Review

Cholecystocutaneous fistula incidence, Etiology, Clinical Manifestations, Diagnosis and treatment. A literature review

Muhamad Zakaria Brimo Alsaman a, Muhammad Mazketly a, Mohammad Ziadeh a,* , Owais Aleter b, Ahmad Ghazal c

a Faculty of Medicine, University of Aleppo, Aleppo, Syria
b Department of Radiology, Aleppo University Hospital, Aleppo, Syria
c Department of Surgery, Aleppo University Hospital, Syria

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ABSTRACT

Cholecystocutaneous Fistula (CCF) is a type of external biliary fistula, which connects the gallbladder with the skin. Thilesus first described this phenomenon in 1670. There is usually a history of calculi in the gallbladder or neglected gallbladder disease.

The incidence of CCF is rare, most patients are elderly females with the mean age of 72.8 years old. They usually present with chronic calculus cholecystitis or a history of a previous surgical intervention. US, CT, MRI, MRCP and (CT or X-ray) fistulogram are used to confirm the diagnosis. CT was more significant than US in identifying the track of the fistula and the fluid that runs throw it.

CCF patients presented with systemic symptoms (fever, nausea and vomiting) or local symptoms. RUQ region is the most common site of external opening.

Open cholecystectomy with excision of the fistulous tract is considered an acceptable option for treatment and it is curative in most cases. However, laparoscopic approach can be another option with experience surgeons.

1. Introduction

Fistula is an abnormal condition, which results from abnormal connection between two epithelialized surfaces. Biliary fistulas are rare complications of gallstone, that connect between the biliary tract and other organs, there are two main groups of biliary fistulas: external and internal [1].

Internal biliary fistula connects the gallbladder with gastrointestinal tract, it is induced by chronic cholecystitis [2].

External biliary fistula connects the gallbladder with abdominal wall, it could be spontaneous, postoperative or post-traumatic or caused by iatrogenic injury of biliary tract [1,3].

Cholecystocutaneous fistula is a type of external biliary fistula, which connects the gallbladder with skin (Fig. 1).

Untreated or neglected gallbladder disease may lead to CCF are the main risk for CCF cases. Most patient presented with a history of calculi in the gallbladder or neglected gallbladder disease and they treated with conservative or surgical way.

There are less than 100 cases of cholecystocutaneous fistula reported in the medical literature [4]. The first reported case of CCF was in 1670 by Thilesus, who described this phenomenon for the first time.

CCF can be spontaneous after cholethiasis and neglected gallbladder disease (5), or following previous surgery such as percutaneous cholecystostomy drain removal [4].

This study reviews the Incidence, Etiology, Clinical Manifestations, Diagnosis and Management for Cholecystocutaneous Fistula patients, using data of pervious case report in the medical literature.

2. Methods

We conducted a literature search for relevant studies that have been published between 1954 and 2020 in Pubmed database by using the following search term “Cholecystocutaneous Fistula”. There were no restrictions on country, or language. Articles were excluded if they were animal studies or uncompleted data. We reviewed 48 case report articles that were published between 1954 and 2020.
However, patients may present with pain and swelling in the RUQ or epigastric region [6,18], discharging sinus from the anterior abdominal wall [15,19], erythematous mass [20], subcostal abscess [18] (Table 1). The most common site of external opening is in the right upper quadrant of the abdominal wall. It can also be seen in right flank, right subcostal area, epigastric region, right breast, para-umbilical site (Table 3).

2.3. Diagnosis

CCF is diagnosed usually using imaging studies, or exploratory laparotomy in special cases.

2.4. Imaging studies include

- Ultrasonography (US)
- Computed tomography (CT)
- Fistulogram
- Magnetic resonance imaging (MRI)

US provides good assessment for CCF diagnosis by showing abnormal findings such as abscess, gallbladder stones, edema, thickened in gallbladder wall and dilated biliary ducts [5,15,17,21] but often fails to confirm the CCF diagnosis. In a few cases, US was able to demonstrate the track of CCF [12,19].

CT confirmed the diagnosis by identifying the track between the gallbladder and the skin in several cases [22–25]. Furthermore, CT fistulogram can also show the track of CCF which confirm the diagnosis [21]. CT couldn’t identify the track of CCF in a few cases where it just showed abnormal findings which point toward the diagnosis [19,23,26,27].

In total, CT was more significant than US in identifying the track of the fistula and the fluid that runs throw it.

MRI was able to detect gallstones, gallbladder perforation, and the fluid, which extruded through the abdominal wall [5,18].

MRI could be more accurate when CT detects no abnormalities.

