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Surgical management of Caroli disease in a low-mid income country: a single-center study and review of literature

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Abstract

Introduction Caroli disease is an uncommon congenital condition characterized by non-obstructive intrahepatic bile duct dilation. When coupled with liver fibrosis or cirrhosis, it is termed Caroli syndrome. This disorder can lead to the development of gallstones, inflammation of the bile ducts, and an elevated susceptibility to cholangiocarcinoma. Typically, Caroli disease presents with involvement in less than 20% of the liver, predominantly affecting a single lobe (either left or right). Monolobar disease can often be effectively addressed through liver resection, while bilobar disease may necessitate the consideration of liver transplantation.

Methods A retrospective study was undertaken involving patients diagnosed with Caroli disease who underwent liver resection. The research included cases from Surgery B Department at Ibn Sina University Hospital in Rabat, covering the period from January 2010 to January 2023.

Results Nine patients who underwent liver resection for Caroli disease were identified, with an average age of 54 years (range: 17–76), and 44.4% ($n=4$) being females. The study comprised 6 cases with disease limited to the left lobe and 3 to the right. The average time interval between initial symptoms and the definitive diagnosis was 4 years (range: 0–24 years). Surgical procedures included left lobectomy in 4 cases, left hepatectomy in 3 cases, right hepatectomy in 1 case, and sub-segmentectomy in 2 cases. Biliodigestive anastomosis was performed in 4 cases. Complications occurred in 2 patients (22.2%), and synchronous cholangiocarcinoma was observed in a single case (11.1%).

Conclusion Consideration of Caroli disease as part of the differential diagnosis is crucial in cases of recurrent cholangitis. Liver resection stands out as the treatment of choice for patients with localized Caroli disease. The critical importance of early intervention is highlighted by the potentially fatal consequences of delayed diagnosis or treatment.

Keywords Caroli disease, Caroli syndrome, Liver resection, Transplantation

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Introduction

First described by Vachell and Stephens [1] in 1906, Caroli disease (CD) was eponymously named by Jacques Caroli [2] in 1958, a French gastroenterologist who saw non obstructive segmental dilatation of intrahepatic bile ducts attributed to total or partial arrest of ductal plate remodeling [3, 4]. In 1977, Todani et al. [5, 6] integrated CD and its variant, Caroli syndrome (CS), into a comprehensive classification system for bile duct cysts, commonly recognized today as Todani Type 5 (Fig. 1). The proposed etiology for the biliary ductal dilatation posits a malformation of the intrahepatic bile ductal plate, leading to focal inflammation and subsequent destruction [7, 8]. CD presents in two primary types [9]; Type I, the archetypal form, exclusively involves bile ducts, while Type II, known as Caroli syndrome (CS), is intricately linked with hepatic fibrosis, cirrhosis, portal hypertension, esophageal varices, cholangiocarcinoma (CCA), intrahepatic duct calculi, cholangitis, pancreatic cysts, and autosomal recessive polycystic kidney disease or other hepatorenal ciliopathies [10]. The critical differentiation between these types is paramount for ensuring patient survival. Typically manifesting as a diffuse liver involvement, CD may, albeit rarely, be localized in a solitary segment or lobe, with a predilection for the left lobe [11, 12].

