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CLINICAL STUDY

Perforation of gallbladder

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Abstract: *Objective:* Gallbladder perforation is a rare but life threatening complication of acute cholecystitis. Aim of this study is to present our clinical experience with gallbladder perforation.
Material and methods: Thirty-seven of retrospectively reviewed 1042 acute cholecystitis patients were found to have gallbladder (GB) perforation. Perforations due to trauma, iatrogenic causes, and gallbladder carcinoma were excluded.
Results: Abdominal ultrasound (US) showed gall stones in all of the patients with type-I and type-II gallbladder perforations (GBP), extensive intraperitoneal free fluid in 9 patients with type-I GBP, and a small amount of pericholecystic free fluid in 7 patients with type-II GBP. Abdominal US did not show GB wall defect in any of the patients, but showed intraperitoneal free gall stone in one type-I and one type-II GBP patients. CT revealed GB wall thickening in all of the patients, gall stones in 7 patients, extensive intraperitoneal free fluid in 7 patients, a small amount of pericholecystic free fluid in 8 patients, and GB perforation sites in 4 patients. Abdominal CT and US detected subhepatic abscesses in 3 patients.
Conclusion: Early diagnosis of gallbladder perforation and immediate surgical intervention are of crucial importance. Unfortunately, the limited success of US and CT for detecting the GBP let us advocate early and urgent surgery *(Tab. 3, Ref. 13).* Full Text (Free, PDF) *www.bmj.sk.*
Key words: gallbladder perforation, acute cholecystitis, ultrasonography, computerized tomography, surgery.

Gallbladder perforation (GBP) is a rare but life threatening complication of acute cholecystitis. In 1934, Neimeier (1) presented his classic description of acute perforation of the gall bladder and proposed a classification based on his findings. He 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.

Roslyn et al (2) reviewed the risk factors for gallbladder perforation. They found that patients aged over 60 years with acute perforation more commonly had associated severe systemic diseases such as diabetes and atherosclerotic heart disease. In this group perforated gallbladder was thought to be a result of a compromised blood supply. There was a second group of younger patients who were also at risk for acute perforations. Most of these patients were immunosuppressed for one reason or another and it was believed that the inability to combat infection played a major role in the perforation. Because of high morbidity and mortality rates due to delay in diagnosis, GBP still continues to be an important problem for the surgeons. Most cases can only be diagnosed during surgery (2, 3).

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Aim of this study is to present our clinical experience with GBP.

Material and method

Records of a total number of 1042 patients who received medical and/or surgical treatment with the diagnosis of acute cholecystitis in two medical centers between January 1990 and September 2007 were reviewed retrospectively. In thirty-seven (3.55 %) of these patients a gallbladder perforation was detected. Perforations due to trauma, iatrogenic causes, and gallbladder (GB) carcinoma were excluded. We wanted to assess the incidence of spontaneous gallbladder perforations.

The original classification of Neimeier was used to identify the patients. Direct abdominal X-ray series, abdominal ultrasound scanning (US), abdominal contrast-enhanced computerized tomography (CT), routine complete blood count, and blood chemistry tests which had been performed, were evaluated. The parameters including age, gender, time from the onset of symptoms until the surgery, diagnostic procedures, surgical treatment, postoperative morbidity and mortality were also evaluated.

Results

There were 20 male and 17 female patients. Their mean age was 64 (range, 42–91) years. Their complaints were abdominal pain, poor general condition, high fever, nausea, and vomiting on admission. Cholelithiasis was unknown prior to perforation in

Tab. 1. Clinical Features of the patients, number (%).

