

Emphysematous Cholecystitis Resulting in Secondary Biliary Cirrhosis: A Rare Complication of Endoscopic Retrograde Cholangiopancreatography

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Abstract

A 48-year-old female developed acute emphysematous cholecystitis after an endoscopic retrograde cholangiopancreatography (ERCP) for evaluation of sphincter of Oddi dysfunction. Cholecystectomy was performed 2 days later. Cultures grew *Clostridium perfringens*. The patient received broad-spectrum antibiotics but developed recurrent cholangitic abscesses and intra- and extra-hepatic biliary necrosis. She was managed by percutaneous transhepatic biliary drains. For next 3 years, patient had recurrent episodes of biliary obstruction, cholangitis, and sepsis, resulting in secondary biliary cirrhosis requiring a liver transplantation. Emphysematous cholecystitis is a rare complication of ERCP. Prompt diagnosis and surgical management can prevent further spread of infection to biliary tree.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a widely used technique for evaluation and treatment of pancreatic and biliary tract disease. Procedure-specific complications occur in up to 7% of patients, and mortality is estimated to be around 0.3%.¹ Common complications include pancreatitis, bleeding, sepsis, perforation, aspiration, and cardiac arrhythmias.¹ Emphysematous cholecystitis is a rare form of cholecystitis characterized by infection of the gallbladder by gas-forming bacteria such as *Clostridium perfringens*, *Pseudomonas*, *Klebsiella*, or *E. coli*.² Cholecystitis as a complication of ERCP is rare, and to date, only 3 cases of emphysematous cholecystitis after ERCP have been reported.³⁻⁵ We present a case of a woman who not only developed emphysematous cholecystitis after ERCP, but also sustained intra- and extra-hepatic biliary ductal injury resulting in recurrent cholangitis and liver abscesses.

Case Report

A 48-year-old female presented for an elective outpatient ERCP for evaluation of sphincter of Oddi dysfunction. The indication for the procedure was recent acute pancreatitis and episodic abdominal pain. Using a Lehman perfusion aspiration manometry catheter (Cook Medical, Winston-Salem, NC), the common bile and pancreatic ducts were cannulated and basal sphincter pressures were measured and found to be normal (<40 mmHg). Cholangiography and pancreatography were normal. The cystic duct was cannulated and after cholecystokinin infusion, bile was aspirated and sent for microlithiasis analysis. No immediate complications were appreciated.

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Due to mild post-procedure discomfort, the patient was admitted to the hospital for overnight observation. The patient developed chest pain several hours after the procedure. Blood work revealed white blood cell count of $14.5 \times 1,000/\mu\text{L}$, hematocrit 32.9%, aspartate aminotransferase (AST) 176 U/L, alanine aminotransferase (ALT) 32 U/L, total bilirubin 0.46 mg/dL, serum lipase 93 U/dL, and serum troponin 2.3 ng/mL. A cardiology evaluation was requested and the patient was found to have a non-ST elevation myocardial infarction, which was treated medically. The following day, approximately 24 hours after the procedure, the patient developed abdominal pain with peritoneal signs. Laboratory tests revealed an AST 250 U/L, ALT 55 U/L, total bilirubin 3.34 mg/dL, direct bilirubin 2.85 mg/dL, and lipase of 192 U/dL. A computerized tomography (CT) scan of the abdomen identified a large amount of air within and around the gallbladder. Extensive free air was noted in the lesser sac, retroperitoneum, intraperitoneal cavity, and the bile duct (Figure 1). In the posterior segment of the right hepatic lobe, a loculated area of air that did not conform to the biliary tree was seen. A presumptive diagnosis of emphysematous cholecystitis was made with suspicion of bowel perforation, given the large amounts of intra-abdominal air. The patient was started on broad spectrum antibiotics (ampicillin/sulbactam).

