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Short Communication

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Pitfalls and fatal complications after iterative endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography management of biliary tract cysts. When to do open surgery (cyst resection; hepaticojejunostomy) or liver transplant?

Andrea Cariati, Giuliano Bottino, Pietro Diviacco, Antonella De Negri, Eva Moraglia, Valerio Belgrano, Irene Leale, Elisa Piromalli, Rosario Fornaro, Mauro Nahun, Enzo Andorno

ABSTRACT

Biliary tract cysts are a group of rare congenital diseases that have been classified by Todani in 8 types. Hepaticojejunostomy has been the preferred intervention for Type I and IV biliary cysts. It has been postulated that, due to the low incidence of cancerization of Types II and III biliary cysts, a less invasive approach could be suggested, namely cyst resection in Type II, and endoscopic sphincterotomy with opening of choledochocele in small (<3 cm) Type III cysts from old patients. Moreover, Caroli disease has been proposed to be treated by percutaneous biliary drainages. The aim of the present study is to propose the therapeutics strategies to follow for the management of biliary tract cysts, in case of failure of percutaneous transhepatic cholangiography (PTC) and endoscopic retrograde cholangiopancreatography (ERCP). From 2008 to May 2014, three patients with congenital biliary tract cysts were followed. Two patients were found to be affected by bilateral liver Caroli disease and another young patient was found to be affected by a Type III biliary cyst (choledochocele). Patients affected by Caroli disease presented cholangitis, jaundice and fever and have been submitted to PTC. PTC, after an initial brief relief of the symptoms, failed in both cases. One of these patients with recurrent post PTC cholangitis was then successfully treated by orthotopic liver transplant. The other patient affected by Caroli disease died after multiple PTC. The young patient affected by choledochocele suffered from pancreatitis and jaundice and was submitted to ERCP. Endoscopic resection of choledochocele was followed by hemorrhagia and a fatal fungal sepsis. Minimally invasive approaches have been widely used in the management of biliary tract cysts. Diffuse bilateral Caroli disease of the liver can be initially managed by percutaneous drainage but if cholangitis recurs, in our opinion, it is useful to consider an open surgery procedure such as orthotopic liver transplant. Type III biliary cyst (choledococele) can be managed by ERCP if patient is old and the cyst is small (<3 cm) but when the cyst is larger than 3 cm, symptomatic, and the patient is young, one approach to take into consideration is open duodenostomy with choledochocele resection and reimplantation of the common bile and of Wirsung ducts into the duodenal mucosa.

Key words: *Biliary tract cysts, Caroli disease, choledochocele, endoscopic retrograde cholangiopancreatography, duodenostomy, percutaneous transhepatic cholangiography, orthotopic liver transplant*

Introduction

Biliary tract cysts account for the 1% of benign biliary diseases and have been generally considered to be of congenital origin. Biliary cysts occur most frequently in females (female:male ratio; 3-4:1) and in Asia (10 times more frequent than in Western countries). The most widely accepted theory about congenital biliary tract cysts is the "common channel" Babbitt's theo-

Author affiliations : *Department of General Surgery, Hepato-Biliary-Pancreatic Surgery and Liver Transplantation Surgical Unit, A.O. San Martino, IST, University of Genoa, Italy*

Correspondence : *Andrea Cariati, MD, Hepatobiliarypancreatic Surgery and Liver Transplant Unit, General Surgery Dept, A.O. San Martino, IST, University, Genoa, Italy. e-mail: andrea.cariati@libero.it*

