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Post-Cholecystectomy Mirizzi Syndrome: A Case Report and Review of the Literature

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 44
Final Diagnosis: Post-cholecystectomy Mirizzi syndrome
Symptoms: Abdominal pain • nausea • vomiting
Medication: Tramadol • hydromorphone • prochlorperazine
Clinical Procedure: US • MRCP • ERCP• choledochoscopy
Specialty: Gastroenterology and Hepatology

Objective: Management of emergency care

Background: Mirizzi syndrome is biliary obstruction caused by extrinsic compression of the distal common hepatic duct by a gallstone in the adjacent cystic duct or infundibulum of the gallbladder. Post-cholecystectomy Mirizzi syndrome (PCMS) is Mirizzi syndrome in the post-surgical absence of a gallbladder. This case report of PCMS and review of the literature illustrates the diagnostic and therapeutic challenges in evaluating and managing Mirizzi syndrome.

Case Report: A 44-year-old female with a remote history of laparoscopic cholecystectomy presented to a community teaching hospital with acute and severe upper abdominal pain and tenderness. Laboratory data revealed markedly elevated transaminases of a magnitude most often observed with hepatitis from acute viral infection, ischemia, or exposure to a hepatotoxin. PCMS was ultimately diagnosed at endoscopic retrograde cholangiopancreatography after being misdiagnosed as choledocholithiasis on magnetic resonance cholangiopancreatography. After transfer to an academic quaternary care referral hospital, the patient's extrahepatic biliary tree was reportedly cleared of gallstones following endoscopically-directed shock-wave lithotripsy performed at repeat endoscopic retrograde cholangiography.

Conclusions: Recognizing post-cholecystectomy syndrome, in general, and PCMS, in particular, is critical when caring for patients presenting with persistent or recurrent symptoms or signs of biliary obstruction following cholecystectomy. Expediently identifying and definitively relieving the biliary obstruction, while limiting the risk of iatrogenic complication, is the priority when caring for patients with PCMS.

MeSH Keywords: Cholangiopancreatography, Endoscopic Retrograde • Mirizzi Syndrome • Postcholecystectomy Syndrome

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Background

Mirizzi syndrome is biliary obstruction caused by extrinsic compression of the distal common hepatic duct by a gallstone in the adjacent cystic duct or infundibulum of the gallbladder (Hartmann's pouch). Post-cholecystectomy Mirizzi syndrome (PCMS) is Mirizzi syndrome in the post-surgical absence of a gallbladder. Complications of Mirizzi syndrome may include fibrotic stricture of the bile duct, cholecystobiliary fistula, cholecystitis, or cholangitis. Methods to identify and treat PCMS have evolved over decades from open surgical exploration to less invasive alternatives. We describe an atypical case of PCMS, compare it to the 64 cases of PCMS we identified in 15 previously published case reports and series of PCMS, discuss the incidence, risk factors, clinical presentation, biochemical abnormalities, imaging characteristics, natural history and complications of PCMS, and focus on the diagnostic and treatment options currently available to evaluate and manage PCMS.

Case Report

A 44-year-old female in otherwise good health with a history of cholecystectomy 25 years prior to presentation arrived at the emergency department reporting 12 hours of severe abdominal pain beginning 3 hours after eating lunch. The pain was constant, sharp, burning, and up to a 10 out of a possible 10 in intensity, radiating from the epigastrium to the substernal chest, right abdomen, and mid-back. The pain was worsened by eating, unrelieved by simethicone, and associated with nausea, an episode of bilious vomiting, and fatigue. The patient denied fever, jaundice, change in the color of her urine, and change in the color of her stool.

Two weeks prior to presentation, she had an attack of abdominal pain that was similar in quality but milder in intensity and shorter in duration. Her symptoms were reminiscent of those with which she presented when suffering from acute calculous cholecystitis at the age of 19 years, for which she had an uneventful laparoscopic cholecystectomy and recovery.

The patient's past medical and surgical histories also included exercise-induced asthma and bilateral tubal ligation. She drank a total of 3 to 4 alcoholic beverages each weekend, most recently 3 days prior to admission, and did not drink alcohol during the work week. She did not take any medication or herbal supplement. She denied a history of jaundice, tattoo, intravenous drug use, blood transfusion, sexual contact with an individual known to have liver disease, and travel to an area in which viral hepatitis is endemic. She had no known family history of gastrointestinal, hepatic, biliary, or pancreatic disease.

