Pitfalls of Diagnosis of Acalculous Cholecystitis. Case Presentation and Literature Review.

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Citation

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Abstract

Acute acalculous cholecystitis (AAC) is an acute inflammation of the gallbladder in absence of gallstones. It is a potentially fatal form of acute cholecystitis that usually occurs in critically ill patients. The disease may often go unrecognized due to the complexity of the patient's medical and surgical problems. Recently, there is a reported increase in the incidence of acalculous cholecystitis in outpatients without typical predisposing critical illness. We report a case of congestive heart failure and pulmonary embolism which was diagnosed initially as acaculous cholecystitis discussing the pitfalls of diagnosis of the disease which usually result in under-estimation of the condition in seriously ill patients (appropriate patients) and over-estimation of the condition in the outpatients without typical predisposing critical illness (inappropriate patients).

INTRODUCTION

Diagnosis is of acalculous cholecystitis is difficult. Clinical examination is often not helpful, as many patients are receiving mechanical ventilation and have decreased mental awareness. The diagnosis is usually made by radiological tests, most often by sonographic examination of the gallbladder. The role of the various imaging modalities in acute acalculous cholecystitis is still somewhat controversial. In general, no single imaging study is ideal. The three primary imaging modalities (ultrasound, CT scan and cholescintigraphy) often are complementary. Early diagnosis and management is of vital importance as without immediate treatment the condition rapidly progresses to perforation or gangrenous cholecystitis with very high mortality. A timely diagnosis will depend on a high index of suspicion in the appropriate patient, and the combined results of clinical findings (admittedly nonspecific), plus properly interpreted imaging.

CASE PRESENTATION

A 68-year-old female was presented to the emergency department at KFMC, Riyadh, with complaints of recurrent upper abdominal pain and vomiting for two months which got worse 4 days before her presentation. She had no past history of medical illness or surgery. On admission to the emergency department, she was fully conscious, oriented, not jaundiced or cyanosed. Her pulse was 93/minute, blood pressure 104/70 mm of Hg, temperature 37.6°C, respiratory rate 22/minute and oxygen saturation 98% at room air. The chest was clear and abdominal examination revealed tenderness in the right hypochondrium and epigastric region, and a positive Murphy's sign. The rest of the abdomen was soft and not tender.

CBC showed an Hb of 10.2 g/dl, WBCs of 10.8 x10³ and platelets of 27 x10³. Urea and electrolytes and liver function test showed elevated urea, creatinine and liver enzymes with marginally elevated serum bilirubin and alkaline phospatase (table 1).

Figure 1

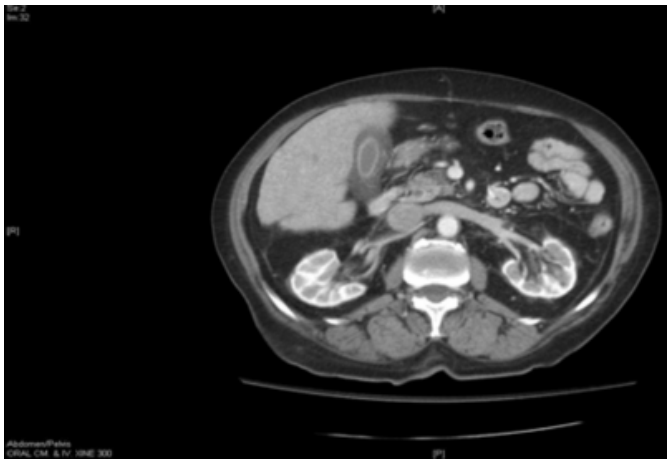
Test Name	Result	Unit	Reference Range
Glucose, STAT plasma	5.9	mmol/L	3.6-6.7
Albumin, plasma	31	g/L	34-50
Bilirubin Total, plasma	19.0	umol/L	0-17.1
Alkaline Phosphatase, plasma	167	U/L	50-136
ALT (SGPT), plasma	94	U/L	30-65
Sodium, plasma	136	mmol/L	135-145
Potassium, plasma	3.3	mmol/L	3.6-5.2
Bicarbonate, plasma	22.2	mmol/L	21-32
Chloride, plasma	104	mmol/L	98-106
Creatinine, plasma	123	umol/L	53-88
Urea, plasma	11.7	mmol/L	2.5-6.4
AST (SGOT), plasma	69	U/L	15-37
LDH, plasma	769	U/L	100-190
Gamma GT, plasma	163	U/L	7-32
Creatine Kinase MB, plasma	4.3	ug/L	0-3.6
Creatine Kinase, plasma	22	U/L	21-215
Troponin I, plasma	0.06	ug/L	0-0.09
Lipase, plasma	212	U/L	114-286
Bilirubin Direct, plasma	5.8	umol/L	0-5

