

Bilio-enteric fistulas, a rare complication of cholelithiasis

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Abstract. Introduction: Bilio-enteric fistulas are a rare complication of untreated cholelithiasis. They are usually classified as primary or secondary and can affect either the biliary or the gastrointestinal tract. Most common they are localized at duodenum level and jejunum level, where they can be associated with biliary ileus. Material and Method: This paper presents a mini-series of 4 patients that presented in our department with biliary ileus caused by bilio-enteric fistulas with multiple localizations, within a 3-year time frame. All the patients underwent surgical treatment and the diagnostic and therapeutic management of each of them was analyzed. Results: Four patients, three women and one man were identified with cholecystoduodenal fistula. Their mean age was 85 years. Two of the patients presented with biliary ileus, one with Bouveret Syndrome, and one with subocclusive episodes and acute cholecystitis. Conclusion: The incidence of bilio-enteric fistula was similar to that reported in the medical literature. They are most often a complication of cholelithiasis with a reduced frequency and its' diagnosis is difficult due to its' nonspecific symptomatology. Given the advanced age of the patients and the existence of comorbidities in practically each of them, the surgical therapy must be customized to each patient.

Key Words: bilio-enteric fistulas, cholelithiasis, ileus.

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Introduction

A biliary fistula is a pathologic communication between any portion of the biliary tree and surrounding organs.

Fistula formation is the result of an insidious inflammatory process triggered by underlying cholelithiasis. External or secondary biliary fistulas are mainly due to iatrogenic lesions or trauma.

The symptoms of bilio-enteric fistula are quite unspecific and the diagnosis is difficult to make and is usually facilitated by contrast-enhanced CT scans and/or MRCP. Biliary ileus is a major complication of internal fistulas in which stones formed in the gallbladder or very rarely in the CBD, reach the digestive tract leading to obstructing. Biliary ileus carries a lifetime risk of development of 0.4% in patients with cholelithiasis (Umer et al 2018) and of 0.15% -8% in patients with patent biliary-digestive fistulas (Aguilar-Espinosa et al 2017).

The etiopathogenesis behind the formation of internal fistulas is represented by the encasement of large stones in Hartmann's pouch which by compression produces ischemia of the gallbladder wall leading to inflammation and then necrosis; stone migration follows this path most commonly towards the second portion of the duodenum (0-10.5%), jejunum or right colon (Nuño-Guzmán 2016). The migration of large stones through the main bile duct and the ampulla of Vater has been described, but is an extremely rare scenario (Chang et al 2018).

The aim of the current paper is to review the existing medical literature, identify the indications and recommendations of diagnosis and management and to compare these with our

mini-series of 4 patients, operated in our department between March 2019 and October 2021.

Patients' Case Presentation

Patient no. 1

A 79-year-old female patient presents with diffuse abdominal pain, nausea, vomiting, and the absence of intestinal transit for faeces and flatus. The onset of the symptoms began 6 days prior to admission. The patient had a personal history of biliary ileus, for which entero-lithotomy was performed with enterorrhaphy (2019). Laboratory findings revealed an increase in WBC serum levels (15,000/mm³ with left shift), hyperglycaemia (123 mg/dl), hypoproteinaemia (6 g/dl); cholestasis syndrome (total serum Bilirubin levels = 1.7 mg/dl, conjugated serum bilirubin levels = 0.7 mg/dl); inflammatory syndrome (C Reactive Protein levels = 61 mg/L). An abdominal ultrasound was performed in the Emergency Department, revealing intestinal loops with a diameter of 38 mm, absent peristaltic movements, low quantity free fluid between small bowel loops, pneumoobilia, without detecting any hyper-echoic structures resembling to gallstones. On plain abdominal X-Ray, multiple fluid-air levels at mesogastric level and at left flank were identified (Figure 1). The patient undergoes emergency surgery via an open approach; Adhesiolysis; Entero-lithotomy – enterorrhaphy. The postoperative diagnosis was that of Bowel obstruction caused by recurrent biliary ileus with stone migrated in the terminal ileum through a cholecysto-duodenal fistula.



