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Choledochal cysts in children: Intrahepatic ductal dilatation does not indicate true intrahepatic biliary duct disease

BILIARY

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Original Article

ABSTRACT

Background/Aims: Choledochal cysts (CCs) are rare abnormalities of the biliary tract. Presenting our clinical experience with CCs herein, we aimed to identify if intrahepatic ductal dilatation indicates true intrahepatic biliary duct disease.

Materials and Methods: We retrospectively reviewed all cases of CCs in children diagnosed at a single center (Başkent University Faculty of Medicine, Department of Pediatric Surgery) institution from 2005 to 2015.

Results: Of 18 patients with CCs, 7 were males (39%). The age range was 3 months to 17 years (mean age, 6.2±3.8 years). Intrahepatic bile duct dilatation was detected in 13 (72%) patients by preoperative scanning. Type I, II, III, and IVA cysts were diagnosed in 13, 1, 1, and 3 patients, respectively. In all patients, total cyst excision and Roux-en-Y hepaticoenterostomy were performed.

Conclusion: In this study, most intrahepatic ductal dilatations seen on preoperative imaging were thought to be caused by a distal obstruction, not true intrahepatic biliary duct disease. This study supports the hypothesis that preoperatively distinguishing between type I and type IVA CCs is not necessary; it does not affect the initial treatment. We consider that complete cyst excision with Roux-en-Y hepaticojejunostomy is safe and should be performed soon after diagnosis, irrespective of symptom severity to avoid future complications.

Keywords: Choledochal cysts, Roux-en-Y hepaticojejunostomy, intrahepatic dilatation

INTRODUCTION

Choledochal cysts (CCs) are rare cystic dilatations of the extrahepatic biliary tree, intrahepatic biliary tree, or both. Although the incidence of CCs is as high as 1 in 1000 in the Asian population, it is only 1 in 100,000 to 1 in 150,000 in the Western population (1). In Asia, approximately two-thirds of CC diagnoses occur in Japan (2). The reason for this geographic distribution is unknown.

The etiology of CCs remains under speculation, and many theories and explanations have been proposed (1). However, Babbitt's theory remains the most popular and widely accepted (2). This theory attributes CC formation to the presence of an abnormal pancreaticobiliary duct junction outside the ampulla of Vater, resulting in a long common channel that allows the reflux of pancreatic juice into the bile duct. This reflux in turn activates pancreatic enzymes, causing inflammation and weakness of the bile duct wall and leading to cyst formation (2).

The Todani classification system of CCs is widely accepted and currently used (2). Type I CCs, the most common type, are characterized by dilatation of the extrahepatic biliary tree. This differs from type IV CCs, which lack intrahepatic ductal involvement (3). Type IVA CCs are characterized by multiple cystic dilatations of the intra- and extrahepatic ducts. Type IVA CCs are defined as the presence of multiple segmental communicating biliary dilatations located in the intra- and extrahepatic biliary tracts (4) and relative stricture at the junction (5). Type IVB CCs involve multiple dilatations of the extrahepatic ducts (6). Complications and follow-up are considered to differ between type I and IVA CCs (6). Type II CCs are discrete diverticula of the extrahepatic ducts with a narrow stalk connection to the common bile duct. Type III CCs, also called choledochoceles, are characterized by

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distal common bile duct dilatation confined to the wall of the duodenum, often bulging into the duodenal lumen. Type V CCs occur in patients with Caroli disease, which is characterized by multiple saccular or cystic dilatations of the intrahepatic bile ducts.

Patients with cystic dilatation of the biliary tract are predisposed to biliary stasis, which leads to repeated cholangitis, stone formation, and ultimately to secondary biliary cirrhosis. Moreover, the tendency of cholangiocarcinoma development in these abnormal biliary tracts is well documented. At present, all surgeons agree that patients with CCs require complete cyst excision (4). However, the need to preoperatively distinguish between type I and IVA CCs is controversial not only because it is difficult to preoperatively predict true intrahepatic involvement but also because distinguishing between these CCs does not affect the initial treatment (6).