On physical examination, the patient appeared to be in pain. Blood pressure was 146/99 mmHg, pulse was 96 beats/minute, respirations were 20 breaths/minute, and temperature was 96.9°F. Weight was 75 kilograms and body mass index was 29.2 kg/m^2. The skin was normal, without jaundice, telangiectasia, or palmar erythema. The sclerae were non-icteric. Auscultation of the heart and posterior lung fields were normal. The abdomen appeared overweight without distension. Bowel sounds were normal. The epigastrium and right upper quadrant were tender, without appreciable mass, organomegaly, guarding, or rebound tenderness.

Initial laboratory results revealed white blood cells 11.7×10^3/uL (normal range, 4.0–10.5×10^3/uL)), 79% (25–62%) of which were segmented neutrophils, hemoglobin 14.5 g/dL (12.5–16.0 g/dL), platelets 327×10^3/uL (150–450×10^3/uL), international normalized ratio (INR) 0.9 (0.8–1.1), albumin 4.3 g/dL (3.5–5.0 g/dL), total bilirubin 2.2 mg/dL (0.3–1.0 mg/dL), direct bilirubin 1.4 mg/dL (0.0–0.2 mg/dL), alkaline phosphatase 163 U/L (34–104 U/L), aspartate aminotransferase (AST) 779 U/L (13–39 U/L), alanine aminotransferase (ALT) 644 U/L (7–52 U/L), lipase 8 U/L (11–82 U/L), and troponin <0.03 ng/mL (<0.03 ng/mL).

A sample of urine obtained by straight catheterization of the bladder appeared clear and yellow. Chemical analysis demonstrated no nitrites, protein, glucose, ketones, or conjugated bilirubin and 150 red blood cells/uL. Microscopic analysis revealed no white blood cell, 6–10 (normal range, 0–2) red blood cells, up to 5 epithelial cells, and 2+ bacteria per high-powered field.

An ultrasound of the abdomen identified a hyperechoic region 2.3 cm in maximal dimension within the right hepatic lobe suspected to be either a hemangioma or focal fatty infiltration. Intrahepatic bile ducts were normal. Surgical absence of the gallbladder was noted. The common bile duct was described as normal, measuring 7 mm in diameter. Color flow Doppler spectral analysis of the portal vein was normal.

A broad differential diagnosis of acute cholestatic hepatitis was entertained, including acute viral infectious hepatitis, ischemic hepatitis, and occult hepatotoxicity, given transaminase concentrations approaching 1,000 U/L. Extrahepatic biliary obstruction, with atypically high transaminases, was also considered. Acute alcoholic or autoimmune hepatitis was thought to be much less likely.

Asymptomatic bacteriuria was diagnosed, given the absence of dysuria, polyuria, flank pain, and pyuria. Microscopic hematuria was suspected to have been the result of a traumatic catheterization. Antibiotics were not administered.

After the administration of tramadol 50 mg orally, hydromorphone 1 mg intravenously and prochlorperazine intravenously,

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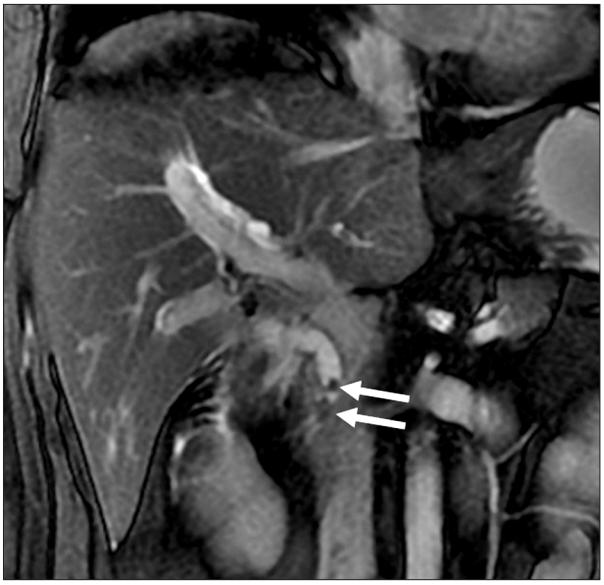

Figure 1. First magnetic resonance image, revealing a dilated 9 mm-wide extra-hepatic bile duct, assumed to be the common bile duct, proximal to 2 faceted signal defects compatible with 4×6 mm and 6×9 mm calculi (arrows) and a decompressed bile duct distal to the presumed gallstones.

