

Clinical characteristics and treatment approaches in patients with post-cholecystectomy syndrome due to remnant gallbladder

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Abstract

Aim: A remnant gallbladder is a rare problem encountered in the diagnosis and treatment of the post-cholecystectomy syndrome. This study aimed to evaluate the clinical features and treatment modalities of patients with a symptomatic remnant gallbladder after cholecystectomy.

Material and Methods: The data of 11 patients who were operated following the diagnosis of a remnant gallbladder between January 2013 and January 2019 were evaluated retrospectively. Clinical characteristics, diagnosis and treatment management, laparoscopy to open conversion rate and hospital stay were evaluated.

Results: The median age was 55.3 years (range, 36 to 77 years), and the male/female ratio was 1/10. Right upper quadrant pain and jaundice were the most common symptoms. The time interval between cholecystectomy and symptom recurrence was 46.8 (range, 1 to 420) months. A remnant gallbladder was determined by ultrasonography in seven patients (63.6%) and by magnetic resonance cholangiopancreatography in 11 patients (100%). Preoperatively, ERCP was performed in six patients due to suspicion of stones in the main bile duct, except for the remnant gallbladder. Complementary cholecystectomy was performed by laparoscopically in seven patients, and only four patients had a conversion to open surgery. The median duration of hospital stay was four days (range, 2 to 9 days).

Conclusion: The remnant gallbladder, which is the rare and a cause of the post-cholecystectomy syndrome, is a pathology that should be considered in patients with postoperative symptoms. Patients with a symptomatic remnant gallbladder should be treated with a multidisciplinary approach, including a careful choice of imaging modalities and surgical or endoscopic treatment methods.

Keywords: Remnant gallbladder; post-cholecystectomy syndrome; diagnose; treatment.

INTRODUCTION

The gold standard for the treatment of patients with symptomatic cholelithiasis is laparoscopic cholecystectomy (LC). While LC provides successful results in approximately 85-90% of patients, pre-operative symptoms persisted or recurred after cholecystectomy in 10 to 15% of patients (1). This undesirable condition, called as post-cholecystectomy syndrome, was first described by Womar and Crider (2). The incidence of the syndrome shows a wide range (between 5% and 47%) and symptomatic status might occur within 2 to 25 years from cholecystectomy (3). The causes of post-cholecystectomy syndrome, including biliary or non-biliary diseases. Gastroesophageal reflux disease, irritable

bowel disease, liver diseases, peptic ulcer disease, and chronic pancreatitis, might also be considered for non-biliary diseases. Biliary stricture, choledocholithiasis, Oddi sphincter dysfunction, long cystic duct stump, and the remnant gallbladder (RGB) rarely have a biliary origin (4). Among these, the incidence of remnant gallbladder after laparoscopic cholecystectomy is approximately 2-13.3% (5). A major problem is that the anatomy of the dissection performed for the Calot triangle often cannot be determined precisely because of Mirizzi syndrome, liver cirrhosis, inflammation or insufficient surgery.

RGB stone is responsible for the recurrence of symptoms after surgery. The most common symptoms are right upper quadrant or epigastric pain and jaundice. Nausea-vomiting,

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bloating, and other dyspeptic complaints might be seen less frequently. For the diagnosis of remnant gallbladder, this condition should be suspected first. Abdominal ultrasonography (USG), computed tomography (CT), endoscopic retrograde cholangiopancreatography (ERCP), and magnetic resonance cholangiopancreatography (MRCP) are used in the diagnosis (6,7). Apart from these, diagnostic methods, such as endoscopic ultrasonography (EUS), intraoperative ultrasonography, intraoperative cholangiography, and percutaneous trans-hepatic cholangiography, are used less frequently (8). The treatment of patients with a symptomatic remnant gallbladder requires surgery. Treatment methods include open or laparoscopic complementary cholecystectomy and/or endoscopic stone extraction, papillotomy, extracorporeal shock wave lithotripsy, and laser lithotripsy. However, studies on laparoscopic exploration for surgical intervention of patients diagnosed with symptomatic RGB are limited.

