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A SELF-TEST ON A CLINICAL CASE

Recurrent abdominal pain after laparoscopic cholecystectomy

Four months after undergoing laparoscopic cholecystectomy for symptomatic gallstones, an otherwise healthy 26-year-old woman begins to have episodes of epigastric and back pain similar to what she experienced before the surgery. The surgery was without complications, and her classic biliary colic disappeared afterward. Histologic evaluation of the surgical specimen revealed chronic cholecystitis with multiple small, mixed gallstones.

Now she describes a burning pain in her epigastrium and mid to upper back, starting about 30 minutes after a meal and lasting up to 4 hours. Sometimes it awakens her at night. She avoids eating for fear of inducing the pain. She has occasional chills but no fever, nausea, vomiting, jaundice, or changes in urine or stool color.

Three years ago she was diagnosed with a gastric ulcer induced by taking a nonsteroidal anti-inflammatory drug (NSAID). The ulcer was treated with a proton pump inhibitor for 1 month. She says the ulcer pain was dull and aching, different from her current pain.

Upper endoscopy 4 months ago (ie, before her laparoscopic cholecystectomy) showed no evidence of esophagitis or peptic ulcer disease.

Apart from her gallbladder operation, she has had no other surgery. According to the surgeon's notes, intraoperative cholangiography was not performed, and no macroscopic changes of acute cholecystitis or difficult biliary anatomy were noted.

The patient does not smoke, does not drink alcohol, is not currently taking any medications, including NSAIDs or over-the-counter medications, and has not taken any recently. Her mother also had symptomatic gallstones requiring cholecystectomy.

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On physical examination, only fever

On examination, her temperature is 101.2°F (38.4°C), blood pressure 117/80 mm Hg, heart rate 82 beats per minute, and blood oxygen saturation 99% on room air. Her weight is 138 lb (62.6 kg), height 5 feet 6 inches (168 cm).

There is no jaundice or pallor. Her heart and lung examinations are normal.

Her abdomen is soft and mildly tender to palpation of the epigastrium, with no distention or hepatosplenomegaly and no rebound tenderness or guarding. The scars from her laparoscopic surgery have healed well. Her bowel sounds are normal.

No costovertebral angle or spinal tenderness can be elicited.

Her laboratory values are shown in TABLE 1.

Four months after gallbladder surgery, her pain is back. Why?

POSTCHOLECYSTECTOMY SYNDROME

1 After cholecystectomy, preoperative symptoms recur in what percentage of patients?

- ☐ 10% to 40%
- ☐ 50%
- ☐ 60%
- ☐ 80%

Postcholecystectomy syndrome—the recurrence of symptoms similar to those before the procedure—occurs in 10% to 40% of patients. The time to the onset of symptoms can range from 2 days to up to 25 years.[1–4] Women may be at higher risk, with symptoms recurring in 43% vs 28% in men.[5]

Postcholecystectomy syndrome can have

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TABLE 1

Her laboratory values before laparoscopic cholecystectomy and now, 4 months later

	PREOPERATIVE	CURRENT	REFERENCE RANGE
White blood cell count	8.04	8.83	3.7–11.0 × 10^9/L
Neutrophils		69.5	39.5%–74.0%
Hemoglobin	12.5	13.2	11.5–15.5 g/dL
Hematocrit	37.9	39.8	36.0%–46.0%
Platelet count	401	373	150–400 × 10^9/L
Protein, total	7.3	7.2	6–8.4 g/dL
Albumin	4.7	5	3.5–5 g/dL
Calcium	9.8	9.6	8.5–10.5 mg/dL
Bilirubin, total	0.7	2.4	0.0–1.5 mg/dL
Alkaline phosphatase	42	99	40–150 U/L
Aspartate aminotransferase	28	274	7–40 U/L
Alanine aminotransferase	63	391	0–45 U/L
Amylase	59	44	0–137 U/L
Lipase	58	31	12–70 U/L
Glucose	86	96	75–100 mg/dL
Blood urea nitrogen	13	11	8–25 mg/dL
Creatinine	0.69	0.59	0.7–1.4 mg/dL

a biliary or a nonbiliary cause. Biliary causes include strictures, retained calculi, dropped calculi, tumors, sphincter of Oddi dysfunction, and calculi in the cystic duct remnant. Nonbiliary causes include functional and organic disorders such as peptic ulcer disease, gastroesophageal reflux, pancreatic disease, hepatocellular disorders, coronary artery disease, irritable bowel syndrome, and intercostal neuritis.

