

RAPID COMMUNICATION

## Diagnosis and treatment of gallbladder perforation

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### Abstract

**AIM:** To present our clinical experience with gallbladder perforation cases.

**METHODS:** Records of 332 patients who received medical and/or surgical treatment with the diagnosis of acute cholecystitis in our clinic between 1997 and 2006 were reviewed retrospectively. Sixteen (4.8%) of those patients had gallbladder perforation. The parameters including age, gender, time from the onset of symptoms to the time of surgery, diagnostic procedures, surgical treatment, morbidity, and mortality were evaluated.

**RESULTS:** Seven patients had type I gallbladder perforation, 7 type II gallbladder perforation, and 2 type III gallbladder perforation according to Niemeier's classification. The patients underwent surgery after administration of intravenous electrolyte solutions, and were treated with analgesics and antibiotics within the first 36 h (mean 9 h) after admission. Two patients died of sepsis and multiple organ failure in the early postoperative period. Subhepatic abscess, pelvic abscess, pneumonia, pancreatitis, and acute renal failure were found in 6 patients.

**CONCLUSION:** Early diagnosis and emergency surgical treatment of gallbladder perforation are of crucial importance. Upper abdominal computerized tomography for acute cholecystitis patients may contribute to the preoperative diagnosis of gallbladder perforation.

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**Key words:** Acute cholecystitis; Gallbladder perforation; Early diagnosis; Computed tomography; Emergency surgery

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### INTRODUCTION

Gallbladder perforation (GBP) is a rare but life threatening complication of acute cholecystitis. Sometimes GBP may not be different from uncomplicated acute cholecystitis with high morbidity and mortality rates because of delay in diagnosis<sup>[1-3]</sup>. Thus GBP still continues to be an important problem for the surgeons. Most cases can only be diagnosed during surgery<sup>[1,4]</sup>. Male acute cholecystitis cases with high fever, high white blood cell (WBC) count, and associated systemic diseases should be meticulously investigated<sup>[1,5,6]</sup>.

Niemeier<sup>[7]</sup> in 1934, classified free gallbladder perforation and generalized biliary peritonitis as acute or type I GBP, pericholecystic abscess and localized peritonitis as subacute or type II GBP, and cholecystoenteric fistula as chronic or type III GBP. This classification is still in use. We aimed to present our clinical experience with GBP in this study.

### MATERIALS AND METHODS

#### Subjects

Records of 332 patients who received medical and/or surgical treatment with the diagnosis acute cholecystitis in our clinic between January 1997 and February 2006 were reviewed retrospectively. Sixteen (4.8%) of those patients were found to have gallbladder perforation. Perforations due to trauma, iatrogenic causes, and gallbladder (GB) carcinoma were excluded.

#### Methods

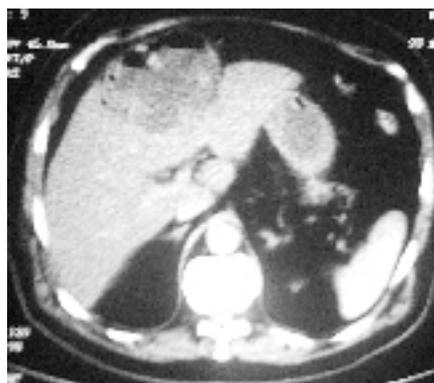
The original classification of Niemeier<sup>[7]</sup> was used to identify the patients. The parameters including age, gender, time from the onset of symptoms to the time of surgery, diagnostic procedures, surgical treatment, postoperative morbidity and mortality were evaluated. Direct abdominal X-ray series, abdominal ultrasound scanning (US), abdominal contrast-enhanced computerized tomography (CT), routine blood cell count, and blood chemistry tests were performed. Peritoneal spaces were lavaged thoroughly with isotonic saline and drains were placed for postoperative drainage in all of the patients.

### RESULTS

There were 10 male and 6 female patients. Their mean age was 69 (range, 54-85) years. Their complaints were abdominal pain, poor general condition, high fever, nausea, and vomiting on admission. Cholelithiasis was unknown prior to perforation in 5 patients. The patients



**Figure 1** Contrast-enhanced CT image at the level of gallbladder.



**Figure 2** Contrast-enhanced CT image of hepatic abscess adjacent to the superior part of gallbladder.

had several associated diseases, of which atherosclerotic heart disease (AHD) was the most common. One patient with type I gallbladder perforation was on long term steroid treatment for systemic lupus erythematosus. White blood cell (WBC) count was high in 14 patients, and 10 patients had high fever. Patients with type I gallbladder perforation had signs of peritoneal irritation such as extensive abdominal tenderness, guarding and rebound tenderness. Patients with type II gallbladder perforation had local tenderness, guarding, positive Murphy's sign and 4 of them had palpable right subcostal mass while one patient had jaundice with a total bilirubin level of 28 mg/dL. Two patients with type III gallbladder perforation had epigastric tenderness and one of them also had abdominal distension. Four patients had systemic inflammatory response syndrome, of them two patients with type I gallbladder perforation and two with type II and type III gallbladder perforations. The number of patients and their clinical features in each type of gallbladder perforation are shown in Table 1.

