

Original Article



Perforated Choledochal Cyst: Its Clinical Implications in Pediatric Patient

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Conflict of Interest

The authors have no financial conflicts of interest.

ABSTRACT

Purpose: Perforation of choledochal cyst (CC) is a relatively rare clinical presentation in pediatric populations and difficult to predict preoperatively. We assess the clinical implications by comparing clinical parameters based on a single-center experience between perforated and nonperforated CC to facilitate the appropriate management for future interventions.

Methods: A total of 92 cases of CC in pediatric patients (aged <18 years) who received surgical management between January 2003 and December 2018 at a Pusan National University Children's Hospital were reviewed. After screening the clinical features of perforated cases, we compared the demographic findings, clinical characteristics, and some laboratory results between the perforated and nonperforated groups.

Results: Perforated CC was identified in 8 patients (8.7%), and nonperforated CC in 84 patients (91.3%). Perforation can be classified into three categories: free perforation of cyst (3 cases), pinpoint perforation of cyst (2 cases), and necrotic change of cyst (3 cases). CC perforation occurred significantly more commonly in patients aged <24 months. Clinically, the perforated group showed significantly higher frequency of fever and higher C-reactive protein (CRP) level during the initial visit.

Conclusion: Perforation is more likely to be suspected in patients aged <24 months presenting together with fever and high CRP level in the initial visit. It is also necessary to keep in mind that it indicates not only a possibility of complicated disease status regardless of its association with stones but also a difficulty of applying a minimal invasive procedure and relatively increased length of hospital stay.

Keywords: Perforated; Choledochal cyst; Fever; C-reactive protein; Initial; Visit

INTRODUCTION

Pediatric patients with choledochal cyst (CC) typically present with classic symptoms of abdominal pain in the right upper quadrant, mass, and jaundice. However, some cases are asymptomatic with incidental findings or unusually complicated situations [1,2].

Furthermore, spontaneous perforation of CC is a relatively rare clinical presentation in pediatric populations and difficult to predict preoperatively. It could present as surgical abdomen secondary to bile peritonitis or delayed pseudocyst, which may affect clinical

progress and require an alternative management strategy. Previous studies have suggested several possible causes of perforation, however, a prominent cause remains unclear [3-9].

In this study, we evaluated the clinical characteristics of perforated CC, including its manifestations, basic laboratory findings, and other results related to biliary tract disease and radiologic and operative findings in pediatric patients. Furthermore, this study attempted to assess clinical implications by comparing some clinical parameters between perforated and nonperforated CC to facilitate appropriate management for future interventions.

MATERIALS AND METHODS

Patient selection

We reviewed cases of CC in pediatric patients (age, <18 years) who received surgical management between January 2003 and December 2018 at a Pusan National University Children's Hospital. There were 92 patients with CC during this period, who were classified into two clinical groups: perforated and nonperforated CC. This study was approved by the Institutional Review Board (IRB No. 05-2019-159), and the data were managed with personal information protection.

Evaluation of clinical characteristics and comparison

The current study was retrospectively conducted by reviewing patients' clinical data. We analyzed basic demographic characteristics, including sex, age, and body weight during the surgery, and clinical characteristics including signs and symptoms, laboratory markers, and radiologic findings at the initial visit. After screening the clinical features of perforated cases, we compared the demographic characteristics; clinical findings, such as a presenting symptoms and sign; presence of fever and associated choledocholithiasis; start of diet; and hospital stay between the two groups. Moreover, some laboratory results, including a white blood cell (WBC) count, C-reactive protein (CRP) level, and other parameters associated with biliary tract disease were analyzed.

Statistical analysis

Analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Co., Armonk, NY, USA). Fisher's exact test for comparison of the frequencies of variables and Mann-Whitney U-test for measured laboratory values were performed. A p -value <0.05 was considered statistically significant.

RESULTS

Of 92 patients, 8 (8.7%) had perforated CC, and 84 (91.3%) had nonperforated CC.

