Acute cholecystitis complicated with gallbladder empyema due to *Mycobacterium tuberculosis* in a patient with diabetes mellitus: a case report

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**Abstract:** Acute cholecystitis severity ranges from mild to very severe, and its most dreadful complication is gallbladder empyema. It can be caused by several etiologic agents, but *Mycobacterium tuberculosis* is not common among them. Here we present a 61-year-old female who lives in an area of high tuberculosis endemity and has type 2 diabetes mellitus. She came to our hospital with a 2-day history of moderate-to-severe colicky right upper quadrant abdominal pain and other clinical manifestations compatible with AC. Imaging studies confirmed the diagnosis. An emergency open cholecystectomy was performed and the gallbladder was sent for histopathologic examination. *M. tuberculosis* was identified by molecular studies and the treatment was adjusted. The patient recovered uneventfully. The clinical history and physical examination are essential for raising the index of suspicion, but complementary evaluation with imaging studies is necessary to confirm the diagnosis and evaluate its complications. Tuberculosis is a major health problem worldwide, and health professionals should be aware of its clinical spectrum to approach and manage common and uncommon presentations within their scope of attention.

**Keywords:** abdominal tuberculosis, acute cholecystitis, gallbladder disease, gallbladder empyema, *Mycobacterium tuberculosis*, tuberculosis

**Introduction**

Acute cholecystitis (AC) is one of the most common surgical entities seen in the Emergency Department, it is an acute inflammatory disease caused after cystic duct obstruction due to gallstones or lithogenic bile.1,2 The most dreadful complication is gallbladder empyema, which accounts for 6.3–26.6% of complicated AC with mortality of nearly 3%. It occurs when the obstructed gallbladder becomes infected and bacteria-containing bile with purulent material accumulates.3–5 The most frequent etiologic agents are Gram-negative enteropathogens: *Escherichia coli*, Klebsiella spp., and *Streptococcus faecalis*.2,6 However, other pathogens can affect the gallbladder and cause complications.

Gallbladder tuberculosis (TB) is a very rare entity due to the intrinsic role of bile acids that inhibits the growth of the *Mycobacterium* spp.7 It can present as acute or chronic cholecystitis,8,9 biliary strictures, choledocholithiasis,10 gallbladder perforation,11 and can also mimic gallbladder carcinoma, one of the most important differential diagnoses of this disease.12 However, only two cases of gallbladder empyema have been reported in the literature.13,14 Here, we report a case of AC with gallbladder empyema in a patient that lives with diabetes mellitus (DM) due to *Mycobacterium tuberculosis* – a very rare cause of this disease. This case report has been reported in line with the SCARE Criteria.15

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**Case report**

We present a 61-year-old female from San Luis Potosí, Mexico, with type 2 DM, hypertension, and 2-year history of gallstone disease with no other comorbidities. Her surgical history was not significant. She presented at the Emergency Department of our hospital with a 2-day history of moderate-to-severe colicky RUQ abdominal pain that started an hour after eating a large, fatty meal for breakfast. It radiated to the mid-back and right shoulder and had no alleviating or aggravating factors. Also, she complained of nausea, vomiting, and food intolerance. The patient had previous self-limited episodes of RUQ abdominal pain.

On general examination, she had a poor general status and was diaphoretic and dehydrated with unstable vital signs: a respiratory rate of 20 r/min, a heart rate of 127 bpm, an oxygen saturation of 92%, a blood pressure of 84/52 mmHg, and a body temperature of 38.1°C. The abdominal physical examination revealed tenderness to palpation in the epigastric region with a firm and painful palpable mass in the RUQ abdominal region. Laboratory tests showed an elevated white blood count (WBC) count of 15,670 mcl with 15,400 mcl (98.0%) neutrophils and 235 mcl (1.5%) of lymphocytes, 287,000 mcl platelets, lactate blood levels of 2.3 mmol/l, total bilirubin of 1.09 mg/dl, conjugated bilirubin of 0.45 mg/dl, unconjugated bilirubin of 0.64 mg/dl, creatinine of 0.89 mg/dl, urea of 53.6 mg/dl, prothrombin time of 14.2 seconds, partial thromboplastin time of 35 seconds, and C-reactive protein of 305 mg/L with no other alterations. Blood cultures were obtained prior the start of antibiotics. There was no ultrasound available, but an abdominal computed tomography (CT) scan was performed and showed an enlarged gallbladder with marked wall thickening. Also, a gallstone obstructing the gallbladder neck was shown (Figure 1).

