• CLINICAL RESEARCH •

Clinical predictors of severe gallbladder complications in acute acalculous cholecystitis

Ay-Jiun Wang, Tsang-En Wang, Ching-Chung Lin, Shee-Chan Lin, Shou-Chuan Shih

Ay-Jiun Wang, Tsang-En Wang, Ching-Chung Lin, Shee-Chan Lin, Shou-Chuan Shih, Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan, China
Correspondence to: Dr. Ay-Jiun Wang, Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital. 92, Sec. 2, Chung San North Road, Taipei, Taiwan, China. ajw@ms2.mmh.org.tw
Telephone: +86-2-25433535   **Fax:** +86-2-25574800
Received: 2003-08-26   **Accepted:** 2003-10-12

Abstract

AIM: To evaluate the relationship between clinical information (including age, laboratory data, and sonographic findings) and severe complications, such as gangrene, perforation, or abscess, in patients with acute acalculous cholecystitis (AAC).

METHODS: The medical records of patients hospitalized from January1997 to December 2002 with a diagnosis of acute cholecystitis were retrospectively reviewed to find those with AAC, confirmed at operation or by histologic examination. Data collected included age, sex, white blood cell count, AST, total bilirubin, alkaline phosphatase, bacteriology, mortality, and sonographic findings. The sonographic findings were recorded on a 3-point scale with 1 point each for gallbladder distention, gallbladder wall thickness >3.5 mm, and sludge. The patients were divided into 2 groups based on the presence (group A) or absence (group B) of severe gallbladder complications, defined as perforation, gangrene, or abscess.

RESULTS: There were 52 cases of AAC, accounting for 3.7 % of all cases of acute cholecystitis. Males predominated. Most patients were diagnosed by ultrasonography (48 of 52) or computed tomography (17 of 52). Severe gallbladder complications were present in 27 patients (52 %, group A) and absent in 25 (group B). Six patients died with a mortality of 12 %. Four of the 6 who died were in group A. Patients in group A were significantly older than those in group B (mean 60.88 y *vs.* 54.12 y, P=0.04) and had a significantly higher white blood cell count (mean 15 885.19 *vs.* 9 948.40, P=0.0005). All the 6 patients who died had normal white blood cell counts with an elevated percentage of band forms. The most commonly cultured bacteria in both blood and bile were *E. coli* and *Klebsiella pneumoniae.* The cumulative sonographic points did not reliably distinguish between groups A and B, even though group A tended to have more points.

CONCLUSION: Older patients with a high white cell count are more likely to have severe gallbladder complications. In these patients, earlier surgical intervention should be considered if the sonographic findings support the diagnosis of AAC.

INTRODUCTION

Acute acalculous cholecystitis (AAC) is rare, occurring in only 5 % to 10 % of patients with acute cholecystitis[1]. It is more likely to be found in patients with recent severe trauma, critical illness, cardiovascular surgery[2,3] or severe burns. AAC has also been found in association with total parenteral nutrition[4], mechanical ventilation, and the use of narcotic analgesics. Major cardiovascular disorders, complicated diabetes mellitus, autoimmune disease[5-8], and AIDS[9] have all been recognized as possible inciting factors for AAC.

AAC is a surgical emergency. Without immediate treatment, there may be rapid progression to perforation or gangrenous cholecystitis, with a mortality as high as 65 %[10]. With early diagnosis and intervention, the mortality drops to 7 %[11]. Therefore, it is important to understand the clinical variables that may assist in making an early diagnosis of this condition. The aim of the present retrospective study was to assess what clinical information might accurately predict AAC.

MATERIALS AND METHODS

We retrospectively reviewed the charts of patients in a medical center from January1997 to December 2002 and found 1395 cases of acute cholecystitis. Gallstones were present in 1234 cases. We excluded patients with carcinoma of the gallbladder, pancreas, or biliary tract, common bile duct stones, intrahepatic stones, and patients who recovered without surgery, leaving 52 cases of AAC confirmed surgically or histologically. We divided the patients into two groups based on the presence (group A) or absence (group B) of severe complications involving the gallbladder, defined as perforation, gangrene, or abscess. We recorded the following data: age, sex, white blood cell count, AST, total bilirubin, alkaline phosphatase, sonographic findings, bacteriology, and mortality. The sonographic findings were scored, with 1 point each given for gallbladder distention, wall thickness greater than 3.5 mm, and sludge.

