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Cystobiliary communication in hepatic hydatid cyst: predictors and outcome

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ABSTRACT

Background/Aims: Cystobiliary communication (CBF) with hepatic hydatid disease is responsible for postoperative bile leakage after surgical management. This study aims to detect various predictors of CBF and its outcome after surgical management.

Materials and Methods: This is a retrospective, cohort study of all patients who underwent surgical management for hydatid disease of the liver. Patient data were recorded on an internal web-based registry system supplemented by paper records. Patients were classified into two groups according to the presence of CBF: group (A) patients with CBF and group (B) patients without CBF.

Results: There were 123 patients with a hepatic hydatid cyst with a mean age of 39.92±14.59 years. Patients were classified into group (A), 26 patients (21.1%) with CBF, and group (B), 97 patients (78.9%) without CBF. The age group (p=0.04), presence of jaundice (p=0.001), serum glutamic-pyruvic transaminase (SGPT) (p=0.001), cyst size (p=0.0001), and cyst size group (>10 cm) (p=0.0001) were associated with CBF. That cyst size was the only independent predictor of the occurrence of CBF. Intraoperative suturing and the T tube led to complete healing of CBF, and postoperative endoscopic retrograde cholangio-pancreatography (ERCP) and tubal drainage led to a rapid reduction in the bile output and the healing of the fistulas after 9±2.6 days.

Conclusion: That cyst size was the only independent predictor for the occurrence of CBF. Management is related to the size of the fistula, the site of the cyst, and the experience of the hepatobiliary surgeon. ERCP is an important option for the management of CBF.

Keywords: Hydatid cyst, cystobiliary communication, bile leakage, ERCP

Original Article

INTRODUCTION

Hydatid disease, a parasitic infestation caused by *Echinococcus granulosus*, is an endemic disease in cattle breeding areas in the Middle East, India, Australia, and Turkey (1). As the transmission of the disease to humans (the intermediate host) occurs via an oral mechanism, the liver is the most common organ affected (50%-70%) (2). Hydatid disease is not endemic in our country, but we encounter the disease because of travel to countries in which the hydatid disease is endemic, such as Mediterranean countries, the Middle and Far East, Australia, and South America (1-4).

Hepatic hydatid disease is usually presented by right upper abdominal pain, hepatomegaly, or a palpable mass. As the cyst enlarges, the risk of cyst wall dehiscence with a subsequent rupture increases. The cyst may rupture into the peritoneal cavity, pleural cavity, blood stream or, most commonly, the biliary system, which causes cyst biliary fistula (CBF) (3).

Cystobiliary fistula is reported in 5%-42% of hepatic hydatid disease cases (4-6). The pathogenesis of CBF formation is thought to be due to a pressure necrosis effect of the enlarging cyst on the adjacent biliary radicles or entrapment of the biliary radicles within the pericystic wall (7).

Cyst biliary fistula is classified into two main types: (1) minor (simple or occult) fistula and (2) major (frank) fistula. A minor fistula (10%-37% of the hepatic hydatid

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cyst cases) (5,8-10) is usually asymptomatic and may be diagnosed intra-operatively (bile within the cyst) or post-operatively by an external biliary fistula through a drain or wound. Frank or major fistula is a wide communication between the cyst and the biliary system that allows the contents of the cyst to drain into the biliary system causing obstructive jaundice, cholangitis, secondary infection of the cyst, or even anaphylaxis (11).

As the presence of CBF in hepatic hydatid disease cases increases the risk of peri-operative morbidity and requires additional management, several studies were conducted to identify the predictors of CBF in hepatic hydatid disease. These predictors included cyst size >10 cm, calcified wall, recurrent disease, pre-operative jaundice, and pre-operative elevated serum alkaline phosphatase (ALP) (3,7,12-14).

The aim of the current study is to identify the predictors for the occurrence of CBF and assess their impact on the surgical management and outcome in hepatic hydatid disease cases referred to our tertiary referral hospital.

MATERIALS AND METHODS

All patients referred to our center for surgical treatment of hydatid disease of the liver in the period between January 2006 and May 2016 were included in this retrospective study. The patients` data were collected in a web based registry system supplemented by paper records. A written informed consent was obtained from all patients. The study was approved by the institutional review board.