In this study, we aimed to evaluate the clinical features, diagnostic, and treatment modalities of patients with a remnant gallbladder who have significant difficulties in diagnosis and treatment after laparoscopic or open cholecystectomy.

MATERIAL and METHODS

Between January 2013 and January 2019, data from patients diagnosed with post-cholecystectomy syndrome in our clinic were retrospectively obtained from hospital records. Eleven of the patients diagnosed with post-cholecystectomy syndrome, the etiological cause was determined as remnant gallbladder. Eleven patients undergoing surgical intervention for remnant gallbladder were included in our study. The initial cholecystectomy of seven patients was performed outside our clinic. Patients undergoing intraoperative choledochal exploration, who underwent cholecystectomy with the diagnosis of gallbladder carcinoma histopathologically, stone-free gallbladder disease, or other surgical procedures (such as Whipple operation) were excluded from the study.

We recorded the demographic data of the patients, recurrent symptoms (pain, jaundice, nausea, vomiting and dyspeptic symptoms), time between cholecystectomy and symptoms (month), liver function tests such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total and direct bilirubin, results of radiological diagnostic methods (such as USG, CT, MRCP and ERCP), data of treatment management (open and laparoscopic surgery), and length of hospital stay. The planned complementary cholecystectomy was started with laparoscopic exploration in all patients. In four of these patients there was intense adhesion, and in one patient the main bile duct injury was exposed. SPSS software, version 20 (SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis. Descriptive data were expressed as median, and categorical data as percentages.

RESULTS

The mean age at the time of diagnosis was 55.3 (range 36 to 77) years, and the male/female ratio was 1/10 at the time of diagnosis. According to the data obtained from the patient records, the first cholecystectomies of only four patients were performed in our clinic. Therefore, the first operative details were unavailable for seven patients. In four patients the indication for partial cholecystectomy was inflammation (n=2) and poor anatomic visualization (n=2). In these four patients first operation details, a partial cholecystectomy performed by leaving the posterior wall intact with the liver (n=1) and dividing infundibulum circumferentially then close by using suture (n=3). The mean time between initial cholecystectomy and symptomatic RGB detection was 46.8 months (range, 1 to 420 months). Pain in the right upper quadrant and the epigastric region was observed in all patients, while three patients had jaundice. The serum AST, ALT, ALP, total and direct bilirubin levels were 65.8 ± 33.6 , 69.7 ± 43.6 , 155 ± 108 , 1.7 ± 1.5 and 0.77 ± 0.92 , respectively. The clinical characteristics of the patients are shown in Table 1 and Table 2.

Table 1. Demographics of variables of patients

Variables	Patients (n=11)
Age, year, median (range)	58 (36-77)
Gender, M/F	1/10
Clinical symptoms	
Abdominal pain	11
Jaundice	3
Cholangitis	2
Nausea-vomiting	7
Indication for subtotal cholecystectomy	
Inflammation	2
Poor anatomic visualization	2
Unknown	7
Interval of cholecystectomy, month, mean \pm SD (range)	46.8 \pm 124.4 (1-420)
Imaging technique for diagnose	
Ultrasound	11
Computed tomography	5
MRCP	11
ERCP	6
Remnant gallbladder size, cm	2.93 \pm 0.49
Serum AST (U/L), mean \pm SD	65.8 \pm 33.6
Serum ALT (U/L), mean \pm SD	69.7 \pm 43.6
ALP (U/L), mean \pm SD	155.8 \pm 108
Total bilirubin (mg/dL), mean \pm SD	1.7 \pm 1.5
Direct bilirubin (mg/dL), mean \pm SD	0.77 \pm 0.92

AST; Aspartate aminotransferase, ALT; Alanine aminotransferase, ALP; Alkaline phosphatase, MRCP; Magnetic resonance cholangiopancreatography, ERCP; endoscopic retrograde cholangiopancreatography