Student's *t*-test was used to analyze differences in means between the two groups. Sonographic scores for the severity of gallbladder condition were analyzed using the χ^2 test. A P value <0.05 was considered significant.

RESULTS

The 52 cases of AAC in our study accounted for 3.7 % of the totally 1 359 cases of acute cholecystitis seen during the study period. Males predominated, with 37 cases. The mean age of males was 56.5 years and of females, 60.5 years (Table 2). Most of our cases were diagnosed by ultrasonography (48 of 52) or computed tomography (17 of 52), with 13 patients having both examinations. Severe complications of the gallbladder were encountered in 27 (52 %) patients (group A). Six patients (12 %), all men, died, of whom 4 were in group A. The underlying conditions in these 4 patients were major surgery in 2, sepsis in 1, and bacteremia caused by *Salmonella gr. D* in 1. Of the 2 patients in group B who died, 1 had severe burns and 1 had *Aeromonas* bacteremia. The predisposing conditions for all

the patients are shown in Table 1.

There were no significant differences between the two groups in terms of liver biochemistry, length of hospital stay, or thickness of the gallbladder wall. The white blood cell count and age were significantly higher in group A ($P<0.05$, Table 2). In 10 patients in both groups, the percentage of band forms was over 10 %, including the 6 patients who died. Blood cultures were positive in 24 % and bile cultures in 66 % (Table 3). *E. coli.* and *Klebsiella pneumoniae* were the most frequently cultivated organisms in both blood and bile (Tables 4 and 5).

Most patients had a score of at least 2 points for sonographic findings. There was a tendency for group A to have higher scores, but the difference was not statistically significant (Table 6).

Table 1 Predisposing factors in patients with acute acalculous cholecystitis

Predisposing factor	Total (n)
Shock	7
Trauma	2
Burn	1
Major surgery	2
Bacteremia	11
DM	8
HTN	13
Heart disease[a]	14
CVA	3
TPN	1
Hyperlipidemia	5

a: Heart disease includes atrial fibrillation, congestive heart failure, hypertensive cardiovascular disease, hypertrophic cardiomyopathy and dilated cardiomyopathy.

Table 2 Demographic and clinical data in patients with acute acalculous cholecystitis with and without severe complications

	Group A n=27	Group B n=25	P
Gender			
Female	8	7	0.28
Male	19	18	0.71
Age (years)	60.88	54.12	0.04
Hospital stay (days)	19.74	18.84	0.42
WBC/mm^3	15 885.19	9 948.40	0.0005
AST (u/l)	138.04	141.87	0.48
Bilirubin (mg/dl)	2.46	2.37	0.46
Alkaline phosphatase (u/l)	106.19	130.59	0.07
Gallbladder wall (mm)	8.8	8.55	0.38

Table 3 Results of blood and bile culture for bacteria in patients with acute acalculous cholecystitis

Culture	Blood (n)	Bile (n)
No growth	34 (76%)	14 (34%)
Bacteria(+)	11 (24%)	27 (66%)

Table 4 Bacteria cultured from blood in patients with acute acalculous cholecystitis

	Group A (n)	Group B (n)	Total (n)
E.coli	3	3	6
Klebsiella pneumoniae	1	2	3
Aeromonas sp	0	1	1
Salmonella gr.D	1	0	1
G(+) Bacilli	1	0	1

Table 5 Bacteria cultured from bile in patients with acute acalculous cholecystitis

	Group A (n)	Group B (n)	Total (n)
E.coli	12	1	13
Klebsiella pneumoniae	6	1	7
Aeromonas	0	1	1
Salmonella gr.D	1	1	2
Enterobacter sp.	2	0	2
Pseudomonas sp.	1	1	2
Burkholderia cepacia	1	0	1
Candida albican	0	1	1
Citro. Freundii	1	0	1
Enterococcus	1	0	1
Providencia	0	1	1
Stophy. Coagulase (-)	1	0	1

Table 6 Sonographic findings recorded including gallbladder thickening, distention, and sludge

Sonographic finding	1 point	2 points	3 points	Total
Group A	4	11	9	24
Group B	9	11	4	24
Subtotal	13	22	13	48
$\chi^2=3.85$	$P>0.05$			

DISCUSSION

Most of our patients had multiple conditions that probably predisposed them to AAC (Table 1). Bile stasis, gallbladder ischemia, cystic duct obstruction, and systemic infection have been considered to be the most important factors in the pathogenesis of AAC[12].

