64.7%) children had congenital CBDD and 30 (35.3%) had CBDD due to other secondary causes. The clinical and cholangiographic characteristics of the 85 patients are summarized in Table 2. The most common presenting clinical manifestations in both groups at the time of diagnosis were abdominal pain and jaundice. Some patients in both groups also presented with pancreatitis. This was regarded as a complication in the patients with choledochal cyst but as the underlying disease in the patients with obstructive CBDD. The two groups did not differ significantly in terms of clinical characteristics except for sex: the patients with congenital CBDD were significantly more likely to be female than the patients with obstructive CBDD (80% vs 26.7%, P = 0.032).

The congenital and obstructive CBDD groups did not differ significantly in terms of mean CBD diameter (19.3 ± 9.6 mm vs 12.2 ± 4.1 mm). However, the congenital group had a significantly higher mean CBD SI (3.62 ± 1.64) than the obstructive CBDD group (1.98 ± 0.71). In addition, as the SI increased, so did the prevalence of choledochal cyst among children with CBDD (Figure 1). All patients with an SI of ≥ 3 had a choledochal cyst, unlike patients with an SI of 1-2 or 2-3 (both P < 0.05). ROC analysis showed that an SI of 2.32 could serve as a cut-off value with a sensitivity of 68%, a specificity of 96.7%, and an area under the curve of 0.87. Of the 55 children with congenital CBDD, 34 (61.8%) had an SI of ≥ 2.32. By contrast, only one of 30 children (3.3%) with obstructive CBDD had such a high SI.

Despite the high specificity of the CBDD SI ≥ 2.32, its low sensitivity means that additional efforts are needed to distinguish between the two types of CBDD in children with SI < 2.32. We observed that anomalous union of pancreaticobiliary duct (APBDU) was very common in congenital CBDD: of the 21 children with congenital CBDD and SI < 2.32, 15 (71.4%) had APBDU. Multivariate analysis revealed that SI ≥ 2.32 (OR = 2.4, 95%CI: 1.2-5.52) and APBDU comorbidity (OR= 5.7, 95%CI: 1.92-24.81) were independent factors that predicted congenital CBDD (Table 2).

The two groups did not differ significantly in terms of any of the other cholangiographic findings. The patients with obstructive CBDD tended to have CBDs with cylindrical-fusiform features more frequently than the patients with congenital CBDD (93.3% vs 78.2%) but this difference did not achieve statistical significance. Moreover, patients with congenital CBDD tended to have cystic features more frequently than the patients with obstructive CBDD (21.8% vs 6.7%) but this too did not achieve statistical significance. The two cases of obstructive CBDD with cystic features had had severe choledolithiasis, which had normalized after endoscopic removal of the stone; recurrence was not observed during the follow-up period. Notably, although choledolithiasis occurred in three-quarters of the children with obstructive CBDD (76.6%), more than half of the congenital CBDD cases (61.8%) also...
Graphic features may be helpful for assessing CBDD, especially for the differential diagnosis of CBDD in children. Firstly, the SI of CBDD was helpful for discriminating congenital CBDD from obstructive CBDD. Secondly, APBDU comorbidity was also an important factor for this differential diagnosis. This had choledolithiasis. Thus, choledolithiasis was not useful for differential diagnosis in CBDD. It was also difficult to differentiate between the obstructive and congenital CBDD patients with SI < 2.32 on the basis of their CBDD features: there were 46 patients with SI < 2.32, of whom 14 had congenital CBDD and 28 had obstructive CBDD. Ten of the 14 congenital CBDD patients (71.4%) and 21 of the 28 obstructive CBDD patients (75%) had cylindrical-fusiform CBDD features. Indeed, in our experience, it was sometimes difficult to differentiate between congenital and obstructive CBDD by only measuring their CBDD diameters (Figure 2).

**DISCUSSION**

The present study indicates that several cholangiographic features may be helpful for assessing CBDD, especially for the differential diagnosis of CBDD in children. Firstly, the SI of CBDD was helpful for discriminating congenital CBDD from obstructive CBDD. Secondly, APBDU comorbidity was also an important factor for this differential diagnosis. This

| Characteristics total (n = 85) | Congenital CBDD ( n = 55) | Obstructive CBDD ( n = 30) | Univariate P value | Multivariate P value |
|--------------------------------|---------------------------|---------------------------|--------------------|----------------------|
| Clinical                       |                           |                           |                    |                      |
| Age, mean ± SD (mo)            | 63.8 ± 36.4               | 82.4 ± 46.0               | NS                 |                      |
| Sex, M:F                       | 11:44                     | 22:8                      | 0.042              |                      |
| Abdominal pain                 | 50 (91.0)                 | 24 (80.0)                 | NS                 |                      |
| Jaundice                       | 23 (41.8)                 | 13 (43.3)                 | NS                 |                      |
| Abdominal mass                 | 2 (3.6)                   | 0 (0)                     | NS                 |                      |
| Vomiting                       | 11 (20.0)                 | 4 (13.3)                  | NS                 |                      |
| Cholangitis                    | 5 (9.0)                   | 1 (3.3)                   | NS                 |                      |
| Pancreatitis                   | 23 (43.6)                 | 9 (30.0)                  | NS                 |                      |
| Cholangiographic               |                           |                           |                    |                      |
| CBD diameter                   | 19.3 ± 9.6                | 12.2 ± 4.1                | NS                 |                      |
| Severity index ≥ 2.32          | 34 (61.8)                 | 1 (3.3)                   | 0.012              | 0.024                |
| Cystic features                | 14 (21.8)                 | 2 (6.7)                   | NS                 |                      |
| Cylindrical-fusiform feature   | 43 (78.2)                 | 28 (93.3)                 | NS                 |                      |
| APBDU                          | 39 (70.9)                 | 0 (0)                     | 0.005              | 0.001                |
| Choledolithiasis               | 34 (61.8)                 | 23 (76.6)                 | NS                 |                      |
| Cholelithiasis                 | 3 (5.5)                   | 7 (23.3)                  | NS                 |                      |
| Pancreatic duct dilatation     | 5 (9)                     | 2 (6.7)                   | NS                 |                      |

APBDU: Anomalous union of pancreaticobiliary duct; CBD: Common bile duct; CBDD: Common bile duct dilatation; NS: Not significant.