Table 2. Demographics, symptoms, mode of diagnosis and intervention

Follow up time, month	Surgery	Interval cholecystectomy time, year	Remnant gallbladder size, mm	Imaging	Symptom	Gender	Age	Patients
46	Lap to open	35	22x20	USG/ MRCP/ERCP	Pain, jaundice	F	62	1
63	Lap	4	28x22	USG/MRCP/ CT/ERCP	Pain, nausea	F	42	2
72	Lap to open	12	20x12	USG/MRCP/ERCP	Pain, jaundice	F	82	3
74	Lap	16	24x25	USG/CT/MRCP/ERCP	Pain, jaundice	F	44	4
48	Lap to open	2	20x10	USG/CT/MRCP	Pain	F	66	5
45	Open	8 month	30x20	USG/MRCP	Pain	F	58	6
92	Open	15 year	30x10	USG/MRCP/CT/ERCP	Pain, jaundice	F	80	7
48	Lap to open	25 day	42x20	USG/MRCP	Pain	E	36	8
56	Lap	5	20x15	USG/MRCP/ERCP	Pain	F	48	9
44	Lap	3	30x15	USG/CT/MRCP	Pain	F	60	10
56	Lap to open	4	22x18	USG/MRCP	Pain	F	62	11

Abdominal USG, CT, MRCP, and ERCP imaging methods were used in the diagnosis. All patients underwent abdominal USG and MRCP, but RGB was not detected by USG in four (36.3%) patients. MRCP was adequate in each of the eleven patients for diagnosis. The remnant gallbladder was identified in all patients and gallstones were distinguished in 8 of the eleven patients by MRCP. The MRCP image of one of these patients is shown in figure 1.



Figure 1. Postoperative magnetic resonance cholangiopancreatography revealed the presence of remnant gallbladder. The thin arrow shows the remnant gallbladder, the thick arrow shows the stone in the common bile duct

In three patients (27.2%), there was no stone in the remnant gallbladder, but there were stones in the cystic canal. The mean size of the determined remnant pouch was 2.93 cm (range, 2 to 4 cm). ERCP was performed in six patients (54.5%) on suspicion of choledocholithiasis.

Nine patients underwent laparoscopic cholecystectomy but 6 of these patients required conversion to open technique and in 2 patients the operation initiated with open technique (table 2). Due to the inability to determine the anatomy and intense adhesions in six patients, it was necessary to undergo conversion to open surgery. One patient had a bile duct injury. In this patient, primary repair was performed intraoperatively, and a t-tube was inserted. Intraoperative cholangiogram was not routinely performed in each patient. Jackson Pratt's drains were placed in the subhepatic area in all patients. Except for one patient with a main bile duct injury, patients started to receive liquid food in the eighth postoperative hour. The median time of discharge from the hospital was 4 days (range, 2 to 9 days).

DISCUSSION

Laparoscopic cholecystectomy is one of the most common operations in Turkey and worldwide. After cholecystectomy, the patient's symptoms typically disappear. However, approximately 5-10% of the patients continue to complain of symptoms 2 days to 25 years after cholecystectomy (4,9). This might be due to remnant stone remains or gallbladder formation. In our study, the mean time interval between the recurrences of symptoms was 46.8 months (range, 1 to 420 months). The reason why this period is longer than in the literature is that the time between the first operation of our one patient and the symptomatic period is quite long. The common symptom is pain, jaundice, nausea, and vomiting in the right upper quadrant and epigastric region. These complaints can be seen alone or together. Abdominal pain was the common symptom in all patients (10). In other study, the symptoms which were seen in patients was jaundice, abdominal pain, cholangitis (11). The most common symptoms were pain in the right hypochondrium, recurrent biliary colic and jaundice in a study (8) and another study reported that abdominal pain and persistent dyspepsia were the common presenting symptoms (12). All of the patients in

our study had pain in the right upper quadrant, and three patients complained of jaundice. Inflammation caused by falling stones in the remnant sac (or later formed into the main bile duct or cystic stump) is one of the main causes of obstructive jaundice. The incidence of disease in women (43%) is higher than men (28%) (13). Of the 11 patients included in our study, ten were female and only one patient was male. Why the remnant gallbladder is more common in the females than males? The answer could be greater incidence of cholelithiasis in women than in men. Our study does not provide a clear-cut answer for this question but we think that the prevalence of cholelithiasis is higher in women.