WHAT IS THE NEXT STEP?

2 Which is the most appropriate next step in the workup of this patient?

- ☐ Ultrasonography of the right upper quadrant
- ☐ Magnetic resonance cholangiopancreatography (MRCP)
- ☐ Endoscopic retrograde cholangiopancreatography (ERCP)
- ☐ Observation and reassurance
- ☐ Review the operative record and consult with the surgeon

Although the patient is presenting with pain and fever, two features of the classic Charcot triad (pain, fever, jaundice) seen in cholangitis (infection of a bile duct), and although cholangitis almost confirms the diagnosis of common bile duct stones in a patient with gallstones (before or after cholecystectomy), other diagnoses to consider are bile duct injury, bile leak, and biloma.

Biloma can be detected with ultrasonography. Bile duct injuries are identified intraoperatively in up to 25% of patients. For those with an unrecognized injury, the clinical presentation is variable and depends on the type of injury. If a bile leak is present, patients present early, at a median of 3 days postoperatively. However, our patient presented with symptoms 4 months after her surgery. Patients with bile duct strictures without bile leak have a longer symptom-free interval and usually present with signs of biliary obstruction. Ultrasonography can then detect biliary dilatation.[6]

It would be very helpful to review the operative record and to talk to the surgeon to confirm that intraoperative cholangiography had not been done and to determine the level of difficulty of the surgery. (Intraoperative cholangiography involves the introduction of contrast dye into the biliary system by cannulation of the cystic duct or by direct injection into the common bile duct. An intraoperative cholangiogram is considered normal if the entire intrahepatic and extrahepatic biliary tree is seen to be filled with contrast.) A normal cholangiogram has a negative predictive value of 99.8% for the detection of ductal stones. Thus, a normal intraoperative cholangiogram can prevent unnecessary postoperative ECRP, since it almost always indicates a clean bile duct.[7]

Ultrasonography of the right upper quadrant has a low sensitivity (< 50%) for detecting common bile duct stones. However, it is highly operator-dependent, and it may be twice as sensitive if done by expert radiologists than by less experienced ones. Its limitations include poor visualization of the distal portion of the duct and low sensitivity in patients in whom the common bile duct is minimally di-

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lated and also in patients with small stones. In most studies, however, it had a very high specificity—ie, greater than 95%.[8]

MRCP has a sensitivity of 82.6% and a specificity of 97.5% in detecting stones in the common bile duct.[9] Therefore, normal results on abdominal ultrasonography and MRCP do not completely rule out stones.

Although this patient has a high pretest probability of having common bile duct stones, ERCP should be done only after a thorough review of the previous operative procedure.

Observation and reassurance are not appropriate in a patient with cholangitis, such as this patient, because waiting increases the risk of septicemia.

The patient undergoes ERCP with stone removal

Review of the operative report and discussion with the surgeon confirm that the laparoscopic procedure was uneventful and that intraoperative cholangiography was not done.

Therefore, the patient undergoes ERCP. The major papilla is normal. Cholangiography reveals nondilated common bile and intrahepatic ducts, with faint filling defects in the mid to distal common bile duct. Endoscopic sphincterotomy is performed, and three small stones are extracted from the common bile duct. Repeat balloon-occlusion cholangiography is normal.

The patient tolerates the procedure well and resumes a normal diet and normal activities.

Her pain persists, prompting an emergency room visit

Five days after her ERCP procedure, however, the same burning epigastric pain returns. As before, the pain occurs after eating and does not occur with fasting. At this time, she has no fever or chills.

The patient continues to have recurrent episodes of pain, on one occasion so severe she visits the emergency department. During this visit she reports she has no symptoms other than pain, and the examination is normal. Laboratory tests (TABLE 2) show that her liver function measures have normalized.