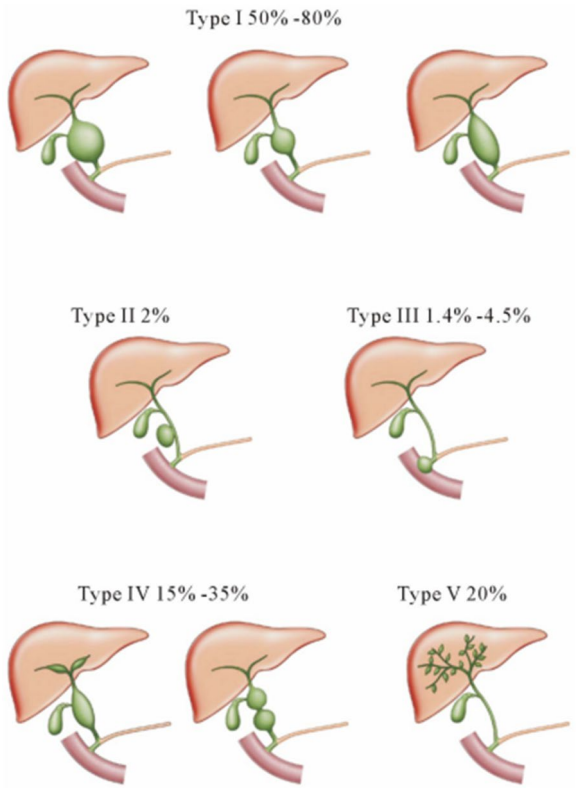

Fig. 1 Illustration of the Todani classification of bile duct cysts [6]. Type 1: cystic, saccular or fusiform dilation; Type 2: extraduodenal choledochal cyst; Type 3: intraduodenal choledochal cyst; Type 4: intra and extrahepatic cysts and multiple extrahepatic cysts; Type 5: Caroli disease

Surgical treatment options are liver resection for localized disease and liver transplantation for diffuse liver involvement [13]. Complete resection of localized CD can be curative and therefore has the potential to eliminate the risk of CCA [14, 15]. Biliary drainage interventions, whether conducted through endoscopy, radiology-guided percutaneous procedures, or surgical biliary drainage operations, entail inherent risks of morbidity and mortality due to infectious complications and elevated recurrence rates [16, 17]. In instances of complicated bilobar disease coupled with liver fibrosis and portal hypertension, the optimal therapeutic approach is liver transplantation (LT) [13].

This retrospective study sought to scrutinize the clinical patterns and outcomes of 9 patients who underwent anatomical liver resection for monolobar CD.

Patients and methods

Single center analysis

We retrospectively reviewed the clinical data of 9 patients diagnosed with monolobar CD who were treated at our hospital between 2010 and 2023. The patients'demographic details, clinical presentations, biochemical markers, and other relevant characteristics are summarized in Table 1. Preoperative imaging primarily involved ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), and cholangiography. We calculated the time between the start of symptoms and operation (interval from diagnosis to liver resection). The diagnosis of CD was definitively confirmed through histopathological analysis. Morbidity and mortality were evaluated and are reported according to the Clavien-Dindo classification [18]. Follow-up was calculated from the date of operation until the date of last follow-up. For this, the patients were contacted via telephone. The main focus of this study was to assess the primary surgical outcomes.

Literature review

To assess the current state of knowledge, an electronic PubMed search was conducted with following terms: '*Caroli Disease*,' '*Caroli Syndrome*,' '*Intrahepatic cystic dilation*,' and '*Dilation of intrahepatic bile ducts*.' It was restricted to studies written in English, excluding animal studies. Articles were reviewed and classified as relevant/non-relevant (e.g. comments/letter to the editors).

Table 1 Patients' characteristics

	Patients **(*n* = 9)**	**(%)**
Sex (Male/Female)	5/4	55.5/44.4
CD/CS	9/0	100/0
Mean age, (y)	54	
Prior cholecystectomy	3	33.3
Prior endoscopic intervention	7	77.7
Clinical presentation		
Abdominal pain	9	100
Fever	4	44.4
Severe cholangitis or jaundice	3	33.3
Biology		
Cholestasis	4	44.4
Hepatic cytolysis	3	33.3
↑ Carbohydrate antigen (CA) 19–9	1	11.1
↑ Carcinoembryonic antigen (CEA)	1	11.1
Imaging findings		
Intrahepatic bile duct stones	4	44.4
Choledocholithiasis	2	22.2
Gallbladder lithiasis	2	22.2
Dilatation of bile ducts	6	66.6
Dot sign	1	11.1
Hepatic abscess	2	22.2
Hepatic mass	1	11.1
Thrombosis of the right portal vein	1	11.1
Stenosis of the left bile duct	1	11.1
Interval until diagnosis, mean (y)	4	44.4
Unilobar (Left/Right)	6/3	66.6/33.3

Table 2 Surgical methods

	Patients **(n = 9)**	**%**
Approach (Open/Laparoscopic)	9/0	100/0
Treatment (patients with Roux-en-Y biliodigestive anastomosis)		
Right hepatectomy	1	11.1
Left hepatectomy	2 (1)	22.2 (11.1)
Left hepatectomy extended to S1	1	11.1
Left lobectomy	3 (2)	33.3 (22.2)
Left lobectomy extended to S1	1 (1)	11.1 (11.1)
Other treatments		
Cholecystectomy and choledochotomy	3	33.3
Liver biopsy	1	11.1

Results

Nine cases of CD were included in our retrospective analysis, 6 localized to the left lobe (66,6%) and 3 to the right (33,3%). The study included 5 men (55,5%) and 4 women (44,4%) with an average age of 54 (range: 17–76) years. The average interval between the onset of symptoms and reaching a diagnosis was 4 years (range: 0–24 years). Patients presented with abdominal pain (n= 9; 100%), cholangitis (n= 3; 33,3%), severe jaundice (n= 3; 33,3%) and fever (n= 4; 44,4%).