Figure 1: Plain abdominal X-Ray

Patient no. 2

A 92-year-old female patient presents with nausea, vomiting, diffuse abdominal pain, lack of transit for faeces and flatus, with symptoms' onset 3 days prior to the Emergency department admission. The patient's biological status reveals nitrogen retention syndrome (BUN = 139 mg/dl, Serum Creatinine = 3.15 mg/dl), inflammatory syndrome with incipient sepsis (C Reactive Protein = 282 mg/L, Procalcitonin = 6.3 ng/ml), non-compensated metabolic acidosis, hypoproteinaemia with hypoalbuminemia (total protein count = 5.3 g/dl, serum albumin = 27 g/L), elevated WBC (18200/uL), moderate anaemia (Hb 9.5 g/dl). An abdominal CT scan without intravenous contrast was undertaken, describing a biliary-digestive fistula between the gallbladder and the duodenum with a stone migrated in the first jejunal loop, paraumbilical to the right; intra and extrahepatic pneumobilia with no signs of pneumoperitoneum or free abdominal fluid; nonobstructive left kidney stones (Figure 2, Figure 3). The patient underwent laparotomy with jejuno-lithotomy and jejunorrhaphy (Figure 4, Figure 5, Figure 6). The final postoperative diagnosis was that of Biliary ileus caused by cholecystoduodenal fistula (gallstone migrated to the proximal jejunum), Gallbladder cholelithiasis.



Figure 2- Abdominal CT without intravenous contrast (arrows pointing towards the “porcelain” gallbladder with intraluminal remnant gallstones)

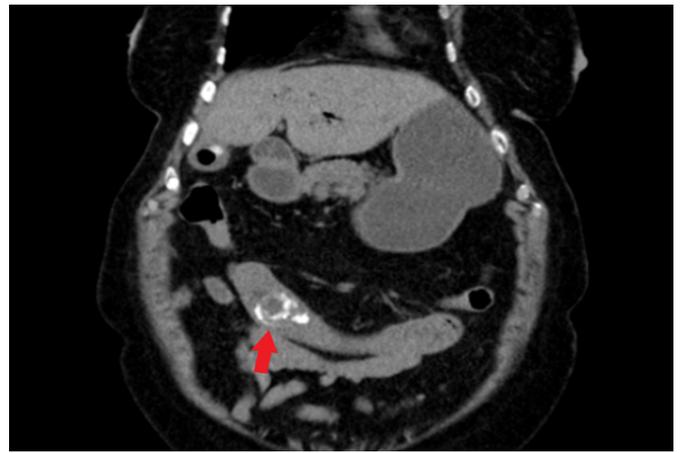


Figure 3 - Abdominal CT without intravenous contrast (arrows pointing towards the migrated gallstone in the proximal jejunum; NB – distended stomach cranially)



Figure 4: Gallstone at the level of the unopened proximal jejunum (arrows)

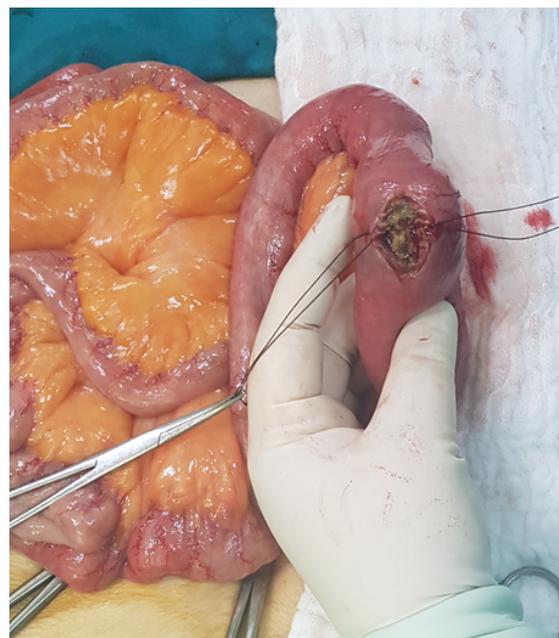


Figure 5: Enterotomy and extraction of the gallstone (note future traction sutures)



Figure 6. Gallstone (broken)

