Insidious Presentation of Emphysematous Cholecystitis in A Type 2 Diabetic Man

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Abstract

We present the clinical course of a 77-year-old diabetic man with jaundice and nausea for one week. An abdominal ultrasound examination revealed a hyperechoic gallbladder wall and a normal common bile duct. Computed tomography disclosed air in the gallbladder lumen as well as intramural air; these are consistent with emphysematous cholecystitis. He was treated with antibiotics and percutaneous gallbladder drainage and finally was discharged uneventfully. We discuss the unusual insidious presentation of emphysematous cholecystitis in this patient, together with the pitfalls related to imaging studies of emphysematous cholecystitis as compared with gallbladder adenomyomatosis. Computed tomography should be considered early when examining diabetic patients who have acoustic artifacts and reverberation shadows on ultrasonography when this is linked to abnormal liver function tests, even when the clinical features are not serious. Percutaneous gallbladder drainage is an alternative therapy to cholecystectomy that can be used with selected patients. (J Intern Med Taiwan 2013; 24: 424-429)

Key Words: Emphysematous cholecystitis; Diabetes mellitus

Introduction

Emphysematous cholecystitis is characterized by having a presentation of gas within the gallbladder lumen, the gallbladder wall or pericholecystic tissues without the presence of communication between the biliary tract and the gastrointestinal tract¹. It is a relatively rare but serious variant of acute cholecystitis that involves infection with a gas-forming bacterial species such as Clostridium spp., Escherichia coli or Klebsiella pneumoniae; the infection is followed by ischemic changes in the gallbladder due to primary vascular compromise². As compared with acute cholecystitis, emphysematous cholecystitis is more commonly associated with diabetes mellitus and arteriosclerosis, has a higher mortality rate, has a higher risk of perforation, and shows a more rapid progression²,³. The initial clinical findings of emphysematous cholecystitis are non-specific and are similar to those of acute...
cholecystitis. We herein report an elderly diabetic patient with acute emphysematous cholecystitis who atypically presented with painless jaundice.

Case report

A 77-year-old man who has suffered from type 2 diabetes mellitus for 10 years with background diabetic retinopathy for 1 year presented with progressive jaundice and nausea for one week. He was referred from a regional hospital where an abdominal ultrasound had revealed a hyper-echoic gallbladder wall and adenomyomatosis was suggested. His regular medication history included glimepiride 2 mg twice per day and metformin 500 mg twice per day. On the arrival at the emergency department, a physical examination showed a blood pressure of 121/65 mmHg, a pulse rate of 67 beats/min, a temperature of 35.6 °C, and a respiration rate of 20 breaths/min as well as remarkable yellowish skin discoloration and icteric sclera. An abdominal examination revealed normoactive bowel sound without abdominal tenderness. All other physical examinations were unremarkable except edema of the legs. Laboratory blood tests revealed elevated levels of total bilirubin (7.6 mg/dL, normal range 0.2-1.6), direct bilirubin (6.15 mg/dL, normal range 0-0.3), alanine aminotransferase (ALT, 49 IU/L, normal range 0-40), alkaline phosphatase (Alk-P, 275 mg/dL, normal range 10-100), gamma-glutamyl transpeptidase (GGT, 177 u/L, normal range 8-60) and C-reactive protein (CRP, 2.66 mg/dL, normal range 0-0.5) but a normal white blood cell (WBC) count (9200/μL, normal range 4,500-11,000) with 58% neutrophils. Furthermore, the patient’s serum creatinine was normal (1.2 mg/dL, normal range 0.7-1.5). An abdominal ultrasound was performed by a radiologist and this revealed a hyperechoic gallbladder wall and the presence of gas in the gallbladder wall was suspected (Fig. 1). Intravenous contrast computed tomography disclosed distension of the gallbladder and the presence of small gallstones. There was also thickening of the gallbladder wall with hyperemia. Air was present in the gallbladder lumen as well as intramurally, which is consistent with emphysematous cholecystitis (Fig. 2). There was neither common bile duct dilation nor the presence of common bile duct stones. The patient was treated with intravenous broad spectrum antibiotics, namely amoxicillin/clavulanic acid, and a surgeon was consulted. Although he had no past history and symptoms of cardiovascular diseases, a nuclear medicine study as part of his pre-operation evaluation revealed a left ventricle ejection fraction of 24% (normal range: > 50%) and generalized severe hypokinesia of the left ventricle, which are compatible with congestive heart failure. Based on this, percutaneous gallbladder drainage was performed on hospital day 4. A microbial culture of the bile showed the presence of *Escherichia coli* and *Klebsiella pneumoniae*. By hospital day 18, the patient’s total bilirubin level had declined to 2.1 mg/dL and by day 29 it dropped further and was 1.6 mg/dL. Antegrade cholangiography via the percutaneous gallbladder drainage was performed on hospital day 17 and this disclosed the presence of filling defects in

![Figure 1. Ultrasonography revealed a hyperechoic appearance secondary to gas in the gallbladder wall (arrow) that was associated with a "tail ring-down artifact."](image)
the gallbladder and a cystic duct; however, there was an absence of stone(s) inside the common bile duct. Serum markers for viral hepatitis including HBsAg, anti-HBc IgM, anti-HAV IgM, and anti-HCV were negative. His glycated hemoglobin (HbA1C) was 10.1%. Urinalysis showed overt proteinuria. The drainage tube was removed on hospital day 23. The patient was hospitalized for a total of 58 days and was finally discharged uneventfully.