Laboratory values were within the normal range for 2 patients (22,2%). Cholestasis was present in 44,4% of patients (n= 4) and cytolysis was observed in 33,3% of patients (n= 3). One patient had a high level of CA 19–9 (= 10xN) and one had a high level of CEA (= 1368xN) (11,1%). Previous surgeries were cholecystectomy (n= 3; 33,3%) and endoscopic sphincterotomy (n= 7; 77,7%).

In 33,3% of cases (n= 3), a left hepatectomy was conducted, with one extended to segment I (Table 2). A right hepatectomy was performed in 11,1% of cases (n= 1). Furthermore, left lobectomy was carried out in 44,4% of cases (n= 4), including one extended to segment I (Fig. 2A). During hemilobectomy, 4 Roux-en-Y biliodigestive anastomosis were necessary (44,4%). Cholecystectomy and choledochotomy were performed in 3 cases (33,3%) and liver biopsy in 1 case (11,1%) after the discovery of a hepatic mass. 33.3% (n= 3) of patients developed recurrent cholestasis (bilirubin levels > 85 µmol/L), which was managed with endoscopic sphincterotomy.

Histopathological reports of all surgical specimens showed cystic dilatation of the segmental and subsegmental intrahepatic bile ducts (Fig. 2B). The hepatic parenchyma was described as normal in 8 cases (88,8%). In one case (11,1%), a synchronous CCA was observed (Fig. 2C). The postoperative mortality rate was 22.2%, attributed to CCA and cardiac complications. We noted a grade 1 on the Clavien-Dindo scale in 6 patients (Table 3), a grade 2 in 1 patient who received a blood transfusion, and a grade 5 in 2 patients. After an average follow-up period of 5 years, we observed that 7 patients from the cohort are presently alive and free from symptoms.

The gathered findings of the literature review are documented in Table 4, providing an up-to-date overview of the existing literature on CD.

Discussion

Caroli disease (CD) is less common than Caroli syndrome (CS), and both are extremely rare with an approximate prevalence of less than one in a million in the general population [25]. CD is characterized as a rare autosomal recessive congenital disorder, marked by an incomplete and faulty remodeling of the embryonic ductal plate. The prevalence of CD/CS appears to be increasing, and this is likely due to improvements in cross-sectional imaging and better understanding of the disease. This condition exhibits a higher prevalence among individuals of Asian descent. The peak incidence typically occurs in early adulthood, with more than 80% of patients presenting before the age of 30 [26, 27]. Since its initial description,

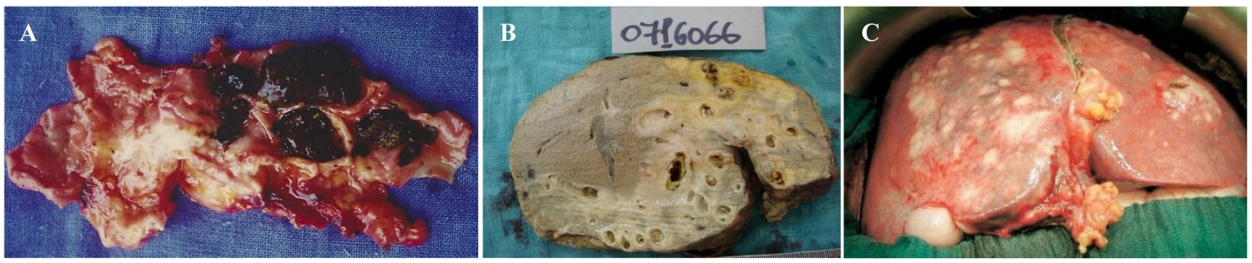

Fig. 2 Macroscopic images. **A** Open resection specimen: Fibrously remodeled Spiegel lobe with multiple saccular dilations and containing lithiasis molds. **B** Macroscopic appearance of the left liver showing dilated ducts containing numerous calculi. **C** Intraoperative discovery of a CCA secondary to CD

Table 3 Short-term outcomes of surgical treatment of unilobar CD

Clavien-Dindo classification	n (%)
Grade 1	6 (66.6)
Grade 2	1 (11.1)
Grade 3	0
Grade 4	0
Grade 5	2 (22.2)

numerous case reports have been published, often included in bile duct cysts reports. However, only a limited number of series with long-term result reports have been made available, indicating the scarcity of comprehensive studies on this rare disorder.