A CT scan of the abdomen reported an echo-free gallbladder with thickened wall, mucosal enhancement, and pericholecystic fluid. The liver showed no obvious intrahepatic bile duct dilatation or focal lesion. The findings were suggestive of acalculous cholecystitis; however, further

correlation with ultrasound study of the biliary system together with the laboratory and the clinical findings was recommended by the radiologist (Figure1).

Figure 2

Figure 1: Abdominal CT scan showing mucosal enhancement of the gall bladder wall with pericholecystic fluid and fat stranding



The ultrasound showed a normal liver without focal lesions or biliary duct dilatation. The gallbladder was echo-free with a thickened wall (figures 2 and 3). There was free fluid seen in Morison's pouch, the infrahepatic area, around the left and right kidneys (figure 4 and 5), and also in the pelvis. The ultrasound findings confirmed the CT findings of features of acalculous cholecystitis.

Figure 3

Figure 2: Ultrasonography showing an echo-free gall bladder with edematous thickened wall

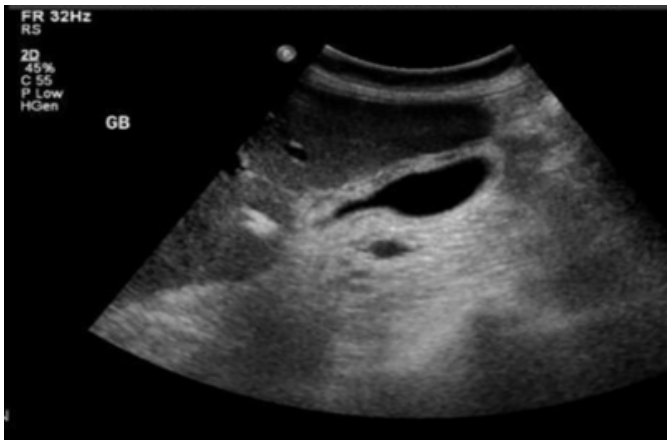


Figure 4

Figure 3: Ultrasonography showing thickened gallbladder wall surrounded with pericholecystic fluid together with right perinephric fluid.

