Perforation of the gallbladder: analysis of 19 cases

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Perforation of the gallbladder occurred in 19 (3.8%) of 496 patients with acute cholecystitis treated at one hospital in an 8-year period. The average age of the 19 patients was 69 years and the female:male ratio was 3:2. Most had a history suggestive of gallbladder disease and most had coexisting cardiac, pulmonary, renal, nutritional or metabolic disease. The duration of the present illness was short, perforation occurring within 72 hours of the onset of symptoms in half the patients; the diagnosis was not suspected preoperatively in any. In the elderly patient with acute cholecystitis who has a long history of gallbladder disease, cholecystectomy should be performed early, before gangrene and perforation of the gallbladder can occur.

Une perforation de la vésicule biliaire est survenue chez 19 (3.8%) sur 496 patients souffrant de cholécystite aiguë traités dans un hôpital au cours d'une période de 8 ans. La moyenne d'âge chez les 19 était de 69 ans et le rapport femme:homme était de 3:2. La plupart présentait une anamnèse compatible avec une affection de la vésicule biliaire et la plupart également souffrait aussi de maladies cardiaque, pulmonaire, rénale, nutritive ou métabolique. Les malaises entraînant l'hospitalisation ont été de courte durée, la perforation survenant dans les 72 heures qui ont suivi le début des symptômes chez la moitié des patients; dans aucun cas le diagnostic n'a été soupçonné avant l'opération. Chez les personnes âgées souffrant de cholécystite aiguë présentant une longue anamnèse d'affection de la vésicule biliaire, une cholécystectomie devrait être effectuée tôt, avant que la gangrène et qu'une perforation de la vésicule biliaire ne surviennent.

Perforation of the gallbladder is a not uncommon complication of acute calculous cholecystitis and constitutes a definite hazard in the management of this condition.

Acute cholecystitis usually develops when a stone blocks the cystic duct so that the gallbladder can no longer empty. Because its mucosa continues to function the gallbladder becomes distended with bile-stained mucus. When the intraluminal pressure of the gallbladder equals and then exceeds the blood pressure of the cystic vessels supplying its wall the gallbladder becomes first edematous, then ischemic and fully gangrenous; the fundus is usually affected first since it is the most distal portion of the gallbladder supplied by the cystic artery. The gangrene provokes local inflammation and the neighbouring organs become attached to the gallbladder by adhesions in an attempt to wall off the inflammatory process. If the obstruction in the cystic duct is not relieved the gangrene advances and weakens the gallbladder wall until the increased intraluminal pressure causes perforation.[1]

In 1934 Niemeier[2] classified perforation of the gallbladder into three types: type 1, acute free perforation (with generalized peritonitis); type 2, subacute perforation (with abscess formation); and type 3, chronic perforation (with fistula formation).

In this paper we report the results of an analysis of 19 cases of perforation of the gallbladder to emphasize that acute cholecystitis is a serious problem in the aged. The following brief case report illustrates the problem.

Case report

A 90-year-old man was admitted to hospital because of severe abdominal pain, vomiting, constipation and melena for 5 days. His general condition was extremely poor and conservative management was started. However, his condition worsened rapidly and he died within 24 hours of admission. Autopsy revealed choledocholithiasis with acute cholecystitis and rupture of the gallbladder, subphrenic abscess, and peritonitis. There were also multiple hemorrhagic gastric and duodenal ulcers.

Table I—Perforation of the gallbladder in acute cholecystitis

Year of report	Acute cholecystitis, no. of cases	Perforation of gallbladder, no. of cases (and incidence [%])
1941[3]	415	64 (15.4)
1942[4]	350	25 (7.1)
1954[5]	1480	90 (6.1)
1957[6]	542	25 (4.6)
1960[7]	1072	24 (2.2)
1966[1]	1529	51 (3.3)
1976 (present study)	496	19 (3.8)

Analysis of series

Incidence

A final diagnosis of perforation of the gallbladder was made in 19 patients at the Ottawa Civic Hospital from 1966 through 1973; the diagnosis was made at operation in 18 and at necropsy in 1. During this time 496 patients with acute cholecystitis and 4890 with chronic cholecystitis were seen. Thus the incidence of perforation of the gallbladder during acute cholecystitis was 3.8%, as compared with 2.2 to 15.4% in other series (Table I).

