Acalculous cholecystitis - a review

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Abstract

Acute acalculous cholecystitis (AAC) may develop in critically ill or injured patients including children. This condition, which is basically acute cholecystitis without gallstones as an aetiological factor, is an uncommon but serious illness and appears to be increasing in incidence. Chronic acalculous cholecystitis (CAC) is a clinical entity characterized by recurrent postprandial biliary colic in patients with sonographically normal gallbladders and low ejection fraction by quantitative radionuclide scanning of the biliary tree following cholecystokinin administration. The development of AAC is not limited to surgical or injured patients, or even to the intensive care unit. Other aetiological factors include diabetes mellitus, malignant tumours of several types, abdominal vasculitis, congestive heart failure, cholesterol embolization, and shock. The pathogenesis of AAC is a paradigm of complexity. Though bile stasis, opioid therapy, positive-pressure ventilation, and total parenteral nutrition have all been implicated, ischaemia-reperfusion injury, or the effects of eicosanoid proinflammatory mediators appear to be the central triggering mechanisms. Ultrasound of the gallbladder is the most accurate diagnostic modality in the critically ill patient, with gallbladder wall thickness of 3.5 mm or greater and pericholecystic fluid being the two most reliable criteria. The mainstay of therapy for AAC has been cholecystectomy, but percutaneous cholecystostomy is gaining acceptance as an alternative to open procedures. Chronic acalculous cholecystitis is a diagnosis of exclusion and usually managed by laparoscopic cholecsystectomy with overall results being similar to those operated upon for calculous disease. The current review encompasses both acute and chronic clinical entities with an emphasis on their pathogenesis and current management concepts.

Key words: acalculous, cholecystitis, gallbladder, acute, chronic

Introduction

Acute cholecystitis may develop at any time in a patient harbouring gallstones. Not surprisingly, complications of this condition are commoner and more serious during a critical illness or following major surgery. Acute cholecystitis may also develop in the absence of gallstones in a condition known as acute acalculous cholecystitis (AAC).

Acute acalculous cholecystitis is an infrequent condition with a guarded prognosis. Its successful management depends upon sound surgical judgment and expertise (Glenn, 1979). Although reports of such cases were rare before 1950, AAC is now recognized to complicate serious medical and surgical illness. The incidence of AAC appears to be increasing (Glenn & Becker, 1982) but the reasons for this are unclear. It is likely that increased awareness and improved imaging modalities are identifying more cases (Kalliafas *et al.*, 1998). It is also possible that, as increasingly ill patients are admitted to intensive care units, the association between AAC and serious illness lead to an increased detection and hence, incidence. The mortality rate remains in the range of 6.9 to 50 percent because the diagnosis remains challenging, the affected patients are critically ill, and the disease itself can progress rapidly due to a high incidence of gangrene (>50%) and perforation (>10%), reflecting the gallbladder ischaemia that is central to the pathogenesis of AAC (Barie & Fischer, 1995).

Patients with chronic acalculous cholecystitis (CAC) often have associated gastrointestinal symptoms of nausea, vomiting, fatty food intolerance and bowel irregularity. These patients have typical scintigraphic evidence of biliary dysfunction as determined by quantitative radionuclide scanning of the biliary tree following cholecystokinin administration (Siegel *et al.*, 2000). A low (< 35%) gallbladder ejection fraction often identifies patient with biliary dyskinesia (Jones *et al.*, 1996).

Spectrum of clinical illness

Acute acalculous cholecystitis accounts for approximately 5 to 10 percent of cases of acute cholecystitis. The condition is also known as necrotizing cholecystitis, signifying the serious clinical sequelae that may ensue following its onset. This terminology is however rarely employed nowadays with AAC being the preferred nomenclature.

