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CASE REPORT | BILIARY

Different Approaches to the Management of Cholecystoenteric Fistula

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ABSTRACT

A cholecystoenteric fistula is an anomalous communicating tract between the gallbladder and any segment of the gastrointestinal tract. It is a rare complication of gallstone disease and typically affects elderly patients with multiple medical comorbidities. These fistulae can present in a variety of ways, and the diagnosis is often made only after extensive workup. Despite notable advances in imaging techniques in the last half-century, a considerable number of cases are still discovered incidentally during open or laparoscopic surgery. We present a series of 3 cases, each with different etiologies and presentations, but all of whom were found to have a cholecystoenteric fistula. Each case was managed differently, highlighting the diversity of this intriguing condition.

KEYWORDS: abdominal pain; Bouveret syndrome; cholecystoenteric fistula; endoscopic treatment; gallstones; gastric outlet obstruction

INTRODUCTION

Cholecystoenteric fistulae (CEFs) are a rare complication of cholelithiasis. They were first described by Thomas Bartholin in 1654. Their prevalence varies across several reports, but they are estimated to affect 3%–5% of patients with cholelithiasis.[1] Most cases occur between the gallbladder and the duodenum. Less commonly, they may occur between the gallbladder and the colon (typically the hepatic flexure) or stomach.[2]

The classical patient with a CEF is an elderly woman in the seventh or eighth decade of her life, often with a known medical history of biliary disease and multiple medical comorbidities.[3] However, multiple cases have been shown to occur in younger persons, and even in infants.[4] The clinical presentation of CEF is variable. Some patients, particularly those with coexisting luminal obstruction by enteric gall stones, present with acute or subacute features, suggestive of gastric outlet or bowel obstruction (depending on the level of obstruction). Others present with chronic abdominal pain and are only found to have CEF after extensive workup including imaging studies or intraoperatively.[2–5]

We present 3 cases of CEF, each with different etiologies and presentations. The management of each case was different and goes to highlight the diversity of this intriguing condition.

CASE REPORTS

Patient 1: A 65-year-old man with a history of hypertension, previous stroke with residual right-sided weakness, chronic calculous cholecystitis, and $T_{4a}N_2M_0$ squamous cell carcinoma of the palate status post chemotherapy and radiotherapy at 63 years of age requiring subsequent tracheostomy and percutaneous endoscopic gastrostomy (PEG) tube placement presented with a 5-day history of epigastric pain, nausea, vomiting, and inability to tolerate his tube feeds. He was afebrile and hemodynamically stable. He had mild tenderness in the epigastric region. His PEG tube was in situ with no erythema, tenderness, or purulence around the site. Initial laboratory investigations were significant for mild hyponatremia to 130 mEq/L and leukocytosis to 11,600 cells/μL with 81.5% neutrophils. His liver function test and lipase were normal. Computed tomography (CT) of the abdomen and pelvis showed features

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concerning for acute-on-chronic cholecystitis, a 26 mm calcified gallstone in the proximal duodenum, and pneumobilia suggestive of a cholecystoduodenal fistula with Bouveret syndrome (Figure 1). The PEG tube was seen with the tip and balloon in the gastric lumen. He was volume resuscitated with intravenous fluids, electrolyte derangements were corrected, and he commenced on intravenous antibiotics, analgesics, and antiemetics. His PEG tube was placed to gravity.

A day after presentation, an esophagogastroduodenoscopy was performed, and a large gallstone was noted to be impacted in the duodenal sweep. A cholecystoduodenal fistula was noted in the distal duodenal bulb immediately proximal to the stone, draining bile. A 3 × 6 cm web basket was used to grasp and capture the gallstone securely. Under constant traction, the gallstone was brought out into the stomach, where a series of mechanical lithotripsy was performed under endoscopic guidance until the stone fragments were small enough to be extracted with the use of Roth nets (Figure 2).

Given his high-risk surgical state, the decision was taken to not pursue surgical intervention with cholecystectomy and fistula repair. He remained stable after the endoscopic procedure and was discharged 3 days after presentation. He continues to follow-up with otorhinolaryngology and medical oncology outpatient. Six months postdischarge, he remains tracheostomy-dependent and has not developed any gastrointestinal complaints since then.