In this population literature study comprising 288 patients, a notable male predominance was evident, with a Sex Ratio of 5:4, mirroring the same Sex Ratio observed in our specific cohort. Among the patients, 186 (64.5%) exhibited unilobar disease, with a significant majority (82.2%) located in the left lobe. Our study yielded similar findings, with 66.6% of cases displaying involvement in the left liver lobe. Nevertheless, it's noteworthy to mention that Kassahun et al. [15] suggested a more balanced distribution in a series of 25 cases of single-lobe CD, where the ratio between left and right lobes was nearly equal at 13:12. Contrary to a consistent lobar preference, CD appears to demonstrate variable involvement, as evidenced by conflicting reports in the literature. Some studies suggest a slight right lobe dominance with a 3:1 ratio, while others propose an even distribution, emphasizing the variability in presentation among individuals. The mean age in this literature review was 50.98 compared to 54 years in our study. Despite occasional reports of neonatal presentation [28], CD usually remains asymptomatic until early adulthood [29].

Diagnosis often faces delays, leading to prolonged intervals from symptom onset to definitive treatment, spanning from 20 days to 24 years in our study. The observed mortality rate in our study stands at 22%, which is comparatively higher than the 9% reported by Lewin et al. [20]. Other studies in this literature review did not record any mortality. The largest series published so far is by Mabrut et al. [24], in 2013; in this multicenter study with 155 patients, the morbidity for resection is 15,3% and mortality 0%. However, in cases involving LT, morbidity surged to 39.3%, accompanied by a mortality rate of 10.7%. It's worth noting that our series did not observe complications such as biliary fistulas, which were predominant in other reports. Remarkably, the risk of developing intrahepatic CCA is markedly elevated by 100-fold in patients diagnosed with CD, underscoring the importance of vigilant monitoring and early intervention in the management of this rare condition [30].

The incidence of CCA in the literature varies; Mabrut et al. [24] described an incidence of 5,2% in their study with 155 patients. Even more alarming, Bockhorn et al. [31] reported an incidence of 25% in 12 patients and Fahrner et al. 19% in 21 patients, the highest among the reported studies [8, 32]. Our study echoed a similar result, with a CCA rate of 11%, accompanied by an intraoperative discovery after 24 years of progression. This correlation suggests a potential association between prolonged chronic inflammation, biliary epithelium injury, and the development of dysplasia leading to epithelial carcinogenesis [33]. The findings align with data presented by Fard-Aghale et al. [34], underscoring the significance of early and stage-dependent curative treatment. In 2017, Petrick et al. investigated the '*risk factors for intrahepatic and extrahepatic cholangiocarcinoma in the United States*'. They searched the database of *the National Cancer Institute: Surveillance, Epidemiology, and End Results* (*SEER*) and were able to show that CD '*… was associated with the strongest associations of any medical condition …* '. It showed a 38-fold and 97-fold increase in risk to develop