AAC can be further classified as being primary or secondary. Primary AAC is associated with ischaemic atherosclerotic vascular diseases, salmonella infection, HIV and infectious colitis. Secondary AAC is more commonly seen in intensive care patients, and the predisposing conditions include recent major surgery or trauma, burns, sepsis, blood transfusions, prolonged hypotension, hyper-alimentation, mechanical ventilation, large doses of narcotics and antibiotics, the post-partum state and diabetes.

Reports of acute cholecystitis complicating surgery, multiple trauma, or burns are widespread. Acute acalculous cholecystitis also shows a striking predilection to occur after trauma (Fabian *et al.*, 1986) and burns (McDermott *et al.*, 1985). One report suggested that the incidence of AAC after acute spinal cord injury is approximately 4% (Romero-Ganuza *et al.*, 1997). AAC is responsible for approximately 90% of cholecystitis that is found in trauma patients. It develops primarily in men following trauma and severe burns, as well as after surgery. The higher incidence of AAC in young men amongst the trauma population is understandable considering that men are more likely to be involved in serious trauma requiring hospital admission. Meanwhile, the incidence of acute calculi related cholecystitis is higher in women as cholelithiasis is commoner in females.

Postoperative cholecystitis, regardless of the antecedent surgical procedure, appears equally likely to develop in the presence or absence of gallstones (Gately & Thomas, 1983). In patients with gallstones, the incidence of postoperative cholecystitis is similar for men and women. However, nearly 83% of patients who develop AAC after other non-trauma-related surgical procedures are men (Babb, 1992). In two series, the incidence of AAC after abdominal aortic reconstruction was, 0.7% and 0.9%, respectively (Ouriel *et al.*, 1984; Hagino *et al.*, 1997). These reports are also similar in that there is a striking predilection for the development of AAC in male patients, especially after an emergency operation or an elective operation complicated by hypotension and increased blood loss. AAC after cardiac surgery, including transplantation, have also been reported. Barie (1993) found the incidence of acute cholecystitis to be 0.12% (42% AAC) in his large series of patients, with an overall mortality rate of 45%. Although cholecystitis is rare after cardiac surgery, certain subgroups of patients may be at particular risk, especially those patients undergoing cardiac valve replacement with or without bypass grafting (Leitman *et al.*, 1987).

Diabetes, congestive heart failure, cholesterol embolization in severe atherosclerosis (Moolenaar & Lamers, 1996), resuscitation from hemorrhagic shock or cardiac arrest (Smith & Bodai, 1982) and percutaneous transhepatic catheter decompression of extrahepatic biliary obstruction (Lillemoe *et al.*, 1989) have all been associated with AAC. Other clinical conditions that have been implicated include abdominal vasculitis such as lupus erythematosus or polyarteritis nodosa (Papaioannou *et al.*, 1979; Dessailloud *et al.*, 1998) and acute myelogenous leukaemia (Topeli *et al.*, 1996). Patients with cancer are at risk for several possible reasons, including metastasis to the porta hepatis. Therapy with interleukin-2 and lymphokine-activated killer cells for metastatic disease has also been implicated as a causative factor (Chung-Park *et al.*, 1990). In bone marrow transplant recipients, the incidence of AAC is as high as 4%, and appears to be associated with concomitant veno-occlusive disease (Wiboltt & Jeffrey, 1997).

Acalculous cholecystitis has been reported in disseminated fungal infections caused by several *Candida* species (Hiatt *et al.*, 1991), in systemic leptospirosis (Baelen & Roustan, 1997), in chronic biliary tract carriers of typhoidal (Yulevich *et al.*, 1992) and non-typhoidal *Salmonella* (McCarron & Love, 1997), during active cholera infection (West *et al.*, 1998), and in tuberculosis (Vallejo, 1950). Extrahepatic biliary obstruction caused by haemophilia (Nursal *et al.*, 2002), ascariasis and echinococcal cysts have also been reported as causes of AAC (Kuzu *et al.*, 1996).