TABLE 2

Her laboratory values 5 days after endoscopic sphincterotomy and stone removal

	VALUE	REFERENCE RANGE
White blood cell count	8.58	3.7–11.0 × 10^9/L
Neutrophils	52.7	39.5%–74.0%
Hemoglobin	12.7	11.5–15.5 g/dL
Hematocrit	37.4	36.0%–46.0%
Platelet count	406	150–400 × 10^9/L
Bilirubin, total	1.2	0.0–1.5 mg/dL
Alkaline phosphatase	61	40–150 U/L
Aspartate aminotransferase	19	7–40 U/L
Alanine aminotransferase	30	0–45 U/L
Amylase	53	0–137 U/L
Lipase	45	12–70 U/L
Blood urea nitrogen	20	8–25 mg/dL
Creatinine	0.55	0.7–1.4 mg/dL

WHAT IS CAUSING HER PAIN?

3 Which is the most likely cause of her persistent pain?

- ☐ Acute pancreatitis after ERCP
- ☐ Peptic ulcer disease
- ☐ Sphincter of Oddi dysfunction
- ☐ Biliary stones

The laparoscopic procedure was deemed successful and was done without intraoperative cholangiography

The most likely cause is persistent biliary stones. The common bile duct was recently explored and stones were removed, but she may still have stones in the intrahepatic ducts or in the cystic duct remnant, both of which were unopacified during the ERCP procedure, indicating that either the test was incomplete or a stone is obstructing the passage of contrast. Her persistent symptoms warrant repeating her liver function tests.

Acute pancreatitis is the most common and feared complication of ERCP, and it should be suspected in any patient who develops abdominal pain within 6 hours of the procedure. It is much less likely to develop after 12 hours, however. Risk factors for post-ERCP pancreatitis include patient factors (young age, female sex, history of recurrent pancreatitis), procedural factors (difficult cannulation,

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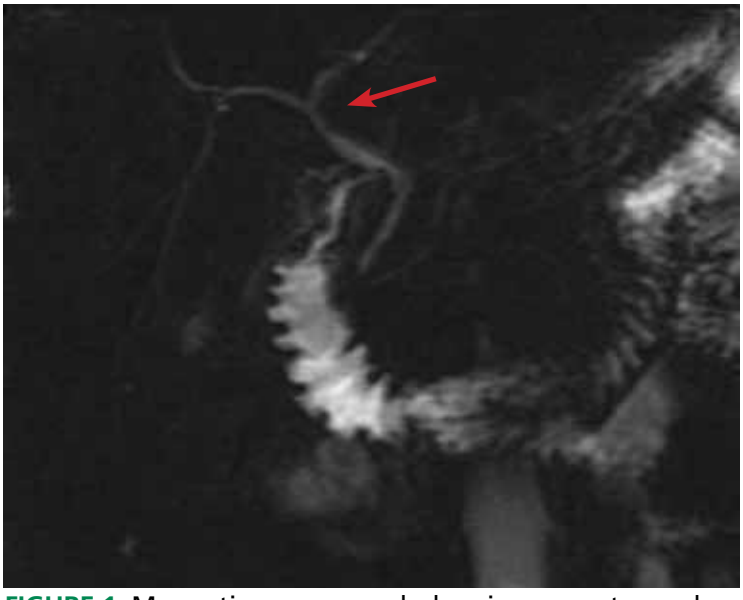


FIGURE 1. Magnetic resonance cholangiopancreatography shows a normal biliary tree (arrow) and pancreatic duct. The cystic duct cannot be seen.