Features	Type-I	Type-II	Type-III
Number (%)	12 (32.44)	21 (56.76)	4 (10.8)
Mean age (year)	58.4	65.1	74.75
Gender (female/male)	5/7	9/12	3/1
Mean duration of symptoms (hour)	109.6	204.2	341
Fever (over 38 °C)	10 (83.3)	8 (38)	–
Mean white blood cell count	24318	14896	12410
Systemic disorders*			
Hypertension	8 (66.6)	13 (61.9)	3(75)
Diabetes mellitus	6 (50)	11 (52.4)	2(50)
Atherosclerotic heart disease	5 (41.6)	11 (52.4)	3(75)
Chronic obstructive pulmonary disease	3 (25)	5 (23.8)	1(25)
Cerebrovascular disorders	–	3 (14.3)	2(50)
Preoperative diagnosis			
Gallbladder perforation	1 (8.3)	5 (23.8)	–
Peptic ulcer perforation	6 (50)	–	–
Acute cholecystitis	1 (8.3)	11 (52.4)	–
Perforated appendicitis	3 (25)	–	–
Mechanical bowel obstruction	1 (8.3)	–	1 (25)
Chronic cholecystitis	–	5 (23.8)	2 (25)
Gastric outlet syndrome	–	–	1 (25)
Surgery			
Laparoscopic cholecystectomy	1 (8.3)	2 (9.5)	–
Conventional cholecystectomy	11 (91.7)	19 (90.5)	4 (100)
Perforation site			
Fundus	8 (66.7)	7 (33.3)	–
Corpus	3 (25)	6 (28.6)	–
Infundibulum	1 (8.3)	5 (23.8)	2 (50)
Cystic duct	–	3 (14.3)	2 (50)
Morbidity			
Pneumonia	2 (16.7)	3 (14.3)	–
Subhepatic abscess	–	2 (9.5)	1 (25)
Pancreatitis	–	4 (19)	1 (25)

* Some patients had more than one systemic disorder.

4 patients. The patients had several associated diseases (Tab. 1). Hypertension was the most frequent one. Diabetes mellitus and atherosclerotic heart disease come the second. Some patients had more than one systemic disorder.

Patients with type-I gallbladder perforation had signs of peritoneal irritation such as extensive abdominal tenderness, guarding and rebound tenderness. US was performed to assess the etiology of peritoneal irritation. Patients with type-II GBP had local tenderness, guarding, positive Murphy's sign and 9 of them had palpable right subcostal mass. Two patients with type-III GBP had epigastric tenderness and one of them also had abdominal distension. The number of patients and their clinical features in each type of GBP are shown in Table 1.

Abdominal X-ray series and abdominal US were performed in all of the patients and abdominal CT scanning in 8 patients. Technical problems are the cause of low number of CT scans. Only one patient with type-III GBP 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 9 patients with type-I GBP, and a small amount of pericholecystic free fluid in 7 patients with type-II GBP. US findings of our patients are summarized in Table 2. Abdominal US did not show GB wall defect in any of the patients, but showed intraperitoneal free gall stone in one Type-I and one type-II GBP patients. CT revealed GB wall thickening in all of the patients, gall stones in 7 patients, extensive intraperitoneal free fluid in 7 patients, a small amount of pericholecystic free fluid in 8 patients, and GB perforation sites in 4 patients. Abdominal CT and US detected subhepatic abscesses in 3 patients. Abdominal CT showed dilated intestinal loops suggesting mechanical obstruction in one patient with type-III gallbladder perforation.

The most common preoperative diagnoses were peptic ulcer perforation in patients with type-I GBP and acute cholecystitis in patients with type-II GBP. Laparoscopic cholecystectomy was tried to be performed in 11 patients; two of them had type-I GBP, and nine of them type-II GBP, but conversion was required in 8 of them due to unclear anatomy. Two patients with type-II GBP and one with type-III GBP also had subhepatic abscesses, which were covered by the omentum. Subhepatic abscesses were also

Tab. 2. US findings of the patients, number %.