Clinical features of perforated CC

The clinical presentation was usually abdominal pain, localized right upper quadrant pain or generalized rigidity, and fever. Surgical management intervals varied from a few hours to 15 days. Radiologic findings, usually via computed tomography, showed massive ascites or localized fluid collection around the subhepatic space in all cases. Additionally, it showed dilatation of the common bile duct in 7 cases and collapsed gallbladder in 4 cases. Combined choledocholithiasis was found in only one case. According to operative findings, perforation

Perforated Choledochal Cyst

Table 1. Clinical features of perforated choledochal cyst

| Case | Sex/age | Main Sx&Sn | Sx duration | Perforation site | Radiologic finding |
|------|---------|---------------------------|-------------|---|--|
| 1 | M/10 mo | Vomiting | 10 d | Ant. wall of the cyst: free perforation | Localized perihepatic fluid collection+CBD dilatation |
| 2 | F/22 mo | Abd pain, fever | 15 d | Necrotic change | GB collapse, ascites |
| 3 | F/18 mo | Rigidity, vomiting, fever | 4 d | CHD necrosis: loss of ductal structure | Massive ascites (+) GB and CBD dilatation Type 1 |
| 4 | F/32 mo | RUQ pain, vomiting, fever | 5 d | Post. wall of the CBD: free perforation | Massive ascites GB collapse Mild dilatation of CBD |
| 5 | F/20 mo | RUQ pain | 2 d | Rt. Lateral: free perforation | Massive ascites GB collapse Type 1 |
| 6 | F/18 mo | Abd pain, diarrhea, fever | 2 d | Ant. wall: pinpoint | Massive ascites Type IV Multiple CBD stones |
| 7 | F/19 mo | Rigidity, vomiting, fever | 4 hr | Rt. post. wall: pinpoint | Massive ascites Type 1 |
| 8 | M/6 mo | Fever | 13 d | Necrosis: loss of structure | Localized fluid collection Collapsed GB |

Sx: symptom, Sn: sign, M: male, F: female, Abd: abdominal, RUQ: right upper quadrant, Ant.: anterior, CHD: common hepatic duct, Post.: posterior, CBD: common bile duct, Rt.: right, GB: gallbladder.

can be classified into three categories: free perforation of cyst (3 cases), pinpoint perforation of cyst (2 cases), and necrotic change of cyst (3 cases). While perforation occurred at any site on the cyst, we could not find any clinical differences according to perforation type. All patients underwent a one-stage operation, cyst excision with hepaticojejunostomy, and had a good clinical course without major complications (**Table 1**).

Comparison between the two groups

In basic demographic findings, there was no significant difference in sex and body weight. Patients were younger in the perforated group than the nonperforated group and a significantly high rate of perforation was seen in patients aged <24 months ($p<0.05$) (**Table 2**).

Table 2. Demographic findings

| Variable | Perforated group (n=8) | Nonperforated group (n=84) | p-value |
|------------------|------------------------|----------------------------|---------|
| Composition | 8.7 | 91.3 | - |
| Sex | | | |
| Male | 2 (25.0) | 13 (15.5) | 0.612 |
| Female | 6 (75.0) | 71 (84.5) | |
| Age (mo) | 19.5±8.7 (6.0–32) | 54.2±52.5 (0–192) | 0.161 |
| Age group | | | |
| Neonate | - | 2 (2.4) | 0.005 |
| Infant (-12 mo) | 2 (25.0) | 21 (25.0) | |
| Childhood | | | |
| -24 mo | 5 (62.5) | 10 (11.9) | 0.005 |
| >24 mo | 1 (12.5) | 51 (60.7) | |
| Perforation rate | | | |
| Neonate | | 0/2 (0.0) | 0.005 |
| Infant (-12 mo) | | 2/23 (8.7) | |
| Childhood | | | |
| -24 mo | | 5/15 (33.3) | 0.005 |
| >24 mo | | 1/52 (1.9) | |
| Body weight (kg) | 10.6±1.5 (5.0–12.1) | 19.2±14.8 (2.4–52.1) | 0.307 |

Values are presented as number (%) or mean±standard deviation (range).