Discussion

In the case described here, the clinical manifestations were insidious and the abdominal physical examination findings were equivocal. Furthermore, the patient’s WBC count was normal and his CRP level was only mildly elevated. These, when taken together, would make diagnosis a challenge if image studies were not undertaken. Patients with diabetes mellitus who have suffered from myocardial infarction may have an insidious clinical presentation. Cardiac autonomic dysfunction resulting from the destruction of the afferent nerve fibers that are involved in cardiac nociception can result in some diabetic patients suffering from silent myocardial ischemia\(^4,5\). Silent mesentery ischemia in a diabetic patient, which is suggestive of visceral afferent

![Figure 2](image)

**Figure 2.** Computed tomography demonstrated thickening of the gallbladder wall with hyperemia, gas within the gallbladder wall and lumen (white arrow), and small gallstones (black arrow). 2A and 2C, without contrast-enhancement; 2B and 2D, with contrast-enhancement.
nerve fiber damage, has been previously reported\(^6\). Although our patient did not receive an cardiac autonomic examination, the presence of retinopathy and nephropathy is suggestive of autonomic neuropathy that might present as and result in an insidious presentation of cholecystitis.

We found that the patient had elevation of conjugated bilirubin, which prompted further imaging study despite the unremarkable abdominal physical findings. The causes of elevated conjugated bilirubin included biliary obstruction, intrahepatic cholestasis, and hepatocellular injury\(^7\). The causes of the episodic jaundice in this patient is likely to be a number of combined factors. Endotoxin and inflammatory mediators are able to impair basolateral and canicular bile acid and organic anion transport\(^8-10\), thus sepsis itself is likely to have contributed to the intrahepatic cholestasis. The coexistent elevation in this patient of serum bilirubin, Alk-P and GGT, but an unremarkable elevation of ALT, suggests that the jaundice was due to biliary tract disease. The serum bilirubin levels in this patient declined quickly after treatment, while cholangiography was performed when the total bilirubin level had declined to 2.1 mg/\(\text{dL}\). This might be attributable to the unremarkable imaging findings in relation to the extrahepatic bile duct. However, a non-dilated biliary duct does not exclude extrahepatic biliary obstruction\(^7\). Since the cholangiography was suggestive of the presence of a cystic duct stone, the possibility remains that transient or incomplete biliary obstruction in this patient cannot be excluded.

The final diagnosis of emphysematous cholecystitis was based on the imaging studies, which demonstrated the presence of gas within the lumen and/or wall of the gallbladder. A highly echogenic gas collection with a reverberation shadow (artifact) and an effervescent gallbladder are the typical ultrasonographic findings of an emphysematous cholecystitis\(^11,12\). However, these findings may be mistaken for adenomyomatosis, as was the case with our patient at the regional hospital. Clinical history and laboratory tests can be helpful when distinguishing emphysematous cholecystitis from gallbladder adenomyomatosis. Both conditions show acoustic artifacts and reverberation shadows during ultrasonography, but each disease require a very different management regimen\(^13\). The intramural diverticulae of adenomyomatosis, which contain biliary sludge, gallstones and/or papillary projections, appear as hyperechoic spaces\(^14\). Alternatively, acoustic shadow can result from small gallstones within the intramural diverticulae, whereas reverberation artifacts result from tiny echogenic foci or front-like mucosal projections within the intramural diverticulae\(^15\). The V-shaped reverberation artifacts of adenomyomatosis need to be compared with the dirty shadow that occurs with emphysematous cholecystitis, which is more linear in shape with the air being mobile and non-dependent\(^16\). Computed tomography should be considered as the image modality of choice when the ultrasonography is indecisive.

An immediate cholecystectomy in association with broad spectrum antibiotic treatment is the recommended treatment for emphysematous cholecystitis. Percutaneous gallbladder drainage may be used as a temporary procedure before cholecystectomy in patients who are critically ill, or used to successfully treat patients when a necrosis-mediated perforation is absent\(^17\). This patient exhibited a prolonged hospitalization. The suggested regimen for the initial empiric antibiotics treatment of biliary infection is 3\(^{\text{rd}}\) generation cephalosporin plus metronidazole, or beta-lactam/beta-lactamase inhibitor (a good choice is ampicillin-sulbactan, piperacillin-tazobactam, ticarcillin-clavulanate). Ciprofloxacin, levofloxacin, or cefepime, each in combination with metronidazole, imipenem-cilastatin, or meropenem are alternative agents\(^18\). The duration of antibiotic therapy should be based on clinical improvement. Furthermore, the definitive treatment of emphysematous cholecystitis requires surgical intervention\(^1\).
Although high risk for general anesthesia and emergent cholecystectomy is not indicated for this patient, an elective cholecystectomy could be arranged after the patient’s condition improves. Poor control diabetes mellitus and old age also contribute to the prolonged hospitalization.

Emphysematous cholecystitis should be considered as a possible diagnosis in diabetic patients with acoustic artifacts and reverberation shadows on ultrasonography when abnormal liver function tests are present; this is true even when the patient is not seriously ill.

References
糖尿病病患罹患氣腫性膽囊炎的隱伏表現

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摘 要

一位77歲男性糖尿病病患因黃疸與噁心一週就醫，腹部超音波顯示高迴音的膽囊壁及正常的膽管。電腦斷層顯示在膽囊腔與膽囊壁出現氣體，符合氣腫性膽囊炎的表現。該病患接受抗生素與經皮膽囊引流治療，順利出院。我們在此討論本氣腫性膽囊炎病例不常見的隱伏表現，以及影像學檢查在鑑別診斷氣腫性膽囊炎與膽囊癌等病變的陷阱。當糖尿病病患出現異常肝功能檢查，且超音波檢查發現膽囊壁有聲波偽影及反射陰影時，即使臨床表現不甚嚴重，仍應考慮儘早安排電腦斷層檢查。對於不適合接受膽囊切除且臨床不甚危急的病患，可以採用經皮膽囊引流治療。