Incidence of incomplete gallbladder removal following cholecystectomy appears very low (14,15). In laparoscopic surgery, incidence of unintentional incomplete gallbladder removal seems slightly more than the ones reported with open cholecystectomy (16-20). Incomplete resection of gallbladder occurs in up to 13.3% of laparoscopic cholecystectomies (20). It is reported that a partial cholecystectomy is a safe option if the anatomy of the Calot's triangle is not fully revealed during cholecystectomy (21-25). Particularly in the case of acute cholecystitis, the Calot's triangle is more likely to be evident from the laparoscopic approach. This is more likely to occur in the presence of inflammation or fibrosis. Laparoscopic partial cholecystectomy is recommended as an alternative to conversion to open surgery for those who have difficult gallbladder (acute cholecystitis, Mirizzi syndrome and cirrhotic, etc) (25). This allows the resection of gallbladder without injury of bile duct but the incidence of this condition is unknown. Moddy et al. claimed that the most striking example of the post-cholecystectomy syndrome is the remnant gallbladder, which causes post-cholecystectomy syndromes (26). In another study supporting 103 women with post-cholecystectomy syndrome, 26 (25%) reported that remnant gallbladder was present (13). In our study, the remnant gallbladder was found in 11 (6.8%) of 161 patients with post-cholecystectomy syndrome. During partial cholecystectomy, it is suggested that there is no clinical significance of small stones and secretions remaining in the remnant sac (27,28), while other authors have suggested that this causes the formation of post-cholecystectomy syndrome by missing the stones in the pouch (29). We believe that the stones that remain in the remnant sac (or stones formed later) cause the patients' symptoms. In a meta-analysis, the authors reported a rate of 1.7% that stones were seen in remnant sac after laparoscopic partial cholecystectomy and 3.8% after open cholecystectomy (30). In another study, 12 of the 14 symptomatic patients were found to have stones in the main bile duct, and this was suggested to be the result of the long-term remnant sac falling into the canal after surgery (27). In our study, a stone was detected in the remnant sac in seven of 11 patients and in the cystic canal in four patients, in both choledochal and remnant sacs.

The increase in the diagnosis of post-cholecystectomy syndrome and the accurate determination of its etiology

has been the result of advances in radiological imaging methods (6,31). Abdominal ultrasound, computed tomography, ERCP, Endo-ultrasonography and MRCP is useful and give satisfactory information in diagnosis of this rare disease. Frequently, abdominal USG is the first-choice method and remnant is insufficient in the gallbladder in 50% of patients (11). If the posterior cholecystectomy syndrome is still suspected despite the absence of remnant gallbladder with USG, EUS or MRCP should be considered without delay. The sensitivity of the EUS is 96.2%, and its specificity is 88.9% (27). Similar sensitivity and specificity rates are reported for MRCP and ERCP however, MRCP is preferred because of its easy application, no sedation is required, and it is noninvasive. Palanivelu et al. showed that MRCP was accurate in 92% of the cases and USG was accurate in 60% of the cases (11). Parmar et al. found that MRCP accuracy was 94% and USG accuracy was 64% (12). In our study, all patients underwent abdominal ultrasonography, but no remnant gallbladder was found in four patients. The presence of remnant pouch in all patients was also visualized by MRCP. MRCP provides a good anatomical and pathological image for biliary tree in these cases as it is noninvasive and safe. In recent years, advances in MRCP have limited the use of ERCP, which is an invasive procedure with risks of morbidity and mortality. However, ERCP continues to maintain its place as an important diagnostic tool in these patients, since it allows both diagnosis and treatment. Carrying out cystic duct cannulation and stone extraction from remnant pouch or cystic duct is difficult. Therefore, ERCP is more useful in patients with choledocholithiasis with a remnant gallbladder. Therefore, ERCP is more useful in patients with choledocholithiasis with remnant gallbladder. In our study, ERCP was performed in six patients (54.5%). However, only two of these patients had cystic channels.