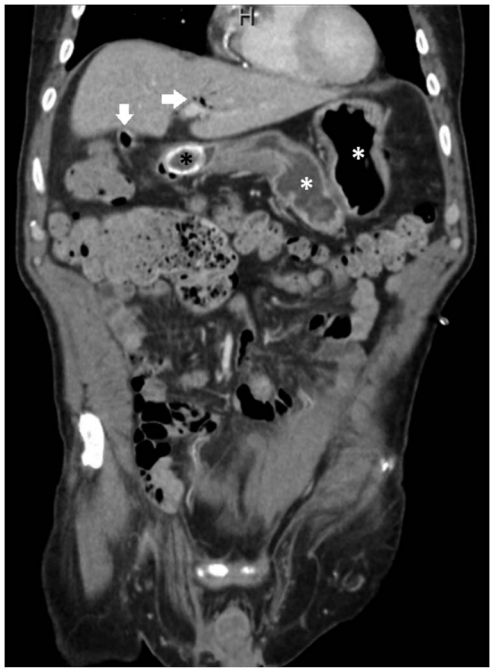

Figure 1. Coronal section computed tomogram showing a calcified gallstone in the proximal duodenum (black asterisk), distended stomach (white asterisks), and pneumobilia (white arrows) concerning for a cholecystoduodenal fistula with the Bouveret syndrome.

Patient 2: A 63-year-old woman with medical history including hypertension, obesity, and low-grade phyllodes tumor of the breast (status post excisional biopsy at 60 years of age) presented with epigastric pain that radiated to the back and right flank, nausea, and coffee grounds emesis of 2 days duration. She endorsed a previous self-limited episode of right upper quadrant abdominal pain 2–3 weeks before her current presentation. She denied any history of using tobacco, alcohol, or other recreational substances. She was afebrile and hemodynamically stable but seemed dehydrated. Her abdomen was moderately distended and tender in the epigastric/right upper quadrant region without rebound tenderness or guarding. Laboratory investigations were significant for leukocytosis to 17,400 cells/μL with 87.4% neutrophils, elevated blood urea nitrogen to 27 mg/dL with normal creatinine of 0.8 mg/dL, mild hypokalemia to 3.3 mEq/L, hypochloremic metabolic alkalosis, and elevated lactate to 2.2 mmol/L (normal = 0.5–1.6 mmol/L). Her hemoglobin concentration, liver function tests, and lipase were normal. CT of the abdomen and pelvis showed marked distension of the stomach, gallbladder wall thickening and mucosal hyperenhancement with cholelithiasis, extensive intrahepatic and extrahepatic pneumobilia, biliary mucosal hyperenhancement, and an obstructing 40 mm calcified gallstone in the duodenal bulb (Figure 3). Imaging findings of the Rigler triad (a gallstone obstructing the gastric outlet, gastric distension, and pneumobilia) raised concern for a fistulous communication between the gallbladder with the stomach and/or duodenum and a diagnosis of the Bouveret syndrome.

She received intravenous fluid resuscitation, analgesics, antiemetics, and antibiotics, and her electrolyte abnormalities were corrected. A nasogastric tube was placed to decompress her stomach. Surgical intervention was deemed more feasible than endoscopic intervention, given the size of the stone. On day 2 postadmission, she had exploratory laparotomy with gastrotomy, extraction of 60 mm gallstone from the first part of the duodenum, and gastrotomy repair with omental patch. She was seen in the general surgery outpatient clinic 2 weeks after discharge and has been doing well. There is no plan for fistula takedown or cholecystectomy unless she develops symptoms concerning for biliary disease.

Patient 3: A 68-year-old man with medical history of type 2 diabetes, recurrent urolithiasis, and appendectomy at 30 years of age presented with progressively worsening diffuse abdominal pain of 5 weeks duration. The pain was said to be worst in the right upper quadrant with no clear radiation or aggravating/relieving factors. He endorsed associated poor oral intake and unintentional weight loss of 10 pounds over the month preceding the presentation. He denied any nausea, vomiting, diarrhea, melena, hematochezia, jaundice, urinary frequency, urinary urgency, dysuria, or hematuria. He smoked 5 cigarettes daily for the past 50 years (12.5 pack-years) and consumed about 70 g of alcohol per day for the last 40 years.