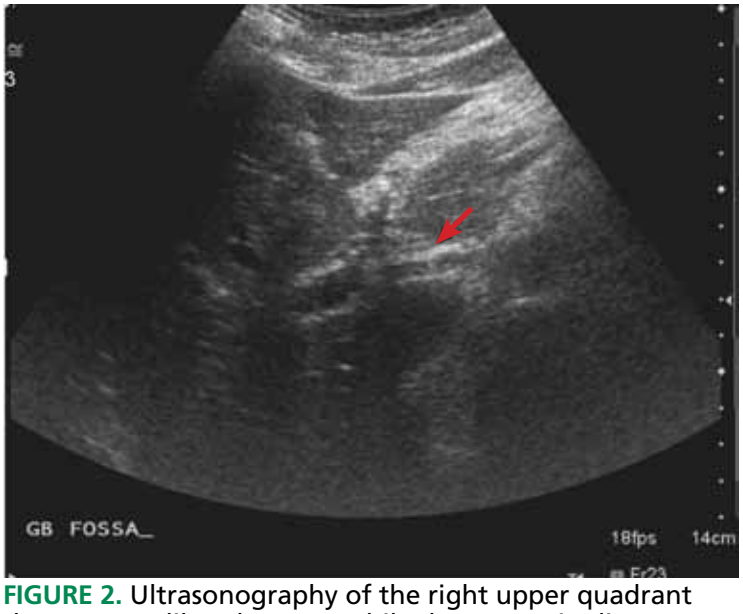


FIGURE 2. Ultrasonography of the right upper quadrant shows a nondilated common bile duct 4 mm in diameter (arrow). No stones are visible.

minor papilla sphincterotomy), and, less likely, operator-related factors.[10–13] In general, the more likely a patient is to have an abnormal and irregular common bile duct or pancreatic duct, the lower the risk of post-ERCP pancreatitis. The importance of operator-dependent factors is not yet clear.[10–13]

Despite the postprandial pattern of our patient's pain and her history of gastric ulcer, peptic ulcer disease is unlikely in view of a normal esophagogastroduodenoscopic examination done 4 months earlier, and since she has no recent exposure to NSAIDs.

Sphincter of Oddi dysfunction may explain her symptoms, but she recently underwent endoscopic sphincterotomy, which is regarded as the most definitive treatment.[14]

WHAT SHOULD BE DONE NEXT?

4 What would be the best next step in her management?

- ☐ Repeat ERCP
- ☐ MRCP
- ☐ Endoscopic ultrasonography
- ☐ Observation and reassurance

MRCP is the most appropriate next step, given her recurrent symptoms. Repeat ERCP is not appropriate, since there is no evidence of cholangitis, and since her liver function tests had completely normalized.

A recent systematic review of endoscopic ultrasonography and MRCP for diagnosing choledocholithiasis found both tests to be highly accurate, with no statistically significant differences in sensitivity or specificity between the two.[15] However, MRCP has the advantage of being noninvasive and of being able to show intrahepatic stones.

Park et al,[16] in a prospective study of 66 patients with primary intrahepatic stones, concluded that MRCP findings were comparable to those of percutaneous transhepatic cholangioscopy, the reference standard for locating intrahepatic stones. The sensitivity, specificity, and accuracy of MRCP for detecting and locating intrahepatic stones were high (97%, 99%, and 98%, respectively).[16] However, after sphincterotomy, pneumobilia may create an appearance that can be mistaken for intraductal stones.

Merely reassuring the patient is not appropriate at this point, given her level of pain.

She undergoes MRCP

MRCP shows a normal biliary tree without stones (FIGURE 1). Similarly, ultrasonography of the right upper quadrant shows no stones and a nondilated common bile duct (FIGURE 2).

The patient continues to have pain, and

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she has lost 5 pounds because she is still avoiding eating. At this point, she is beginning to wonder if her symptoms are psychogenic, since all the test results have been normal.

ERCP, MRCP, ULTRASONOGRAPHY?

5 What would be the best next step?

- ☐ Reassurance
- ☐ Referral to a psychiatrist
- ☐ Referral to a pain management clinic
- ☐ Endoscopic ultrasonography
- ☐ Repeat ERCP

Endoscopic ultrasonography is needed to look for cystic duct stones. Although several tests have shown normal results, the patient's pain continues as in the previous episodes, making stone disease the most likely cause.

Although no stones were seen on MRCP and ultrasonography, a detailed evaluation for stones in a cystic duct or retained gallbladder remnant was not done satisfactorily.

Reassurance and referral to a psychiatrist or pain management clinic are not appropriate, since an organic cause of her pain has not been completely ruled out.

ERCP should not be used as a diagnostic test in a situation such as this.

Findings on endoscopic ultrasonography

Endoscopic ultrasonography is performed and reveals a large (7-mm) stone in the area of the cystic duct remnant or gallbladder remnant (FIGURE 3). The common bile duct is normal.