Pre-Operative Evaluation

Diagnosis of hepatic hydatid disease was based on a pre-operative abdominal CT scan with features specific to a hydatid cyst, a past history of traveling to endemic areas, and an enzyme linked immunosorbent assay for echinococcal antigens. Whenever the presence of CBF was suspected (history of jaundice, cholangitis, or elevated liver enzymes), it was assessed using magnetic resonance cholangiopancreatography (MRCP). Other routine laboratory investigations included a complete blood picture and liver and kidney function tests.

Operative Technique

The principles of liver hydatid surgery include inactivation of protoscolices within the cyst fluid, evacuation of the cyst contents, prevention of content spillage, secure closure of any cystobiliary communications, and management of the residual cyst cavity (4-6). After a laparotomy and packing with hypertonic saline impregnated packs, two main types of procedures were done in this study group, radical surgery (peri-cystectomy and liver resection) and conservative surgery (deroofing and endocystectomy) with subsequent management of the resultant cavity by either marsuplization, omentoplasty, or drainage. Hypertonic saline was used as a scolicidal agent in all cases. First, the cyst was aspirated, and then hypertonic saline was injected and left for 10 minutes before the cyst was opened.

Intra-operative identification of CBF was done by observation of the bile stained hydatid fluid, bile staining, or oozing from the cyst wall or intra-operative cholangiography for cases with pre-operative suspicion of CBF. Small CBF were managed by primary sutures only when detected.

Post-Operative Care and Follow up

Vital parameters and drain outputs were carefully recorded post-operatively. Whenever needed, an abdominal ultrasonography was done to identify the presence of abdominal collections. Oral intake commenced after the return of intestinal motility. All patients were started on Albendazole therapy on the day of discharge.

Patients follow ups were at 1 week and then 3, 6 and 12 months post-operatively.

Primary and Secondary Outcomes

The primary outcome was the peri-operative diagnosis of CBF. The secondary outcomes were the predictors of CBF (age, gender, pre-operative aspartate aminotransferase, alanine aminotransferase, ALP, bilirubin, complete blood cell count, cyst location (right and left or both), cyst diameter, cyst number), post-operative complications, length of hospital stay, and hospital mortality. The severity of the complications was graded according to the Dindo-Clavien complication classification system (15).

Statistical Analysis

Statistical analysis in this study was performed using Statistical Package for the Social Sciences software, (IBM SPSS Statistics; Armonk, NY, USA) version 20. Descriptive data were presented as the mean and standard deviation or medians with ranges. Cross-tabulation and an independent T test were used for univariate analysis of the variables of concern. Multiple logistic regression analysis was done to detect independent predictors of cysto-biliary fistula. A p value less than 0.05 was considered to be statistically significant.

RESULTS

Patient`s Characteristics

In the study period, 123 patients were admitted to our institution for surgical management of hepatic hydatid disease. The patients' characteristics and demography are represented in Table 1. Of these, 21 patients (21.1%) were diagnosed with CBF. Right upper abdominal pain was the most common presentation (97.6%). Although pre-operative jaundice was present in only 7 cases (5.7%), it was significantly higher in the CBF group (p=0.001). Serum alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were significantly elevated in cases diagnosed with CBF (p=0.001, p=0.002 respectively).

Analysis of Operative Data

Analysis of the operative data is shown in Table 1. Ninety-two patients (74.8%) underwent conservative surgery compared to only 31 patients (25.2%) who underwent radical surgery. The right lobe was the common location of the hydatid cyst