Abdominal X-ray series and abdominal US were performed for all of the patients and abdominal CT scanning for 14 patients. Only one patient with type III gallbladder perforation had air-fluid levels on direct abdominal radiograms. Abdominal US showed gall stones in all of the patients with type I and type II gallbladder perforations, extensive intraperitoneal free fluid in 7 patients with type I gallbladder perforation, and a small amount of pericholecystic free fluid in 6 patients with type II gallbladder perforation. Abdominal US did not show GB wall defect in any of the patients. CT revealed GB wall thickening in all of the patients, gall stones in 10 patients, extensive intraperitoneal free fluid in 5 patients, a small amount of pericholecystic free fluid in 7 patients, and GB perforation sites in 5 patients. Abdominal CT and US detected liver abscesses in 2 patients, dilated extra and intrahepatic bile ducts in 1 patient. Abdominal CT showed dilated intestinal loops suggesting mechanical obstruction in one patient with type III gallbladder perforation. Abdominal CT showed dilated stomach suggesting gastric outlet syndrome in another patient. The stomach was dilated with a normal mucosa, but the gall stone could not be seen during upper gastrointestinal endoscopy of this patient.

**Table 1** Clinical features of the patients, *n* (%)

Feature	Type I	Type II	Type III
<i>n</i> (%)	7 (43.7)	7 (43.7)	2 (12.6)
Mean age (yr)	67.5	68.4	76.5
Gender (Male/Female)	5/2	5/2	0/2
Fever (more than 38°C), <i>n</i> (%)	5 (71.4)	5 (71.4)	-
White blood cell count (mean)	23966	17314	13200
Mean duration of symptoms (d)	5	8.6	15
Systemic disorders <sup>1</sup> , <i>n</i> (%)			
Atherosclerotic heart disease	4 (14.3)	4 (57.1)	1 (50)
Diabetes mellitus	2 (28.6)	1 (14.3)	1 (50)
Hypertension	1 (14.3)	1 (14.3)	1 (50)
Systemic lupus erythematosus	1 (14.3)	-	-
Chronic obstructive pulmonary disease	1 (14.3)	2 (28.6)	1 (50)
Systemic inflammatory response syndrome	2 (28.6)	1 (14.3)	1 (50)
Preoperative diagnoses, <i>n</i> (%)			
Gallbladder perforation	4 (14.3)	1 (14.3)	-
Acute cholecystitis	2 (28.6)	4 (14.3)	-
Cholangitis	-	1 (14.3)	-
Peptic ulcer perforation	1 (14.3)	-	-
Perforated appendicitis	-	1 (14.3)	-
Mechanical bowel obstruction	-	-	1 (50)
Gastric outlet syndrome	-	-	1 (50)
Sites of perforation, <i>n</i> (%)			
Fundus	6 (85.7)	3 (42.9)	-
Corpus	1 (14.3)	2 (28.6)	-
Infundibulum	-	1 (14.3)	2 (100)
Cystic duct	-	1 (14.3)	-

<sup>1</sup>Some patients had more than one systemic disorder.

Enlarged gallbladder, irregularity of the gallbladder walls at the fundic region, air density lateral to the fundus and corpus, and increased density of the mesentery anterior to the fundus suggesting free fluid on CT image of a patient with type II gallbladder perforation are shown in Figure 1. The abdominal CT image of a patient with hepatic abscess adjacent to the superior part of GB is shown in Figure 2.