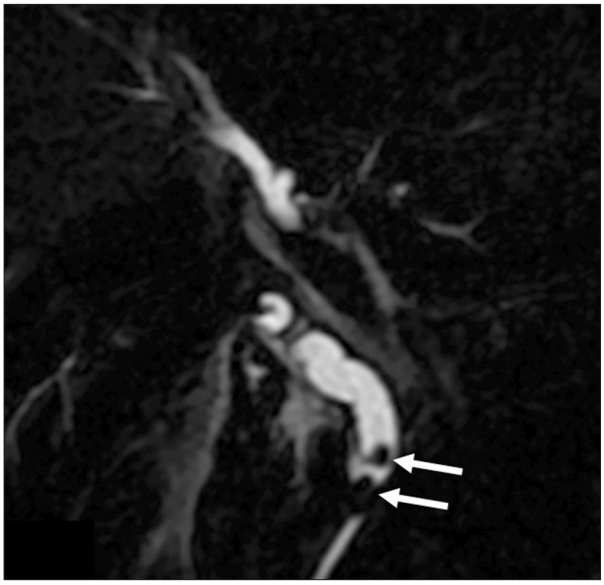

Figure 2. First magnetic resonance cholangiopancreatography, confirming a dilated 9 mm-wide bile duct proximal to 2 signal defects compatible with calculi (arrows), assumed to be in the common bile duct despite the 3 cm-long length of decompressed bile duct distal to the gallstones.

the patient's abdominal pain lessened and the nausea resolved, after which doses of tramadol were repeated every 8 hours and hydromorphone every 3 hours to control persistent pain.

By the following day, vital signs had normalized. The physical examination was unchanged. Repeat blood test results revealed white blood cells 6.9 k/uL, 65% of which were segmented neutrophils, hemoglobin 13.3 g/dL, total bilirubin 5.0 mg/dL, direct bilirubin 3.4 mg/dL, alkaline phosphatase 209 U/L, AST 929 U/L, and ALT 1,169 U/L. Blood tests screening for alcohol, acetaminophen, salicylates, and acute hepatitis A, B and C were negative.

Magnetic resonance imaging of the abdomen with magnetic resonance cholangiopancreatography (MRCP) was performed on the second day of hospitalization, the interpretation of which initially described a 6×9 mm calculus in the common bile duct (CBD) located at the level of the pancreatic head, upstream from which the common hepatic duct (CHD) was 11 mm and the intrahepatic bile ducts (IHDs) were moderately dilated, and downstream from which the distal CBD was normal, measuring 3 mm (Figures 1, 2).

Later that day, endoscopic retrograde cholangiopancreatography (ERCP) using a therapeutic video duodenoscope revealed a normal distal common bile duct 3–4 mm wide, a narrowed section in the mid-extrahepatic bile duct, and dilated common hepatic and intrahepatic ducts. Upon injection of additional contrast, the previously narrowed section of extrahepatic bile duct widened to a normal diameter and a filling defect was noted in the now opacified cystic duct remnant, the insertion of which was relatively low on the extrahepatic biliary tree (Figure 3). A bloodless 1 cm long biliary sphincterotomy was performed, after which the common hepatic and common bile ducts were swept with a 9–12 mm biliary balloon over a guidewire with expression of minimal sludge and no stone. Occlusion cholangiography revealed 2 sub-centimeter filling defects consistent with mobile gallstones in the cystic duct remnant which was approximately 5 cm long and up to 8 mm wide. The cystic duct remnant was swept several times, first with the catheter's balloon inflated to 9 mm and then with a trapezoidal biliary basket, neither of which extracted a stone. Contrast drained rapidly from the biliary tree. As the extrahepatic biliary obstruction appeared to have resolved during endoscopic manipulation of the biliary tree, presumably by dislodging the impacted gallstone(s) up into the cystic duct remnant, a common bile duct stent was not placed (Figure 4).

On the following day, the patient remained symptomatic. Total bilirubin increased to 6.1 mg/dL. Alkaline phosphatase remained unchanged. Repeat MRCP confirmed a dilated cystic duct remnant 7 mm wide containing a round filling defect 6 mm wide near its insertion into the junction of the CHD and CBD, consistent with a gallstone, and no dilatation of the CBD, CHD, or intrahepatic biliary ducts (Figure 5).