Patient no. 3

A 89-year-old female patient, complains of pain in the right upper quadrant (RUQ) and epigastrium, nausea, vomiting, headache, symptoms that have been ongoing for the past 7 days prior to hospital admission; bowel transit for faeces and flatus was present. Biological status revealed Left shift without increased WBC (9,360/uL), hyperglycaemia (142 mg/dl), inflammatory syndrome (C Reactive Protein levels = 14 mg/L). An abdominal CT scan without contrast was performed that identifying a cholecysto-duodenal fistula with one gallstone blocked at an intracholecystic level; another migrated gallstone was found below the level of the fistula tract on the third duodenal segment; other relevant CT findings included a small axial hiatal hernia, sigmoid diverticulosis, bilateral uncomplicated inguinal hernias with properitoneal fat in the sack (Figure 7, Figure 8). The surgical approach consisted of: emergency laparotomy followed subsequently by, fundus-down cholecystectomy, gastrotomy with retrograde duodenal gallstone mobilization and extraction, primary double-layer gastrorrhaphy and suture of the primary duodenal fistula point of entry. The post-operative diagnosis was that of Bouveret's Syndrome due to cholecysto-duodenal fistula. Scleroatrophic cholecystitis.

Patient no. 4

A 80-year-old male patient presents with pain in the ROQ associating fever (39°C), nausea, vomiting with an onset 5 days



Figure 7 - Abdominal contrast enhanced CT (arrows pointing towards migrated gallstones, coronary view)

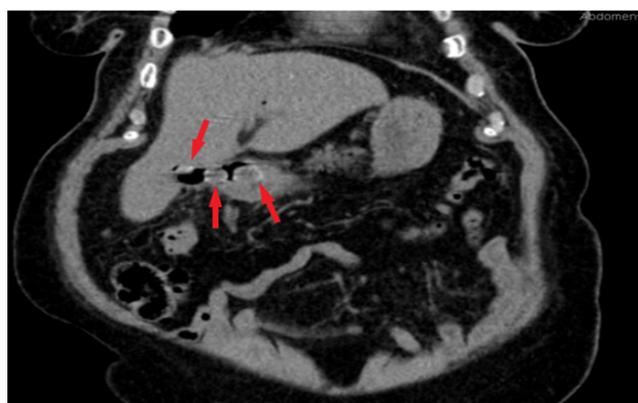


Figure 8 - Abdominal contrast enhanced CT (arrows pointing towards migrated gallstones, frontal view; dilated stomach is eloquent for Bouveret's Syndrome)

prior to hospital admission. The patient is known with a personal history of similar episodes associated to diminished bowel movements for the past 3 months. The patient's biological status revealed elevated BUN and GGT levels. Abdominal ultrasonography described a distended gallbladder with bladder wall thickness of over 5 mm, with multiple hyper-echoic images suggestive for gallstones up to 7 mm, portal vein 12 mm, CBD 7.5 mm, intrahepatic bile ducts without any segmentary or global distensions. Contrast-enhanced abdominal CT scan revealed an acute cholecystitis with a pericholecystic abscess. An exploratory laparotomy is performed with concomitant fundus-down partial cholecystectomy and stone extraction; intraoperative, the presence of a cholecysto-duodenal fistula is confirmed, but was not addressed per primam. The post-operative diagnosis was that of cholecysto-duodenal fistula with subocclusive episodes and acute cholecystitis.

Results

In the postoperative setting, Patient no.1 presented with a slow favourable evolution, with restored bowel movements on postop day 6. On postop day 8, the patient presented melena, with favourable remission after Hydrogen Pump Inhibitors (Omeprazole 40 mg bid) administration, without performing a gastroscopy prior to discharge on the 13th postoperative day (respiratory and haemodynamic stability, afebrile, wound healing).