The patient was started with IV antibiotic therapy of ciprofloxacin and metronidazole. Preoperative resuscitation followed by an emergency open cholecystectomy was performed for source control. Surgical exploration revealed omentum and duodenum adherences to the enlarged gallbladder. The gallbladder was also necrotic without perforation. Retrograde gallbladder dissection with subtotal fenestrating cholecystectomy was performed because of the impossibility to identify the common hepatic bile duct, cystic duct, and cystic artery. Intraoperative drainage of the gallbladder was performed, obtaining 60 ml of purulent fluid. Cultures were collected from the content of gallbladder. Saratoga sump drainage was collocated on the liver bed for wound drainage. Because of the risk of bile duct injury along with the procedure and risk of biliary fistula, the patient was taken for an endoscopic retrograde cholangiopancreatography (ERCP), where an endoscopic biliary prosthesis was inserted. All blood and fluid cultures and Gram-stain yield negative. The patient recovered uneventfully without pain and fever and was discharged on the fifth postoperative day.

The gallbladder specimen removed during cholecystectomy was sent for histopathologic examination to the Pathology Department of our hospital. The presence of a gallstone of $5.5 \times 3 \times 3$ cm, a wall thickness of 4–10 mm, and a nodular cheesy-looking lesion of 9 mm were noted. The reported histopathologic diagnosis was AC with areas of caseous necrosis. Routine staining was performed and showed intracellular acid-fast bacilli (AFB). (Figure 2) The gallbladder specimen was sent for molecular testing, where *M. tuberculosis* was identified by polymerase chain reaction. A diagnosis of AC complicated with gallbladder empyema due to *M. tuberculosis* was performed and treatment was adjusted. An epidemiological report was sent to our Epidemiology Department and the authorities of the National Secretary of Health for follow-up and starting the antituberculous therapy. They started the shortened primary TB treatment which comprises an intensive therapy with isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months, followed by 4 months of continuation phase with isoniazid and rifampicin. The patient had completed the intensive phase and currently is in the second month of continuation phase. During follow-up, the patient has not presented any complications due the disease or the treatment.

**Discussion**

The case report that we present here belongs to an area with a high prevalence of TB and highlights one of the complications that can develop in the natural course of this disease. It also demonstrates the importance of making a good clinical history in all critically ill patients with AC complicated with gallbladder empyema. Early identification of
Figure 1. (a) Axial view of the abdominal CT at level of T12 vertebrae, showing an enlarged gallbladder filled with large amounts of fluid, with marked diffuse uniform wall thickening and a hyperdense gallstone partially obstructing the gallbladder neck. (b) Axial view of the abdominal CT at level of L1 vertebrae showing enlarged gallbladder with wall edema and pericholecystic fluid. CT, computed tomography.

Figure 2. Histopathologic gallbladder tissue examination. (a) Hematoxylin and eosin (HE), gallbladder with marked areas of chronic and acute granulomatous inflammation and caseous-necrosis. (b) Ziehl–Neelsen, gallbladder showing intracellular acid-fast bacilli. (c) HE, marked intimal and a diffuse subendothelial proliferation compatible with tuberculous endarteritis.
potential complications can allow appropriate and prompt medical and surgical management, reducing its morbidity and mortality.