Sex and age of patients

The ratio of women to men in our series was 3:2. This is comparable with the ratio in other series[1,7] and probably reflects the higher incidence of cholecystitis in women.

All our patients were over the age of 40 years and 26% were over 80; one patient was 90 years old. The average age was 69, and 64% were between the ages of 60 and 79.

Clinical history and findings

Previous gallbladder disease: Although all the patients were admitted to hospital with acute cholecystitis 11 had a history suggestive of gallbladder disease and 3 had a previous diagnosis of chronic cholecystitis. This correlates well with the finding of Stone and Douglass[8] that most of their patients gave a history of pre-existing chronic cholecystitis.

Duration of present illness: In half of our patients perforation occurred within 72 hours of the onset of symptoms. However, nine others had waited more than 3 days after the onset of symptoms to come to hospital.

Symptoms: Nausea, usually with vomiting, and persistent pain in the right upper quadrant of the abdomen were the commonest symptoms. Pain radiating to the back occurred in 37% of patients. However, the presence of pain is of little aid in deciding whether perforation has occurred.

Signs: No definite pattern of signs could be found that would facilitate the diagnosis of impending perforation of the gallbladder. Elevations of pulse rate, temperature and respiratory rate were of some help but were not invariable signs. The leukocyte count in

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our series averaged between 17.0 and 21.0 x $10^9/l$. Right upper quadrant tenderness was present in 79% of patients, a right upper quadrant mass in 36%, generalized abdominal tenderness in 15%, distension in 21% and jaundice in only 10%.

Radiologic findings: Radiologic examination did not usually aid in diagnosis. The findings ranged from nonspecific ileus in 58% to gallstones in 21% of patients.

Preoperative diagnosis: Eliason and McLaughlin[9] stated that "a correct preoperative diagnosis of a perforated gallbladder is quite unusual". In our series the preoperative diagnosis was acute cholecystitis in 15 cases (80%) and empyema of the gallbladder, ruptured appendix, bleeding duodenal ulcer or gastritis in 1 case (5%) each. Cowley and Harkins[10] reported that in only 12% of their cases was the correct diagnosis of perforated gallbladder even considered in the written preoperative diagnosis.

Previous and associated diseases. Four patients had a history of myocardial infarction or congestive heart failure; one of these was currently having angina pectoris. Two patients had chronic obstructive lung disease and five patients were obese.

Management and findings

Surgical procedures: In 8 patients an operation was performed within 48 hours of admission, while in 10 patients the operation was delayed for 72 hours after admission because of their state of hydration at admission or because of associated diseases that required stabilization.

In most patients a cholecystectomy was performed with common duct exploration and insertion of a T-drain. One patient also had a duodenotomy and excision of an acute bleeding ulcer.

An operation was not performed in one patient, the subject of the case report.

Findings at operation: Most of our patients had type 2 perforation of the gallbladder (Table II), which agrees with most other reviews of the subject.[5-11] The low incidence of type 1 perforation in our series may be explained on the basis of Cave's[12] comment that "the majority of perforations of this viscus occur so gradually that protective adhesions between the gallbladder, omentum and colon are formed and usually result in a localized abscess". The only death in our series occurred in the subject of the case report, who had a type 1 perforation.

Stones were present in 16 patients and absent in 2. Stones were found not only in the gallbladder but also in the ducts and outside the gallbladder. All but 1 of Schaeffer's[11] 20 patients had gallstones. Cowley and Harkins[10] found stones in 23 of their 25 patients.

Acute and chronic cholecystitis were present in 17 instances and acute gangrenous cholecystitis was described in 1. The sites of perforation were the fundus in 53%, Hartmann's pouch in 21% and other sites in 26%.