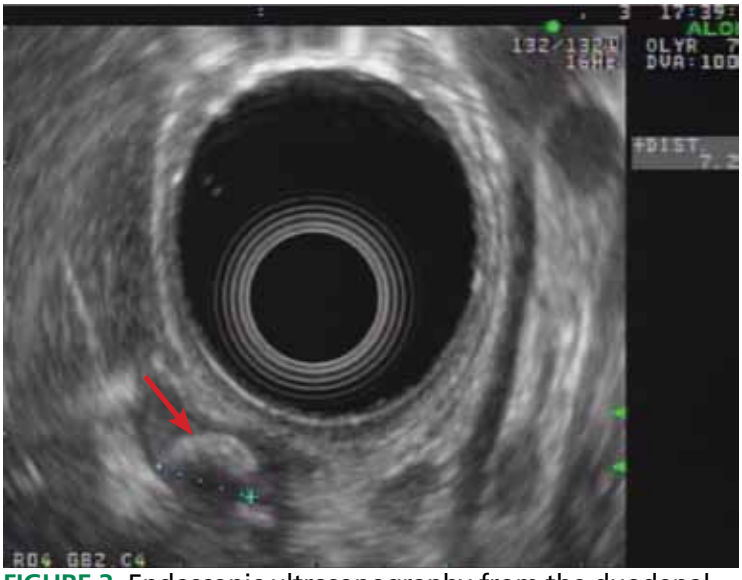


FIGURE 3. Endoscopic ultrasonography from the duodenal bulb shows a 7-mm stone (arrow) in the cystic duct remnant or gallbladder remnant.

CAUSES OF RETAINED GALLBLADDER AND CYSTIC DUCT REMNANT

6 What may have predisposed this patient to a retained gallbladder or cystic duct remnant after her surgery?

- ☐ Laparoscopic cholecystectomy
- ☐ Not doing intraoperative cholangiography
- ☐ Cholecystectomy for acute cholecystitis
- ☐ All of the above

All of the above may have contributed.

Postcholecystectomy syndrome can pose a diagnostic and therapeutic challenge, as in our patient. Although it has been reported since the advent of the operation, it is more common after laparoscopic cholecystectomy than after open surgery. One possible cause is stones in a cystic duct remnant, ie, a stub longer than 1 cm.

During open cholecystectomy, the cystic duct is ligated and cut as close to the common bile duct as possible, leaving only a small remnant. In laparoscopic cholecystectomy, it is divided closer to the gallbladder to avoid iatrogenic injury to the common bile duct, leaving a longer remnant. A long cystic duct remnant can be prevented by accurately locating the junction of the gallbladder and the cystic duct during cholecystectomy and by routinely doing intraoperative cholangiography. The presence of stones in a cystic duct or retained gallbladder remnant is a rare cause of postcholecystectomy syndrome, and suspicion is required to make the diagnosis.[17–19]

Only 5 days after ERCP with stone removal, her symptoms return

We should note that stones may also lurk in the short cystic duct remnant left after open cholecystectomy. In fact, the first case of cystic duct remnant, the so-called reformed gallbladder containing stones, was described in 1912 by Flörcken.[20]

Intraoperative cholangiography was introduced in 1931 by Mirizzi,[21] who recommended its routine use. Since the advent of laparoscopic cholecystectomy in 1988, the routine use of intraoperative cholangiography has been debated. Advocates point to its ability

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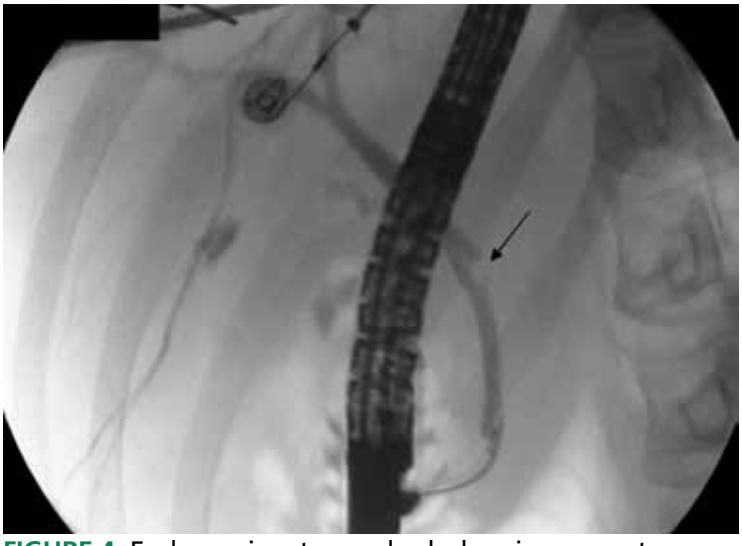