Two forms of acalculous biliary disease occur in patients with acquired immune deficiency syndrome (AIDS). One form is cholestasis similar to sclerosing cholangitis (Cello, 1989), which can be impossible to distinguish from bacterial cholangitis in an acutely jaundiced patient. Alternatively, patients

with AIDS may present with AAC (Kavin *et al.*, 1986). Both of these clinical entities have been associated with cytomegalovirus (Keshavjee *et al.*, 1993), *Cryptosporidium* sp. or microsporidial (Soave, 1988) infections. These opportunistic infections account for the majority of cases of AAC in cases associated with AIDS. Acute cholecystitis is now the most common indication for laparotomy in patients with AIDS (Lowy & Barie, 1994).

The increased incidence of AAC occurring de novo has been recognized only recently (Parithivel *et al.*, 1999). One study has found that 77% of patients with AAC developed the disease without evidence of preceding acute illness and trauma (Savoca *et al.*, 1990).

Acute acalculous cholecystitis affects the paediatric age group as well, representing 50% to 70% of all cases of acute cholecystitis in children (Tsakayannis *et al.*, 1996). Acalculous cholecystitis was traditionally considered a disease of older children (Trayneys & Hrabovsky, 1985), but is now increasingly recognised in young children and neonates (Strauss, 1969). Dehydration and infective conditions predisposing to the development of AAC include acute bacterial infections such as otitis or scarlet fever, brucellosis (Ashley *et al.*, 2000), upper respiratory tract infections and viral illnesses such as hepatitis (Ciftci *et al.*, 2001). Cystic duct obstruction secondary to portal lymphadenitis, metabolic abnormalities, neoplasms and trauma are other factors implicated in the development of acute acalculous cholecystitis. Among the other predisposing factors, congenital anomalies such as congenital diaphragm of the gallbladder (Soares *et al.*, 2000) and choledochal cyst (Lin *et al.*, 2000) have also been uncommonly reported. Recent reports of several cases in the immediate postoperative period suggest that the pathogenesis may be similar to that in adults.

Pathogenesis

The pathophysiology of AAC is a paradigm of complex interrelationships as the clinical complexity of the critically ill patient makes it difficult to define a single aetiology in relation to its pathogenesis (Table 1). Only approximately one-half of cases of postoperative cholecystitis develop in patients with gallstones. It is possible that the pathogenesis of acute cholecystitis is identical in such patients, and that the presence of gallstones is irrelevant.

Bile stasis

Bile stasis has been implicated in the pathogenesis of acalculous cholecystitis in experimental and clinical studies (Wagner *et al.*, 1962). Volume depletion may lead to concentration of bile, which can inspissate in the absence of gallbladder emptying. Opioid analgesics, which are frequently employed in critically ill and postoperative patients, can induce increased biliary pressure caused by spasm of the sphincter of Oddi. Bile stasis may be induced by positive-pressure mechanical ventilation with positive end-expiratory pressure (PEEP) (Johnson & Hedley-White, 1975). Ventilation with 7 to 10 cm H_2O of PEEP decreases portal perfusion by increasing hepatic venous pressure (Johnson & Hedley-White, 1972). In euvolaemic subjects treated in this manner, mean common bile duct pressure increased by about 3 cm H_2O, and choledochal flow resistance at the ampulla of Vater increased by about 30% (Johnson & Hedley-White, 1975), perhaps confirming the role of mechanical ventilation in the pathogenesis of AAC.

Alteration in Bile Composition

Bile stasis may alter the chemical composition of bile, which may promote local injury of the gallbladder mucosa. Lysophosphatidyl choline is present in bile of patients with AAC, and has potent effects on gallbladder structure and function (Niderheiser, 1986), disrupting normal water transport across gallbladder mucosa resulting in oedema of the gallbladder wall, mucosal necrosis, and an acute inflammatory infiltrate. Beta-glucuronidase has been implicated in the pathogenesis of AAC. This acid hydrolase, located in the apices of the epithelial cells of the gallbladder wall, causes increased lysosomal activity with epithelial disruption. This alters the chemical composition of bile, further enhancing a vicious cycle of stasis, oedema, inflammation and necrosis of the gall bladder wall (Kouromalis *et al.*, 1983).