Bacteriologic findings: Positive cultures of bile were reported in 10 cases, the organisms being *Escherichia coli* in 4, *Aerobacter aerogenes* in 4 and *Klebsiella pneumoniae* in 2. *E. coli* and *A. aerogenes* were also among the common organisms found in the studies of Cowley and colleagues.[1,10]

Postoperative complications: Subphrenic abscesses in two patients were incised and drained. Transurethral resection was performed in two other patients, on the 18th and 19th postoperative days, respectively.

Duration of hospitalization: Duration of hospitalization was usually between 10 and 20 days (Table III). In the series of 25 cases reported by Cowley and Harkins[10] in 1943 the average stay was between 14 and 30 days.

Discussion

In the aged population perforation of the gallbladder is a not uncommon complication of acute cholecystitis.[13] The early signs and symptoms of impending perforation in the elderly are obscure and thus increase the difficulty of early recognition.

The patient with acute cholecystitis has pain, tenderness and frequently a mass palpable in the right upper quadrant of the abdomen. In many instances gangrene and perforation cause the same signs and symptoms. Strohl and colleagues[14] pointed out that the most helpful factor in diagnosing gangrene and perforation is evidence of progression of the disease, as manifested by an increase in pulse rate, enlargement of the mass in the right upper quadrant and pronounced increase in tenderness. When bile peritonitis follows inflammation and perforation of the gallbladder the patient's condition worsens abruptly. Seven of our patients had a palpable abdominal mass and all had evidence of progression of the disease.

Cholecystography is of limited value is establishing the diagnosis of acute cholecystitis because an acutely inflamed gallbladder cannot concentrate the dye; because the cystic duct or ampulla is obstructed owing to edema and inflammation the dye is unable to enter the organ. A plain radiograph of the abdomen should be made because it may reveal a radiopaque stone or gas in the gallbladder or biliary tree.

The aged patient with acute cholecystitis should be treated aggressively to prevent perforation.[15] When the status of previous and associated diseases is stabilized and the best possible physical condition has been attained, there should be no delay in operating. Signs of generalized peritonitis call for surgical intervention as soon as the patient's condition permits. Special attention should be focused on rehydration and correction of deficiencies in protein, carbohydrate or oxygen-carrying erythrocytes. The condition of elderly patients with compromised cardiac and pulmonary reserves should be evaluated carefully to prevent overloading with water and electrolytes.

Whether operation should be early or delayed in acute cholecystitis continues to be debated. However, MacDonald[16] and Vallefo and Dickie[15] stated from experience that performing the operation within 24 to 48 hours of admission will result in considerable saving of time, pain and expense. The risk of early operation is not as great as that of acute perforation. Indeed, it has been shown in both clinical and experimental studies[10] that type 1 perforation of the gallbladder, though of relatively low incidence, is associated with a high mortality because it is rarely diagnosed preoperatively and it is frequently indistinguishable from nonperforated acute cholecystitis.

The operation of choice is cholecystectomy for acute cholecystitis and cholelithiasis. However, the very old debilitated patient with an acutely distended gallbladder may be more safely treated by cholecystostomy; then, after the infection has subsided, the patient is in better physical condition to have a cholecystectomy.

Table II—Grouping of cases according to Niemeier's classification[2]

Type of perforation	No. (and %) of cases
1. Acute free perforation with generalized peritonitis	3 (16)
2. Subacute perforation with abscess formation	13 (68)
3. Chronic perforation with fistula	3 (16)

Table III—Duration of hospitalization

Duration (d)	No. (and %) of cases
< 10	1 (5)
10-20	14 (74)
20-30	3 (16)
> 30	1 (5)

The most important lesson to be learned from this and other studies is not the management of these patients, because this has to be tailored to the needs of the individual, but that cholecystectomy should be done more frequently in cases of recurrent chronic cholecystitis.