FIGURE 4. Endoscopic retrograde cholangiopancreatography shows an oval filling defect in the cystic duct remnant at its insertion into the common bile duct (arrow).

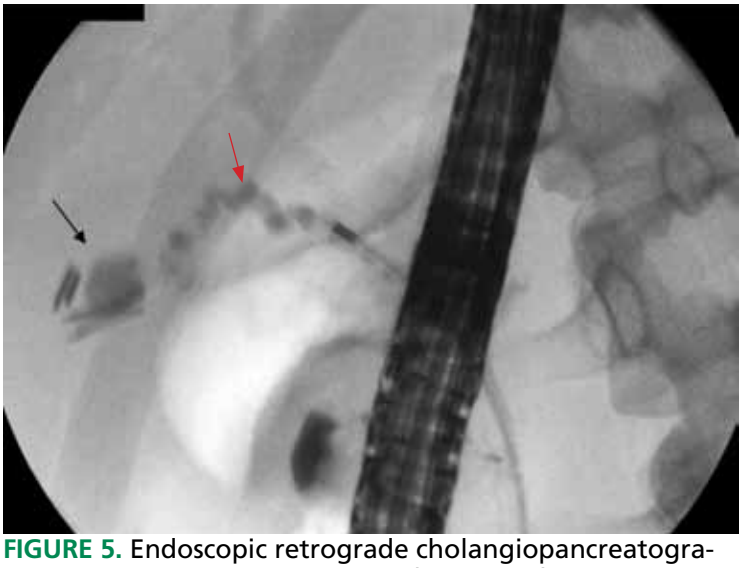


FIGURE 5. Endoscopic retrograde cholangiopancreatography reveals a long duct remnant (red arrow) and a small gallbladder remnant (black arrow). The stone has already been extracted.

to detect unsuspected calculi and to delineate the biliary anatomy, thus reducing the risk of biliary duct injury.[7,22–25] Those who argue against its routine use emphasize the low reported rates of unsuspected stones in the common bile duct (2% to 3%), a longer operative time, the additional cost, and false-positive results that may lead to unnecessary common bile duct exploration. Another argument against its routine use is that most small ductal stones pass spontaneously without significant sequelae.[26–28] Surgeons who use intraoperative cholangiography only selectively use it in patients with unclear biliary anatomy and preoperative biochemical or radiologic evidence of choledocholithiasis.

Another potential explanation for the retained gallbladder remnant is that the cholecystectomy was done while the patient had acute cholecystitis, in which inflammation may obscure anatomic landmarks. Hence, cholangiography during laparoscopic cholecystectomy has been widely recognized as a means of delineating the biliary anatomy.

Case continued: She undergoes repeat ERCP

The patient undergoes ERCP again (FIGURE 4 and FIGURE 5). Cholangiography shows a normal common bile duct with low insertion of the cystic duct and an oval filling defect in the cystic duct just proximal to its insertion into the common bile duct. Cystic duct opacification reveals a long cystic duct remnant and a small gallbladder remnant. The stone in the cystic duct is successfully removed.

IF STONES ARE DIFFICULT TO EXTRACT

7 If the cystic duct stone were not amenable to endoscopic extraction, what would be the best alternative?

- ☐ Extracorporeal shock-wave lithotripsy (ESWL)
- ☐ Endoscopic biliary laser lithotripsy
- ☐ Repeat laparoscopic cholecystectomy
- ☐ All of the above

All of the above are alternatives.

A symptomatic stone in a cystic duct remnant is uncommon and is mentioned in the literature only in case series and case reports.