The patients underwent surgery after administration of intravenous crystalloid solutions, and were treated with analgesics and antibiotic (third generation cephalo-

sporins) within the first 36 h (mean 9 h) after admission. The patients who had associated diseases such as diabetes, chronic obstructive pulmonary disease (COPD), and AHD underwent surgery after specific medical treatment was started. Antibiotic treatment was changed when required, according to the results of microbiological assessment of the infected bile specimens obtained from the gall bladder. The most common preoperative diagnoses were perforated cholecystitis in patients with type I gallbladder perforations, and acute cholecystitis in patients with type II gallbladder perforations. Laparoscopic cholecystectomy was performed in 6 patients, two of them had type I gallbladder perforation, and four type II gallbladder perforation. Conversion was required in 2 of them due to unclear anatomy. Laparotomy was performed in the remaining 10 patients. Perforations were recognized intraoperatively in 11 patients. The perforated site of the GB was the fundus in 9 patients, the corpus in 3 patients, the infundibulum in 3 patients, and the cystic duct in 1 patient. Two patients with type II gallbladder perforation also had hepatic abscesses, which were covered by the omentum. Hepatic abscesses were also drained in these patients. All of the patients received a cholecystectomy. Common bile duct exploration was performed, gall stones were extracted, and a T-tube was placed into the common bile duct in addition to cholecystectomy in 1 patient with obstructive jaundice. One of the 2 patients had a cholecystoduodenal fistula (type III gallbladder perforations) underwent surgery for gastrointestinal tract obstruction due to bile stones in the jejunum, which were removed through an enterotomy. Gall stones were also found in the duodenum of the other patient with type III gallbladder perforation and removed through a duodenotomy.

The median hospital stay was 15 d (4-26 d). Two patients (12.5%) died of sepsis and multiple organ failure in the early postoperative period. One was a female patient at the age of 79 with type III gallbladder perforation and COPD. The other was a 84 year-old male patient with delayed type II gallbladder perforation and pericholecystic abscess associated with AHD and diabetes. Subhepatic abscess, pelvic abscess, pneumonia, pancreatitis and acute renal failure were found in 6 patients (Table 2). Subhepatic and pelvic abscesses were drained percutaneously under ultrasound guidance. The other diseases were treated conservatively.

## DISCUSSION

Inflammation may progress and cause ischemia and necrosis, thus resulting GBP in 2% to 11% of acute cholecystitis patients<sup>[6,8,9]</sup>. GBP also develops following acalculous cholecystitis, although rare<sup>[10,11]</sup>. GB fundus, the most distal part with regard to blood supply, is the most common site of perforation<sup>[8,12]</sup>. The incidence of GBP was 4.5% and the most frequent site of perforation was the fundus (60%) in our study. Six of the 7 type I gallbladder perforations and 3 of 7 type II gallbladder perforations were at the fundus. When GB is perforated at the fundus, it is less possibly covered by the omentum, thus the bile drains into the peritoneal space. If the perforation site is not at the fun-

**Table 2** Surgical procedures and morbidities of the patients *n* (%)

	Type I	Type II	Type III
Surgery			
Laparoscopic cholecystectomy	2 (12.5)	4 (25)	-
Laparotomy and cholecystectomy	5 (31.2)	3 (18.7)	2 (12.5)
Morbidity <sup>1</sup>			
Subhepatic abscess		1 (11.1)	1 (11.1)
Pelvic abscess		1 (11.1)	1 (11.1)
Pneumonia	1 (11.1)	1 (11.1)	1 (11.1)
Pancreatitis		1 (11.1)	
Acute renal failure	1 (11.1)		

<sup>1</sup>Some patients had more than one morbidity.

cus, it is easily sealed by the omentum or the intestines and the condition remains limited in the right upper quadrant with formation of a plastrone and pericholecystic fluid. This observation suggests that if the perforation site is at the fundus, it is more likely to end up with a type I perforation. The relation between the site and the type of GBP has not been defined. Although statistical analysis was not possible because of the insufficient number of patients in this series, this observation may be supported by larger series.

Acute uncomplicated cholecystitis is more common among females with a female to male ratio of 2:1<sup>[13]</sup>. However, GBP is more frequent in male gender<sup>[1,6]</sup>. In our study, male patients made up of 60% and the two patients with type III gallbladder perforation were females. GBP is usually seen over 60 years of age<sup>[4,14]</sup>. Roslyn *et al*<sup>[1]</sup> reported that type I and II GBP tend to occur in younger patients, especially more or less at the age of 50 years, whereas type III gallbladder perforations are more common in the elderly. The patients with type I gallbladder perforation were relatively younger than those with type II and III gallbladder perforations in our study.