There are well-known risk factors for TB such as low socioeconomic status, TB family history, malnutrition, smoking, and poorly controlled DM. The association of TB with DM has been known for centuries due to the immunosuppression caused by the poor glycemic control. Globally, according to the World Health Organization, DM is associated with a twofold to threefold risk of developing complications due to TB, including death during treatment and risk of developing multidrug-resistant TB (MDR-TB), it is also associated with a fourfold risk of TB relapse after treatment completion. Mexico is among the countries with the highest prevalence of DM, with 15.7% in 2020, where the population attributable risk of DM on TB reaches 25% which is higher than the one from human immunodeficiency virus infection. MDR-TB was one of our primary concerns in this patient follow-up because, in San Luis Potosí, the most common risk factor associated with MDR-TB has been DM, which was found in 47.2% of MDR-TB patients.

Abdominal TB prevalence has increased in both immunocompetent and immunocompromised hosts worldwide, mostly in endemic countries. However, the real prevalence and implications are still unknown. Gastrointestinal TB comprises nearly 2% of total TB cases and it is often associated with disseminated disease, with less than 20% associated with pulmonary TB. The most affected organ is the liver, in counterpart to the gallbladder, which is rarely affected. People living with DM are less likely to present with extrapulmonary TB, which contrasts with our case because our patients didn’t have signs of pulmonary TB. Gallbladder TB can develop by affecting the biliary epithelium causing acute or chronic inflammation or by involving the adjacent perportal and pericholedochal lymph nodes. Typically, patients complain of a slow and insidious clinical presentation with jaundice, fever, anorexia, recurrent abdominal pain, and weight loss. However, the clinical findings are nonspecific and clinical findings are indistinguishable from other gallbladder diseases.

Regarding imaging studies, three different CT scan morphology findings of the gallbladder TB have been described in the literature: micronodular lesions of the gallbladder wall with or without enhancement of the lesion, a thickened gallbladder wall, and a gallbladder mass, being the thickening of the gallbladder wall the most common finding. Our patient’s CT scan showed an enlarged gallbladder with marked gallbladder wall thickening and small amounts of pericholecystic fluid. However, laboratory tests can be normal or they may demonstrate anemia, elevation of the liver enzymes, such as aspartate aminotransferase and alanine aminotransferase, and elevation of inflammatory biomarkers, such as C-reactive protein and erythrocyte sedimentation rate, and neutrophil-predominant leukocytosis.

Traditionally, all gallbladder specimens are sent for histopathologic examination after cholecystectomy to rule out the presence of malignant diseases when a macroscopic abnormality is present. The histopathologic findings can confirm the presence of gallbladder TB. Similar to our case, caseous necrosis, multiple granulomas, and intracellular AFB are the typical histopathologic findings, highlighting the importance of doing the AFB routine staining.

Abdominal TB is generally responsive to medical treatment alone, so early diagnosis can prevent unnecessary surgical intervention. According to our national policy, the diagnosed cases of abdominal TB, including gallbladder TB, should receive the shortened primary treatment of antituberculous therapy, which is strictly supervised and monthly follow-up is recommended. However, because the diagnosis of gallbladder TB is mostly done postoperatively, surgery is mandatory. In our case, we performed a subtotal fenestrating open cholecystectomy as a bail-out procedure in view of our patient’s safety due to the impossibility of achieving and optimal view of the hepatobiliary anatomy. It is recommended in cases with a lot of inflammation or loss of the anatomy. Biliary fistula or stenosis is known as postoperative complications of this procedure, making a priority to perform an ERCP.

Conclusion
This case report describes an AC complicated with gallbladder empyema due to M. tuberculosis in a patient that lives with DM in an area of high endemicity for TB. The clinical, imaging, and
laboratory findings are nonspecific for gallbladder TB empyema. The diagnosis can only be made postoperatively after a histopathologic check and confirmation. This highlights the importance of sending all gallbladder specimens for histopathologic routine examination after performing a cholecystectomy due to its implications for treatment and prognosis. TB is a major health problem worldwide, and health professionals should be aware of its clinical spectrum to approach and manage common and uncommon presentations within their scope of attention. Surgeons should have a high index of suspicion for patients with AC and gallbladder empyema that live in endemic countries or that have risk factors for TB as they can change their outcome.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Author contributions
Alejandro Ortiz-Hernández: Conceptualization; Investigation; Methodology; Project administration; Resources; Supervision; Visualization; Writing – original draft; Writing – review & editing.

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