Patient's no. 2 postoperative evolution was good, with no major events, with the resumption of diuresis in normal quantity over a 24 hour time interval; bowel movements recovered on postoperative day5. The patient is discharged on the 11th postoperative day – with no fever, haemodynamic and respiratory stable, without subjective complaints. On the 13th postoperative day, the patient returns in the Emergency Department with nausea, vomiting, diffuse abdominal pain, lack of transit for flatus and stool for the past day. Lab findings revealed an elevated BUN level, anemia, thrombocytosis, inflammatory syndrome, hyperglycaemia, metabolic acidosis, hypoproteinaemia with hypoalbuminemia. On the abdominal CT scan, without contrast, we have identified moderate pneumobilia in the CBD in the intrahepatic bile ducts of the left hepatic lobe; corresponding to left iliac fossa, at the level of a jejunal loop, a calculus with a diameter of 30 mm was noticed, with concomitant proximal small bowel dilatation (proximal bowel short axis diameter of

33 mm over a distance of 97 mm (Figure 9)). Surgical reintervention was undertaken. Re-Laparotomy; Jejunotomy with calculus extraction (28 cm from Treitz's angle); Segmental jejunal resection with end-to-end hand-sewn jejuno-jejunal anastomosis; Douglas's pouch drainage. The postoperative evolution was slowly favourable, under antibiotic, analgesic, antipyretic treatment, hydro-electrolytic and acid-base balancing. On postoperative day 3 a surgical site infection (SSI, Clavien Dindo 2) was noticed at the level of the superficial tissue (*Pseudomonas aeruginosa* detected), which required local drainage, lavage with antiseptic solutions and oral antibiotic therapy. Neurology consult was requested, which does not confirm the suspicion of a stroke (the patient manifested apathy, adynamism, drowsiness). She was discharged on the 19th postoperative day.

Patient no. 3 had a favourable post-operative evolution, without any major events, resumed her intestinal movements on the 4th postoperative day and was discharged on the 7th postoperative day.

Patient 4 also shows a favourable evolution, being discharged on the 7th postoperative day.

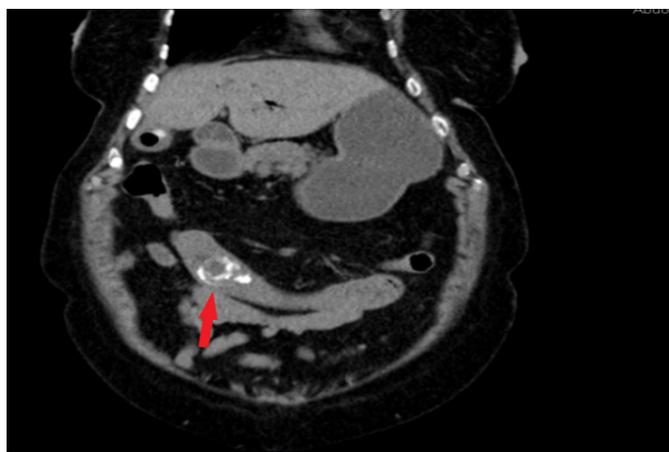


Figure 9 - Abdominal CT without contrast - biliary ileus

Discussions

In our institution, between March 2019 and October 2021, a number of 350 cholecystectomies were performed for cholelithiasis. The percentage represented by those with biliary fistulas being of 1.14%. The percentages reported by other case series found in the literature are between 0.15% - 8% (Umer et al 2018).

The age of the patients in our short case series is between 79 and 92 years, with similar age at diagnosis, reported by other. The predominance of female patients was higher, 3:1. The onset of the symptoms was insidious and unspecific. The period between the onset of symptoms and surgery was between 4 and 7 days. This interval is extremely important, because delaying surgery contributes to the increase of postoperative morbidity and mortality. All patients also had significant comorbidities that lead to some sort of postoperative complications – such as sepsis, pulmonary complications (ARDS) and an early onset of acute renal failure. Clinical diagnosis is difficult to establish, this is why, imaging studies are the most important tool in clearly delineating the final etiology of the disease. Symptoms are dominated by pain, associated in most cases with nausea and vomiting (Nuño-Guzmán 2016; Alemi et al 2019). In our

mini-series, 3 patients had biliary ileus, two had stones in the ileum and jejunum and one had Bouveret's syndrome (i.e. the obstruction of the first duodenal segment caused by the calculus, leading to acute gastric outlet syndrome). The calculus needs to measure at least 4 to 6 cm in size, in order to lead to intestinal obstruction (Iancu et al 2008). In our cases, the obstructive calculus had sizes that ranged from 4 to 5 cm. The first therapeutic measure upon hospital admission, for patients presenting with ileus, a parenteral hydro-electrolytic rebalancing therapy was implemented associated to a mandatory naso-gastric decompression tube, cranial from the site of obstruction. The same approach was reported by the vast majority of the authors cited by Inukai et al 2019.