We aimed to identify that most of the intrahepatic ductal dilatation seen on preoperative imaging is caused by distal obstruction, not true intrahepatic biliary duct disease.

MATERIALS AND METHODS

This study was conducted at Başkent University Medical Faculty after the approval of the ethical committee and is in conformance with the Declaration of Helsinki. All parents of patients provided informed consent for this study. Medical records were retrospectively reviewed for all patients who underwent surgical resection of CC at a tertiary center (Başkent University Faculty of Medicine, Pediatric Surgery Clinic) from January 2005 to April 2015. No patient who underwent CC excision during the study period was excluded. Data collected included sex, age, presenting symptoms, preoperative laboratory and imaging study results, preoperative diagnosis (cyst type), operation performed, postoperative complications, follow-up length, and postoperative imaging and laboratory study results. All preoperative imaging reports were reviewed, including ultrasound (US), computed tomography (CT), endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance cholangiopancreatography (MRCP), and gastrointestinal contrast studies. The classification of CC type was based on the surgeon's and radiologist's interpretation of the preoperative images. The cysts classified as Todani and type IVA choledochal cysts were defined as the presence of segmental communicating biliary dilatations located in the intra- and extrahepatic biliary tracts based on preoperative imaging studies and intra-operative exploration. Acquired dilatations of the intra- and/or extrahepatic biliary tree induced by proximal biliary obstruction, such as stricture or obstructive primary biliary stones, were excluded. Also excluded were those patients with a dilated extrahepatic bile duct that continuously extended to the intrahepatic main biliary convergence without a clear demarcation between non-dilated hepatic or sectorial ducts and diseased biliary divisions. Patients with type I, II, III, or IVA disease underwent complete excision of the extrahepatic biliary tree with widely patent hepaticoenterostomy. All perioperative care was provided by the pediatric surgery service.

Statistical analysis was performed using Microsoft Office Excel version 2007, (Microsoft Corporation; Redmond, WA, USA). All numerical data are expressed as mean values±SD or as proportions.

RESULTS

In total, 18 patients (7 males and 11 females) were evaluated. The patients' ages ranged from 3 months to 17 years (mean age, 6.2±3.8 years). Three (17%) patients were younger than 1 year. Although all patients presented with abdominal pain, the classic triad (recurrent episodes of jaundice, right upper quadrant pain, and a palpable mass in the right upper quadrant) was detected in only 4 (22%) patients; the mean age of these patients was 2.4±1.1 years.

Laboratory findings demonstrated normal hemoglobin, thrombocyte, and blood coagulation parameters. The C-reactive protein level was elevated in 4 patients. Four patients had elevated levels of direct bilirubin, alanine transaminase (ALT), and aspartate transaminase (AST), and 9 had elevated levels of ALT and AST. The blood amylase level was elevated in 2 patients (Table 1).

Ultrasound was used in the initial evaluation of all patients. Biliary stones and intrahepatic bile duct dilatation were additionally detected in 9 (50%) and 13 (72%) patients, respectively. MRCP was performed in all patients as an additional imaging modality and confirmed the presence of intrahepatic dilatation in 13 patients in whom dilatation was initially detected by US. Thirteen of the 18 patients had intrahepatic ductal dilatation on preoperative imaging, but the dilatation in 10 of these patients was thought to be caused by distal obstruction, not true intrahepatic disease, according to the presence or absence of segmental communicating biliary dilatations located in the intra- and extrahepatic biliary tracts and relative stricture at the junction (Table 2) (6,7). Additionally, in 7 patients, acquired dilatations of the intra- and/or extrahepatic biliary tree induced by distal biliary obstruction, such as stricture or obstructive primary biliary stones, were shown by percutaneous transhepatic cholangiography (PTC). For this reason, only 3 patients were diagnosed with type IVA CCs (Figure 1), and the intrahepatic dilatations were completely resolved following operative resection. We performed CT and an upper gastrointestinal contrast study in only 1 patient to rule out a duodenal duplication cyst (Figure 2). Thirteen patients (72.2%) had a type I CC, 1 (5.5%) had a type II CC, 1 (5.5%) had a type III CC, and 3 (16.7%) had a type IVA CC. Percutaneous transhepatic biliary drainage followed by cholangiography was performed in 7 patients in the interventional radiology department, and it revealed either cholangitis or obstructive jaundice (Figure 3).