Table 1. Demographic and laboratory data of study population

Variables	Total	With biliary communication 26 (21.1%)	Without biliary communication 97 (78.9%)	p
Age (years)	39.92±14.59	40.15±15.19	39.86±14.5	0.92
<45 years	69 (56.1%)	10 (38.5%)	59 (60.8%)	0.04
>45 years	54 (43.9%)	16 (61.5%)	38 (39.2%)	
Sex				
Male	89 (72.4%)	17 (65.4%)	72 (74.2%)	0.37
Female	34 (27.6%)	9 (34.6%)	25 (25.8%)	
Pain	120 (97.6%)	26 (100)	94 (96.6%)	0.36
Jaundice	7 (5.7%)	5 (19.2%)	2 (2.1%)	0.001
Cholangitis	6 (4.9%)	3 (11.5%)	3 (3.1%)	0.08
Preoperative serum bilirubin	1.32±2.15	1.79±1.29	1.19±2.31	0.21
Preoperative SGPT	40.71±24.9	56.34±32.26	36.52±20.81	0.001
Preoperative alkaline phosphatase	9.73±7.78	13.86±10.54	8.62±6.2	0.002
Preoperative WBC	7.72±3.19	8.58±4.25	7.49±2.82	0.12
Size of the cyst	11.77±7.07	18±9.21	10.1±5.31	0.0001
<10 cm	75 (61%)	8 (30.8%)	67 (69.1%)	0.0001
>10 cm	48 (39%)	18 (69.2%)	30 (30.9%)	
Site				
Right lobe	70 (56.9%)	18 (69.2%)	52 (63.6%)	
Left lobe	28 (22.8%)	1 (3.8%)	27 (27.8%)	0.06
Both lobes	25 (20.3%)	7 (26.9%)	18 (18.5%)	
Number of cyst				
Single	84 (68.3%)	12 (46.2%)	72 (74.2%)	0.006
Multiple	39 (31.71%)	14 (53.8%)	25 (25.8%)	
Type of surgery				
Radical	31 (25.2%)	6 (23.1%)	25 (25.8%)	0.15
Conservative	92 (74.8%)	20 (76.9%)	74.2%)	
Management of the cavity				
Nothing	58 (47.2%)	13 (50 %)	45 (46.4%)	0.8
Omentoplasty	62 (50.4%)	12 (46.2%)	50 (51.5%)	
Obliteration and drainage	3 (2.4%)	1 (3.8%)	2 (2.1%)	

SGPT: serum glutamic-pyruvic transaminase; WBC: white blood cells

(56.9%). Only 86.3% of the cases presented a single cyst; however, CBF was more frequently encountered in cases with multiple hepatic hydatid cysts (p=0.006).

Regarding the size of the cyst, which was an important predictor for the presence of CBF, the mean cyst size was 18±9.21cm for the CBF group and 10.1±5.31 cm with a high statistical significance (p<0.001) for the group without CBF.

Table 2. Multivariate logistic regression for predictors of cystobiliary communication

Variables	p	Oddis ratio	95% C.I.for EXP (B) Lower	Upper
Age group (<45)	0.271	1.894	.607	5.910
SGPT	0.397	1.012	.985	1.039
ALP	0.304	1.044	.962	1.134
Size of the cyst	0.010	1.148	1.034	1.275
Size group	0.639	1.442	.312	6.660
jaundice	0.981	1.032	.075	14.128
Number of cysts	0.100	2.557	.836	7.820

SGPT: serum glutamic-pyruvic transaminase; ALP: alkaline phosphatase

Predictors of CBF

After the multivariate analysis of significant independent variables (Table 2), the size of the cyst was the only significant predictor for the occurrence of CBF (p=0.01).

Analysis of the Post-Operative Outcomes

The overall complication rate in our series (shown in Table 3) was 15.4% (n=19). The incidence of post-operative morbidity was significantly higher in the group with CBF (p<0.001). Major complications (Dindo-Clavien class IIIb or higher) were significantly higher in the presence of CBF (p<0.001). Bile leakage was detected in 14 patients (53.8%) in the CBF group, while none of the patients without CBF were associated with evidence of intra- or post-operative bile leaks (p<0.001). The incidence of abdominal collections was significantly higher in the CBF group compared to the group without CBF (34.6% vs. 3.1%, respectively, p=0.001). The mean length of the hospital stay was 7 days longer in the CBF group (p<0.001).

Management of CBF

Cyst biliary fistula was detected intra-operatively in 26 patients, and 7 cases were managed by direct suturing only, 5 cases were managed by suturing the fistula and transcystic tube decompression and 3 cases were managed by suturing and T-tube placement through a choledechotomy. We found that biliary decompression significantly increased the success rates for controlling post-operative bile leaks and reducing the length of the hospital stay (p<0.001) (Table 4).