On presentation, his vital signs were stable. Physical examination revealed generalized abdominal tenderness most marked

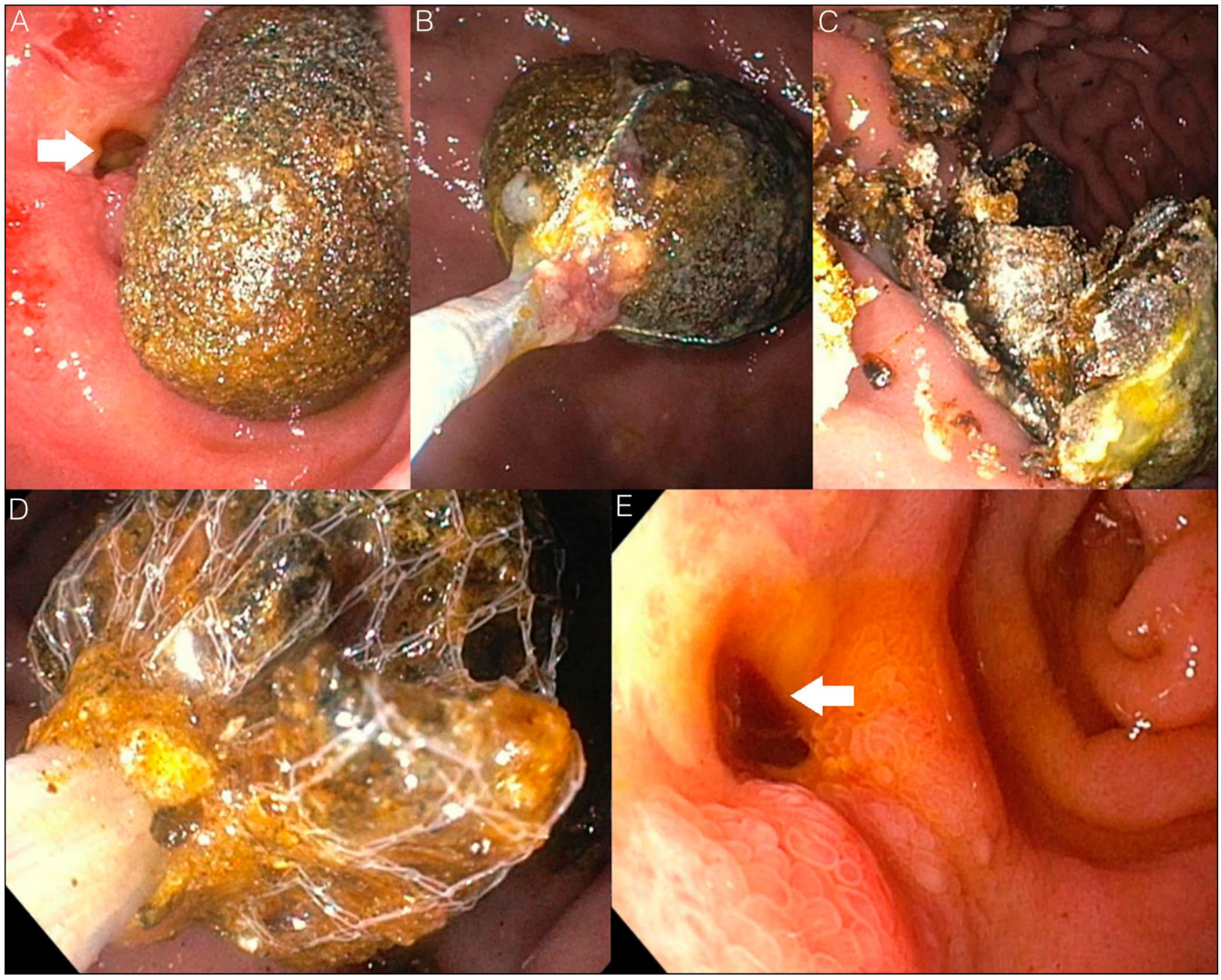

Figure 2. Esophagogastroduodenoscopy findings. (A) Large gallstone impacted in the distal duodenal bulb with a cholecystoduodenal fistula (white arrow) immediately proximal to the stone. (B) The stone pulled into the stomach with a web basket. (C) Postmechanical lithotripsy. (D) Stone fragments being extracted with the use of Roth nets. (E) Postextraction image of the duodenal bulb showing the cholecystoduodenal fistula (white arrow) draining bile into a clear duodenal lumen.

in the right upper quadrant without guarding or rebound tenderness. Initial laboratory investigations showed normal basal metabolic profile (except for hyperglycemia to 153 mg/dL) and complete blood count. His liver function tests were only significant for mildly elevated alkaline phosphatase (133 U/L; normal = 20–120) and gamma glutaryl transferase (78 U/L; normal = 3–60). His urinalysis was normal.

CT of the abdomen and pelvis with intravenous contrast showed an ill-defined necrotic mass in the gallbladder fossa of the liver in direct fistulous communication with the transverse colon measuring 6.0 × 7.0 cm (Figure 4). The gallbladder was not visualized. There were calcifications within this region likely representing calculi previously seen within the gallbladder. There