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Clindamycin plus gentamicin as expectant therapy for presumed mixed infections

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The prevalence of obligate anaerobes was studied prospectively in 60 patients with severe sepsis of intra-abdominal, soft tissue, female genital or oropulmonary origin. In addition, the efficacy of clindamycin (for anaerobes) plus gentamicin (for aerobic bacteria, especially coliforms) as initial empiric therapy in these patients was evaluated. Among 54 patients with cultural proof of infection, anaerobic pathogens were recovered from 52%. Nineteen patients had bacteremia; *Bacteroides fragilis* and *Klebsiella pneumoniae* were the most prevalent pathogens, being isolated in five patients each. Infection was eradicated in 56 of the 60 patients (93%). Mortality related to sepsis was 7% in the entire group, 16% in patients with bacteremia and 2% in patients without bacteremia. Eighty-five percent of aerobic isolates tested were susceptible in vitro to either gentamicin or clindamycin; 97% of anaerobic isolates were inhibited by 5 μg/ml of clindamycin.

Une étude prospective de la prévalence des bactéries anaérobies obligatoires a été faite chez 60 patients atteints d'infections graves ayant pour origine l'abdomen, les tissus mous, les organes génitaux féminins ou les tissus oropulmonaires. De plus, on a évalué l'efficacité de la clindamycine (pour les anaérobies) et de la gentamicine (pour les bactéries aérobies et spécialement les coliformes) utilisées empiriquement comme traitement d'attaque. Parmi 54 patients dont l'infection a été démontrée par culture on a retrouvé des bactéries anaérobies pathogènes chez 52%. Dix-neuf patients souffraient de bactérémie; *Bacteroides fragilis* et *Klebsiella pneumoniae* ont été les bactéries les plus fréquemment retrouvées alors qu'elles ont été isolées chez cinq patients chacune. L'infection a été enrayée chez 56 des 60 patients (93%). La mortalité due à l'infection a été de 7% pour le groupe complet, de 16% chez les patients souffrant de bactérémie et de 2% chez les sujets ne présentant pas de bactérémie. Quatre-vingt-cinq pourcent des souches aérobies testées étaient sensibles in vitro, soit à la gentamicine, soit à la clindamycine, alors que 97% des anaérobies étaient inhibées par 5 μg/ml de clindamycine.

Recent technologic advances have greatly facilitated the isolation and identification of obligate anaerobes from clinical material.[1] However, with few exceptions,[2-4] the prevalence of anaerobic bacteria in specific infections has not been adequately investigated by prospective study. For this reason, although antibiotics efficacious against anaerobic bacteria (such as clindamycin and chloramphenicol) are readily available, the necessity to include these agents in the initial empiric treatment of suspected or presumed sepsis remains controversial.[5]

We report the results of a prospective evaluation of the prevalence of obligate anaerobes in presumed sepsis of intra-abdominal, soft tissue, female genital or oropulmonary origin. Fastidious techniques were used to isolate both aerobic and anaerobic microorganisms, and special precautions were taken to avoid contamination of specimens by normal flora. In addition, the efficacy of clindamycin plus gentamicin as initial empiric therapy in these infections was examined prospectively. Clindamycin was chosen because of its demonstrated efficacy, both in vitro and in vivo, against anaerobic pathogens[6-10] and the lack of antagonism, at least in vitro, between clindamycin and gentamicin against both aerobic and anaerobic bacteria.[11,12]

Patients and methods

Patient population

Sixty patients admitted consecutively to hospital in 1973 with presumed sepsis of intra-abdominal, soft tissue, female genital or oropulmonary origin were studied. The mean age was 41 years for the entire group, 35 years for the 19 females and 43 years for the 41 males. Informed consent was obtained from all patients. All were seriously ill, requiring immediate institution of empiric antibiotic therapy prior to availability of cultural data. Ten patients had received prior antibiotic therapy (three, penicillin; four, ampicillin; and three, cephalothin) within 10 days of combination therapy but were included in the study because of continued clinical deterioration or relapse despite use of these antibiotics. Patients who had received prior therapy with chloramphenicol, tetracycline, lincomycin or other antibiotics were excluded from the study. Pregnant women, infants and patients with known toxic or

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