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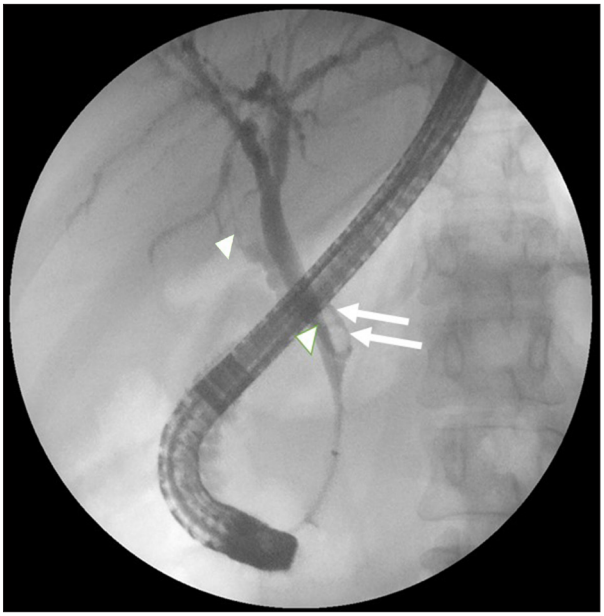

Figure 3. First endoscopic retrograde cholangiopancreatography, revealing a normal 2–3 mm-wide common bile duct, dilated 8 mm-wide common hepatic duct, dilated 6 mm-wide intrahepatic ducts, and a long and dilated cystic duct remnant (arrow heads) up to 8 mm-wide containing 2 filling defects, 4×6 mm and 6×9 mm, consistent with gallstones (arrows), that no longer appear to extrinsically compress the common hepatic duct.

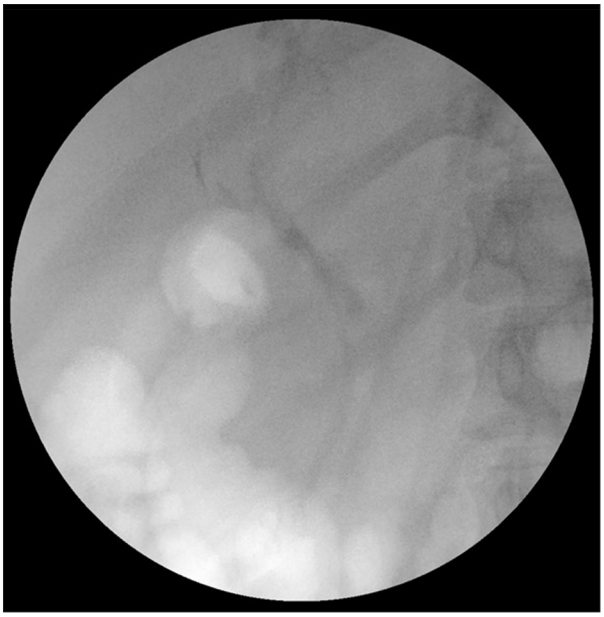

Figure 4. Two minutes post-first endoscopic retrograde cholangiopancreatography, demonstrating rapid drainage without evidence of a residual biliary stricture.

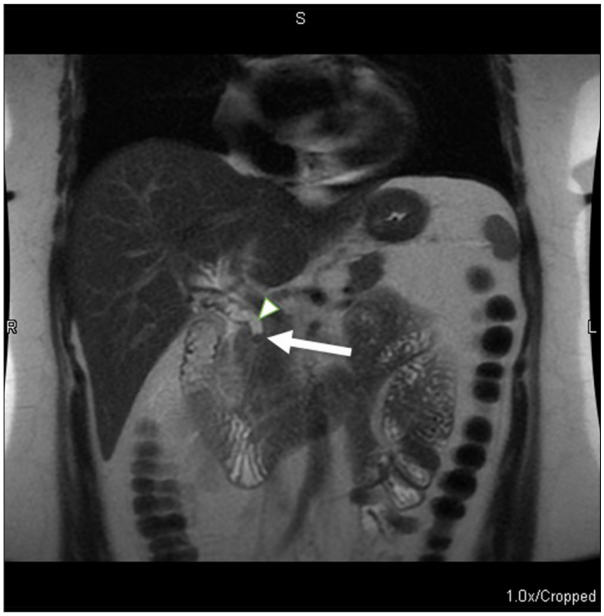

Figure 5. Second magnetic resonance image, confirming a long and dilated cystic duct remnant (arrowhead) with filling defect (arrow) near its insertion into the junction of the common hepatic and common bile ducts.

After discussing alternative therapeutic options, the patient requested transfer to a nearby academic quaternary care referral hospital, which occurred later that day. During ERCP there, 2 gallstones within the cystic duct remnant were fractured using electrohydraulic shockwaves created and delivered by a 0.63 mm-wide catheter advanced into the cystic duct through the 1.2 mm-wide accessory channel of a 3.5 mm-wide video cholangioscope which, itself, was passed through the accessory channel of a therapeutic video duodenoscope. The stone fragments were removed, after which the common bile duct was stented to prevent any risk of recurrent extrahepatic biliary obstruction from post-lithotripsy traumatic acute edema of the bile duct wall.