In all patients, total cyst excision and Roux-en-Y hepaticoenterostomy were performed through open surgery.

Table 1. Laboratory test results

Age (years)	Amylase (30.00–110.00 U/L)	CRP (0.00–6.00 mg/L)	Direct bilirubin (0.10–0.50 mg/dL)	Total bilirubin (0.40–1.35 mg/dL)	AST (10.00–42.00 IU/L)	ALT (10.00–60.00 IU/L)	ALP (80–350 IU/L)	Biliary drainage
0.25	45.00	5.0	**5.60**	**7.40**	**319**	**211**	**787**	+
0.83	60.00	3.0	0.40	5.50	31	12	200	
1.00	50.00	3.0	**4.60**	**6.20**	**261**	**300**	**1164**	+
1.50	51.00	3.0	0.10	0.40	32	20	223	
1.50	**136.00**	3.0	0.30	0.40	59	64	89	
3.00	50.00	3.0	0.10	0.40	23	11	241	
3.00	75.00	**45.0**	0.40	0.60	**53**	**109**	231	+
5.00	30.00	3.0	0.20	0.40	**104**	**113**	214	
7.00	45.00	3.0	0.10	0.40	18	10	110	
7.00	60.00	3.0	0.40	0.30	18	22	120	
8.00	40.00	3.0	0.20	0.40	**62**	**108**	190	
8.00	40.00	2.6	0.60	1.30	**372**	**236**	416	+
8.00	80.00	3.0	0.80	1.40	60	65	80	
10.00	50.00	**13.0**	**12.00**	**13.00**	**153**	**205**	205	+
10.00	60.00	3.0	0.10	0.40	**141**	**213**	495	+
10.00	40.00	3.0	0.40	0.20	10	20	100	
12.00	**318.00**	**21.0**	0.50	1.00	17	12		
17.00	33.00	**320.0**	**6.05**	**6.44**	**170**	**230**		+

CRP: C-reactive protein; AST: aspartate transaminase; ALT: alanine transaminase; ALP: alkaline phosphatase
The boldfaced numbers indicate levels exceeding the high end of the reference range.

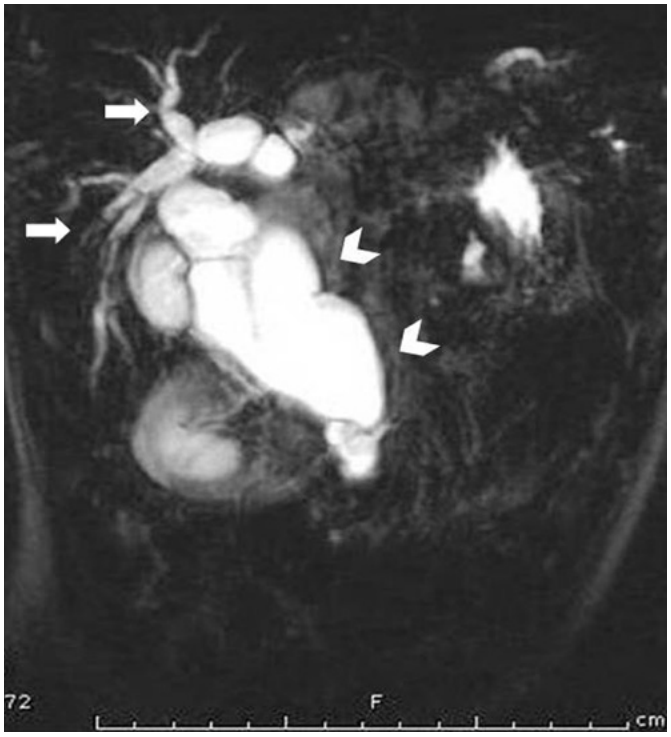

Figure 1. Magnetic resonance cholangiopancreatography maximum intensity projection images showed combined intrahepatic (arrows) and extrahepatic duct (arrow heads) dilation.