A laparotomy performed 2 days after the initial ERCP revealed a completely gangrenous gallbladder without any evi-



Figure 1. Computed tomography (CT) image showing extensive gas in gallbladder, gallbladder wall, and intraperitoneal cavity.

dence of bowel perforation. Cholecystectomy was performed with no gallstones present. Examination of the common bile duct (CBD) was without any abnormalities; however, the common hepatic duct (CHD) was markedly inflamed with possible gangrene. Histopathologic examination of the gallbladder revealed gangrenous cholecystitis with gram-positive rods invading the gallbladder wall. Cultures from the gallbladder and blood grew *Clostridium perfringens*. The patient continued to improve and was discharged home 14 days after her surgery.

One week after discharge, the patient presented with abdominal pain and fever. An abdominal CT scan revealed 2 large abscesses, one in the left lobe and the other in the right lobe of the liver. One percutaneous drainage catheter was placed in each abscess by interventional radiology. The catheter in the left lobe abscess started to drain bilious fluid. Cholangiography via percutaneous drain a few days later showed communication of the left lobe abscess with the left intrahepatic biliary system along with extravasation of contrast in the peribiliary area, indicating disruption and necrosis of intrahepatic ducts (Figure 2). The CHD and CBD demonstrated necrosis and infarction with intramural tracking of contrast. A trans-hepatic 8F locking loop draining

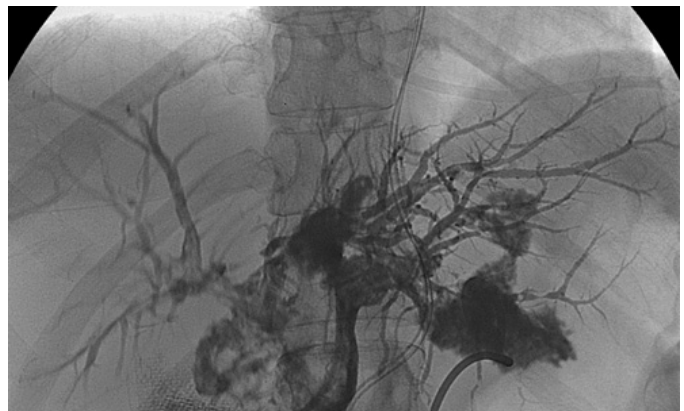


Figure 2. Contrast injection through percutaneous abscess drain showing communication between abscess, left biliary system, and extravasation of contrast.

catheter was placed through the peripheral left bile duct, with the loop in the cavity of the disrupted common hepatic duct. The patient was continued on antibiotics and supportive measures. A couple of weeks later the CHD drain was exchanged for an internal external percutaneous drain. The patient was discharged home; however, she presented to the emergency room 4 weeks later with worsening abdominal pain and fever, and was found to have a serum creatinine of 3.5 mg/dL and leukocytosis of $20,000/\mu\text{L}$. She required treatment of septic shock with broad spectrum antibiotics, supportive measures, and revision of biliary drain catheters.

Over the next 3 years, the patient had recurrent hospital admissions due to cholangitis; recurring hepatic abscesses, sepsis with *Enterococcus*, *Pseudomonas*, *Klebsiella*, and *Candida*; and severe hypotension, renal failure and respiratory failure managed by percutaneous drains, antibiotics, and supportive care. Most of these episodes within the first year required medical care in intensive care units. An ERCP was done 15 months after the index ERCP, which revealed formation of multiple strictures and beading in the intra- and extra-hepatic biliary tree. The hepatic abscesses resolved, but the biliary strictures required management by placement and exchange of biliary stents every 3 months. The patient, however, continued to show evidence of progressive sclerosing cholangitis and developed end-stage liver disease. Three years after the initial insult, the patient underwent successful living donor liver transplantation. Explant histopathology revealed secondary biliary cirrhosis, bile duct necrosis, fungal hyphae, and bacterial organisms. The patient has maintained normal hepatobiliary function and has overall been feeling well in 3 years of follow-up after liver transplantation.