Total Parenteral Nutrition

Surgical nutrition or total parenteral nutrition (TPN) is associated with the development of acute cholecystitis in both adults and children (Long *et al.*, 1978). Non-critically ill patients receiving long-term TPN is associated with a 30% incidence of cholecystitis, often in the form of AAC (Roslyn *et al.*, 1983). Messing *et al*, (1983) reinforced this hypothesis by performing serial gallbladder ultrasound studies in patients

on long-term TPN. The incidence of gallbladder "sludge," only 6% during the first week of TPN therapy, increased to 50% at 4 weeks and 100% at 6 weeks. More than 40% of patients developed gallstones (Doty *et al.*, 1984). Moreover, enteral hyperalimentation of critically ill patients, which preserves gallbladder motility, does not prevent AAC (Merrill *et al.*, 1989).

Systemic infection and mediators

Although bacterial infection is a secondary phenomenon, the humoral response to gram-negative bacteraemia or splanchnic ischaemia and vasoactive mediator release may play a role in the pathogenesis of AAC. Lipopolysaccharide induces a marked host response, including the activation of the coagulation cascade producing AAC (Becker *et al.*, 1980) in animals and *in vitro* stimulated secretion of both eicosanoids and platelet-activating factor (Kaminski *et al.*, 1994). Ellagic acid or rutin, plant polyphenols that directly activate Factor XII can produce immediate spasm of the cystic artery (Ratnoff & Crum, 1964) causing cholecystitis. Acute acalculous cholecystitis has also been produced in cats by infusion of platelet-activating factor into the cystic artery (Kaminski *et al.*, 1990). This has an implication in humans as platelet-activating factor has been incriminated in the pathogenesis of splanchnic hypoperfusion in sepsis and other low-flow states. The inflammation appears to be mediated by proinflammatory eicosanoids, as non-specific cyclooxygenase inhibitors inhibit it.

Gallbladder Ischaemia

Gallbladder ischaemia is a critical factor in the pathogenesis of AAC. Orlando *et al.* (1983) suggested an interrelationship between ischaemia and stasis as expressed by low gallbladder perfusion pressure (mean cystic artery pressure minus gallbladder intraluminal pressure), leading to hypoperfusion. The causes of hypoperfusion include hypotension, dehydration, or the administration of vasoactive drugs, whereas intraluminal pressure is increased by bile stasis. Alternatively, reperfusion injury may be the critical issue. Taoka (1991) noted that 45 minutes of ischaemia followed by 90 minutes of reperfusion reproducibly produced AAC, whereas ischaemia alone did not.

Clinical low-flow states support the hypothesis of gallbladder ischaemia (Leitman *et al.*, 1987; Dessailloud *et al.*, 1998) as a critical factor in the pathogenesis of gallbladder necrosis and perforation. There is diffuse infiltration of vascular structures and the gallbladder wall by neutrophils. Focal necrosis of the gallbladder walls due to arterial obstruction and venous congestion can ensue with associated focal necrosis of gallbladder mucosa or even transmural gangrene with perforation of the gallbladder. Gallbladder specimen arteriography reveals marked differences between acute calculous cholecystitis and AAC in humans (Hakala *et al.*, 1997). AAC is associated with multiple arterial occlusions and minimal-to-absent venous filling, suggesting that vascular occlusion and disruption of the microcirculation is central to the pathogenesis of AAC (Warren, 1992; Hakala *et al.*, 1997).