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ry, who stated that cystic dilation of the biliary tract resulted from an abnormal pancreaticobiliary junction of biliary and pancreatic ducts outside the ampulla of Vater that lead to the mixture of pancreatic and biliary juices within the biliary tract. Chronic activation of pancreatic enzymes causes inflammation of biliary tract wall that deteriorates and becomes enlarged [1]. A long common pancreatobiliary channel is "an external junction of the pancreatic and biliary ducts in the duodenum, apparently beyond the scope of intramural sphincter function [2]. These malformations have been classified using Todani's modification [3] of Alonzo-Lej classification [4]and comprise eight variants [3]. The most frequent clinical findings are jaundice, abdominal pain, abdominal mass and fever. Symptoms often result from complications such as: Cholangitis, choledocholithiasis, hepatolithiasis, pancreatitis, hepatic abscess, biliary cirrhosis and cholangiocarcinoma [5]. Diagnostic evaluations comprise laboratory investigation (serum bilirubin, alkaline phosphatase, gamma-glutamyltranspeptidase, alanine and aspartate aminotransferase, amylase, reactive C protein), abdominal ultrasound, computed tomography, magnetic resonance and cholangiopancreatography imaging [5,6]. In addition, endoscopic retrograde cholangiopancreatography (ERCP) is an invasive investigation, widely used, that has a therapeutic possibility in small Type III (choledochocele) biliary tract cysts [7]. Percutaneous transhepatic cholangiography (PTC) is useful in intrahepatic biliary tract dilatations and allows to drain infection, remove intrahepatic gallstones and to plan liver resection [5]. However, there is still a debate about the role of ERCP, PTC or magnetic resonance in the diagnosis of biliary tract cysts [5,8]. In particular, it is necessary to delineate when to stop with iterative therapeutic actions of ERCP and PTC and to switch to open surgery options. The aim of this study is to report a cases series and to propose the therapeutic strategies to follow in case of failure of PTC and ERCP.

Case Reports

From 2008 to May 2014 three patients with congenital biliary tract cysts have been observed in General Surgery Department of San Martino, IST, University Hospital of Genoa, Italy.

Case 1

A 17-year-old male was admitted to the emergency department because of jaundice, abdominal pain and pancreatitis. Laboratory examinations, ultrasonography and abdominal computed tomography (CT) demonstrated an acute pancreatitis with congenital absence of the right kidney and the presence of a large (>3 cm) Todani Type III biliary tract cyst (choledochocele) (Figure 1). Magnetic resonance imaging confirmed diagnosis (Figure 2) and ERCP was advocated to complete diagnosis and to try to remove choledochocele. Unfortunately, ERCP was not completely performed at the first attempt (Figure 3). Subsequently, an internal meeting was held to discuss the strategies to follow in this case (open surgery with trans-duodenal approach or iterative ERCP). It was then decided by the Dean of the department to follow iterative ERCP. Over the period of a month, ERCP was repeated 3 times; at the

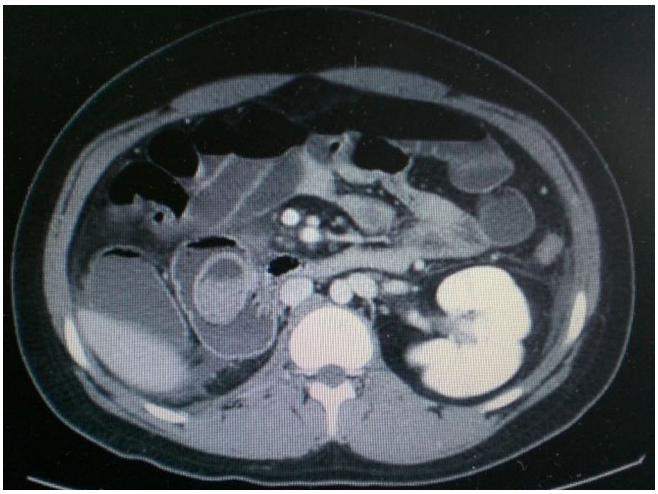

Figure 1. Abdominal computed tomography scan: Type III cyst, choledochocele.