The bacteria we cultured from blood and bile were similar to those reported by others. Gastrointestinal flora such as *E. coli* and *Klebsiella pneumoniae* were most commonly cultured, as was true in our series. However, uncommon microorganisms have also been isolated from the bile, including *Leptospira spp*[13,14], *Salmonella spp*[15], *Vibrio cholerae*[16], or *Listeria monocytogenes*. We had two patients with *Salmonella group D* infection, one of whom died of gangrene of the gallbladder with sepsis.

Rapid and accurate diagnosis is essential because ischemia may progress rapidly to gangrene and perforation. If an operation was performed within 48 hours from the onset of symptoms, severe complications would be reduced[17]. AAC should be considered in every patient who is critically ill or injured and who has clinical findings of sepsis with no obvious source. Fever, right upper quadrant pain, and leukocytosis are common manifestations but are very nonspecific. However, our study revealed that a high white blood cell count and older age were associated with a higher incidence of gallbladder gangrene and perforation. More aggressive management should be considered in these patients. Patients with greater than 10 % band neutrophils might have an especially poor outcome.

Abdominal ultrasonography is the primary diagnostic modality for AAC. The most significant ultrasonographic findings are thickening of the gallbladder wall of more than 3.5 mm, gallbladder distention, a positive sonographic Murphy's sign, pericholecystic fluid, and a sonolucent intraluminal layer[18,19]. We did not find the 3 sonographic findings we used were adequate to predict those patients likely to have severe gallbladder complications, although there was a trend toward higher scores in the group with complications. It may be that a study with a larger sample might find this to be a useful criterion.

In a discussion of diagnostic strategies for AAC, Kalliafas *et al* reported that morphine cholescintigraphy had the highest sensitivity (9 of 10, 90 %), followed by computed tomography (8 of 12, 67 %) and ultrasonography (2 of 7, 29 %). They reported a mortality of 41 % and a morbidity (that is, gangrene, perforation, or abscess) of 82 %[20]. However, in our series, the mortality was only 11.5 % and morbidity 52 %. Why are the results so different? We diagnosed most of our cases by ultrasonography (48 of 52) or computed tomography (17 of 52), only two patients had cholescintigraphy. Further studies are needed to elucidate the relationship between the diagnostic modality and prediction of the morbidity and mortality of AAC.

The mainstay of therapy for AAC is cholecystectomy, which was traditionally performed by open laparotomy[21]. Recently, laparoscopic cholecystectomy was performed in a small study with no complications from the procedure[22]. Cholecystostomy has be come a potentially lifesaving alternative in patients too weak to undergo general anesthesia[23]. Percutaneous cholecystostomy by computed tomography or echo guidance is gaining acceptance as an alternative to an open procedure[24]. In the future, laparoscopy for early diagnosis and treatment may be further developed as a useful method to decrease the mortality of AAC.

Finally, early diagnosis and early operation are the key to managing acute acalculous cholecystitis. Older patients with a high white cell count are more likely to have severe gallbladder complications. In these patients, earlier surgical intervention should be considered if the sonographic findings support the diagnosis of AAC.

REFERENCES

1   **Howard R**. Acute acalculous cholecystitis. *Am J Surg* 1981; **141**: 194-198

2   **Saito A**, Shirai Y, Ohzeki H, Hoyashi J, Eguchi S. Acute acalculous cholecystitis after cardiovascular surgery. *Surg Today* 1997; **27**: 907-909

3   **Hagino RT**, Valentine RJ, Clagett GP. Acalculous cholecystitis after aortic reconstruction. *J Am Coll Surg* 1997; **184**: 245-248

4   **Hatada T**, Kobayashi H, Tanigawa A, Fujiwara Y, Hanada Y, Yamamura T. Acute acalculous cholecystitis in a patient on total parenteral nutrition: case report and review of the Japanese literature. *Hepato-Gastroenterology* 1999; **46**: 2208-2211