Clinically, the perforated group had a significantly higher incidence of fever during the initial visit (75.0% vs. 10.7%, $p < 0.05$). There were 11 CC cases combined with choledocholithiasis in this study: 1 in the perforated group and 10 in the nonperforated group. However, there was no significant difference between the two groups (12.5% vs. 11.9%, $p = 0.591$). The WBC count and CRP level were higher in the nonperforated group than in the perforated group; however, only the CRP level showed a significant difference. In the perforated group, leukocytosis was not severe. Several laboratory markers related with biliary tract disease, such as aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, bilirubin, amylase, and lipase, were compared to determine any association with CC perforation. All these laboratory markers were elevated in the nonperforated group, despite the lack of significance between the two groups. Postoperatively, there was no significant difference in postoperative fasting time, but the length of hospital stay was significantly longer in the nonperforated group (12.2 days vs. 7.8 days, $p < 0.05$) (Table 3).

By comparing clinical and laboratory parameters, such as age <24 months, presence of fever at the initial visit, and combined choledocholithiasis, we examined the risk ratio for developing CC perforation in both groups (Table 4). The results showed a significantly high risk ratio in cases that presented with fever at the initial visit.

Table 3. Comparison of clinical characteristics between the perforated and nonperforated groups

| Variable | Perforated group (n=8) | Nonperforated group (n=84) | p-value |
|---|-----------------------------|-----------------------------|---------|
| Fever at initial visiting | | | |
| Yes | 6 (75.0) | 9 (10.7) | <0.001 |
| No | 2 (25.0) | 75 (89.3) | |
| Choledocholithiasis | | | |
| Yes | 1 (12.5) | 10 (11.9) | 0.961 |
| No | 7 (87.5) | 74 (88.1) | |
| WBC ($10^3/\mu\text{L}$) (mean 6–12)* | 11.7±6.07 (6.2–23.4) | 11.2±4.7 (5.6–25.7) | 1.000 |
| CRP (mg/dL) (0–0.5)* | 3.4±2.6 (0.36–6.4) | 1.1±1.8 (0.01–9.2) | 0.006 |
| AST (IU/L) (15–60)* | 109.1±95.5 (27.0–289.0) | 144.4±133.9 (18.0–626.0) | 0.533 |
| ALT (IU/L) (13–45)* | 140.3±119.7 (8.0–296.0) | 146.4±135.6 (5.0–566.0) | 0.949 |
| ALP (IU/L) (124–341)* | 654.8±345.3 (279.0–1,191.0) | 769.4±610.0 (186.0–3,042.0) | 0.889 |
| GGT (IU/L) (9–64)* | 282.7±109.7 (204.0–408.0) | 460.6±396.5 (10.0–1,256.0) | 0.516 |
| Bilirubin (mg/dL) (0.3–1.2)* | 2.3±1.4 (0.9–4.2) | 2.8±3.5 (0.25–15.1) | 0.422 |
| Amylase (IU/L) (22–80)* | 205.5±206.3 (6.0–583.0) | 371.7±674.1 (2.5–3,492.0) | 0.924 |
| Lipase (IU/L) (7–39)* | 438.0±340.6 (127.0–923.0) | 977.3±1,474.1 (7.0–5,944.0) | 0.927 |
| Postoperative fasting time (d) | 3.9±1.3 (2.0–8.0) | 3.5±1.1 (2.0–6.0) | 0.876 |
| Length of hospital stay (d) | 12.2±4.6 (8.0–22.0) | 7.8±1.2 (6.0–10.0) | 0.001 |

Values are presented as number (%) or mean±standard deviation.

WBC: white blood cell, CRP: C-reactive protein, AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, GGT: gamma-glutamyl transferase.

*Reference value.

Table 4. Predictable value of perforated choledochal cyst

| Variable | Perforated group (n=8) | Nonperforated group (n=84) | Odds ratio | 95% Confidence interval |
|-----------|------------------------|----------------------------|------------|-------------------------|
| Age group | | | | |
| <24 mo | 7 | 33 | 9.8 | 1.153–83.271 |
| >24 mo | 1 | 51 | | |
| Fever | | | | |
| Yes | 6 | 9 | 25.0 | 4.374–142.9 |
| No | 2 | 75 | | |
| Stone | | | | |
| Yes | 1 | 10 | 1.057 | 0.118–9.51 |
| No | 7 | 74 | | |