At the patient's third (and final) ERCP, performed as an outpatient 6 weeks later at the same referral hospital, the prophylactic biliary stent was removed, and cholangiography was normal. Neither persistent gallstone nor biliary stricture was identified. At subsequent follow-up with her primary care physician, the patient reported no recurrence of biliary symptoms and surveillance complete blood cell and liver tests were normal.

Discussion

Our patient's cholecystectomy in the late 1990s was 1 of an estimated 500,000–600,000 performed annually in the United States at that time, most of which were completed laparoscopically [1]. Unfortunately, anywhere from 10–15% of these

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patients likely had persistent or recurrent biliary symptoms or developed new symptoms, like diarrhea, attributed to the surgery [1]. Patients with these post-operative symptoms are considered to have post-cholecystectomy syndrome and may suffer from a variety of structural or functional diseases intrinsic or extrinsic to the residual biliary tree, one of which is PCMS. To better understand its incidence, risk factors, clinical presentation, biochemical abnormalities, imaging characteristics, natural history, management, and complications, we reviewed 64 cases of PCMS from 15 case reports and studies [2–16].

Mirizzi syndrome is named after Pablo Luis Mirizzi, who was a Professor of Surgery at the National University of Cordoba in Argentina. He lived from 1893 to 1964, trained in Argentina, Europe, and the United States of America, and ultimately was honored internationally for his surgical skill, dedication to teaching, and contributions to humanity. After performing the first operative cholangiogram in 1931, he described hepatic duct obstructions in the 1940s to which his name is now eponymously attached. Of note, Dr. Mirizzi mistakenly believed that hepatic duct obstruction associated with adjacent gallstone disease was caused by spasm of a hepatic duct sphincter. Subsequent anatomical studies of the hepatic duct failed to reveal even smooth muscle [17]. Our understanding of Mirizzi syndrome, including PCMS, continues to evolve.

The incidence of Mirizzi syndrome is likely between 0.7% [18] and 2.1% [19] over a 20-year interval among patients ultimately scheduled for cholecystectomy. Estimates of the incidence of PCMS range from <2.5% over a 2-year interval [11] to as high as 7% over a 4-year interval [20] when calculi in the gallbladder remnant or cystic duct following subtotal cholecystectomy and in the cystic duct remnant following complete cholecystectomy are considered together.

Among the 64 case reports of PCMS evaluated for this review, symptoms or signs of PCMS developed as early as a few days [21] and as late as 40 years [10] following cholecystectomy and at an average age of 49 years (with a standard deviation of 18 years), among whom 60% were female. The presence or absence of obesity was reported inconsistently. Patients with PCMS most commonly reported right upper quadrant pain, nausea, vomiting, or jaundice. They less commonly reported epigastric pain, anorexia, pruritus, or weight loss, and occasionally reported fever. The most commonly reported physical examination findings (in descending order of prevalence) were right upper quadrant tenderness, jaundice, fever, and epigastric tenderness.

Regarding surgical and anatomical risk factors for PCMS, laparoscopic cholecystectomy, particularly when subtotal [9], a cystic duct remnant longer than 1 cm [20], and a low insertion of the cystic duct on the extrahepatic bile duct (resulting, by definition, in a relatively short common bile duct and a relatively long common hepatic duct) [9] were frequently reported in patients with post-cholecystectomy syndrome, some of whom had PCMS. The authors of this case report are unaware of any report that residual gallstone size is a risk factor for PCMS.

Consistent with these observations, our patient was female and asymptomatic for 25 years after her laparoscopic cholecystectomy. She complained of abdominal pain and had tenderness in the epigastrium and right upper quadrant accompanied by nausea and vomiting. Imaging ultimately identified a long cystic duct remnant with a low insertion on the extrahepatic bile duct.

Biochemical patterns vary in PCMS. Among the 49 of 64 patients with PCMS reviewed for this report for whom laboratory data were reported, the most common abnormality was an elevated alkaline phosphatase concentration. Among the 30 patients for whom alkaline phosphatase was reported, the values ranged from 10 (upper limit of normal, 126 U/L) [5] to 5,011 U/L (upper limit of normal, 114 U/L) [10]. Among the 25 patients for whom transaminases were reported, the majority (56%) had normal transaminase concentrations, 24% had mildly to moderately elevated transaminases (1×< upper limit of normal ≤10×) and 20% had markedly elevated transaminases (>10× upper limit of normal). Our patient's transaminases, at 22 times the upper limit of normal, were elevated to an extent more commonly observed with hepatitis from acute viral infection, ischemia, or exposure to a hepatotoxin than from biliary obstruction [22].