Diagnosis

Acute acalculous cholecystitis poses enormous diagnostic difficulties. The majority of these patients are critically ill and unable to communicate their symptoms. Cholecystitis is but one of many potential causes of systemic inflammatory response syndrome or sepsis that may develop in such patients. Moreover, the differential diagnosis of jaundice in the critically ill patient is complex, and includes intrahepatic cholestasis from sepsis or drug toxicity and "fatty liver" induced by TPN, in addition to AAC. Rapid and accurate diagnosis is essential, as ischaemia can progress rapidly to gangrene and perforation. Acalculous cholecystitis is sufficiently common that the diagnosis should be considered in every critically ill or injured patient with a clinical picture of sepsis and no other obvious source. Physical examination and laboratory evaluation are unreliable (Long *et al.*, 1978). Fever, leukocytosis and hyperbilirubinemia are commonplace, but non-specific in the setting of critical illness. Other biochemical assays of hepatic enzymes are of little help. The diagnosis of AAC thus often rests on radiologic studies such as ultrasound, radionuclide studies and computed tomography apart from surgical intervention that could involve laparoscopy.

CAC is a diagnosis by exclusion. Histopathological examination of cases secondary to CAC, apart from demonstrating abnormalities associated with chronic inflammation, may also reveal cholesterol crystals, small gallstones, cholesteorosis or polyps (Jones *et al.*, 1996).

Ultrasound

Ultrasound of the gallbladder is the most accurate modality to diagnose AAC in the critically ill patient and its sensitivity varies from 25 to100 percent. Thickening of the gallbladder wall is a more reliable criterion in serial ultrasonographic studies. Deitch and Engel (1981) reported specificity of 90% using 3.0 mm wall thickness and 98.5% at a 3.5 mm wall thickness, whereas sensitivity was 100% at 3.0 mm but only 80% at 3.5 mm. Based on the above findings, the authors recommended utilising a gallbladder wall thickness of 3.5 mm or greater as definitive evidence of acute cholecystitis, whereas 3.0 mm could be considered as suggestive but not conclusive evidence. Distension of the gallbladder of more than 5 cm in transverse diameter has also been reported (Deitch & Engel, 1981) to be associated with AAC. False-positives may occur when conditions including sludge (Fiske *et al.*, 1980), nonshadowing stones, cholesterolosis, hypoalbuminemia, or ascites mimic a thickened wall (Deitch & Engel, 1980). Other helpful ultrasonographic findings for AAC include pericholecystic fluid, the presence of intramural gas or a sonolucent intramural layer or "halo" that represents intramural oedema (Deitch & Engel, 1981).

Gallbladder imaging studies

Hepatobiliary imaging has limited value in critically ill or injured patients (Ohrt *et al.*, 1983; Shuman *et al.*, 1984) because of a high incidence of false-positive scans, which may be caused by fasting, alcoholism, other forms of liver disease, or parenteral feeding. A sensitivity rate as low as 68% has been reported in studies of hepatobiliary imaging for AAC (Shuman *et al.*, 1984), even though Swanye's (1986) review of seven small series suggested a 90% sensitivity rate. Intravenous morphine may increase the accuracy of cholescintigraphy in critically ill patients by enhanced gallbladder filling caused by increased biliary secretory pressure (Flancbaum *et al.*, 1994; Krishnamurthy & Krishnamurthy, 1996). The technique is however not practiced widely (Fig *et al.*, 1990). Hepatobiliary imaging for CAC is useful as it has typical scintigraphic evidence of biliary dysfunction. Gallium or indium-111 leukocyte scan may also be potentially helpful in the diagnosis of AAC (Babb, 1992).

Computed tomography

Computed tomography (CT) is as accurate as ultrasound in the diagnosis of AAC (Mirvis *et al.*, 1987). Only a single retrospective study has compared all three modalities (ultrasonography, hepatobiliary scanning, and CT) (Mirvis *et al.*, 1986). Ultrasonography and CT have been consistently found to be comparably accurate and superior to hepatobiliary imaging. Due to its sensitivity, low cost and the ability to perform the investigation rapidly and accurately at the bedside, ultrasonography is considered as the diagnostic modality of choice in confirming or refuting a diagnosis of possible AAC. Preference may be given to CT if other diagnoses of thoracic or abdominal pathology are considered likely or to be concurrently present.