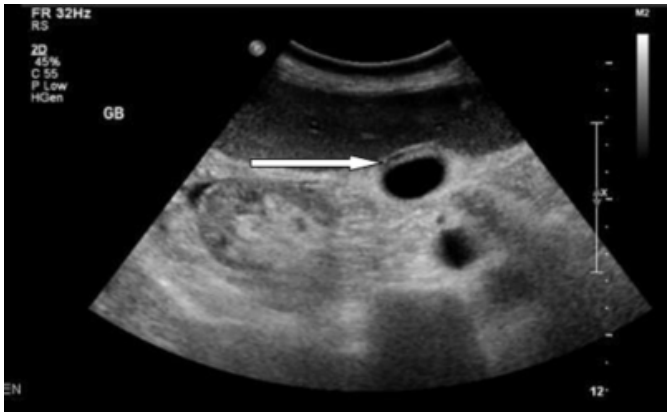


Figure 5

Figure 4: Ultrasonography showing right perinephric fluid

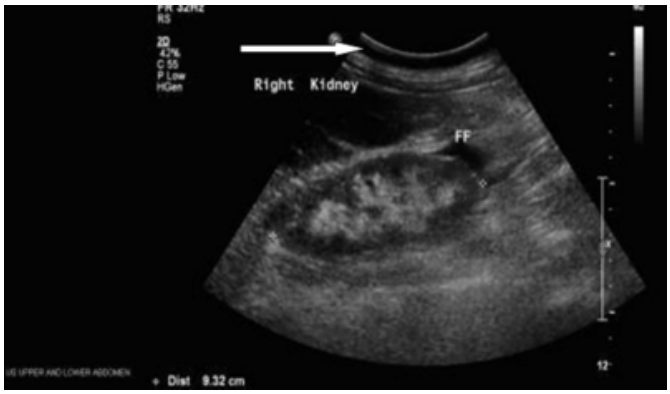
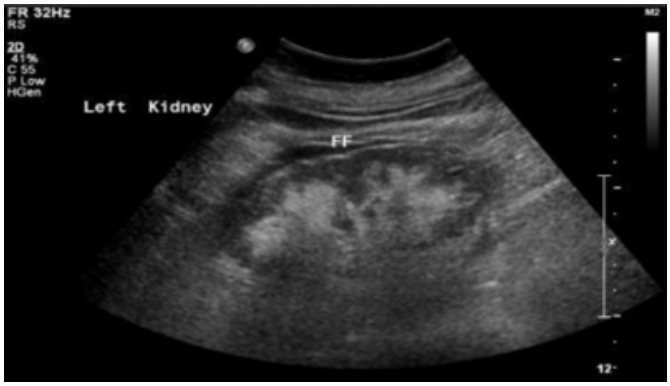


Figure 6

Figure 5: Ultrasonography showing fluid around the left kidney

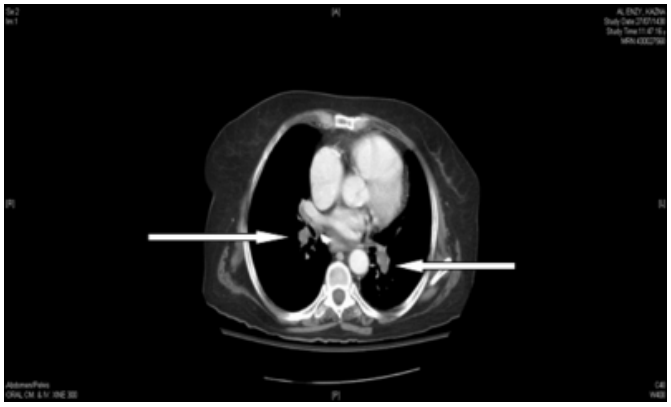


Up to this stage the patient was only seen by the emergency physicians and junior surgical staff. Admission to the surgical ward was planned on the assumptive diagnosis of acalculous cholecystitis. Fortunately enough, the patient was

seen by a clinically oriented senior surgical staff member who discovered that what was thought to be a positive Murphy's sign was in fact enlarged tender liver and that there was obvious increase in jugular venous pressure and bilateral lower limb edema. Diagnosis of congestive heart failure was established and immediate cardiac consultation was sought. A bedside echocardiogram showed a dilated right ventricle and atrium together with a right atrial mass (thrombus) extending through the tricuspid valve into the right ventricle. Immediately after performing the echocardiogram, her oxygen saturation dropped and the patient required endotracheal intubation and ventilation. A spiral chest CT scan was ordered to rule out pulmonary embolism, but on reviewing the upper cuts of the abdominal CT scan by a senior radiologist, it was obvious that there were pulmonary emboli almost completely occluding both the right and left pulmonary arteries (figure 6).

Figure 7

Figure 6: Upper cuts of abdominal CT showing emboli almost completely occluding the right and left pulmonary arteries (arrows)



The patient was admitted to the CCU with a multidisciplinary team including cardiology, pulmonology, hematology and surgery. Retrospectively, it was very clear that the radiological findings of acalculous cholecystitis had distracted the junior staff from a more serious medical issue that was immediately endangering the patient's life.

DISCUSSION

Acute acalculous cholecystitis (AAC) is an acute inflammation of the gallbladder in the absence of gallstones (1). It was first described by Duncan in 1844 complicating surgery on a patient with incarcerated hernia (2). Acute acalculous cholecystitis is rare, occurring in only 5 % to 10 % of patients with acute cholecystitis (3). It is a potentially fatal form of acute cholecystitis that usually occurs in critically ill patients (4).

Acalculous cholecystitis is more likely to be found in patients with recent severe trauma, critical illness, cardiovascular surgery (5, 6, and 7) or severe burns. It has also been found in association with total parenteral nutrition (8), mechanical ventilation, and the use of narcotic analgesics, as well as in major cardiovascular disorders, complicated diabetes mellitus, autoimmune disease (9-12), AIDS (13) and after radiotherapy (14).