The gallbladder was dissected to assist with the dissection of the cyst from the portal vein and hepatic artery. The cyst was dissected from the liver hilum down to the retroduodenal part of the bile duct. The cystic bile duct was ligated at the most distal level, excised, and reflected up toward the porta hepatis. The whole segment comprising the cystic bile duct, cystic duct, gallbladder, and part of the common hepatic duct was excised. A Roux-en-Y jejunal loop was prepared 40-cm distal to the ligament of Treitz. The proximal limb of the Roux-en-Y loop was carried in a retrocolic fashion to the liver hilum to reach the common hepatic duct. An end-to-side hepaticojejunostomy was performed with interrupted mucosa-to-mucosa Vicryl sutures (Figure 4). The abdominal incision was closed with drain placement, and the excised specimen was sent out for histopathological examination. The operative time ranged from 150 to 300 min (mean, 218±44 min). Operative times were particularly longer in patients with a history of repetitive cholangitis attacks than in asymptomatic patients. Histopathological examination of the excised tissues confirmed the diagnosis of a benign CC involving the common bile and hepatic ducts with a normal gallbladder tissue.

All patients were postoperatively followed-up by laboratory and US examinations. Ileus and bile leakage were detected

Table 2. Patient's clinical presentation, age, radiologic tests showing biliary abnormality, bile duct size (mm) compared with normal ranges of bile ducts by age

				MRCP					PTC		Other image		
Age	Gender	Clinic	Type	Gallbladder	Stone/sludge in the biliary tract	Intrahepatic bile duct dilatation	CBD (mm)	*CBD normally range for age (mm)	Obstruction	Drain	CT	GIS contrast study	USG
0.25	Female	Classical triad	I	Normal	No	Yes	10	<2	+	+	-	-	+
0.83	Female	Abdominal pain	IV-A	Normal	No	Yes	35		-	-	-	-	+
1	Female	Classical triad	I	Normal	Yes	Yes	21		+	+	-	-	+
1.5	Female	Abdominal pain	I	Normal	Yes	Yes	8		-	-	-	-	+
1.5	Female	Classical triad	I	Normal	Yes	No	46		-	-	-	-	+
3	Male	Abdominal pain	I	Normal	Yes	Yes	16	<4	-	-	-	-	+
3	Female	Classical triad	I	Normal	Yes	Yes	15		+	+	-	-	+
5	Male	Abdominal pain	II	Normal	No	No	100		-	-	-	-	+
7	Female	Abdominal pain	I	Normal	No	Yes	25		-	-	-	-	+
7	Male	Abdominal pain	I	Hydropic	Yes	Yes	26		-	-	-	-	+
8	Female	Abdominal pain/jaundice	I	Normal	Yes	Yes	30		-	-	-	-	+
8	Male	Abdominal pain/jaundice	IV-A	Normal	No	No	75		+	+	-	-	+
8	Male	Abdominal pain	I	Hydropic	No	Yes	16		-	-	-	-	+
10	Male	Abdominal pain	I	Hydropic	Yes	Yes	11		+	+	-	-	+
10	Female	Abdominal pain	IV-A	Normal	No	Yes	65		+	+	-	-	+
10	Female	Abdominal pain	I	Normal	No	No	14		-	-	-	-	+
12	Male	Abdominal pain	III	Normal	No	No	38		-	-	+	+	+
17	Female	Abdominal pain	I	Hydropic	Yes	Yes	37	<7	+	+	-	-	+

MRCP: magnetic resonance cholangiopancreatography; PTC: percutaneous transhepatic cholangiography; CT: computed tomography; USG: ultrasound; CBD: common bile duct
Classical triad. Recurrent episodes of jaundice, right upper quadrant pain, and a palpable mass in the right upper quadrant
*The normal range of CBD size depends on age. Siegel stated that the normal CBD size should be <2 mm in infancy, <4 mm in childhood, and <7 mm after adolescence (7).