Discussion

Emphysematous cholecystitis is a rare but well-described variant of acute cholecystitis. It is characterized by the presence of gas in the gallbladder wall; infection by gas-producing organisms including *Clostridia* species, *Klebsiella*, *E. coli*; a higher incidence of gangrene and perforation; higher incidence of acalculous disease; and higher mortality. Emphysematous cholecystitis is more common in males, and more than one-third of patients with this condition have diabetes mellitus.^{2,6} The exact etiology of emphysematous cholecystitis is unknown, but an initial ischemic insult with secondary infection from gas-forming bacteria has been proposed based on histopathologic findings.⁷ Although a diagnosis can be made on plain films revealing air in the gallbladder wall, a CT scan provides further evaluation for biliary enteric com-

munication, and the presence of gallstones or perforation. The standard management of emphysematous cholecystitis is emergent cholecystectomy.

Emphysematous cholecystitis as a complication of ERCP has been described in only 3 prior case reports.³⁻⁵ A comparison of these 3 cases and our patient is described in Table 1. Our patient differed in multiple ways, including younger age, female gender, non-diabetic, and significant intra- and extra-hepatic biliary injury.

Cholangiopathy with biliary inflammation and necrosis has been recognized as a result of post-liver transplantation ischemic injury, particularly with livers donated after cardiac death (DCD),⁸ surgical complication of laparoscopic cholecystectomy,⁹ advanced HIV/AIDS cholangiopathy,¹⁰ after radiofrequency ablation for hepatocellular carcinoma,¹¹ and in patients with hemophagocytic syndrome.¹² However, to our knowledge, this is the first report of infectious biliary necrosis and cholangiopathy as a complication of ERCP. The mechanism seems to be an initial ischemic insult during ERCP and contrast injection with superimposed bacterial infection causing cholecystitis and rapid spread of infection to the biliary system. Our patient developed myocardial infarction after the initial ERCP, which delayed cholecystectomy and may have promoted the spread of infection to the biliary tree.

Unlike the other reported cases of post-ERCP emphysematous cholecystitis, cystic duct was cannulated for direct aspiration of gallbladder bile in our case, which, theoretically, could increase the chance of bacterial colonization. Aspiration of bile from common bile duct or duodenum after stimulation by cholecystokinin is another effective but less invasive method to evaluate for microlithiasis.¹³ Surprisingly, our patient had none of the risk factors of emphysematous cholecystitis, such as advanced age, diabetes mellitus, and male gender. Our patient did not receive pre-procedure antibiotics. Recent data and American Society of Gastrointesti-

Table 1. Comparison Between 4 Reported Cases of Post-ERCP Emphysematous Cholecystitis

Case Report	Procedure	Indication	Sex	Diabetes Mellitus	Prophylactic Antibiotics Use/ Gallstones	Biliary Injury	Outcome
Baker et al ³	ERCP with cholangiogram	NR	Male	Yes	No / No	No	Died despite emergent cholecystectomy and supportive measures
Alvarez et al ⁴	ERCP with cholangiogram and pancreatogram; no sphincterotomy	Double duct sign, pancreatic head mass	Male	No	No / No	No	Died despite emergent cholecystectomy and supportive measures
Itah et al ⁵	ERCP with cholangiogram and sphincterotomy	Cholangitis	Male	NR	NR/ Yes	No	Uneventful recovery after cholecystectomy
Current case	ERCP with cholangiogram, pancreatogram, and sphincter pressure measurement	Recent pancreatitis	Female	No	No / No	Yes	Emergent cholecystectomy, recurrent hepatic abscesses, liver transplantation

ERCP = endoscopic retrograde cholangiopancreatography; NR = not reported.

nal Endoscopy (ASGE) recommendations suggest a benefit of pre-ERCP antibiotics in only those patients with known or suspected biliary obstruction in which complete drainage may not be achieved.^{14,15}

Though current guidelines do not recommend routine antibiotic use given the low likelihood of infection, infectious complications of ERCP can occur even in low-risk patients undergoing diagnostic procedure without any biliary obstruction. Prompt diagnosis of the complication and treatment is important to prevent long-term complications and mortality.

Disclosures

Author contributions: K. Bari, H. Aslanian, and P. Jamidar conceptualized, initiated, and wrote the article; J. Pollak, R. Salem, S. Emre, and P. Jamidar revised the article for critical intellectual content and approved the final version for publication; and E. Reiner and T. Taddei performed the literature review and conceptualized the article and figures. P. Jamidar is the article guarantor.

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