The choice of treatment in post-cholecystectomy syndrome depends entirely on the etiological cause. Diagnosis and management of calculi, which is localized in the remnant gallbladder, can be challenging. Most of the patients with retained calculi require surgical intervention. If the stone is formed in the remnant sac and is symptomatic; carcinoma, recurrent cholangitis attacks, mucocele formation, recurrent choledocholithiasis and Mirizzi syndrome are present, then complementary cholecystectomy recommended for pathologies such as morbidity and mortality. We conclude that complementary cholecystectomy can be performed by an open or laparoscopic method, depending on the experience of the surgical team and the clinic. After partial cholecystectomy, the cystic duct and Calot's triangle are usually embedded in the inflamed dense adhesion. Because of this, there is a high risk in these cases when re-operated laparoscopically. The preferred method for complementary cholecystectomy in our clinic is to start with laparoscopy. For this reason, seven of our patients were laparoscopically treated, and four of them underwent complementary cholecystectomy.

Although laparoscopic completion cholecystectomy is difficult and risky, it is not impossible with advances in laparoscopic instruments and sealing devices. Nowadays, it is found that laparoscopic cholecystectomy is safe and feasible in excising residual gallbladder. Chowbey et al. in their case series on laparoscopic management of residual gallstones reported that 26 patients underwent a revision or laparoscopic completion cholecystectomy for residual gallstones disease. Out of these, laparoscopic excision of gallbladder remnant was performed in three patients, and excision of cystic duct stump with stone was performed in 18 patients. A formal laparoscopic cholecystectomy was performed in 5 patients who had previously undergone cholecystectomy and cholecystolithotomy (8). Parmar et al. reported that all 40 patients were managed by laparoscopic excision of gallbladder remnant, except for two patients who required conversion to open surgery. These two patients required conversion due to severe dense adhesions (12). The incidence of stones in the sac was higher in patients with RGB size, and it was observed that the duration of symptoms was shorter. For this reason, the size of the sac that is left behind affects the treatment method. Stone extraction and sphincterotomy were performed with ERCP in three of four patients who did not have stones in the RGB. In the other patient, ERCP was performed with the suspicion of stone, despite the absence of stones in the choledoch, and only the sphincterotomy was performed. It is now suggested that it is safe and feasible to remove the gallbladder or gallbladder remnants in such patients laparoscopically (32). Despite some previously reported contrary opinions, the laparoscopic approach to reoperations on the biliary tract appears to be a minimally invasive, safe, feasible, and effective procedure when done by expert laparoscopic surgeons (33). In 9 of our patients, remnant gallbladder extraction was started laparoscopically and 2 of them were started by direct open surgery. Six of 9 patients who underwent laparoscopic surgery had to undergo open surgery. Although it is reported in the literature that reoperations can be performed safely with laparoscopy, the surgeons should not hesitate to switch to open surgery in these patients because of the high rate of vascular and/or main bile duct injuries. For this reason, only 3 of our patients were able to complete the reoperation laparoscopically. Limiting aspects of our study include its retrospective nature, a small sample size, and operations performed by multiple surgeons. Nevertheless, keeping this rare pathology in mind might help in the differential diagnosis of various problems that occur after cholecystectomies.

CONCLUSION

In patients presenting with similar symptoms before cholecystectomy and the remnant gallbladder diagnosis should be considered. Laparoscopic re-exploration should be the first choice in the surgical treatment plan because of advantages such as acceptable revision and short hospital stay. However, a multidisciplinary approach, including the selection of imaging methods and surgical and endoscopic treatment methods, is important for the success of treatment.

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