Laparoscopy

Laparoscopy is possible in critically ill patients and has been used with success for both the diagnosis and therapy of AAC (Brandt *et al.*, 1994; McClain *et al.*, 1997). It can even be performed under local anaesthesia and intravenous sedation at the bedside. This is a modality that should be seriously considered when adequate facilities and expertise are available. It is advisable to attempt laparoscopy if open surgical drainage is otherwise contemplated in a seriously ill patient. "Gasless" laparoscopy may even be performed in patients who have undergone recent abdominal surgery with a reportedly high diagnostic accuracy (Almeida *et al.*, 1995; Brandt *et al.*, 1994). Apart from this, laparoscopic cholecystostomy (Yang & Hodgson, 1996) and cholecystectomy can be performed, but it is more invasive than the percutaneous drainage procedure that is being increasingly employed by interventional radiologists. When contemplating surgical extirpation of the gallbladder, laparoscopic cholecystectomy should only be performed after the patient has been transferred to the operating room where adequate facilities are available to ensure prompt and effective outcome (Almeida *et al.*, 1995). The procedure is also effective in alleviating pain in cases of CAC with minimal associated morbidity (Frassineli *et al.*, 1998).

Differential Diagnosis

Conditions such as pancreatitis, hepatitis or hypoalbuminaemia, congestive heart failure causing diffuse thickening of gallbladder, cholangitis and perforated ulcer can mimic AAC (Kalliafas *et al.*, 1998).

Conversely, the diagnosis of CAC should not be arbitrarily dismissed in the presence of concomitant diseases that cause recurrent gastrointestinal symptoms. CAC should be differentiated from spastic colon and chronic irritable bowel syndrome (Jones *et al.*, 1996).

Treatment

The mainstay of therapy for AAC has been cholecystectomy (Glenn & Becker, 1982). Cholecystostomy can be a lifesaving alternative in the patient considered too unstable to undergo general anaesthesia (Glenn, 1977). Cholecystostomy can be accomplished under local anaesthesia through a short right subcostal incision, but visibility and the ability to explore the remainder of the right upper quadrant are limited. Cholecystostomy also provides inadequate drainage of the common bile duct for concomitant cholangitis. Successful cholecystostomy is usually followed by tube cholangiography after the patient has recovered. If gallstones are present, an elective cholecystectomy should be performed, with the drainage tube remaining in place during the interprocedure interval. Interval cholecystectomy is usually not indicated after AAC (Pearse *et al.*, 1984).

Percutaneous cholecystostomy is gaining acceptance as an alternative to open procedures (Pearse *et al.*, 1984; Vauthey *et al.*, 1993). The advantages of percutaneous cholecystostomy are bedside applicability, local anaesthesia, and avoidance of an open procedure. The technique controls the acute syndrome in about 85% of patients. The gallbladder is punctured under sonographic (occasionally laparoscopic) control via an anterior or anterolateral transhepatic approach through the bed of the gallbladder in order to minimize the leakage of bile. Though the transperitoneal puncture can also be employed, this is generally not recommended, as bile leakage and sepsis are complications that can occur, leading to an unnecessary increase in the morbidity of an already seriously ill patient. After the gallbladder is punctured, an 8-French pigtail catheter is passed into the gallbladder over a guide wire, and its position is confirmed radiographically by instillation of water-soluble contrast, with placement related to gravity drainage. Rapid improvement should be expected when the procedure is performed properly. If percutaneous cholecystostomy does not result in improvement, an open procedure should be performed expediently.