ESWL is effective for treating bile duct calculi.[29] In a cohort of 239 patients with bile duct stones treated by ESWL, Benninger et al[30] concluded that endoscopy plus ESWL was a definitive treatment for all patients except one, who subsequently underwent cholecystectomy. Once fragmented, the stones are extracted endoscopically.

Another fragmentation technique that can be offered to patients with stones in the cystic duct that are difficult to extract is contact fragmentation with a holmium laser placed in a

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transpapillary position under visual guidance.[17]

Repeat cholecystectomy with removal of stones in the cystic duct remnant (and removal of retained gallbladder remnants and reduction of the cystic duct remnant) has good postoperative results.[17,18,31,32]

After incomplete cholecystectomy, the cystic duct remnant and the Calot (cystohepatic) triangle are surrounded by inflamed scar tissue, and this was thought to make laparoscopic reoperation difficult.[33] However, with advances in surgical technique and increasing experience of surgeons, repeat cholecystectomy can be done laparoscopically. It has now been suggested that laparoscopic exploration to remove the gallbladder remnants is safe and feasible in such patients.[34,35]

Discharge and follow-up

The patient is discharged home after the procedure. She is still free of symptoms 31 months later.

LESSONS LEARNED

Remnant cystic duct stones are uncommon

The estimated incidence of a retained calculus within the cystic duct remnant after cholecystectomy is less than 2.5%.[2,36] In a series of 322 patients who underwent repeat surgery because of postcholecystectomy syndrome, Rogy et al[36] found only 8 who had a stone in the cystic duct or gallbladder remnant, and in a series of 371 patients, Zhou el al[2] found 4 who had a stone in the cystic duct remnant.

Stones in the cystic duct remnant are difficult to diagnose

Diagnosing stones in surgical remnants of the cystic duct or gallbladder can be difficult. The sensitivity of abdominal ultrasonography in detecting cystic duct stones is low—only 27% in one study, with a specificity of 100% and an accuracy of 75%.[37] Ultrasonography may occasionally suggest cystic duct stones by showing an acoustic shadow in the anatomic region of the cystic duct. However, the results should be interpreted with caution.

Determining the accuracy of ERCP and MRCP in detecting cystic duct remnant stones is also difficult, as few cases have been reported and data may be conflicting. In a review of seven patients confirmed to have retained stones in a surgical remnant, Walsh et al[17] found that ERCP correctly diagnosed the retained stone in only four out of six patients; MRCP was done in one patient, and it was read as normal.

In three cases of stones in a postsurgical gallbladder remnant, Hassan and Vilmann[38] reported that ERCP and MRCP failed to identify the gallbladder remnant in two out of three cases, likely because the remaining structures are small. The diagnosis was finally made by endoscopic ultrasonography, which the authors concluded was a valuable method to visualize a small gallbladder remnant with stones.

Greater suspicion is needed in patients with typical biliary colic after cholecystectomy

Retained gallbladder remnant is described in the literature as a latent complication. The main problem is not the remnant itself but the chance that it harbors retained stones, which can lead to dilatation and inflammation of the remnant.

The patient can develop symptoms of acute cholecystitis or even acute cholangitis if the stone migrates to the common bile duct. Symptoms can develop as early as 2 weeks or as late as 25 years after laparoscopic cholecystectomy.

Endoscopic ultrasonography may be the best way to look for these remnant stones and to evaluate the bile duct and pancreas. Therefore, it should be part of the diagnostic algorithm in the evaluation of postcholecystectomy pain.

Acute pancreatitis is the most common and feared complication of ERCP

Mixed results with ERCP for extracting cystic duct stones

In case reports of cystic duct calculi after cholecystectomy, ERCP by itself has had mixed results. This traditional means of removing stones may succeed, as in our case. However, the success rate depends largely on anatomic factors such as the position of the stone in the cystic duct, the degree of stone impaction, the diameter of the cystic duct, and the number of valves in the duct.[17]

Stones in the cystic duct that cannot be extracted with ERCP may benefit from fragmentation techniques in situ via holmium laser followed by endoscopic extraction.

Repeat cholecystectomy is generally advised for any residual gallbladder, and it can be done laparoscopically. ■

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