The precise mechanism of the disease is unknown: the commonly postulated theories regarding its pathogenesis are bile stasis, sepsis and ischemia (15, 16, and 17).

Although recognized for more than 150 years, acute acalculous cholecystitis remains an elusive diagnosis. This is likely because of the complex clinical setting in which this entity develops and lack of large prospective controlled trials that evaluate various diagnostic modalities (18).

The disease may often go unrecognized due to the complexity of the patient's medical and surgical problems. Clinical examination is often not helpful, as many patients are receiving mechanical ventilation and have decreased mental awareness. It is usually difficult to elicit right quadrant tenderness or Murphy's sign in those patients. Biochemical markers are nonspecific and contribute to the delay in diagnosis and treatment (19). The diagnosis is usually made by radiological tests, most often by sonographic examination of the gallbladder. A timely diagnosis will depend on a high index of suspicion in the appropriate patient, and the combined results of clinical findings (admittedly nonspecific) plus properly interpreted imaging (18).

Ultrasound is usually the first line of investigation because it is widely available and can be performed at the bedside (20,21). The most significant ultrasonographic findings are thickening of the gallbladder wall of more than 3.5 mm, gallbladder distention, pericholecystic fluid, and a sonolucent intraluminal layer (22, 23). Although ultrasonography is considered as an effective and accurate diagnostic test for acalculous cholecystitis (16), the reported sensitivity and specificity of sonography in the evaluation of acalculous cholecystitis vary from 23-95% and 40-95%, respectively (24).

Computed tomography usually demonstrates the same findings of ultrasound (21, 22). The advantage to CT compared with ultrasound is that it is superior at detecting pathology elsewhere in the abdomen that could be the cause

of the patient's fever or pain, but it cannot be applied at the bedside, which is necessary for many critically ill patients.

The diagnosis of acute acalculous cholecystitis with CT requires that 2 major diagnostic criteria be met or, alternatively, that 1 major criterion and 2 minor criteria be met. These criteria are as follows:

MAJOR CRITERIA

Gallbladder wall thickening greater than 3 mm
Subserosal halo (i.e., gallbladder wall edema)
Pericholecystic fatty inflammation
Pericholecystic fluid (without ascites or hypoalbuminemia)
Mucosal sloughing
Intramural gas

MINOR CRITERIA

Gallbladder distention (>5 cm transverse)
High-attenuation bile (sludge)

Reported sensitivity and specificity 0f CT scan in diagnosis of acalculous cholecystitis vary but generally have been greater than 90-95% (24).

Tc-99m iminodiacetic acid cholescintigraphy is a highly reliable test and is easily performed even in acutely ill patients and should be the test of choice in all patients predisposed to and suspected of acute acalculous cholecystitis (25).

In general, diagnostic quality studies with augmentation yield a sensitivity of 80-90% and a specificity of 90-100%. False positives may occur reducing the specificity of the test. With morphine augmentation, the false-positive rate is decreased and the specificity is improved (26).

Cholescintigraphy is a useful tool for early diagnosis of acalculous cholecystitis in critically ill patients, in whom ultrasonography alone does not provide enough information to permit a sufficiently early decision regarding indications for surgery. Many authors suggest that the combination of ultrasonography and cholescintigraphy improves diagnostic accuracy and reduces false-positive and false-negative rates (27, 28).

The role of the various imaging modalities in acute acalculous cholecystitis is still somewhat controversial. In general, no single imaging study is ideal. The 3 primary imaging modalities often are complementary, with ultrasound (US) or CT providing anatomic information and evaluation of adjacent structures and cholescintigraphy providing functional information (29, 30).

The importance of early diagnosis and immediate treatment is reflected in the fact that without immediate treatment the condition rapidly progresses to perforation or gangrenous cholecystitis, with a mortality as high as 65 %. With early diagnosis and intervention, the mortality drops to 7 % (31).

Radiological changes associated with acalculous cholecystitis are not specific and can occur with many other non-biliary conditions. Thickening of the gallbladder wall may result from a large spectrum of pathological conditions and may have different appearances. Accurate diagnosis is usually established after a correlation of imaging findings, laboratory data and clinical history (32).