The diagnosis of certainty for the presence of a bilio-enteric fistula is sometimes associated to Riegler's triad on imaging studies - which involves identifying the fistula, air-fluid levels and calculus images with ectopic location. The reported sensibility and specificity of Riegler's triad used for an accurate preoperative diagnosis vary between 30% -75%. (Clavien et al 1990; Rodríguez Hermosa et al 2001; Nuño-Guzmán 2016) For patient no. 1, a plain abdominal X-ray was performed, highlighting the air-fluid levels. In this matter, plain radiograms lack in sensibility and specificity in determining the etiology of the bowel obstruction. Other significant details that can be identified on plain radiograms could be pneumobilia or possibly a radiopaque ectopic calculus, which in our case, were not seen on this type of imaging study.

Abdominal CT was performed without any injection of contrast, due to elevated BUN and serum creatinine levels.

In our case, the three elements mentioned in Riegler's triad, were accurately identified on the performed CT scan. For patient no. 1, abdominal ultrasound identified bowel loops with a diameter of 38 mm, without peristalsis, and minimal free fluid. Furthermore, abdominal ultrasound accurately identified the presence of pneumobilia, the presence of the calculus, but could not identify the fistula tract. For patient no. 4, ultrasound correctly described the pericholecystic abscess, the inflammation of the gallbladder, the presence of cholelithiasis, without describing the presence of pneumobilia or fistula. As suspected, the sensibility and specificity aiding the diagnosis is higher when comparing CT scans to ultrasound evaluation (Nuño-Guzmán 2016). Other methods used, that can be useful for an accurate diagnosis, are upper GI endoscopy (that can visualize the obstruction caused by the calculus, the fistulous tract, or indirect signs of the fistula represented by an inflamed mucosa); MRCP is a method that has a diagnosis accuracy equal or, in the cases of radio-transparent calculus, higher than contrast-enhanced CT scans. ERCP is another useful tool that allows an opacification the entire biliary tree with the possibility of the contrast to migrate into the digestive tract, highlighting the fistulous tract.

In our case series we did not use endoscopy, MRCP, ERCP, in the surgical emergency setting.

The treatment of bilio-digestive fistulas is solely surgical. Conservative treatment with good results is rarely suited. As a matter of principle, the treatment should be tailored and adapted for every patient, considering the fact that usually the patient is frail, due to his/her's age, bears concomitant comorbidities and metabolic imbalances, all aggravated by the metabolic acidosis, septic state and intestinal obstruction. A quick and correct

diagnosis is of great value, helping the surgical team perform the surgery in an Emergency setting. Delaying surgery leads to an increase in postoperative morbidity and mortality. Surgical treatment has mainly 3 options.

The first is represented by enterolithotomy with enterorrhaphy. It is the method that bares the lowest rate of postoperative complications and mortality with an in-hospital stay duration shorter compared to other methods of surgical management. Its' disadvantage is that it leaves the gallbladder in situ, which may lead to a recurrence of the ileus. This is most commonly seen in the first 10 postoperative days. Other inconveniences are represented by the development of cholangitis, especially in the event of the presence of a cholecysto-colic fistula, and by malignant transformation of the gallbladder. A rare scenario is the spontaneous closure of the fistula, sometimes possible, reported by several other studies (Roberts & Lambrianides 2012; Aguilar-Espinosa *et al* 2017).