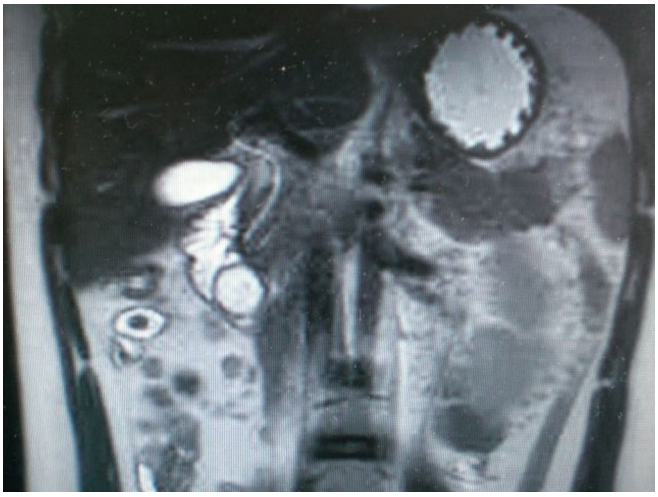

Figure 2. Magnetic resonance imaging: Type III biliary cyst.

third attempt, Vater papilla was cannulated and ERCP was performed, choledochocele was opened and partially removed but the general condition of the young patient rapidly deteriorated with a rapid onset of fungal (Candida) sepsis and hemorrhage; the patient died within 48 h.

Case 2

A 56-year-old female had been diagnosed 8 years before to have bilateral Caroli disease. Liver disease was followed for 7 years and on December 2013 a sepsis developed. After ultrasound, magnetic resonance (Figure 4) and CT (Figure 5) imaging, PTC was performed (January 2014) with removal of some gallstones and biliary drainage. During the first 5 months of 2014, PTC was repeated 3 times and multiple biliary gallstones were removed (Figures 6-7); biliculture was positive every time it was tested and intrahepatic gallstones, jaundice and cholangitis recurred. As iterative PTC seemed to have failed, the decision to make the liver transplant was taken by the chief of the liver transplant unit. The liver transplant was done successfully. Currently, the patient is in good condition.

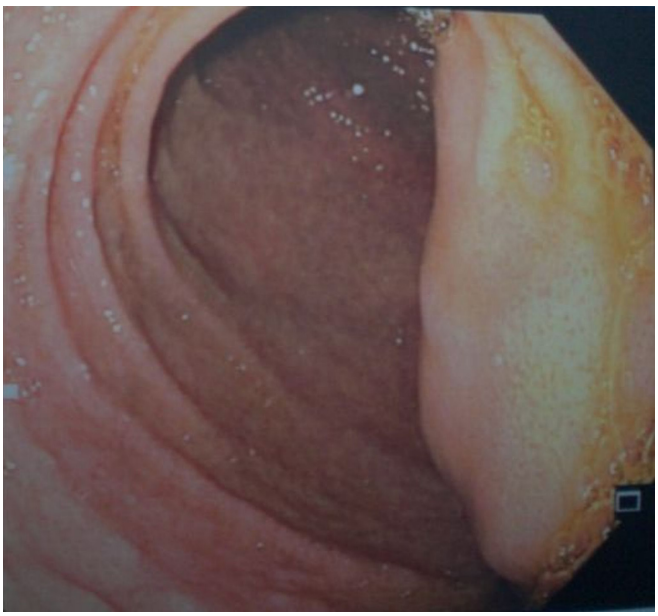

Figure 3. Gastroduodenoscopy during endoscopic retrograde cholangiopancreatography: Type III cyst, choledochocele.

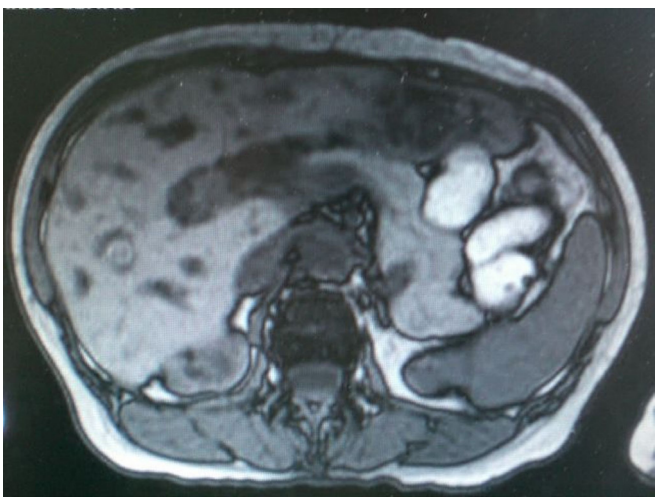

Figure 4. Magnetic resonance imaging: Bilateral Caroli disease.