Thirteen cases with CBF were diagnosed post-operatively by bile leaks. Six patients were managed conservatively, 2 patients required ultrasound guided tube drainage and 5 patients underwent an endoscopic sphincterotomy in addition to ultrasound guided tube drainage. After analysis of the data, we found that endoscopic decompression via a sphincterotomy together with tubal drainage significantly reduced the length of the hospital stay (p<0.001)

Table 3. Postoperative outcome

Variables	Total	With biliary communication 26 (21.1%)	Without biliary communication 97 (78.9%)	p
Complications	19 (15.4%)	14 (53.8%)	5 (5.2%)	0.0001
Complications grade				
I	9 (7.3%)	5 (19.2%)	4 (4.1%)	
II	2 (1.6%)	2 (7.7%)	0	
III	6 (4.9%)	6 (23.1%)	0	0.0001
IV	2 (1.6%)	1 (3.8%)	1(1%)	
V	0	0	0	
Severe complications (>IIIb)				
Minor	11 (8.9%)	7 (26.9%)	4 (4.1%)	0.0001
Major	8 (6.5%)	7(26.9%)	1 (1%)	
Biliary leakage	14 (11.4%)	14 (53.8%)	0	0.0001
Abdominal collection	12 (9.8%)	9 (34.6%)	3 (3.1%)	0.001
Wound infection	11 (8.9%)	6 (23.1%)	5 (5.2%)	0.004
Pulmonary function	8 (6.5%)	2 (7.7%)	6 (6.2%)	0.78
Hospital mortality	0	0	0	
Postoperative stay (day)	6.03±5.24	11.96±8.88	4.44±1.54	0.0001

Table 4. Management and outcome of cystobiliary fistula

Variables	n	Success rate	Amount of drainage (ml)	Hospital stay (days)
Intraoperative				
Suturing	18/26	7 (38.88%)	16720±17305.9	18.4±10.5
Suturing and transcystic	5/26	3 (60%)	7838.9±9226.8	10.4±7.7
Suturing and T tube	3/26	3 (100%)	6983.3±1272.8	10.7±11.6
p			0.0001	0.0001
Postoperative				
Conservative	6/13		22428.6±7044.1	21.9±5.4
Tubal drainage	2/13		25000±14142.1	13
ERCP and tubal drainage	5/13		6600±3847.1	9±2.6
p			0.0001	0.0001

ERCP: endoscopic retrograde cholangio-pancreatography

DISCUSSION

In endemic areas, hepatic hydatid disease (HHD) remains a medical problem of great concern. One of the most common complications of HHD is the communication between the cyst and the biliary system, which is known as cysto-biliary fistula (CBF). CBF is reported to be present in up to 40% of the cases of HHD and is responsible for most of the post-operative complications (4-6,16,17).

Because CBF is a major risk factor for post-operative morbidity, pre-operative and intra-operative diagnosis and management helps to effectively enhance the post-operative outcome. Several reports in the literature addressed the methods to effectively diagnose and predict the presence of CBF (14,18,19).

Predicting the presence of CBF begins with pre-operative factors detected in the history, examination, laboratory, and imaging findings. Obstructive jaundice and/or cholangitis are sensitive indicators of the presence of a frank CBF in more than 60% of the cases (7,11,20,21). In our series, obstructive jaundice was present in 19.2% of the patients with CBF, which was similar to what Atli et al. (5) reported in a case series including 116 patients where 25% of the patients with CBF had a history of obstructive jaundice.

An intracystic pressure around 35 cm H_2O is an indicator of its viability, and this pressure is generally higher than the intraluminal pressure of the biliary radicals. This high pressure is the cause of CBF. Obstructive jaundice, recurrent cholangitis, and elevated ALT and ALP are the expected results of CBF. Endoscopic retrograde cholangio-pancreatography (ERCP) and MRCP are ineffective in predicting pre-operative CBF because of the high pressure inside the cyst. However, ERCP and MRCP can used pre-operatively for patients with obstructive jaundice, a history of cholangitis, or elevated liver enzymes. ERCP and MRCP demonstrate dilated bile ducts and daughter vesicles or a germinative membrane of hydatid cysts inside biliary radicals. If the bile ducts are evaluated with pre-operative ERCP, it is not necessary to do common bile duct exploration (22).

In this study, the pre-operative levels of ALT and ALP were significantly higher in the CBF group (p<0.001). However, after multivariate analysis, a history of jaundice, pre-operative ALT and ALP were found to be non-significant as predictors for CBF, which is consistent with recent reports (13,14,18).