Our patient's complete blood count revealed a mild neutrophilia consistent with pain, hepatitis, or cholangitis. Her platelet count and INR were normal. These tests are useful to check prior to considering therapeutic endoscopy, as the risk of hemorrhage from biliary sphincterotomy is increased in patients with coagulopathy, be it from malnutrition, intrinsic liver disease, chronic biliary obstruction [23], or thrombocytopenia from splenic sequestration in portal hypertension or from disseminated intravascular coagulation in sepsis [24,25]. A patient with progressive jaundice, often appreciated first by an acquaintance who has not seen the patient in the preceding several days, might not present until coagulopathic from malabsorption of vitamin K. Vitamin K is required by hepatocytes to synthesize prothrombin, other pro-coagulants and, for that matter, anti-coagulants. Therefore, treatment with vitamin K is advised for any patient presenting with coagulopathy in the setting of a cholestatic hepatitis. Our patient had no sign of portal hypertension, sepsis or coagulopathy.

When treating a coagulopathic patient, vitamin K may be administered orally (if co-administered with bile acids in the absence, otherwise, of enteral bile), subcutaneously (reportedly with unpredictable absorption), intramuscularly (with

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risk of hematoma and anaphylaxis) or intravenously (with risk of anaphylaxis, even when diluted and infused slowly) [26]. Vitamin K-related coagulopathy often improves, if not resolves, within 24 hours following the first dose of vitamin K [27]. If the INR fails to normalize even after 3 days of daily vitamin K supplementation, then decompensated liver disease or disseminated intravascular coagulation should be suspected.

Patients presenting with upper gastrointestinal symptoms and abnormal liver tests often are imaged initially with transabdominal ultrasound with a reported sensitivity for detecting choledocholithiasis in the cystic duct remnant as low as 29% [28] and as high as 60% [9]. Yet, other studies have reported poor sensitivity (22–55%) for detecting choledocholithiasis, albeit in the common bile duct (29), and less than expected sensitivity (77–87%) for detecting even common bile duct dilation [29]. Whether ordered in place of, preceding, or following abdominal ultrasound, computed tomography (CT) of the abdomen has a reported sensitivity for detecting cholelithiasis in the cystic duct remnant as high as 71% [5], which will be dependent on the degree to which a gallstone is calcified.

If the presence or absence of biliary obstruction remains uncertain after abdominal ultrasound or CT, additional imaging may be helpful. The sensitivity of MRCP for detecting stones in the cystic duct remnant ranges from 89% [5] to 92% [9]. Endoscopic ultrasound (EUS), widely available at tertiary and quaternary care hospitals and offered at some community hospitals, may also identify otherwise occult cystic duct remnant stones with a reported sensitivity of 100% in symptomatic post-cholecystectomy patients [30]. In a patient for whom MRCP is contraindicated and sedation for endoscopy is considered high-risk, cholescintigraphy, also called hepatobiliary scintigraphy or a HIDA scan (HIDA being an acronym for hepatobiliary iminodiacetic acid, a radiotracer which hepatocytes absorb from the blood stream and excrete in the bile), can suggest PCMS when radiolabeled bile collects in a prominent CHD without subsequent migration into the CBD or drainage into the duodenum. Once extrahepatic biliary obstruction is confirmed non-invasively, regardless of the method, ERCP is the preferred intervention to relieve the obstruction [5].

In our patient's case, the initial interpretations of noninvasive abdominal imaging misled the care team to anticipate a routine therapeutic ERCP with biliary sphincterotomy and common bile duct stone extraction. The abdominal ultrasound report mentioned neither the possibility of biliary obstruction nor choledocholithiasis. The MRCP report identified choledocholithiasis but mistook the long cystic duct remnant within which it was located for the common bile duct. It was not until ERCP that the calculi were appreciated to be in the cystic duct remnant, where they remained for the second MRCP, the interpretation of which was informed by the ERCP.

A common bile duct diameter of up to 10 mm in a post-cholecystectomy patient may be considered normal only in the absence of additional signs of biliary obstruction [31]. Our patient's common bile duct diameter of 7 mm, in the setting of cholestatic hepatitis, was abnormal and consistent with biliary obstruction.

Non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are equally effective, and superior to spasmolytics, in treating biliary colic [32]. NSAIDs might decrease biliary pain and even the risk of cholangitis when used to treat PCMS by decreasing prostaglandin synthesis, biliary mucus, edema and smooth muscle tone [33]. Therefore, administration of an NSAID is an excellent choice to treat pain in patients suspected to have PCMS for whom there is neither history nor suspicion of peptic ulcer disease, particularly since NSAIDs are not associated with increased risk of post-sphincterotomy hemorrhage following therapeutic ERCP [34]. Although opioids can cause nausea or provoke spasm of the sphincter of Oddi [35], the latter of which could further increase intraductal biliary pressure in patients with only partial biliary obstruction from PCMS, administration of an opioid remains an excellent option to effect analgesia. Our patient received opioids and an antiemetic without an NSAID.