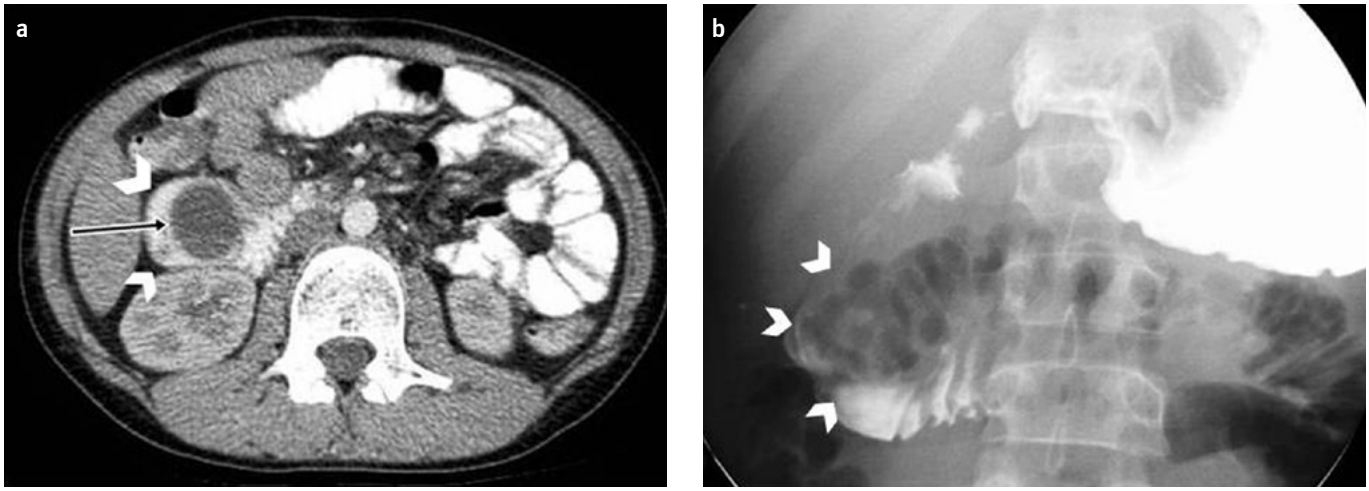

Figure 2. a, b. Abdominal computed tomography revealed a slightly thick-walled, well-defined, 52×38×27-mm cystic mass (long arrow) protruding into the second portion of the duodenum (arrow heads) (a), a gastrointestinal contrast study revealed an obscure limited filling defect that was considered to represent external compression at the medial and second portions of the duodenum (arrowheads) (b), the compression did not result in a significant obstruction.

in the early postoperative period in 1 patient each. Although the ileus was conservatively treated, the bile leakage required reoperation. The average duration of the hospital stay was 7.6 days, excluding the reoperation that was required for the patient with prolonged bile leakage. The patients were followed up for 6 months to 9 years (mean, 4.19±2.50 years) with US imaging and liver function testing. There were no long-term complications.