was asymmetric bowel wall thickening and enhancement near the fistulous connection of the transverse colon and gallbladder fossa measuring up to 15 mm. Also noted was mesenteric nodularity and thickening concerning for omental carcinomatosis in the anterior mesentery (Figure 5).

He was then admitted to the medical floor given concern for biliary or colonic malignancy with cholecystocolonic fistula. Tumor marker carcinoembryonic antigen was elevated (19.8 ng/mL; normal <3 ng/mL), whereas CA19-9 was normal. A day after presentation, he had CT-guided percutaneous core needle biopsy of the necrotic mass within the gallbladder fossa of the liver with findings of small foci of atypical cells in a background of acute inflammation, granulation tissue, hyalinized fibrous tissue, and focal calcium deposits. Some of the atypical cells were immunopositive for epithelial markers AE1/3 and CK7.

Owing to the nondiagnostic CT-guided necrotic mass biopsy, he had a colonoscopy performed. Despite poor bowel preparation throughout the colon, a large ulceration with heaped up

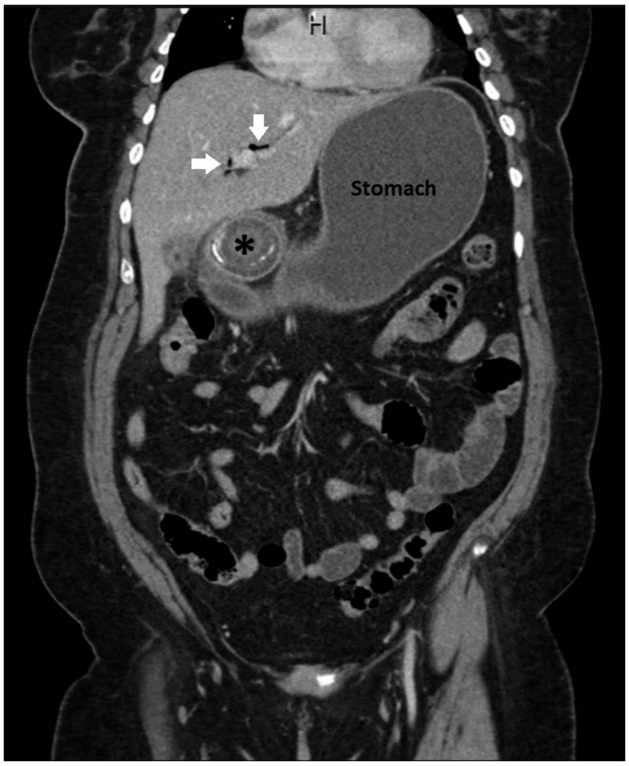

Figure 3. Coronal section computed tomogram of the abdomen and pelvis showed marked distension of the stomach, pneumobilia (white arrows), and an obstructing 40 mm calcified gallstone in the duodenal bulb (black asterisk). This is the Rigler triad that is considered pathognomonic for the Bouveret syndrome.