The bile is normally sterile. If cholangitis is suspected, usually from a mono-microbial infection if in a native biliary tree, a parenteral antibiotic should be selected that is active against Gram-negative bacilli and excreted to at least some degree in the bile, as *Escherichia coli* and Klebsiella species are the most common pathogens. If the biliary tree has been instrumented, then the increased risk of mono-microbial infection with Gram-positive cocci like enterococcus and, to a lesser extent, Streptococcus species, Gram-negative bacilli like Enterobacter species, Bacteroides, Pseudomonas aeruginosa, and Proteus species, Gram-positive bacilli in the Clostridium species, as well as polymicrobial infection, should be considered, for which ticarcillin/clavulanate, piperacillin/tazobactam or ceftriaxone, alone or in combination with metronidazole, is often administered empirically.

In obstructive jaundice caused by gallstone disease, however, ceftriaxone might best be avoided, as it is lithogenic. Precipitation of the calcium salt of ceftriaxone was reported to reversibly induce biliary sludge in up to 46% of patients without pre-existing biliary disease exposed to this medication, some of whom became symptomatic. Patients with a polymorphism in the TATAA box in the promoter region of the UDP-glucuronosyltransferase 1A1 (UGT1A1) gene, associated with Gilbert's syndrome, might be at particular risk. Quinolones, penicillins and alternative cephalosporins with adequate penetration in the bile (like cefazolin and cefuroxime) are alternatives. Still other cephalosporins (like cefotaxime, ceftazidime and cefepime), as well as carbapenems (like imipenem and meropenem), vancomycin and aminoglycosides (like gentamicin and amikacin) are excreted into the bile at less than desirable

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concentrations, and are not the best choices when treating or preventing cholangitis or cholecystitis [36].

In patients suspected to have sepsis from cholangitis, an antibiotic regimen with a sufficiently broad spectrum of empiric activity should be administered rapidly, ideally after obtaining blood cultures and within one hour of identifying this life-threatening concern [37]. An antibiotic with a narrower spectrum of activity may be substituted based upon the subsequent results of blood or bile cultures and antibiotic sensitivities reporting bacteria suspected to represent pathogens and not contaminants. Patients who appear to be recovering from cholangitis after biliary decompression may discontinue antibiotics as soon as blood cultures have ruled out bacteremia or after 5 to 7 days when accompanied by bacteremia [38,39].

Patients with biliary obstruction are particularly prone to intravascular volume depletion, especially when in septic or postoperative states. The risk for acute kidney injury correlates with serum bilirubin concentration and is likely multifactorial, including the natriuretic and diuretic effect of bile salts on the kidney, tendency for hypotension when dehydrated, hypo-perfusion from myocardial dysfunction and endotoxemia [40]. Therefore, in the absence of congestive heart failure, aggressive intravenous fluid administration is appropriate for patients suspected to have PCMS, particularly if there are signs of sepsis.

In a risk prediction model for in-hospital mortality among patients with acute cholangitis using 22 predictors and the Tokyo criteria to stratify them into groups at high- and low-risk for mortality, organ failure was the best predictor of mortality in univariate analysis. Furthermore, confusion, hypotension requiring catecholamines, Quick Sepsis-Related Organ Failure Assessment (Quick SOFA) score below 50%, serum creatinine level above 2 mg/dL, and platelet count $<100\times10^3$/mL all predicted organ failure [41]. Although the authors stratified patients into a high-risk group meriting urgent ERCP and a lower-risk group requiring only elective ERCP, a subsequent retrospective study determined that patients with acute cholangitis who had ERCP within 24 hours of presentation had a lower 30-day mortality compared to patients whose ERCP was performed later in the hospitalization (8% versus 19%, respectively), even after adjusting for other competing clinical risk factors, among 244 consecutive patients with acute cholangitis treated between 2009 and 2016 [41].

In the absence of suspected cholangitis, prophylactic antibiotics prior to ERCP should be administered to patients with PCMS only if biliary drainage is expected to be incomplete following biliary access and, if confirmed, likely should be continued for several days. Prophylactic antibiotics may also be considered in immunosuppressed patients, such as those with an absolute neutrophil count <500 cells/mL, advanced hematologic malignancy, or a history of liver transplantation [42].