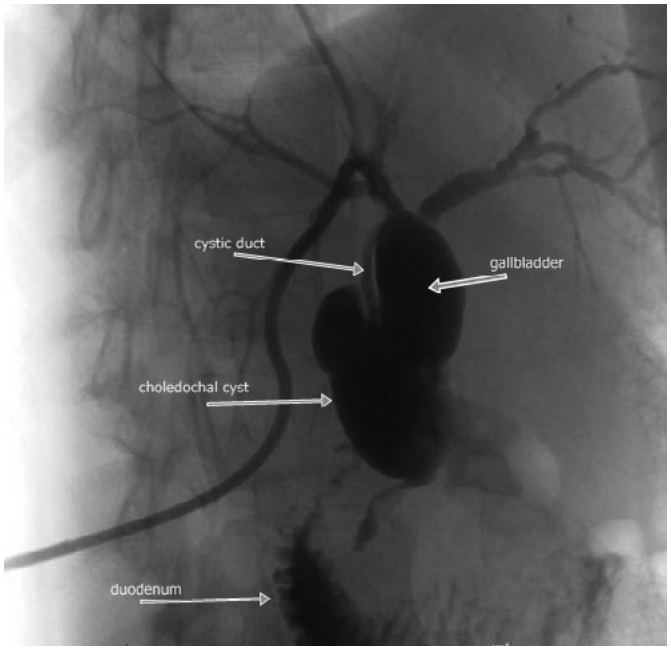

Figure 3. Ultrasound-guided, contrast-enhanced transhepatic cholangiographic images were obtained. The right and left main hepatic ducts were dilated. Cystic dilatation of the proximal choledochal duct and transition of contrast media to the intestine were observed.

DISCUSSION

As previously described, there is a great preponderance among the Asian population to CCs (1). The reason for this remains unclear, although similar diet- or lifestyle-related factors among Asians may contribute to the development of CCs. Literature also supports a female preponderance to biliary cystic disease, commonly reported in a female:male ratio of 4:1 (1). This sex distribution was echoed in the present study but at a slightly lower ratio of 1.6:1.0.

Abdominal pain is the predominant clinical feature in patients with CC and is caused by bile and pancreatic juice reflux and bile stasis, which lead to chronic inflammation and stone and stricture formation (1). However, the classic triad of abdominal pain, jaundice, and a palpable mass was found in only 22% of the patients in the present study. In the reported literature, the classic triad was found in <20% of patients, and most were <1 year old (1). Comparable results were found in our study; 2 of 4 (50%) patients were less than 1 year old.

Although Todani initially felt that the different types of CC represented a spectrum of the same condition, subsequent authors have stated that each type represents a unique condition with a separate etiology, clinical course, and optimal treatment (8). The breakdown of cyst types seen in our series is similar to that established in literature, including other North American series (5). The most common types were I and IVA. Interestingly, although mostly type I and IVA CCs have been previously reported in the pediatric population (1), type II and III CCs were also seen in our study.