Table 4 Literature studies on CD

Study	Fard-Aghaie et al. [19]	Lewin et al. [20]	Wabitsch et al. [21]	Fahrner et al. [22]	Yamaguchi et al. [23]	Mabrut et al. [24]
Year	2022	2021	2021	2019	2018	2013
Country	Germany	France	Germany	Germany	Switzerland	France
No of patients (Male/Female)	14 (6/8)	66 (40/26)	7 (3/4)	21 (7/14)	25 (15/10)	155 (89/66)
CD/CS	12/2	31/35	ND	6/13	23/2	125/30
Median Age	56,5	32,3	49	56	53,4	55,7
Comorbidities/medical history (%)	ND	Cholecystectomy (27%), sphincterotomy (18%), personal history of renal ciliopathies (18%), familial history of liver ciliopathies (9%)	Primary hypertension (28%), type II diabetes (28%), hypothyroidism (28%), paroxysmal atrial fibrillation (14%), Conn syndrome due to a cortical adrenal adenoma (14%), chronic obstructive pulmonary disease (14%), chronic gastritis (14%), arthritis (14%), DVT and pulmonary embolism (14%) **Previous surgery:** cholecystectomy (28%), appendectomy (14%), surgical correction of a rectal prolapse (14%), stripping of lower-limb varices (14%), cataract operation (14%)	ND	**Previous surgery:** cholecystectomy (48%), choledochotomy (12%), surgical sphincterotomy (12%), biliodigestive anastomosis (12%), resection of a main bile duct diverticulum (4%) **Associated lesions:** congenital hepatic fibrosis (8%), intrahepatic pancreatic ectopia (4%), renal cysts (4%) Drainage of a hepatic abscess (4%)	**Associated HBP disease:** biliary lithiasis (56,8%), secondary biliary cirrhosis (47,7%), unilobar liver atrophy (14,2%), acute pancreatitis (3,2%), CHF (2,6%), NASH (1,3%), polycystic liver (1,3%), chronic pancreatitis (1,3%), autoimmune hepatitis (0,6%), undetermined, cholestasis (0,6%) **Previous surgery:** cholecystectomy (42,6%), biliodigestive anastomosis (6,5%), choledochotomy (5,2%), Portosystemic shunt (2,6%), IHS extraction (1,9%), hepatectomy (1,3%)
Presentation (%)	Recurrent lithiasis (42%), recurrent pain (35%), recurrent cholangitis (14%), liver abscess (7%)	Severe cholangitis or jaundice (59%), abdominal pain (18%), asymptomatic (13%), pancreatitis (1%), hematemesis (7)	Biliary lithiasis (57%), cholangitis (42%), systemic sepsis (14%), pancreatic and liver cysts (14%)	Recurrent episodes of cholangitis (58%), pain (63%), fever (26%)	Asymptomatic (4%) Biliary lithiasis (80%), ↑GGT and ALP (4%), cholangitis (4%), pain and recurrent jaundice (4%), acute cholecystitis (4%), acute pancreatitis (4%), hepatic abscess (4%)	Asymptomatic (10,3%) Cholangitis (58,1%), abdominal pain (29%), jaundice (24,5%), acute pancreatitis (11%), loss of weight (6,5%), asthenia (6,5%), gastrointestinal bleeding (4.5%), ascites (3,2%), abdominal mass (1,3%), pruritus (2,6%), biliary peritonitis (0,6%), complicated delay between symptom and diagnosis (60,6%)

Table 4 (continued)

Study	Fard-Aghaie et al. [19]	Lewin et al. [20]	Wabitsch et al. [21]	Fahrner et al. [22]	Yamaguchi et al. [23]	Mabrut et al. [24]
Imaging findings	ND	Bile duct dilations, 'Dot sign', biliary lithiasis, hepatomegaly, liver atrophy, liber abscess, biliary hamartoma, large regenerative nodules, signs of portal hypertension, renal cysts	Intrahepatic gallstones, bile duct dilations	ND	ND	"Central dot sign"
Unilobar (Left/Right)	14 (11/3)	21 (19/2)	7 (5/2)	12 (7/5)	25 (20/5)	107 (91/16)
Laparoscopic approach (n=)	ND	ND	6	ND	ND	ND
Open approach (n=)	ND	ND	0	ND	ND	ND
Conversion to open surgery (n=)	ND	ND	1	ND	ND	ND
Interventions and treatments (%)	ERCP (78%), lithotripsy (7%), PTD (14%), left hepatectomy (64%), right hepatectomy (14%), left lateral sectionectomy (14%), segmentectomy (7%)	Conservative management (53%), hepatectomy (24%), liver transplantation (21%), biliodigestive anastomosis (3%)	Left lateral bisegmentectomy (28%), left hemihepatectomy (28%), left lobectomy (14%), posterolateral hepatectomy (14%), complete right hemihepatectomy (14%), bilio-jejunal anastomoses (14%)	ERCP (89%), stenting of the biliary tree (21%), left lateral segmentectomy (38%), left hepatectomy (33%), right hepatectomy (14%), monosegmentectomy (4%), LT (9%), hepaticojejunostomy (4%)	left lobectomy (40%), left hepatectomy (36%), biliojejunal anastomosis (24%), right hepatectomy (12%), segmentectomy (12%), right hepatectomy (12%), ERCP (8%), drainage of abscess (4%)	Unilateral left LR (81.1%), liver transplantation (18.9%), IHS extraction (32%), unilateral right LR (11.8%), biliary drainage (10.2%), bilobar liver resection (7.5%), surveillance (0,6%), other (6.1%)
Post-operative complications (%)	Bilioma (7%), postoperative bleeding (7%), bile leakage (7%)	Death (9%), severe cholangitis (3%), gastrointestinal hemorrhage (3%), postoperative complications after liver transplant (1%)	Seroma (28%), cholangitis (14%), left-sided pleural effusion (14%)	Biliary leakage (14%), pleural effusion (4%), urinary tract infection (4%)	Intra-abdominal abscess (4%), bilioma (4%), biliary fistula (4%), liver hematoma (4%), intra-abdominal collection (4%)	Biliary fistula (7%), mortality (2%), hepatic artery thrombosis (1,2%), primary nonfunction and acute rejection (1,2%), hemorrhage (0,9%)
Rate of CCA (%)	7%	1,5%	0%	19%	4%	5.2%