Type I gallbladder perforations are usually seen in patients with AHD, diabetes, malignancy, cirrhosis, and immunosuppressive diseases, or during immunosuppressive treatment, without a history of chronic cholecystitis. On the other hand, type III gallbladder perforations most often occur in patients with a previous long time history of gall stones<sup>[1,9,12]</sup>. Severe AHD has been reported in 21% of patients with type I and II gallbladder perforations, and diabetes, in 25% of patients with type I gallbladder perforation<sup>[8,14]</sup>. Such high rates are related to vascular disorders caused by these systemic diseases. It has been reported that type II GBP occurs more frequently<sup>[1,3,9,12]</sup>. The incidence of type I and II gallbladder perforations was equal and the most frequent associated systemic disease was AHD in the present study. Type III gallbladder perforations usually occur in chronic cholecystitis patients with obstructive gastrointestinal symptoms<sup>[9,12,15]</sup>. Since the symptoms of type I - II GBP and uncomplicated cholecystitis are similar, differential diagnosis may be difficult based on physical examination, laboratory tests, and radiological methods and the diagnosis may not be established

preoperatively<sup>[6,12]</sup>. Delay in diagnosis is the major cause of its high morbidity and mortality<sup>[1,4,9,16]</sup>. Tanaka *et al*<sup>[17]</sup> reported that only one patient had a concrete diagnosis preoperatively in their series of 9 patients. The majority of GBP patients include those who undergo early surgery with the diagnosis of acute cholecystitis. The main complaint of the patients is abdominal pain accompanied with nausea and vomiting during the last 7 d<sup>[12,18]</sup>. The duration of symptoms was shorter in patients with type I gallbladder perforation than in patients with type II and III gallbladder perforation in our study. High fever and elevated WBC count are not the diagnostic indications for gallbladder perforation. Parker *et al*<sup>[19]</sup> reported that high fever and high WBC count could be observed in 56% and 59% of patients with acute cholecystitis, respectively. The majority of type I and II gallbladder perforation cases had fever whereas type III gallbladder perforation cases did not in our study. The patients with type I and II gallbladder perforation had elevated WBC count, but those with type III gallbladder perforation had only a mild increase in WBC count.

US findings in acute cholecystitis, such as the GB wall thickening, GB distension, pericholecystic free fluid, and positive sonographic Murphy sign, may also be present in gallbladder perforation cases<sup>[2,9,20]</sup>. Sood *et al*<sup>[2]</sup> noted that the sonographic hole sign, in which the defect in GB wall is visualized, is the only reliable sign of gallbladder perforation. They reported that GB wall defect could be shown with a high resolution ultrasound scanner device in 70% of patients<sup>[2]</sup>. However, Kim *et al*<sup>[21]</sup> reported that the site of defect could not be visualized on US in any patients, which is similar to our study. On the other hand, CT can show more accurate signs of free intraperitoneal fluid, pericholecystic fluid, and abscess<sup>[1,2,22]</sup>. CT can also show GB wall thickness and the defect on the wall due to perforation<sup>[2,20]</sup>. In our study, all of the 5 patients who had the diagnosis of gallbladder perforation preoperatively were diagnosed by CT. Since the patients were admitted for acute abdominal pain, standard pelvic CT rather than upper abdominal CT was applied. Kim *et al*<sup>[21]</sup> reported that the defect could not be visualized on CT in 54% of patients. Doppler ultrasound, magnetic resonance imaging and radionuclide methods have been used in the diagnosis of gallbladder perforation<sup>[23-25]</sup>. The majority of our patients with type II gallbladder perforation were initially treated conservatively and then underwent surgery as no improvement was observed during the first 3 d.

Cholecystectomy, drainage of abscess if present, and abdominal lavage are usually sufficient to treat gallbladder perforation<sup>[1,4]</sup>. Cholecystectomy may be difficult in type III gallbladder perforations. If a cholecystectomy is performed, additional surgical procedures such as repair of the fistula may be required<sup>[15,16]</sup>. Cholecystectomy can be performed after the infection is relieved by US guided percutaneous drainage in type II gallbladder perforations<sup>[22]</sup>. Laparoscopic cholecystectomy can be performed for acute, gangrenous, and/or perforated cholecystitis as well as uncomplicated cholecystitis, but a conversion may be necessary in case of difficulties like an unclear anatomy<sup>[9,16]</sup>. In our study, laparoscopic procedure was initiated in 6 patients but conversion was required in two.

Since the difficulties in diagnosis cause delay in treatment, higher morbidity and mortality rates are often encountered<sup>[1,2,9]</sup>. Glenn and Moore<sup>[26]</sup> have reported that the mortality rate of gallbladder perforation patients is 42%, while other studies reported that the mortality rates are decreased to 12%-16% owing to the developments in anesthesiology and intensive care conditions<sup>[1,3]</sup>. The morbidity and mortality rates were 37.5% and 12.5%, respectively in the present study.

In conclusion, early diagnosis of gallbladder perforation and immediate surgical intervention are of crucial importance. Although standard abdominal CT has an important role in diagnosing gallbladder perforation, upper abdominal CT for acute cholecystitis in which pericholecystic fluid is found by US may increase the rate of preoperative diagnosis of gallbladder perforation.

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