MRCP increases the confirmed cases [7,17,19,28]. The results of MRCP are identical to US and CT.

Hepatobiliary iminodiacetic acid scan was used in two cases; it failed to demonstrate the fistula in one case (4) and showed obstruction in biliary tracks in the second one [29].

In addition, exploratory laparotomy may be the only diagnosis methods especially in old reported cases, in poor countries or with shortage of appropriate equipment and laparoscopic experience.

CT Fistulogram or X-ray Fistulogram have been used to demonstrate track of the fistula accurately [14,21,30], although in most cases Fistulogram was not used and the diagnose was made by another method.

There are problem and the difficulties facing the diagnosis such as absence of radiological expertise, it is uncommon to consider CCF as deferential diagnosis since it is a rare condition and presence of mucous discharge rather than yellowish discharge if there is an obstruction in the cystic duct makes it hard to diagnose especially in the early stages.

2.5. Management

The management of CCF vary according to disease severity, age, and the patient’s preference.

There is no standard base line management for cholecystocutaneous fistula, due to the fewness of the number of cases and the differences in patients’ illness quality.

The medical literature mentioned different ways of CCF management, either conservative or surgical management.

2.6. Conservative management

Conservative management includes antibiotics, fluids or ERCP. Percutaneous abscess drainage is performed immediately with the
Table 1
Age, sex, etiology, presentations, diagnosis and management of Cholecystocutaneous Fistula.

| Authors                  | Age | Sex | Etiology | Presentations | Confirmed diagnosis | Management                        |
|--------------------------|-----|-----|----------|---------------|---------------------|-----------------------------------|
| Wang et al. [18]         | 86  | M   | Calculous cholecystitis | Pain and swelling in the RUQ | MRI                 | Open cholecystectomy               |
| Rinzivillo et al. [5]    | 76  | M   | Calculous cholecystitis | tumefaction of the right hypochondrium, fever, malaise and a right subcostal mass | MRI | Open cholecystectomy               |
| El Fathy et al. [23]     | 78  | M   | Calculous cholecystitis | Fever, malaise and a right subcostal mass | CT | Open cholecystectomy               |
| Ioannidis et al. [8]     | 71  | M   | Calculous cholecystitis | persistent bilious drainage from an old surgical scar, from surgical drainage, of the right upper abdominal quadrant | X-Ray fistulogram | Open cholecystectomy               |
| Cheng et al. [32]        | 21  | F   | Calculous cholecystitis | Soft tissue defect at posterior trunk and sacral area after a major trauma | CT fistulogram | PTGBD                            |
| Chatterjee et al. [11]   | 45  | F   | Calculous cholecystitis | acute onset of pain and swelling in the right hypochondrium fevers, malaise and a right subcostal mass | X-Ray fistulogram | Open cholecystectomy               |
| Ijaz et al. [10]         | 74  | F   | Calculous Cholecystitis | fever, malaise and a right subcostal mass | CT | Open cholecystectomy               |
| Ayoub et al. [26]        | 65  | M   | Gallstones       | Swelling in the right hypochondriac area. | During the surgery | Open cholecystectomy               |
| Pol et al. [21]          | 70  | F   | Gallstones       | Discharging sinus in the right hypochondriac region | CT fistulogram | Laparoscopic cholecystectomy       |
| Kassi et al. [6]         | 46  | _   | Gallstones       | Painful, fluctuating, epigastric swelling of 15 days’ duration. | CT | Open cholecystectomy               |
| Kundi et al. [30]        | 30  | F   | Gallstones       | Pain in the right hypochondrium of years evolution | X-Ray fistulogram | Open cholecystectomy               |
| Dixon et al. [28]        | 94  | F   | Gallstones       | Discharge and non-healing wound | CT | Conservative management            |
| Polite et al. [29]       | 70  | F   | Gallstones       | acute on chronic midegastriac abdominal pain, associated with nausea and vomiting right upper abdominal pain and icterus | Hepatobiliary iminodiacetic acid | Open cholecystectomy               |
| Ozdemir et al. [24]      | 89  | F   | Gallstones       | | CT | Open cholecystectomy               |
| Gordon et al. [33]       | 83  | F   | Gallstones       | Mild, intermittent right upper quadrant pain | CT | Open cholecystectomy               |
| Khan et al. [34]         | 76  | M   | Gallstones       | Necrotizing fasciitis of anterior abdominal wall and cholecystocutaneous fistula | X-Ray fistulogram | Open cholecystectomy               |
| Pezzilli et al. [17]     | 90  | F   | Gallstones       | Diarrhea and low-grade fever | CT | conservative management and Ct drainage of the purulent collection was also carried out |
| Aguilar et al. [35]      | 83  | M   | Gallstones       | Pain in the right upper quadrant and the appearance of a mass | CT | Open cholecystectomy               |
| Hawari et al. [9]        | 84  | M   | Gallstones       | Intermittent right upper quadrant abdominal pain, nausea, darkening of his urine, and increasing jaundice | X-Ray fistulogram | Open cholecystectomy               |
| Sayed et al. [31]        | 85  | F   | Gallstones       | Soft and non-tender mass in her right flank. | MRCP | ERCP and sphincterotomy          |
| Yucseyar et al. [36]     | 70  | F   | Gallstones       | Abscess formation in the right upper quadrant | _ | Open cholecystectomy               |
| Carragher et al. [37]    | 67  | F   | Gallstones       | Right hypochondriac pain. | CT | Conservative management            |
| Hoffman et al. [38]      | 70  | F   | Gallstones       | Chronic epigastric pain. | During the surgery | Open cholecystectomy and choledocholithotomy |
| Jeffery et al. [39]      | 73  | F   | Gallstones       | Ten-day history of dull epigastric pain and anorexia | During the surgery | Laparotomy                        |
| Schippers et al. [40]    | 75  | M   | Cholecystitis     | Necrotizing fasciitis of anterior abdominal pain | During the surgery | Open cholecystostomy               |
| Gerrard et al. [22]      | 80  | F   | Cholecystitis     | Acute cholecystitis | CT | Percutaneous cholecystectomy      |
| Mughal et al. [19]       | 74  | F   | Cholecystitis     | Unremitting pain in the right shoulder that had progressed to the right side of the abdomen pain and swelling in the RUQ, and development of a discharging sinus within it | US + CT | Open cholecystectomy               |
| Maynard et al. [7]       | 68  | F   | Cholecystitis     | Painful swelling in the right upper anterior abdominal wall. | CT | Open cholecystectomy               |
| Jayasinghe et al. [41]   | 87  | F   | Cholecystitis     | Sepsis following a fall | CT | Open abcess drainage              |
| Jayasinghe et al. [41]   | 74  | F   | Cholecystitis     | Sepsis following a fall | CT | Open abcess drainage              |