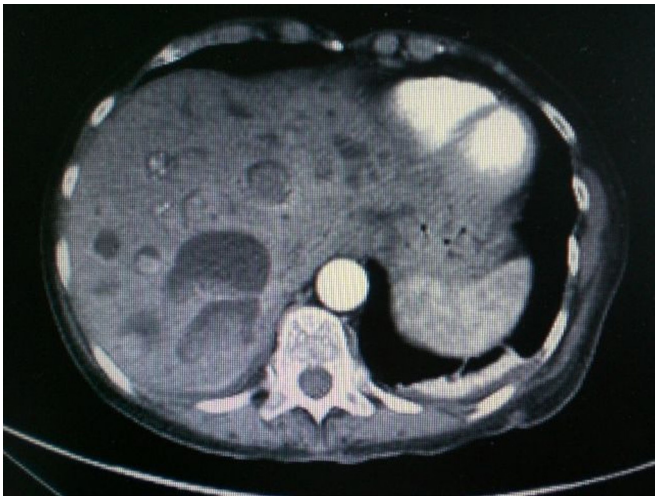

Figure 5. Abdominal computed tomography scan: Bilateral Caroli disease.

Case 3

A female patient was admitted in 2008 for bilateral Caroli disease; PTC biliary drainage with gallstones extraction was performed several times but cholangitis recurred, general conditions and liver function failed before a liver transplant could be provided and the patient died.

Discussion

Biliary tract cysts are a heterogeneous disease. Clinical presentation differs in young and adult patients. Obstructive jaundice and abdominal mass are the most frequent signs in neonatal patients; in adult patients, abdominal pain, fever, nausea are the commonest signs. The reported complications have been: Recurrent cholangitis, pancreatitis, cholecystolithiasis, intracystic lithiasis and choledocholithiasis, cholecystitis and liver cirrhosis. In fact, bile stasis and bile infection predispose to gallstone formation [9,10]. Intraperitoneal or retroperitoneal spontaneous rupture of the cysts presented with pain, peritonitis and sepsis. The overall reported risk of cancer is 10-30%; Nicholl [11] reported a correlation between the patient's age and cancer risk: From 0 to 30 years (0%); from 31 to 50 years (19%); from 51 to 70 years (50%). Hystopathological types are: Ad-

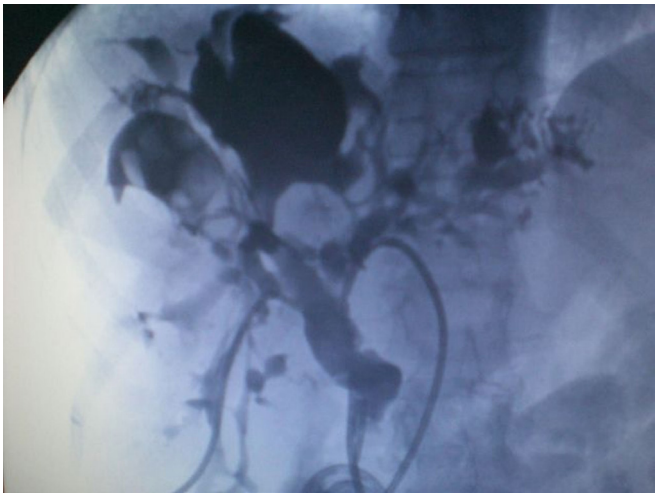

Figure 6. Percutaneous transhepatic cholangiography: Bilateral Caroli disease.