Management options for PCMS have evolved over decades from open surgery to less invasive alternatives. ERCP has been used to retrieve stones in the cystic duct remnant using catheters to perform balloon extraction, basket extraction, and mechanical lithotripsy [5,43]. When attempts to access the cystic duct remnant fail or, once accessed, attempts to clear the stone(s) fail, a temporary plastic stent may be placed in the common bile duct, with the proximal end in the common hepatic duct and the distal end in the duodenal lumen, to traverse the stricture and decompress the biliary tree. Definitive therapy may then be deferred to a later – but not indefinite – date. Most biliary stents are made of polyethylene [44] and tend to occlude within weeks to months after placement, regardless of design [45]. Once biliary stents occlude (or – less commonly – migrate either distally or proximally enough to no longer traverse the stricture), patients become increasingly at risk for cholangitis and life-threatening sepsis [45].

If attempts at trans-papillary biliary access fail, or, once achieved, attempts to cannulate the biliary tree proximal to the extrahepatic biliary stricture fail, the more proximal biliary tree may be accessed through the wall of the stomach or proximal duodenum via EUS, after which a guidewire may be passed distally into the duodenal lumen and used in a rendezvous procedure to complete the ERCP. When the major papilla cannot be reached, a fully covered self-expanding metallic stent may be placed under EUS guidance to effectively create a choledochogastric or choledochoduodenal fistula through which the biliary tree may be decompressed, an approach usually reserved for advanced endoscopists at a tertiary or quaternary care hospital.

Alternatively, transhepatic access via percutaneous cholangiography with placement of an external or external-internal biliary drain may follow the non-therapeutic ERCP. Percutaneous drainage is also appropriate for the patient considered to be at high risk of complication from anesthesia. Any exclusively external biliary drain placed either to limit further instrumentation of the biliary tree in the setting of cholangitis or after repeated failures to traverse a biliary stricture should be revised electively to include internal drainage, whenever possible [46]. The presence of bile within the intestinal lumen allows for its enterohepatic circulation, encourages absorption of fat-soluble vitamins, maintains the integrity of enterocyte tight junctions and reduces endotoxemia [47].

If standard endoscopic approaches to remove retained stones in the cystic duct remnant fail, alternatives include intraductal shock wave lithotripsy delivered through a choledochoscope-passed percutaneously, laparoscopically, or (as in this case) endoscopically, laparoscopy-assisted ERCP, or extracorporeal shock wave lithotripsy (without or with subsequent endoscopic removal of fragmented stones). The requisite equipment and

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expertise for these maneuvers might be available only at a tertiary or quaternary care hospital [4,6].

Endoscopic electrohydraulic lithotripsy (EHL) is achieved by delivering oscillating shockwaves between 2 adjacent electrodes at the tip of a thin catheter positioned under direct endoscopic visualization (choledochoscopy) on or immediately adjacent to a gallstone (and as far from the bile duct wall as possible). The EHL catheter reaches its target after being passed through the accessory channel of a mini-endoscope which, itself, is passed through the accessory channel of a therapeutic duodenoscope (ERCP scope) in standard position, then through the major papilla, common bile duct and, ultimately, into the cystic duct remnant.

PCMS and its management can cause complications. Some are related to the natural history of the disease, like cholangitis further complicated by bacteremia and sepsis or cholecystocholedochal fistula. Others are iatrogenic, like post-ERCP pancreatitis (with a reported incidence of 3.5%), post-sphincterotomy hemorrhage (with a reported incidence of 1.3%) [48], cholangitis after the biliary tree proximal to the obstruction is instrumented but not decompressed (with a reported incidence of 0.5–1.7%) [49], or bile duct perforation. Yet, most patients with PCMS are cured without complication, sometimes with the help of expertise available only at a tertiary or quaternary care hospital where select patients may be referred or transferred.

Conclusion

The present case highlights the importance of including PCMS in the differential diagnosis of persistent or recurrent symptoms or signs of biliary obstruction following cholecystectomy, however remote. Although non-invasive imaging, including abdominal ultrasound, CT, and MRCP will narrow the differential diagnosis, PCMS might be discovered or confirmed only at ERCP. When extra-hepatic biliary obstruction is strongly suspected, gastroenterology consultation and timely ERCP is crucial to decompress the biliary tree and, when from gallstones, to prevent or treat cholangitis. If endoscopic attempts to drain the biliary tree fail, then interventional radiology consultation is appropriate to consider percutaneous cholangiography and biliary stenting. Physicians practicing in a community hospital may refer patients with PCMS and challenging anatomy to a tertiary or quaternary care hospital with the multi-disciplinary expertise and equipment to care for patients with complicated biliary disease.

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