DISCUSSION

CC perforation with subsequent bile peritonitis is a rare clinical presentation in pediatric patients. Its incidence has been known to range between 1.8% and 12.2% in the reported literature [3,4,10-12]. The present study showed 8 cases of perforation (8.7%) that could be classified into three different types without a predilection site: free perforation of cyst (3 cases), pinpoint perforation of cyst (2 cases), and necrotic change of cyst (3 cases). However, there was no significant clinical difference in the location or type of perforation, which may be attributed to the small number of available cases. Therefore, it would be necessary to increase the sample size and prolong the duration of such a study to better determine the nature of CC perforation prevalence in pediatric patients. Nonetheless, it has been generally accepted that CC is more prevalent in teenage girls, aligning with our findings, which also revealed greater number of female patients in both the perforated and nonperforated groups. There were no significant differences in age between the two groups ($p=0.161$) although patients in the nonperforated group were older (54.2 ± 52.5 vs. 19.5 ± 8.7 months). Additionally, there was no significant difference in body weight at the time of the surgery. In this study the oldest patient in the perforated group was aged 32 months. When considering the age of the patients in this study, we could identify a significantly high perforation rate in patients aged <24 months and a rare occurrence of perforation in older patients ($p=0.005$).

To date, risks or predisposing factors causing CC perforation have not been well established. We presume that there are three main possible causes related to perforation. First, the impacted plug in the bile duct and consequent intraluminal high pressure may result in perforation of the fragile cystic wall [3-5]. Considering the physiological characteristics of CC, multiple stones in the distal portion of the cyst and fibrosis or inflammation can be predisposing factors of perforation. The authors investigated the association of stone formation in all cases but could not find a significant relationship between perforation and presence of stone in this study ($p=0.591$). Moreover, CC perforation may be further characterized using the Todani classification, which we were unable to do because we could not primarily determine the type of perforation. The second possible risk factor for perforation is pancreaticobiliary malunion (PBM), which may exacerbate the development of CC [3,6,7]. Although we believed that the relationship between PBM and perforation is significant, we could not present such results in this study group due to its retrospective design, rendering the comparison between the two patient groups unfeasible. The third risk factor for perforation is related to the anterior wall of the common bile duct, which is more susceptible to an ischemic event due to anatomical impairment leading to poor blood supply, only from the marginal artery. In the event of hypoperfusion, it may cause focal ischemia of the common bile duct wall and perforation in severe situations [8,9].

Clinically, a perforated CC usually manifests as a form of bile peritonitis, in which most of our cases showed signs and symptoms of peritonitis, such as generalized abdominal pain and fever. These clinical manifestations are nonspecific, so it is difficult to confidently attribute them to this specific disease. However, there were significantly more patients with fever at the initial visit in the perforated group, which together with younger age may be clinically important. When fever and leukocytosis are simultaneously present, it is usually considered a result of an inflammatory reaction, but the WBC count was not greatly increased to signify inflammation, despite perforation. Thus, a significantly higher CRP level seems to suggest its clinical implication in the perforated group. Besides, laboratory results for biliary tract disease markers did not show significant differences between the two groups in this study,

although most results showed higher levels of the respective biomarkers in the nonperforated group. This might be a result of a transient change due to improvement of bile flow after perforation. In the management of both groups, all patients showed a favorable course after primary one-stage operation irrespective of disease status, as reported in previous studies [13,14]. However, the length of hospital stay was significantly longer in the perforated group in the present study. Because we managed the perforated group by open surgical procedure, it implies the poor likelihood of applying a minimal invasive surgical procedure for CC perforation and might affect the length of hospital stay.

This study was limited by the small number of perforated cases in a single institution and the comparison of limited data due to its retrospective design. A greater number of cases to further validate the clinical implications of our results are necessary in the future.

In conclusion, CC perforation is more likely to be suspected in younger patients, especially those aged <24 months, who present with fever and high CRP level during the initial visit. Furthermore, considering the management for, it is necessary to keep in mind that perforated CC not only implies a complicated disease status regardless of its association with stones but also poses the challenge of using minimal invasive procedure to reduce the associated length of hospital stay.

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