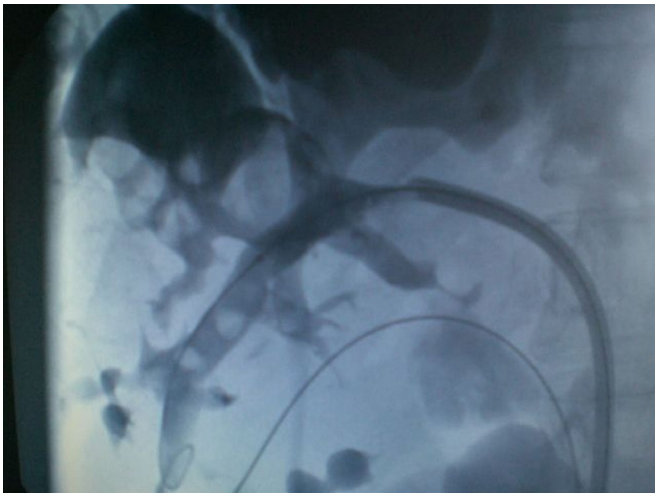

Figure 7. Percutaneous transhepatic cholangiography: Bilateral Caroli disease. Gallstones extraction.

Table 1. Todani classification of biliary cysts. Biliary cysts treatments according to cysts types.

Todani classification	Cyst Resection + hepatico-jejunostomy	Cyst Resection + hepatico-jejunostomy	Cyst resection + hepatico-jejunostomy	Cyst resection and common bile duct suture over T tube	Open duodenostomy, cyst resection re-implant of bile and pancreatic ducts. ERCP	Cyst resection, hepatico-jejunostomy+ liver resection or PTC	Cysts resection + hepatico-jejunostomy	Liver resection or liver transplant
Type I A	Cystic dilatation of all extra-hepatic ducts							
Type I B		Segmental cystic dilatation of distal common bile duct						
Type I C			Fusiform dilatation of extra-hepatic ducts					
Type II				Diverticulum of common bile duct				
Type III					Cystic dilatation of intra-duodenal portion of common bile duct			
Type IV A						Multiple extra- and intrahepatic cysts		
Type IV B							Multi. extra-hepatic cysts	
Type V								Multiple intra-hepatic cysts.

enocarcinoma (nearly 75-80%); anaplastic carcinoma (10%); undifferentiated carcinoma (6%); squamous-cell carcinoma (5%); other carcinoma (1%). Cancers have been reported in the extrahepatic bile duct (50-60%), gallbladder (40-45%) and intrahepatic bile duct (2-3%)[5]. Bile stasis, pancreato-biliary reflux and gallstones produce a chronic irritation of the mucosa that leads to cell regeneration, DNA modification during accelerated replication, dysplasia and cancer (usually cholangiocarcinoma or squamous-cell carcinoma in case of metaplasia)[5,11]. In fact, pancreaticobiliary reflux is associated with oncogene expression and adenocarcinoma onset [12,13]. Biliary cysts require different treatments (Table 1): Types I and IV cysts require total cysts excision with Roux-Y hepatojejunostomy and, in IV A cysts, PTC [14-16]. Type II cyst requires surgical excision of the cyst and of the gallbladder with primary closure of the bile duct over a T-tube [14-16]. Type III