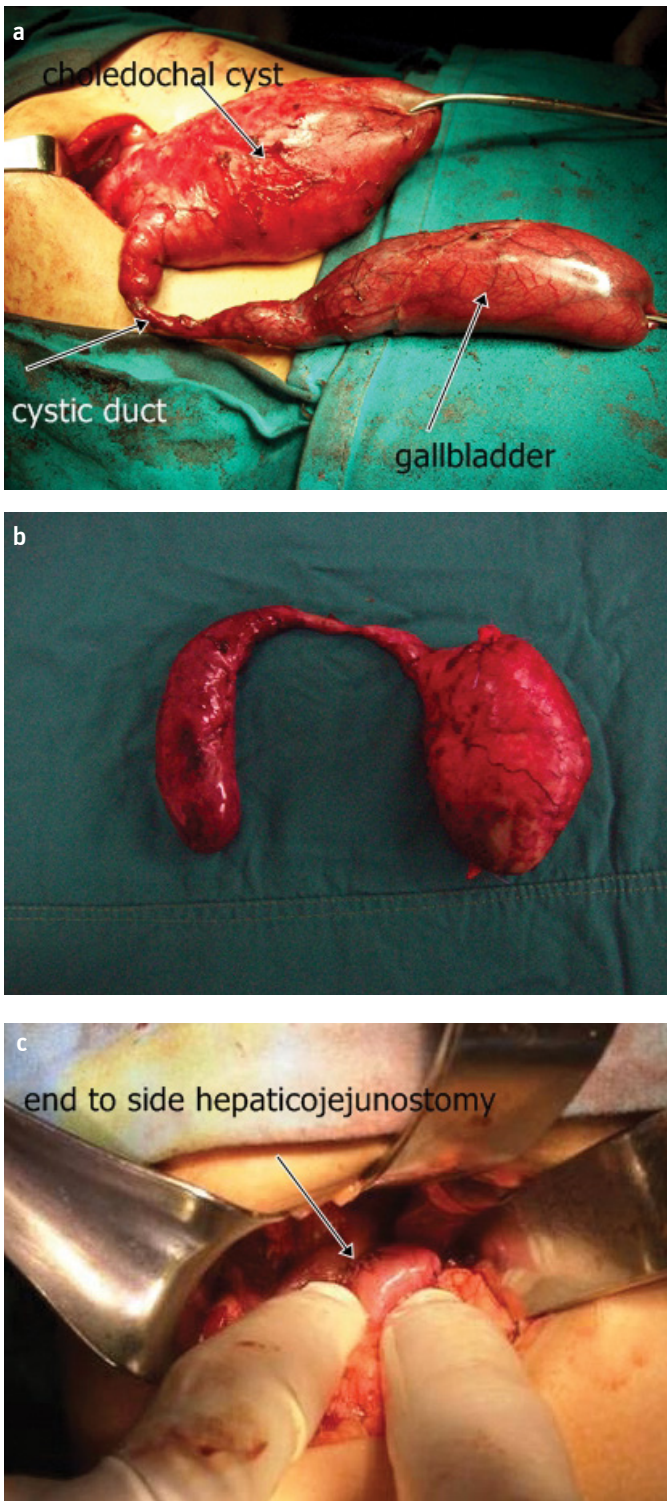

Figure 4. a-c. The whole segment comprising the cystic bile duct, cystic duct, gallbladder, and part of the common hepatic duct was excised, and Roux-en-Y hepaticoenterostomy was performed. A Roux-en-Y jejunal loop was prepared 40-cm distal to the ligament of Treitz. The proximal limb of the Roux-en-Y loop was carried in a retrocolic fashion to the liver hilum to reach the common hepatic duct (a, b), an end-to-side hepaticojejunostomy was performed with interrupted mucosa-to-mucosa Vicryl sutures (c).

Ultrasound is the initial imaging modality of choice for children, whereas ERCP is most commonly used in adults (1). ERCP is difficult to perform in young children and infants because it requires

special equipment and expertise that are unavailable at many institutions (9). In contrast, percutaneous transhepatic cholangiopancreatography is preferred when ERCP is unsuccessful or technically infeasible (10). However, both these procedures are invasive and carry a risk of complications (11). In our study, US was used as the initial imaging technique in all patients with MRCP. MRCP is an innovative technique for evaluating the biliary tree and pancreatic duct (11). The advantages of MRCP are that it is noninvasive, requires no contrast material, is performed without ionizing radiation, and can be performed on an outpatient basis. Its safety is deemed comparable with that of US (12). MRCP was performed in all patients as an additional imaging modality and had a sensitivity of 100% and specificity of 100% (Figure 3). However, more evaluation methods need to be performed to assess the MRCP ability to detect abnormal pancreaticobiliary junctions (APBJs) and choledochoceles. ERCP should be used when MRCP inadequately visualizes the terminal common bile duct or pancreaticobiliary duct junction or when a therapeutic procedure is anticipated (13). Additionally, we performed CT and an upper gastrointestinal contrast study in 1 patient to rule out a duodenal duplication cyst.