Finding/Perforation type	Type-I	Type-II	Type-III
Perforation site	0 (0%)	0 (0%)	0 (0%)
Wall thickness	12 (100%)	21 (100%)	4 (100%)
Extensive intraperitoneal free fluid	9 (75%)	0	0
Small amount of pericholecystic free fluid	9	7	0
Intraperitoneal free gall stone	1	1	0
Stones in gallbladder	12	21	0
Stones in CBD	1 (50%)*	2 (66.6%)*	0

* According to the intraoperative cholangiogram results.

Tab. 3. Blood Chemistry tests of the patients, number.

Tests/Perforation type	Type-I	Type-II	Type-III
ALT (20–65 U/L)	2VH/4H/6N	3VH/8H/10N	1H/3N
AST (5–37 U/L)	2VH/ 5H/5N	3VH/10H/8N	1H/3N
GGT (5–85 U/L)	2VH/3H/7N	3 VH/5H/13N	1H/3N
ALP (25–136 U/L)	2H/10N	6H/15N	4N
LDH (100–190 U/L)	4H/8N	7H/14N	1H/3N
Amylase (25–115 U/L)	6H/6N	13H/8N	1H/3N
Lipase (114–286 U/L)	1H/11N	1H/20N	4N
Total Bilirubin (mg/dl)*	1VH/3H/8N	2VH/ 3H/17N	1H/3N
Direct Bilirubin (mg/dl)**	2VH/2H/8N	4VH/1H/17N	1H/3N

VH – very high, more than two times of the upper limit, H – high, between the upper limit and double the upper limit, N – normal, under upper limit
* upper limit is 1 mg/dl, ** upper limit is 0.3 mg/dl

drained in these patients. All of the patients underwent cholecystectomy and intraoperative cholangiogram. In five patients, gall stones were found at common bile duct (CBD). Also, all had high liver function tests and 4 of them had high bilirubin levels (Tab. 3). CBD exploration was performed and gall stones were extracted.

Mean hospital stay was 17 days (5–38 days). Four patients died (10.8 %). While two of them died of sepsis and multiple organ failure in early postoperative period, others died due to complications of pancreatitis.

Discussion

Inflammation may progress and cause ischemia and necrosis, thus resulting in GBP in 2 % to 11 % of acute cholecystitis patients (4, 5). GBP also develops following acalculous cholecystitis, although rare (6, 7). GB fundus, the most distal part with regard to blood supply, is the most common site of perforation (7). The incidence of GBP was 3.55 % and the most frequent site of perforation was the fundus (40.5 %) in our study. Derici et al suggested that when GB is perforated at the fundus, it is less possibly covered by the omentum, thus the bile drains into the peritoneal space (7). We think that this was the cause why we had preoperative diagnosis like peptic ulcer perforation or perforated acute appendicitis. If the perforation site is not at the fundus, it is easily sealed by the omentum or the intestines and the condition remains limited to 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. Our study supports the study of Derici et al. The relation between the site and the type of GBP has not been defined. Although statistical analysis was not possible because of insufficient number of patients in this series, this observation may be supported by larger series.

While acute uncomplicated cholecystitis is more common among females (m/f=1/2), GBP is more frequent in male gender (2, 4, 7). In our study 54 % of the patients are male gender. GBP is usually seen over 60 years of age (2). Roslyn et al (2) 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. Also, 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 atherosclerotic heart diseases, diabetes, malignancy, cirrhosis, and immunosupressive diseases, or during immunosupressive treatment, without a history of chronic cholecystitis. On the other hand, type-III gallbladder perforations most often occur in patients with a previous long term history of gall stones (2, 5, 7). In our study, there is no statistically significant difference between the three groups in the incidence of these diseases. Beside of this finding, cerebrovascular disorders seem to be more frequently

related with type-II and type-III GBP. Unfortunately, analyzing this relation statistically was not possible because of the insufficient number of patients in this study; this observation may be supported by larger series. Half of type-III GBP patients were diagnosed during elective cholecystectomy and their specimens were histopathologically diagnosed as chronic cholecystitis. All of our patients, who have been diagnosed as chronic cholecystitis, have a history of acute cholecystitis attack.