Wegener et al. performed a comprehensive prospective ultrasonographic study in 93 patients to investigate gallbladder wall thickness and gallbladder volumes in various non-biliary disease states. They found that without changes in gallbladder volume, the mean gallbladder wall thickness was significantly increased in patients with liver cirrhosis, viral hepatitis, chronic congestive heart failure, hypoalbuminemia, and chronic renal failure but not in patients with diabetes mellitus as compared to a control group. They concluded that a variety of non-biliary disorders are associated with significant thickening of the gallbladder wall (33).

Congestive right heart failure can cause thickening of gallbladder wall associated with pericholecystic fluid that mimics acalculus cholecystitis (34, 35), but additional findings of extravascular volume overload, such as pleural or pericardial effusions, ascites, dependent subcutaneous oedema, distended IVC and pulmonary congestion in the lung bases seen in patients with congestive heart failure, help in differentiation between the two conditions. Hypoalbuminaemia in patients on intensive care units may cause gallbladder wall thickening and can cause confusion with acute acalculous cholecystitis, which occurs most commonly in these patients. CT findings are helpful for distinguishing these conditions.

Most of the diagnostic difficulties arise from lack of clinical correlation and proper interpretation of the radiological findings due to decreased mental awareness secondary to trauma or/and diminished patient responses due to sedation and ventilation. Overcautiously, acalculous cholecystitis should be considered in every patient who is critically ill or injured and who has clinical findings of sepsis with no

obvious source (36).

In presence of these diagnostic difficulties we believe that over-diagnosis of acalculous cholecystitis is permissible and may be safer in critically ill patients. We also recommend maintaining a low threshold for instituting empiric, minimally invasive therapy in the form of percutaneous cholecystostomy.

Although acute acalculous cholecystitis is a disease traditionally observed in the critically ill, it has also been reported in outpatients without typical predisposing critical illness (37, 38). Savoca et al. reported a recent increase in the de novo presentation of outpatients with this disease, especially in elderly male outpatients with vascular disease (39). Similarly, Shridhar et al. observed de novo presentation of acalculous cholecystitis in several outpatients, young and middle-aged healthy individuals, in the absence of critical illness or predisposing factors (40).

In spite of the reported increased incidence of acalculous cholecystitis in outpatients without typical predisposing critical illness, we believe that over-diagnosis of the condition in the outpatient set-up is dangerous as it may distract the attention of the treating physician (especially junior medical staff) from more serious medical issues that endanger the patient's life and need immediate attention. We feel that it is safer to consider those patients as inappropriate patients for acalculous cholecystitis and the diagnosis should only be established in presence of strong clinical, labarotary and imaging evidence of the disease.

We would also like to point to another area of concern regarding training of our junior medical staff which was well expressed by Professor Herbert L. Fred in his interesting topic "hyposkillia". We totally agree with him that we should teach them high-touch medicine based on a carefully constructed medical history coupled with a pertinent physical examination and critical assessment of the information thus obtained. One then determines which studies, if any, are indicated. And if studies are deemed necessary, the simpler ones are ordered first; not high-tech medicine essentially bypasses the medical history and physical examination, and, primarily on the basis of the patient's chief complaint, goes directly to a slew of tests that typically include magnetic resonance imaging or computed tomography, or both (41).

SUMMARY

Acute acalculous cholecystitis is a rare variety of gallbladder inflammation. It is a potentially fatal form of acute cholecystitis that usually occurs in critically ill patients. Recently acalculous cholecystitis was reported to have increasing incidence in outpatients without typical predisposing critical illness or trauma. Without immediate treatment, the condition rapidly progresses to perforation or gangrenous cholecystitis, with a mortality as high as 65%. Diagnosis of acalculous cholecystitis may depend mainly on radiological findings due to decreased patient mental awareness secondary to trauma or/and diminished patient responses due to sedation and ventilation which makes eliciting of the clinical signs difficult and sometimes impossible. The pitfalls of radiological diagnosis result in over- or under-estimation of the condition. We believe that over-diagnosis of acalculous cholecystitis is permissible and may be safer in critically ill patients and recommend maintaining a low threshold for instituting empiric, minimally invasive therapy in the form of percutaneous cholecystostomy. On the other hand, over-estimation of the condition in outpatients without typical predisposing critical illness may be dangerous as it may distract the attention of the treating physician from more serious medical issues that need urgent attention and immediate management.

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