edges was noted in the hepatic flexure. The base of the ulcer seemed to tunnel, which represented the known fistula to the gallbladder (Figure 6). Cold forceps biopsies were taken and the specimens were sent for pathology, which showed moderately to poorly differentiated invasive adenocarcinoma likely biliary in origin (CK7 positive; CK20, CA19-9 negative) which mostly

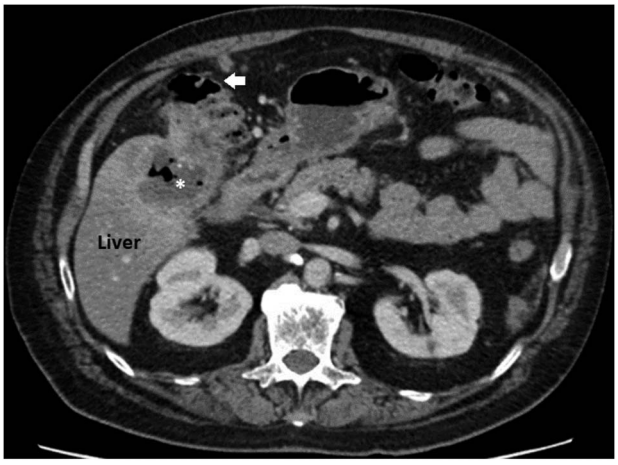

Figure 4. Axial section computed tomogram of the abdomen showing an ill-defined necrotic mass (white asterisk) in the gallbladder fossa of the liver in direct fistulous communication with the transverse colon (white arrow).

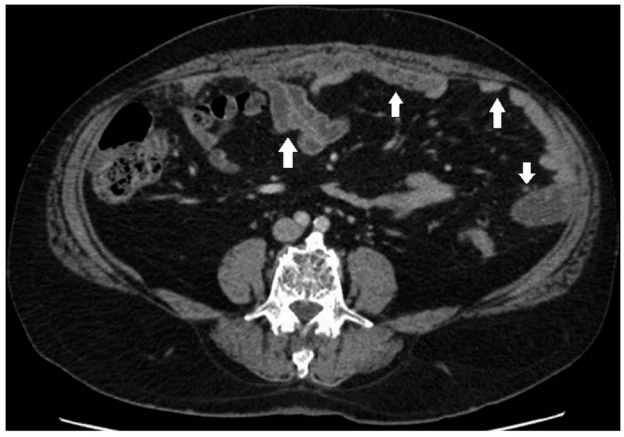

Figure 5. Axial section computed tomogram of the abdomen showing mesenteric nodularity and thickening (white arrows) concerning for omental carcinomatosis.

infiltrated the submucosa with no involvement of surface epithelium.

Staging CT of the chest showed prominent mediastinal and left hilar lymph nodes and bibasilar atelectasis. Positron emission tomogram showed F-fluorodeoxyglucose (FDG) avid, centrally necrotic soft tissue lesion in the gallbladder fossa consistent with malignancy, abnormal FDG uptake extending via the known cholecystocolonic fistula to involve the adjacent colon, extensive FDG avid omental and peritoneal carcinomatosis especially along the posterior aspect of the ventral abdominal wall, and mildly FDG avid mediastinal and hilar lymph nodes.