Lau et al showed in their metaanalysis that early cholecystectomy reduces the total length of hospital stay and averts the risk of recurrent attack or the development of other biliary complications while the patients are awaiting definitive surgical intervention8. They also suggest that it is a more cost-effective approach for the management of acute cholecystitis within 72 h after the onset of symptoms8. As we presented in Table 1 a mean duration of symptoms for Type-I is 109 hours, Type-II 204 hours and Type-III 341 hours. However, in the section of preoperative diagnosis one patient in the group of Type-I and 11 patients of the group of Type-II had acute cholecystitis. We calculated the duration prior to diagnosis by the history of the patients. Chronic disorders like diabetes decrease the feeling of pain and elongate the onset of the symptoms. Thus, we think that the cause of the long duration at our series is the possible misunderstandings of the patients' histories and the chronic disorders like diabetes.

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 (3, 5, 9). Sood et al3 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 patients3. However, Kim et al (10) reported that the site of defect could not be visualized on US in any patients, which is similar to our study. But, abdominal US showed intraperitoneal free gall stone in one Type-I and one type-II GBP patients. On the other hand, CT can show more accurate signs of free intraperitoneal fluid, pericholecystic fluid, and abscess (2, 3). CT can also show GB wall thickness and the defect on the wall due to perforation (3, 9). In our study CT revealed GB wall thickening in all of the patients (8 of 8 patients), but GB perforation sites in only 4 of 8 patients (50 %). Neither US nor CT showed any findings of hematoma within the GB.

Since the difficulties in diagnosis cause delay in treatment, higher morbidity and mortality rates are often encountered (2, 3, 5). Glenn et al 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 (2). In our study morbidity and mortality rates were 35 % and 10.8 % respectively. Many of our patients were diagnosed as gall bladder perforation during the operation. Mean hospital stay was 17 days (5–38 days). We prescribed intravenous antibacterial therapy to all operated patients for at least 5 days. Unfortunately, four patients died (10.8 %). While two of them died of sepsis and multiple organ failure in early postoperative period, others died due to complications of pancreatitis. One of the patients who died of sepsis was a 91-year old woman with cerebrovascular disorders and diabetes mellitus. A multi-drug resistant E.coli was isolated from her blood culture. The other one was a 78-year old woman with atherosclerotic heart disease, hypertension and chronic obstructive pulmonary disease. A multibacterial subhepatic abscess and then sepsis developed, no treatment made any sense. Both of them were type-III GBP patients. No bile leaks were observed in our gall bladder perforation patients, during postoperative period.

The best form of management is early surgery; this would concur with the findings of Larmi et al (11). Addison et al (12) advocated early and urgent cholecystectomy for acute gall bladder disease. They reported the risk of perforation to be between 3 and 12 % in patients treated conservatively for acute cholecystitis. They also showed that the mortality and morbidity for emergency cholecystectomies compared favorably with those for elective surgery and concluded that in well selected patients, emergency cholecystectomy for acute cholecystitis should be advocated as a safe procedure.

Cholecystectomy may be difficult in type-III gallbladder perforations. Under that condition, cholecystostomy can be helpful. Silberfein et al suggested that US-guided percutaneous cholecystostomy is a safe and effective treatment for acute cholecystitis in high-risk surgical patients (13).

We did not come cross any report about the prediction of gall bladder perforation. But, chronic disorders like diabetes decrease the feeling of pain and elongate the onset of the symptoms of acute cholecystitis. Thus, a gall bladder perforation can be occurring.

Conclusion

Early diagnosis of gallbladder perforation and immediate surgical intervention are of crucial importance. Unfortunately, the limited success of US and CT for detecting the GBP and poor guidance of clinical features and laboratory let us advocate early and urgent surgery for acute gall bladder disease. Also, we suggest a diagnostic laparoscopy for patients with gall bladder wall thickness or free fluid.

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