intrahepatic and an extrahepatic CCA, respectively. However, their study population was above 68 years of age [35]. Such interventions become crucial for providing patients with suitable therapy, ensuring acceptable long-term survival, and maintaining a good quality of life.

The pathogenesis of CD involves a complex interplay of both embryologic and acquired factors. Bile duct formation occurs during the 7 th week of gestation, involving the differentiation of hepatoblasts into biliary cells. These cells envelop the vessels of the portal system to form the ductal plate, followed by a remodeling process that separates hepatocytes and bile ducts through connective tissue, with hepatocytes migrating into the portal spaces. While the exact pathophysiological basis remains incompletely understood, genetic factors are implicated in CD, particularly involving a mutation of the PKHD1 gene (Polycystic Kidney and Hepatic Disease 1). This gene mutation affects a protein called fibrocystin, expressed in multiple organ systems including renal tubular cells, liver cholangiocytes, and the pancreas [7]. Abnormalities in fibrocystin due to the PKHD1 mutation lead to fibrocystic changes in the kidney and liver. Notably, the PKHD1 gene is also associated with Autosomal Recessive Polycystic Kidney Disease (ARPKD), often co-occurring with CD. In the context of autosomal recessive CS, characterized by congenital hepatic fibrosis, this genetic anomaly hypothesis aligns with the discontinuous and irregular dilatations observed in the biliary tree characteristic of CD. Early onset of this genetic anomaly can result in defects affecting the right or left bile ducts, or the segmental ducts [28]. A later onset could induce lesion formation consistent with that seen in CHF [35].

Clinical manifestations of CD are often atypical, characterized by right upper quadrant tenderness, a negative Murphy's sign, fever due to recurrent cholangitis, and jaundice. A literature review revealed that recurrent acute cholangitis is the most common mode of presentation (64% of patients) [36].

Additionally, patients may present with severe complications like sepsis, contributing to a generally poor prognosis [37]. Differential diagnoses for similar clinical presentations or imaging findings include primary sclerosing cholangitis, recurrent pyogenic cholangitis, polycystic liver disease, multiple intraductal papillomas in the bile duct, and choledochal cysts. CD can be diagnosed through various imaging modalities, including US, CT, MRI, or ERCP. The characteristic imaging features encompass a tubular or cystic appearance with low echogenicity on ultrasound images and low-attenuation lesions on CT scans. An additional notable finding is the central '*dot sign*', where high-attenuation dots or lines protrude within the dilated bile ducts on contrast-enhanced axial CT images (Fig. 3). These bright dots, exhibiting strong contrast enhancement, are also observable on MRI [38].

Among the diagnostic tools, MRI is regarded as the most precise and noninvasive approach for identifying CD. It offers comprehensive insights into the condition, detecting associated features such as cirrhosis, portal hypertension, renal abnormalities, and CCA. In addition to that, the diagnosis of dilation can be confirmed by intraoperative cholangiography under manometric control. Single-lobe CD can present as localized dilation of intrahepatic bile ducts, and it often does not involve hepatic fibrosis. The bile duct dilation in this form of the disease may appear more tubular than cystic, and the degree of dilation may not be as pronounced, making it challenging to distinguish from other conditions that can cause bile duct dilation.