Given the concern for potential obstruction of his colon and in view of his inoperable tumor, he underwent diagnostic laparoscopy and creation of diverting loop ileostomy. The fistula was left unrepaired because the perforation was clogged by the large tumor mass. He remained in stable condition after the

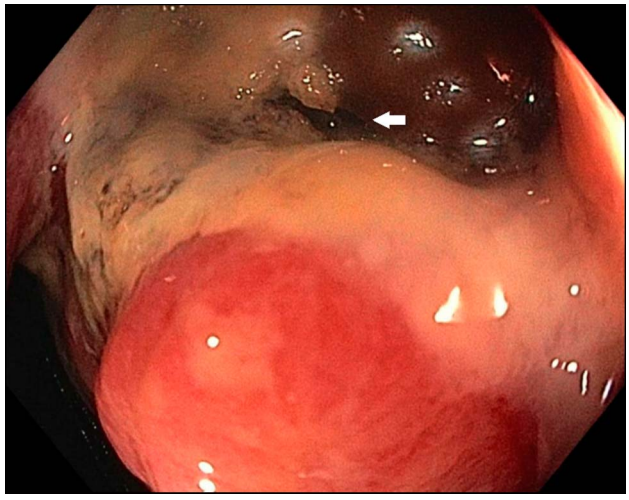

Figure 6. Colonoscopy showing a large ulceration with heaped up edges in the hepatic flexure. The base of the ulcer seemed to tunnel representing the fistula (white arrow) to the gallbladder.

procedure and was discharged to continue outpatient follow-up with colorectal surgery and oncology. He is being worked up for palliative chemotherapy.

DISCUSSION

The variability of cholecystoenteric fistulae is highlighted in the diversity of our 3 cases. Most cases of cholecystoenteric fistulae occur in women in their 60s and 70s. The woman-man ratio of this disorder ranges from 1.9 to 2.5:1.[1,6,7] The overwhelming majority of CEF results in patients with previous cholecystitis or chronic cholecystitis, with pericholecystic inflammation initiating adhesions between the gallbladder and surrounding enteric structures. Gallstone impaction is then followed by pressure necrosis and erosion through the gallbladder and into the bowel wall. More than 60% of these fistulae result in communication between the gallbladder and the duodenum. Cholecystocolonic (10%–20%), cholecystogastric (5%–10%), and choledochoduodenal (less than 5%) fistulae are less common.[6–8] Other risk factors for CEF in patients without evidence of cholelithiasis or a history of cholecystitis include peptic ulceration, malignant neoplasms of the pancreatobiliary tract (as seen in patient 3 above) or the bowel, Crohn's disease, ulcerative colitis, right-sided diverticulitis, abdominal trauma, and previous abdominal surgery.[1,3,8–10] Rarely, cases occur in infants, often as a sequelae of necrotizing enterocolitis.[11]

The clinical presentation of CEF is highly variable. Most patients present acutely or subacutely with signs consistent with gastric outlet or bowel obstruction. Others present with chronic symptoms of epigastric or right upper quadrant pain, dyspepsia, eructation, nausea, vomiting, and obstructive jaundice. Occasionally, there may be features consistent with gastrointestinal bleeding, often because of a marginal ulcer at the site of the fistula or erosion into surrounding vascular structures.[8] Cholecystocolonic fistulae often present with chronic diarrhea and malabsorption resulting from impaired enterohepatic circulation of bile acids.[12] Rarely, a large gallstone in the colon can become impacted at the rectosigmoid junction causing large bowel obstruction.[3]

Physical examination is often nonspecific. Common findings include dry mucous membranes, abdominal distension, abdominal tenderness, high-pitched bowel sounds, and obstructive jaundice. Patients with a chronic picture (especially those because of cholecystocolonic fistulae) may have physical examination findings consistent with intestinal malabsorption.[1–4] For this reason, the diagnosis is often uncertain and is often made after extensive imaging or intraoperatively.[5] When patients with CEF present with small bowel obstruction, the clinical picture is termed "gallstone ileus." Gallstone ileus results in terminal ileum obstruction 50%–70% of the time.[1,2] If the gallstone that passes via the fistula obstructs the pylorus or proximal duodenum resulting in gastric outlet obstruction, the presentation is termed "Bouveret syndrome."[13] Another peculiar syndrome that is often associated with CEF is the Mirizzi syndrome. In this condition, there is a large gallstone in the gallbladder neck or cystic duct leading to a narrowing of the common hepatic duct.[2,14] A retrospective review of emergency or elective cholecystectomies over a 12-year period that included more than 5,000 cholecystectomies found that 1.8% of patients had a cholecystoenteric fistula. Almost 90% of these patients had an associated Mirizzi syndrome.[15]