(continued on next page)
Conservative management: few cases, helped relieve symptoms and improved patient’s condition.

Surgical management:

Guidance of CT, or US, then all patients should receive management by antibiotics to manage infections and cholecystitis [4,7,16,17,23,26].

Conservative management is performed to elderly patients who are unable to tolerate surgery [17].

Few cases were treated by using endoscopic retrograde cholangiopancreatography (ERCP) for CCF treatment, by removing calculi using ERCP balloon trawl and sphincterotomy [31].

Chemotherapy is applied for CCF patients due to carcinoma of the gallbladder [13].

Percutaneous transhepatic gallbladder drainage (PTGBD) can be applied to treat CCF. Where the fistula heals under secondary intention after removing drainage tube [32].

Conservative management cured few cases, helped relieve symptoms and improved patient’s condition.

Surgical management includes open cholecystectomy and laparoscopic cholecystectomy.

Open cholecystectomy with excision of the fistulous tract is considered as a standard option for management and it is curative in most cases. In the other hand, laparoscopic cholecystectomy with excision of the tract can be another acceptable and preferable option with advance experienced laparoscopic surgeons.

Presence of comorbidity in patients lead to failure of healing, also difficulty in performing surgery for cachectic or elderly patients.

Lack of adequate surgical experience can lead to serious complications and difficulty in treatment.