Both monolobar and diffuse CD types commonly exhibit cholangitis, a condition exacerbated by inappropriate therapeutic interventions or opacification of the bile ducts. The identification of isolated lithiasis within

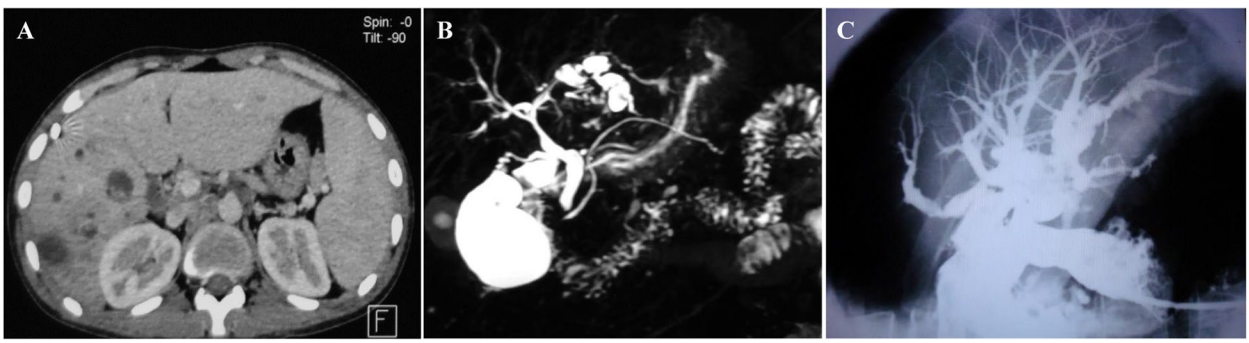

Fig. 3 **A** Abdominal CT scan revealing hypodense lesions in segments VI and VII, along with multiple cystic formations in the right lobe, with the presence of a dot sign (arrow). **B** MRCP showing dilation of the left intrahepatic bile ducts (arrow) with the presence of intrahepatic and gallbladder stones. **C** Intraoperative cholangiography showing dilation of the left intrahepatic bile ducts with numerous calculi

the bile ducts, without involvement of the gallbladder, or the diagnosis of cholangitis in a patient with a history of biliary surgery should evoke suspicion of CD or CS. This suspicion warrants further investigation, ideally employing MRI for a more comprehensive assessment [23].

In our current series, 3 patients underwent cholecystectomy, and 7 had prior endoscopic interventions before the final diagnosis of CD. Remarkably, the postoperative course was uneventful in all cases.

In the case of monolobar CD, the optimal approach involves the comprehensive removal of affected regions. Surgical considerations take into account factors such as localization, disease extension, and the presence of underlying chronic liver conditions, kidney disease, or associated malignancy. Specifically, for left monolobar CD, effective management often entails extended resection, which may include the incorporation of segments I or IV if affected [20].

When dealing with lesions in the right lobe, the extent of resection is intricately guided by the segmental anatomical distribution of biliary ectasia. If the lesion extends to the biliary convergence, opting for a Roux-en-Y biliodigestive anastomosis is recommended. This approach facilitates the restoration of biliary drainage following surgical resection, ensuring an effective and comprehensive management strategy [23]. Hemihepatectomy with or without a bilioenteric anastomosis remains the treatment of choice in unilobar CD in the absence of cirrhosis. Bilioenteric anastomoses following major resections usually involve the extrahepatic bile ducts, i.e., the common hepatic, the left or right hepatic ducts. Anastomoses to the intrahepatic bile ducts or cholangiojejunostomies are uncommon and have largely been described in the context of the Longmire procedure for inoperable hilar cholangiocarcinomas [39, 40] where following a left lobectomy, the intrahepatic ducts of segments II and III on the cut surface of the liver are anastomosed to a Roux-en-Y jejunal loop. Only one case of cholangiojejunostomy has been described after hepatectomy for CD [41].

Like other bilioenteric anastomoses, cholangiojejunostomies are susceptible to early bile leaks and late anastomotic strictures. The incidence of complications specific to this reconstruction is not known because of the negligible reports available but the rates of hepaticojejunostomies after hilar CCA resections may provide references [42–44]. The association of CD with congenital hepatic fibrosis ranges from 1.8% to 57%. Studies indicate that the presence of congenital hepatic fibrosis could worsen portal hypertension after resection in CD patients [35]. In the study led by Yamaguchi [23], 25 adult patients (median age 53 years old) who underwent hepatic resection for Monolobar CD experienced sustained relief from symptoms during a median follow-up period of 18 months. Similarly, in a series conducted by Nagasue [45], 2 patients subjected to hepatic resection for monolobar disease remained free from malignancy for over a decade postoperatively. This observation suggests that the removal of affected segments of the biliary tree may effectively diminish the risk of malignant degeneration, providing further support for the efficacy of surgical intervention in managing monolobar CD. Compared to this data, our series showed that 7 patients were free from symptoms with normal imaging and surgical markers at 5-year follow-up.