The migrated calculus is usually enclaved in the duodenum or terminal ileum due to lower peristalsis and a narrowed lumen of these structures. In the situation of a calculus obstructing the duodenum, the ideal surgical tactic would be to mobilize it by gentle maneuvers in the stomach or jejunum. Most often, these maneuvers lead to alteration of the duodenal wall, which greatly complicates the intervention. A solution for the accidental burst of the duodenal wall is to extract the stone at the level of the wall perforation, followed by a side-to-side duodeno-jejunal Roux en Y anastomosis. A simple duodenorrhaphy with possibly an omental patch have a higher complication rate, the most significant of which is the recurrent enlarging duodenal fistula. Another option is not to mobilize the stone and to perform the Kocher maneuver followed by duodenotomy with stone extraction and duodenorrhaphy. The chances for a postoperative duodenal fistula formation are lower, because the duodenal wall is not traumatized as in the case of an unsuccessful attempt to mobilize the calculus. (Nuño-Guzmán 2016)

Due to these inconveniences, a one-step surgery was proposed, involving enterolithotomy, cholecystectomy with subsequent closure of the remnant fistulous orifice. This approach is a more demanding one, since it comes with a longer operative time than the above-mentioned approaches. The postoperative morbidity and mortality rates are higher, when such one-setting surgery is performed. Same can said about a longer length of hospitalization.

Because of these, a third surgical strategy has been proposed, which involves a two- step surgery. In the initial operative setting, an enterolithotomy with enterorrhaphy is performed. Subsequently at 4-6 months postop, if the fistulous orifice is still patent, a second surgery is performed involving cholecystectomy and closure of the fistulous orifice. Verification of fistula patency is done by contrast-enhanced abdominal CT scan and upper GI endoscopy. This 4-6 month interval between the two surgeries lacks specialists' consensus and is still a subject of debate. There are many surgical teams that propose an earlier reintervention at an interval of 2 months from the first one, motivating this by the fact that if the fistula does not close spontaneously during this time, it has little to no chance of spontaneous closure, thus the delay of the surgical reoperation does not make sense (Crespi *et al* 2016; Inukai 2019).

In patient no.1, the obstruction level was located 15 cm cranial from the ileo-cecal valve. Exploratory laparotomy together with adhesiolysis, enterolithotomy and enterorrhaphy was the chosen surgical strategy. For patient no. 2, the obstacle was located 30 cm distal from Treitz's ligament – thus, the strategy chosen consisted in laparotomy, jejunolithotomy and jejunorrhaphy. Although the patient still had a 3.5 cm stone in the gallbladder, no surgical approach for the bladder was done, mainly because of the patient's frail status and cardiovascular instability. This patient returned 48 hours after discharge showing obvious signs of a recurrent biliary ileus. The on-call surgeon reoperated the patient, identifying the de novo migration of the known gall bladder calculus, at 28 cm distal from Treitz's ligament. Intraoperative, due to the signs of localized wall ischemia at the level of obstruction, segmental enterectomy with end-to-end hand-sewn entero-enteral anastomosis was performed. Segmental enterectomy greatly increases the rate of postoperative complications, not encountered for this patient. Probably a better initial surgical strategy could have been a partial cholecystectomy with the extraction of the remnant calculus, thus avoiding the recurrence of the ileus.

In the case of Patient no. 3 with Bouveret's syndrome, the 3 stones that obstructed the first segment of the duodenum were successfully mobilized in the stomach. Through an antrotomy, they were extracted, with a subsequent gastrorrhaphy followed by cholecystectomy with the closure of the fistulous orifice. The pathology resolution, in this case, was technically feasible to be performed in a single stage.

Patient no. 4, whose preoperative diagnosis was acute cholecystitis with pericholecystic abscess, underwent a partial cholecystectomy with the extraction of stones. Intraoperatively, we found a communication between Hartmann's pouch and the duodenum of about 0.4 cm. Cholecystorrhaphy, abscess evacuation and drainage were the strategies of choice.

Conclusions

Biliary-digestive fistulas are rare complications of chronic cholelithiasis. Their known cited incidence is between 0.5-8%. A redoubtable complication of large calculus co-existing with bilio-enteric fistulas is the onset of the biliary ileus. Surgical treatment strategies have different approaches, all bearing advantages and disadvantages and being a constant debate issue. Given the old age of the patients, frailty and co-existing comorbidities, the chosen surgical approach needs to be tailored for every distinct patient. The widespread use of ultrasound has greatly increased the diagnostic frequency of cholelithiasis in the uncomplicated phase or inflammatory complications in the early phase, leading to increased cholecystectomies before the onset of potential migratory complications, such as bilio-digestive fistulas

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