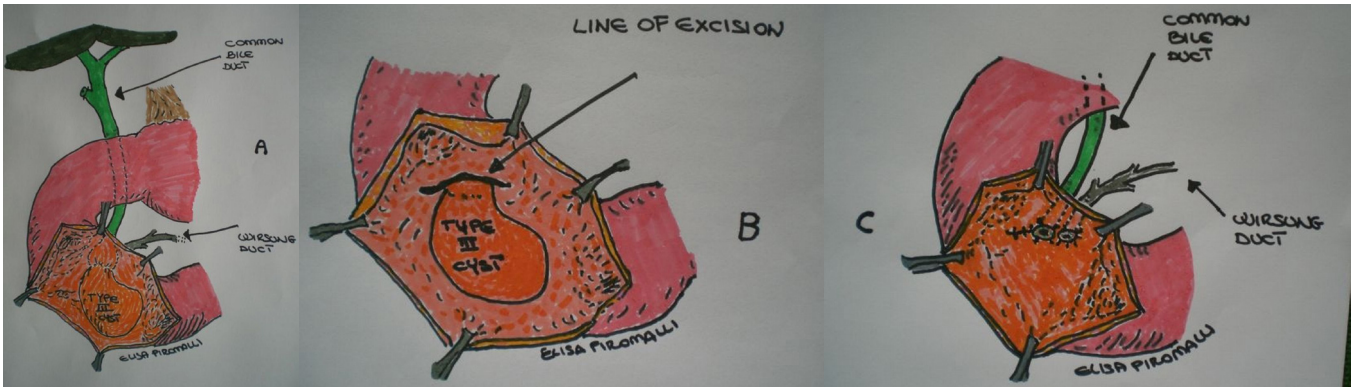

Figure 8. (A) Open surgery, duodenostony with visualization of the Type III cyst after cholecystectomy, **(B)** Open surgery, duodenostomy, level of excision of the Type II biliary cyst at the cyst neck, **(C)** Open surgery, duodenostomy, complete excision of the cyst with replanting of common bile duct and of Wirsung duct into the duodenal mucosa.

cysts have been usually treated by ERCP and endoscopic sphincterotomy to allow free gallstones and biliary drainage [17-19]. ERCP does not permit a complete cyst excision. The incidence of malignancy in patients with symptomatic Type III biliary cyst has been around 2.5% [20, 21]. It has been proposed to follow these patients with endoscopy every 6-12 months [22]. In the light of these considerations and after a revision of pitfalls and complications found during ERCP management of our case, we suggest that Type III cyst could be treated in older patients with small cysts (<3 cm) by endoscopic drainage via sphincterotomy (ERCP), and in younger patients, especially with larger (>3 cm) cysts, by the complete excision of the cyst via duodenostomy and the reinsertion of the common bile duct and the Wirsung duct in the duodenal wall (Figures 8A-C) [14-15, 23]. Segmental or unilobar Caroli's disease after the failure or PTC requires hepatic lobectomy. Diffuse bilateral Caroli's disease can be successfully treated by PTC in 90% of the cases [24], but in case of failure of PTC, when cholangitis recurs frequently (10% of the cases) [24], in our opinion the orthotopic liver transplantation could be entertained [14,25].

Conclusion

In our experience, during the management of patients with biliary cysts endoscopic and percutaneous approaches (ERCP, PTC) should be sometimes abandoned and replaced by open surgery. In fact, the patient with Type III biliary cyst (choledochocele) was submitted to ERCP that failed twice; at the third attempt during the same month, ERCP and sphincterotomy were done but a fatal fungal sepsis developed. Probably the endoscopic excision of the cyst was not sufficient to treat the hemostasis and did not permit the reinsertion into the duodenal mucosa of the common bile and Wirsung ducts. In cases like this, when anatomy is not simple and ERCP fails, we recommend to perform the complete excision of the choledochocele via open duodenostomy and reinsertion of the common bile and Wirsung ducts (as showed in Figures 8A-C). Diffuse Caroli's disease has been treated at the beginning with PTC, biliary drainage of infected cysts, antibiotic therapy and gallstones extraction; usually this procedure is successful in 90% of the cases [24]. In 10% of the cases [24], cholangitis recurred. In our opinion, in case of failure of PTC an orthotopic liver transplant should be considered, as suggested by Lipsett and Pitt [16]. In fact, in our cases series, the patient with Caroli's disease that refused the liver transplant in 2008, choosing iterative PTC died, whilst the patient that, in May 2014, after the failure of iterative PTC, decided to undergo orthotopic liver transplant is in good condition.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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