Diffuse CD may be managed conservatively with ursodeoxycholic acid and internal bile duct drainage procedures such as choledochojejunostomy or Roux-en–Y hepaticojejunostomy (Fig. 4) [46]. However, patients continue to be affected by complications of recurrent biliary obstruction and chronic inflammation which may lead to malignant transformation of the biliary tree [25]. Thus, orthotopic liver transplantation remains the sole definitive treatment of diffuse CD [47, 48].

The laparoscopic approach, including robotic hepatectomy, has shown promise in select cases, offering excellent long-term results with a low rate of conversion. However, the complex nature of CD involving segmental or lobar bile ducts and the presence of severe complications may limit the feasibility of minimally invasive liver surgery. Complex intraoperative biliary procedures, such as cholangioscopy and bilio-enteric anastomosis, further restrict the application of minimally invasive approaches.

Ulrich et al. [49] showed that if the patients suffer from CD rather than CS, the resection seems to be curative. After a median follow-up of 86,5 months the patients had significantly less symptoms and 5-year-survival was 97,5%. In 2005, Kassahun et al. [15] published their data comprising 33 patients treated either with resection or LT. After a median follow-up of

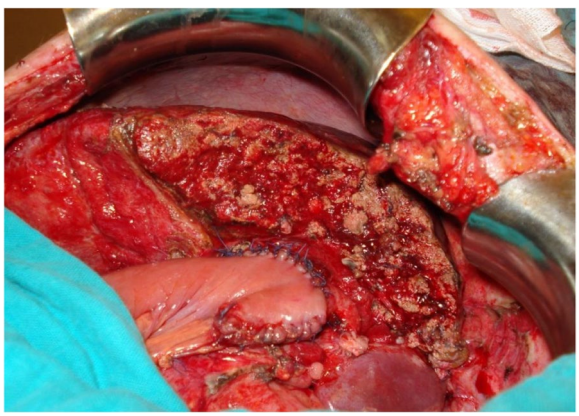

Fig. 4 Roux-en-Y hepaticojejunostomy

3,7 years, 83,9% of the patients remained free from complications.

Conclusion

Despite its rarity, the consideration of CD is crucial in the differential diagnosis, especially when dealing with patients presenting recurrent cholangitis. Given the absence of consistently specific signs or symptoms, preoperative diagnosis requires a high degree of clinical suspicion. Surgical resection emerges as the optimal curative approach for unilateral CD, providing long-term symptom-free survival. In cases of bilateral disease, hepaticojejunostomy may be considered as a potential treatment option before contemplating LT.

Looking ahead, future prospective randomized studies should aim to compare minimally invasive approaches with the traditional open approach. Such studies can provide insights into short- and long-term complications associated with each surgical platform, contributing to the refinement of treatment strategies for CD.

Abbreviations

ALP	Alkaline Phosphatase
ARPKD	Autosomal Recessive Polycystic Kidney Disease
CCA	Cholangiocarcinoma
CD	Caroli Disease
CEA	Carcinoembryonic Antigen
CS	Caroli Syndrome
CT	Computed Tomography
DVT	Deep Vein Thrombosis
ERCP	Endoscopic Retrograde Cholangiopancreatography
IHS	Indicates Intrahepatic Stones
GGT	Gamma-Glutamyl Transferase
LR	Liver Resection
LT	Liver Transplantation
MRI	Magnetic Resonance Imaging
ND	Not Described
PTD	Percutaneous Transhepatic Drains
US	Ultrasound
Y	Year

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Credit authorship contribution statement

S.B did the original draft preparation and the literature review. T.L, A.M and M.H reviewed the manuscript. A.S reviewed and supervised the study. All authors have read and approved the final version of the article.

Conflicts of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Clinical trial number

N/A.

Authors' contributions

The authors of this work have satisfied the ICMJE criteria for authorship. S.B. authored and designed the manuscript. T.L., A.M. and M.H. revised the manuscript. A.S. revised and supervised the manuscript. All authors agree to be accountable for all aspects of the work. All authors read and approved the final manuscript.

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Data availability

The datasets used during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Surgery B Department—Ibn Sina Hospital and adhered to the ethical principles outlined in the Declaration of Helsinki. Informed consent forms were obtained from all patients.

Consent for publication

N/A.

Competing interests

The authors declare no competing interests.

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