The size of the cyst has always been reported as an important predictor for the presence of CBF. The hypothesis is that the increase in the cyst size is associated with an increase in the intracystic pressure causing pressure necrosis of the adjacent biliary radicles with a subsequent rupture of the cyst into the biliary system (23). However, the cut off value for the cyst diameter that predicts CBF has not been settled. In 2001, Atli et al. (5) analyzed the data of 116 patients with HHD, and 24 had CBF. They concluded that a cyst diameter >10.5 cm was a significant predictor for frank rupture, while a cyst diameter of >14.5 cm was significant for occult CBF. In 2006, Demircan et al. (12) reported that a cyst diameter >8.5 cm was a predictor for CBF. In 2008, Kilic et al. (13) reported that a cyst diameter of >7.5 cm was a risk factor for intra-operative bile leakage and postoperative biliary fistula. In another study including 183 cases with occult and asymptomatic cysts, Unalp el al. (10) reported that a cyst diameter of more than 10 cm predicted post-operative bile leak. In the current study, we also found that the cyst diameter was a significant predictor for the presence of CBF. The mean cyst diameter was 18±9.2 cm for the group with CBF versus 10.1±5.3 cm for the group without CBF. Cysts with a diam-

eter >10 cm in our study were found to be associated with a significantly higher incidence of CBF.

The management strategy of CBF depends on when it is diagnosed. Pre-operatively diagnosed frank fistulae presenting with obstructive jaundice and/or cholangitis can be effectively managed by ERCP, which is both diagnostic and therapeutic and can be a scheduled elective surgery (24,25). Some authors recommend routine ERCP in cysts larger than 7.5 cm in diameter to assess the presence of CBF; however, there is no consensus supporting such a recommendation (5,26). Intra-operatively diagnosed CBF can be managed by several techniques. These include simple suturing or suturing with biliary decompression by the means of a transcystic tube (through the cystic duct after cholecystectomy) or a T-tube through a choledechotomy (5,27-29). In our series, suturing and biliary decompression were significantly associated with a lower incidence of post-operative complications and a shorter length of hospital stay ($p<0.001$).

Occult CBF not detected pre- or intra-operatively usually presents with post-operative biliary fistula. Post-operative biliary leakage occurred in 11.4% of our study group, which was similar to the rates reported in several studies (5,12,13,19,29,30). These patients were managed either conservatively, with ultrasound guided tube drainage or ERCP with ultrasound guided drainage of the abdominal bilomas. We found that biliary decompression via ERCP with ultrasound guided tubal drainage of any collection present is the most effective strategy in the management of post-operative biliary leakage compared to conservative treatment or ultrasound guided tubal drainage alone ($p<0.001$). Several studies have emphasized the importance of ERCP in the management of post-operative biliary fistula, especially when the fistula output is more than 300 ml/day or the duration of the fistula is more than 3 weeks (2,20,31,32). However, in our study, early management by ERCP led to earlier resolution of the bile leakage and a shorter hospital stay (9±2.6 days).

International classification of cystic echinococcosis (CE) depending on imaging will facilitate the application of uniform standards and principles of treatment for each cyst type. Two classifications are most frequently used: the Gharbi and the WHO Informal Working Group on Echinococcosis (IWGE) classification (33,34). The first clinical group starts with cyst types CE 1 and 2, and such cysts are active, usually fertile cysts containing viable protoscoleces. This group can be treated successfully and effectively by percutaneous methods. The technique requires experience, and the cyst must be drained through the hepatic parenchyme to avoid peritoneal contamination or anaphylaxis. The second clinical group (CE Type 3) is cysts entering a transitional stage where the integrity of the cyst has been compromised either by the host or by chemotherapy. The third clinical group is comprised of CE Types 4 and 5, which are inactive cysts that lost their fertility and are degenerative. Surgery is still the first choice for type III cysts, type IV cysts, and cysts opening into the bile ducts or peritoneal cavity. There is often no need for therapy for type V hydatid cysts (33-36).

In conclusion, our study suggests that cysts with a diameter >10 cm are strong predictors of the presence of CBF. When present, biliary decompression (intra- or post-operatively) is an effective way to control the fistula and improve the post-operative outcomes.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Mansoura faculty of medicine MFM-IRB (Code number: R/16.06.18).

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

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