3. Conclusion

CCF diagnosis and management represent one of the surgical

### Table 1 (continued)

| Authors             | Age | Sex | Etiology | Presentations | Confirmed diagnosis | Management             |
|---------------------|-----|-----|----------|---------------|---------------------|------------------------|
| Kapoor et al. [15]  | 65  | M   | Cholecystitis | CT            | Cholecystocutaneous fistula excision |
| Flora et al. [27]   | 67  | M   | Cholecystitis | CT            | Open cholecystectomy |
| Malik et al. [43]   | 76  | F   | Cholecystitis | CT            | Laparoscopic cholecystectomy |
| Cruz et al. [25]    | 81  | M   | Cholecystitis | X-Ray fistulogram | Open cholecystectomy |
| Khan et al. [44]    | 90  | F   | Cholecystitis | CT            | Open cholecystectomy |
| Dutiaux et al. [45] | 65  | M   | Cholecystitis | Systemic Pathology Exam | Open cholecystectomy |
| Vasanth et al. [46] | _   | _   | Cholecystitis | -             | - |
| Mathonnet et al. [47]| 87  | F   | Cholecystitis | X-Ray fistulogram | Open cholecystectomy |
| Sedwick et al. [48] | 76  | M   | Cholecystitis | ERCP          | Laparoscopic cholecystectomy |
| Pripotnev et al. [16]| 85  | F   | Cholecystocutaneous fistula developing after the removal of a percutaneous drain for the treatment of acute cholecystitis | During the surgery | Laparoscopic cholecystectomy |
| Sodhi et al. [13]   | 66  | F   | Adenocarcinoma of gallbladder | CT            | Conservative management (chemotherapy) |
| Serrano et al. [49] | 83  | M   | Papillary adenocarcinoma | CT            | Radical cholecystectomy |
| Andersen et al. [50]| 89  | F   | -         | ERCP          | Open cholecystectomy |
| Lofgren et al. [4]  | 60  | F   | Severe cholecystitis the year prior that was managed by a percutaneous cholecystostomy drain | CT with oral contrast | Robotic cholecystectomy |
| Seoane et al. [51]  | 83  | F   | Spontaneous external biliary fistula and a history of ERCP three months before | ERCP          | Laparoscopic cholecystectomy |
| Murphy et al. [52]  | 80  | M   | Cholecystitis | ERCP          | Laparoscopic cholecystectomy |
| Grimes et al. [14]  | 70  | F   | traumatic rupture of the gallbladder | X-Ray fistulogram | Open cholecystectomy |
| Mean age            | 72.8|     |           |                |                      |
| Standard Deviation  | 15  |     |           |                |                      |
obstacles, which we still encountered from time to time. We noticed through our review different ways of diagnosis and management. Most of them were dependent on the surgical experience and the advanced medical investigation equipment.

In conclusion, there is no standard ways for diagnosis and management of CCF but according to our review; we think that each surgeon should choose the best way to deal with CCF patients depending on patients’ quality, available equipment and advanced experienced surgeons.

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Author contribution
MZBA, MM, MZ, OA: Writing - Original Draft. MM, MZBA: Writing - Review & Editing. MM: Formal analysis and Resources. MZBA: Validation and Visualization. AG: Supervision and Project administration. MZ: corresponding author.

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Table 2
Presenting microorganism found in cholecystocutaneous fistula cases.

| Authors | Microorganism |
|---------|---------------|
| Loefgren et al. [4], Micu et al. [12], El Tinay et al. [23] | Escherichia coli |
| Jayasinghe et al. [41] Fabi et al. [53], Ioannidis et al. [8], Hoffman et al. [38], Orville et al. [14] | Helicobacter pylori |
| Flora et al.[27], Murphy et al. [52], Ijaz [10] | Klebsiella pneumonia |
| El Tinay et al. [23], Ioannidis et al. [8] | Staphylococcus hominis, |
| Ioannidis et al. [8] | Staphylococcus aureus |
| Cheng et al. [32] | Strepto-coccus milleri |
| Hawaiari [9] | Entercoccus faecalis |
| Micu et al. [12] | Bac teroides fragilis |
| Lofgren et al. [4] | Fragils |
| Mathonnet et al. [47] | Proteus mirabilis |
| Orville et al. [14] | Viridans streptococci |

Table 3
presenting site of external opening.

| Location | Authors |
|----------|---------|
| RUQ | Ayoub et al. [26], Loefgren et al. [4], Seoane et al. [51], pol et al. [21], Wang et al. [18], Rinzivillo et al. [5], Gerrard et al. [22], El Tinay et al. [23], Meghal et al. [19], Maynard et al. [17], Bermudez et al. [30], Pripotneva et al. [16], Kapoor et al. [15], Poite et al. [29], Kim et al. [42], Sodhi et al. [13], Ioannidis et al. [8], Cheng et al. [32], Serrano et al. [49], Gordon et al. [33], Khan et al. [34], Pezzillia et al. [17], Hawaiari et al. [9], Chatterjee et al. [13], Flora et al. [27], Ijaz et al. [10], Malik et al. [45], Väyeyer et al. [36], Carraher et al. [37], Sedgwick et al. [40], Abri et al. [54], Jeffrey et al. [39], Orville et al. [14], |
| Right flank | Sayed et al. [31], Khan et al. [44], Jayasinghe et al. [41] |
| Right subcostal area | Ondenir et al. [24], Cruz et al. [25], Hoffman et al. [38] |
| Epigastric region | Micu et al. [12], Kansi et al. [6] |
| Right breast | Andersen et al. [50] |
| para-umbilical | Dixon et al. [28] |

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