5   **Kamimura T**, Mimori A, Takeda A, Masuyama J, Yoshio T, Okazaki H, Kano S, Minota S. Acute acalculous cholecystitis in systemic lupus erythematous: a case report and review of the literature. *Lupus* 1998; **7**: 361-363

6   **Date K**, Shirai Y, Hatakeyama K. Antiphospholipid antibody syndrome presenting as acute acalculous cholecystitis. *Am J Gastroenterol* 1997: **92**: 2127-2128

7   **Parangi S**, Oz MC, Blume RS, Bixon R, Laffey KJ, Perzin KH, Buda JA, Markowitz AM, Nowygrod R. Hepatobiliary complications of polyarteritis nodosa. *Arch Surg* 1991; **126**: 909-912

8   **Imai H**, Nakamoto Y, Nakajima Y, Miura AB. Allergic granulomatosis and angiitis (Churg-Strauss syndrome) presenting as acalculous cholecystitis. *J Rheumatol* 1990; **17**: 247-249

9   **Jannuzzi C**, Belghiti J, Erlinger S, Menu Y, Fekete F. Cholangitis associated with cholecystitis in patients with acquired immunodeficiency syndrome. *Arch Surg* 1990; **125**: 1211-1213

10 **Flancbaum L**, Choban PS. Use of morphine cholescintigraphy in the diagnosis of acute cholecystitis in critically ill patients. *Intensive Care Med* 1995; **21**: 120-124

11 **Adam A**, Roddie ME. Acute cholecystitis: radiological management. *Baillieres Clin Gastroenterol* 1991; **5**: 787-816

12 **Barie PS**, Fischer E. Acute acalculous cholecystitis. *J Am Coll Surg* 1995; **180**: 232-244

13 **Vilaichone RK**, Mahachai V, Wilde H. Acute acalculous cholecystitis in leptospirosis. *J Clin Gastroenterol* 1999; **29**: 282-283

14 **Baelen E**, Roustan J. Leptospirosis associated with acute acalculous cholecystitis, Surgical or medical treatment. *J Clin Gastroenterol* 1997; **25**: 704-706

15 **McCarron B**, Love WC. Acalculous nontyphoidal salmonellal cholecystitis requiring surgical intervention despite ciprofloxacin therapy: report of three cases. *Clin Infect Dis* 1997; **24**: 707-709

16 **West BC**, Silberman R, Otterson WN. Acalculous cholecystitis and septicemia caused by non-O1 Vibrio cholerae: first reported case and review of biliary infections with Vibrio cholerae. *Diagn Microbial Infect Dis* 1998; **30**: 187-191

17 **Hsu JC**, Yang TL, Wang TC. Acute acalculous cholecystitis. *Chin Med J* 1993; **51**: 266-2704

18 **Deitch EA**, Engel JM. Acute acalculous cholecystitis: ultrasonic diagnosis. *Am J Surg* 1981; **142**: 290-292

19 **Becker CD**, Burckhardt B, Terrier F. Ultrasound in postoperative acalculous cholecystitis. *Gastrointest Radiol* 1986; **11**: 47-50

20 **Kalliafas S**, Ziegler DW, Flancbaum L, Choban PS. Acute acalculous cholecystitis: incidence, risk factors, diagnosis, and outcome. *Am Surg* 1998; **64**: 471-475

21 **Glenn F**, Becker CG. Acute acalculous cholecystitis: an increasing entity. *Ann Surg* 1982; **195**: 131-136

22 **McClain T**, Gilmore BT, Peetz M. Laparoscopic cholecystectomy in the treatment of acalculous cholecystitis in patients after thermal injury. *J Burn Care Rehabil* 1997; **18**: 141-146

23 **Glenn F**. Cholecystostomy in the high-risk patient with bililary tract disease. *Ann Surg* 1977; **185**: 185-191

24 **Vauthey JN**, Lerut J, Martini M, Becker C, Gertsch P, Blumgart LH. Indications and limitations of percutaneous cholecystostomy for acute cholecystitis. *Surg Gynecol Obstet* 1993; **176**: 49-54