Laboratory studies are also typically nonspecific, but may show evidence of hyperbilirubinemia, liver enzyme derangements, leukocytosis, electrolyte abnormalities, acid-base alterations, and renal failure. These laboratory abnormalities often depend on the acuity of the presentation, the intensity of the inflammatory response, and preexisting comorbidities.[16] Imaging modalities may be useful in the diagnosis of CEF but tend to be more sensitive for detecting acute or subacute presentations with gallstone ileus or Bouveret syndrome than chronic ones or uncomplicated fistulae. The constellation of pneumobilia, an aberrant gallstone, and bowel/gastric outlet obstruction (Rigler triad) is highly suggestive of gallstone ileus or Bouveret syndrome. This finding is appreciated on plain abdominal radiographs in less than 50% of cases, but CT increases sensitivity, specificity, and diagnostic accuracy to above 90%. In addition, CT can also provide vital information about the presence of an abscess, the inflammatory state of the surrounding tissue, and the size and number of gallstones. Ultrasound may show features of cholecystitis, pneumobilia, dilated stomach, and ectopic location of a gallstone but is often suboptimal because of bowel gas. Less commonly used diagnostic imaging tests include barium studies and biliary scintigraphy.[1–3,9,16] However, despite the abundance of available imaging techniques, the final diagnosis is established intraoperatively when a patient is undergoing laparotomy for gastric outlet/small bowel obstruction of an unknown cause in 20%–40% of cases. This particularly applies to patients with gallstones that are isoattenuating and not visible on radiologic imaging.[5,16]

Classically, cholecystoenteric fistulae are definitive managed by open surgery with cholecystectomy, excision of the fistula, enterolithotomy if an obstructing enteric stone is present, common bile duct exploration, operative cholangiography, and reconstruction of the penetrated organ. Open surgery in this patient population is, however, fraught with increased morbidity and mortality (as high as 12%–27%) because up to 80% of patients with CEF harbor multiple comorbidities. Thus, endoscopic or laparoscopic intervention is often first pursued.[2–5,13,17] Endoscopic therapy (mechanical, laser, or extracorporeal shockwave lithotripsy with stone extraction) can be considered in those with a large obstructing enteric gallstone in the gastric outlet or proximal duodenum. Colonoscopy may be attempted for stones causing large bowel obstruction.[3,12] However, open surgery is still favored when there is extensive inflammation and adhesions because these cases are often complicated by perforation and conversion to open surgery (50%–90% of cases).[7,9] Because in our patient presented in case 3, diverting loop ileostomy is an option for patients with a cholecystocolonic fistula, especially in those with other comorbidities or unresectable malignancies obviating more extensive surgical strategies.[5,6]

In conclusion, cholecystoenteric fistulae are a rare entity and remain a diagnostic and therapeutic challenge. Owing to the highly variable and nonspecific nature of their presentation, CEF should be suspected in any patient presenting with abdominal pain, chronic diarrhea, or small bowel/gastric outlet obstruction, especially in those with a history of biliary tract disease and multiple medical comorbidities. Despite increasing awareness of the condition and improvements in imaging techniques, a substantial number of cases are still discovered incidentally during open or laparoscopic surgery. A variety of options exists for the management of cholecystoenteric fistulae. In cases of gallstone ileus and Bouveret syndrome, endoscopic therapy should be considered (especially with stones in the gastric outlet or proximal duodenum) but if it is not feasible, surgical intervention should be pursued. Unfortunately, morbidity and mortality are still high in part because of delay in diagnosis and misdiagnosis resulting from nonspecific symptoms, signs, and laboratory investigations. Further management requires a tailored approach that should consider the patient's clinical state and comorbidities.

DISCLOSURES

Author contributions: PE Ojemolon drafted the manuscript, participated in the review and final approval of the manuscript, and is the article guarantor. R. Kwei-Nsoro, M. Haque, and M. Shah drafted the case presentations and participated in the review and final approval of the manuscript. A. Almoghrabi conceptualized the manuscript, collected the cases, and revised the manuscript for intellectual content.

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