**Figure 1** Prevalence of congenital common bile duct dilatation relative to common bile duct severity index. CBDD: Common bile duct dilatation.

**Figure 2** Two children with different etiologies show similarities in terms of endoscopic retrograde cholangiopancreatography findings. A: Congenital common bile duct dilatation (CBDD) with choledolithiasis; B: Obstructive CBDD due to hereditary spherocytosis.
associated complications.

This is the first time that CBDD has been expressed as an SI that incorporated an age-corrected reference. In the present study, the SI of CBDD showed high specificity in terms of differentiating congenital CBDDD from obstructive CBDDD. This indicated the importance of using age-related CBD reference diameters to assess CBDDD in children. Several other studies have also noted this. In a pediatric study of APBDU, most cases of the non-dilated CBD type of APBDU were found to actually have CBDDD when the CBDDD diameter was corrected by an age-related reference. Two TUS studies also provided cut-off CBD diameter references that would allow the identification of CBDDD: 2 mm in neonates and 3 mm in children under 13 years of age. However, when we employed these TUS references in the present study, the congenital CBDDD group could not be differentiated from the obstructive CBDDD group.

It is generally known that APBDU is often accompanied by congenital CBDDD. Although Todani's classification system divides congenital CBDDD into five types, most patients with choledochal cysts have types Ia, Ic, and Ⅳa CBDDD, and all of these types are accompanied by APBDU in almost all adults with this condition: 50%-80% have type I congenital CBDDD while 15%-35% have type Ⅳ congenital CBDDD. Moreover, 76% of children with types I and Ⅳ CBDDD had APBDU. In the present study, APBDU played a critical role in the differential diagnosis of children with cylindrical-fusiform CBDDD. Of the 21 children with congenital CBDDD with SI < 2, 20 (71.4%) had APBDU, which facilitated the differential diagnosis of our patients with cylindrical-fusiform CBDDD.

No consensus has yet been reached regarding the best approach for identifying APBDU and CBDDD in pediatric patients. In addition, APBDU has not been defined in children in relation to the age-corrected size of the common channel. In adults, however, MRCP and endoscopic ultrasonography have been shown to be useful for diagnosing APBDU. One study showed that MRCP diagnosed APBDU in adults with a sensitivity of 83% and a specificity of 90%. Since much less is known about APBDU in children, it is unclear whether ERCDD can be replaced by MRCP in these patients. Indeed, in a study of children with known or suspected APBDU, only 70% were identified by MRCP. The use of endoscopic ultrasonography in children has not been widely established. As a result, ERCDD remains the standard diagnostic modality for biliary disease in children, even though its usefulness is limited in neonates and by ERCDD-associated complications.

While choledolithiasis with congenital CBDDD was initially thought to be rare in Japan, it was then found to be more common than originally believed when it was assessed on the basis of local referral patterns. The present study also showed a high prevalence of choledolithiasis among congenital CBDDD children (61.8%). The rate of this comorbidity may depend on the age at diagnosis and the degree of pathological progression, as evidenced by the fact that adult patients with congenital CBDDD have CBD stones more frequently than pediatric patients (50% vs 28.6%).

In conclusion, the SI of CBDDD, as measured by ERCDD, together with APBDU comorbidity, may aid the differential diagnosis of congenital CBDDD and obstructive CBDDD. However, the study has several limitations. Firstly, it was not adequately powered because of the small cohort size, its retrospective study design, the discrepancy between the numbers of patients in each group, and the etiological heterogeneity of the obstructive CBDDD group. In addition, this study may have been limited by selection bias, namely, patients with more complications tend to be referred to a tertiary hospital. Therefore, it is not yet possible to state conclusively that ERCDD-measured CBD diameter is useful for differentially diagnosing congenital CBDDD in children. However, further study is warranted given that the accurate diagnosis of children with choledochal cyst on the basis of bile duct measurements would facilitate their early and appropriate surgical management and thus result in low morbidity rates and a good prognosis. Given the current scarcity of related studies, a collaborative study that investigates the usefulness of ERCDD for diagnosing children with CBDDD is needed.

**COMMENTS**

**Background**

While the investigation of common bile duct dilatation (CBDDD) in adults focuses mainly on causes of secondary obstruction of common bile duct (CBDDD), congenital CBDDD must be prioritized in the diagnosis of CBDDD in children. ERCDD remains the standard diagnostic modality for CBDDD in children. However, no consensus has been reached regarding the best approach for identifying CBDDD and the diagnosis of CBDDD is based on the morphology of CBD.

**Research frontiers**

No study to measure the diameter of CBD and to adjust its degree of CBDDD according to age has been done in children.

**Innovations and breakthroughs**

This study shows that rather than simple measurement of dilatation of the CBD, a calculated index adjusted for age would be more specific for differentiating obstructive form congenital pathology.

**Applications**

Not only evaluating the morphology of the CBD, but also measuring the diameter of CBD may be helpful in the differential diagnosis of CBDDD in children.

**Terminology**

CBDDD is mainly caused by a congenital anomaly in children, while in adults it is caused by obstruction secondary to cancer and choledolithiasis.

**Peer-review**

This is an interesting concept regarding discriminating between congenital...
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