Reported causes of failure include gangrenous cholecystitis (Lo *et al.*, 1995), catheter dislodgement, bile leakage causing peritonitis, and an erroneous diagnosis. Perforated ulcer, pancreatic abscess, pneumonia, and pericarditis have been discovered in the aftermath of percutaneous cholecystostomy when patients failed to improve (Werbel *et al.*, 1989). In the largest reported series, major complications were reported in 11 patients (8.7%), including dislodgment of the catheter, acute respiratory distress, bile peritonitis, haemorrhage, cardiac arrhythmia, and hypotension caused by procedure-related bacteraemia. Minor complications occurred in an additional five patients (3.9%). Throughout the literature, the 30-day mortality of percutaneous and open cholecystostomy appears to be similar.

Antibiotic therapy does not substitute for removal or drainage of AAC, but remains an important adjunct. The most common bacteria isolated from bile in acute cholecystitis are *E. coli*, *Klebsiella*, and *Enterococcus faecalis*, thus antibiotic therapy should be directed against these organisms. However, critical illness and prior antibiotic therapy alter host flora, and resistant or opportunistic pathogens may be encountered. *Pseudomonas*, staphylococci (including methicillin-resistant strains), *Enterobacter* and related species, anaerobic organisms (*Clostridium*, *Bacteroides*), and fungi may be recovered. Anaerobes are particularly likely to be isolated from bile in diabetics, in patients older than 70 years, and from patients whose biliary tracts have been instrumented previously.

Complications

The incidence of gallbladder gangrene in AAC exceeds 50%, and leads to additional morbidity including perforation of the gallbladder. One variant, emphysematous cholecystitis, is particularly associated with gangrene and perforation. Though rare, emphysematous cholecystitis shares many traits with AAC with reportedly 28% of patients demonstrating acalculous disease (Barie & Fischer, 1995). More than 70% of cases of emphysematous cholecystitis occur in men, and 20% of patients have diabetes. *Clostridium* species, rather than aerobic gram-negative bacilli, are most commonly isolated in emphysematous cholecystitis (45% of cases, with *Clostridium welchii* predominating). *Escherichia coli* was recovered from approximately one-third of

affected patients. The hallmarks of therapy in emphysematous cholecystitis are early surgery and antimicrobial therapy specific for *Clostridium* (such as penicillin) in addition to agents directed against the typical bacteria flora in acute cholecystitis. Radiographic identification of gas in patients with acute cholecystitis mandates immediate exploration in view of the high incidence and rapid development of gangrene and perforation. Cholecystectomy is advisable because of extensive tissue necrosis.

Perforation of the gallbladder occurred in 20% of cases of AAC (Hagino *et al.*, 1997). The perforation was either localized into the subhepatic space or occurred freely with generalised peritonitis. Perforation into the biliary tract is extremely rare in AAC. Unusual causes of death from gallbladder perforation in AAC include haemorrhage from the liver (Elde *et al.*, 1975), and pulmonary bile embolism (Proia *et al.*, 1986). Serious complications of gallbladder gangrene without perforation include acute pancreatitis (Wagner & Flynn, 1985), colonic perforation (Brady & Welch, 1985), and obstruction of the common hepatic duct (Ippolito, 1993). Empyema of the gallbladder may also complicate AAC (Fry *et al.*, 1981).

Conclusions

Acalculous cholecystitis, especially of the acute type remains a serious condition with a high associated morbidity. With an improvement in overall patient care and a greater increase in the survival of seriously ill patients, an increasing incidence of AAC is being encountered. Medical and surgical conditions can both lead to the development of AAC and a high index of suspicion is required to establish the diagnosis and institute effective therapy. The pathogenesis of AAC, due to a multitude of complex interacting factors, remains to be elucidated to allow for preventive measures to be recommended at this stage. Percutaneous radiological decompression with the aid of ultrasonography is safe and remains as the gold standard in the diagnosis and management of AAC in seriously ill patients requiring intensive care support. Laparoscopic cholecystostomy and cholecystectomy is increasingly being employed successfully in both AAC and CAC when non-surgical modalities fail in effective patient management. It is of utmost importance that either form of intervention is performed expediently to procure an effective outcome leading to a higher rate of patient survival.

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