The standard treatment for type I and IVA CCs is complete cyst excision and reconstruction with hepaticojejunostomy (5); this was performed in all our patients. Although Roux-en-Y hepaticojejunostomy is considered to be the gold standard treatment by many conventional surgeons, hepaticoduodenostomy has gained popularity in recent years. When compared with hepaticojejunostomy, some advantages of hepaticoduodenostomy include a shorter operative time, shorter hospital stay, and lower chance of postoperative adhesions; however, a disadvantage is the development of reflux/gastritis. Although we are unable to directly compare the two surgeries, no problems were observed in the long-term follow-up of patients who underwent Roux-en-Y hepaticoenterostomy in the present study. It seems that further studies are needed to compare the two procedures (14). There is in fact another uncertainty regarding the management of type IVA CCs with extensive involvement of the intrahepatic ducts. If cystic disease is present within the liver, treatment options include extrahepatic biliary tree excision, partial hepatectomy if the disease is confined to a single lobe, or liver transplantation if the disease is bilaterally present (5). However, as previously reported (6), we found that the excision of the extrahepatic portion of the cyst with wide hepaticoenterostomy provides adequate drainage and that the intrahepatic dilatation regressed in all 13 affected patients (100%) in the present study. Postoperatively, one case each of ileus and anastomosis leakage was observed as a short-term complication; however, no long-term complications such as cholangiocarcinoma were noted. Based on the findings of the present study and our overall experience with type I and IV CCs, complete excision with Roux-en-Y hepaticojejunostomy is recommended for all patients with CC. Confirming the information above, the US findings of 3 patients with type IVA CCs showed resolution of the intrahepatic dilatation.

Laparoscopic surgery has recently gained popularity in many fields in addition to the treatment of CCs. However, laparoscopic procedures have a higher level of difficulty than open laparotomy procedures; this is especially true for hepaticojejunostomy (15).

The most serious complications of CCs are cholangitis and biliary cirrhosis, the risks of which increase with an increasing duration and degree of obstruction prior to surgery and following inadequate therapy. We encountered CC-related cholangitis before surgery in 35% of the patients, but no cirrhosis (16). We found stones within the cysts, gallbladder, or both in 50% of the patients, which is higher than the rates reported in literature (8%–26%) (16). This finding is considered to have been associated with the long duration between symptom onset and surgery. No long-term complications were observed in this study, including anastomotic stricture, malignancy, or recurrent cholangitis. We found that the longer the bile stasis and resultant inflammation are allowed to continue, the greater are the risks of fibrosis and adhesion formation, which increase the difficulty of achieving complete excision. When we examined the patients with longer surgery times in detail, we found that they were symptomatic throughout numerous preoperative inflammatory episodes. In this study, 8 (44%) patients' surgery lasted for more than 4 h. Therefore, we recommend that surgery should be performed as soon as possible after the diagnosis of CCs to prevent fibrosis, avoid ongoing inflammation, and facilitate subsequent surgery (1).

The main limitations of this study are its retrospective nature, the fact that it was conducted in a single center, and the inclusion of only Turkish patients.

In conclusion, in this study, we retrospectively analyzed a series of patients in a single tertiary center in Turkey, outside of Asia. We consider that MRCP, with sensitivity (100.0%) and specificity (100.0%), is useful in CC imaging, may replace intraoperative cholangiography, in both preoperative and postoperative follow-up as a noninvasive diagnostic approach. The intrahepatic ductal dilatation seen on preoperative imaging in the present study was thought to have been caused by distal obstruction and not true intrahepatic biliary duct disease. The need to preoperatively distinguish between type I and IVA CCs is controversial because for both, complete excision of the extrahepatic bile duct with wide hepaticoenterostomy and intensive long-term follow-up remains the standard of care at our institution. We recommend complete cyst excision and Roux-en-Y hepaticojejunostomy early after the diagnosis of CC. This is still preferred by most surgeons.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Başkent University Medical Faculty.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.Ö.G.; Design - H.Ö.G.; Supervision - P.O.; Resource - E.İ.; Materials - E.İ.; Data Collection and/or Processing - A.T.; Analysis and/or Interpretation- S.E.; Literature Search - H.Ö.G.; Writing - H.Ö.G.; Critical Reviews - A.H.

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