Prospective Evaluation of Endoscopic Ultrasonography in the Diagnosis of Biliary Microlithiasis in Patients With Normal Transabdominal Ultrasonography

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Prior investigators have proposed microlithiasis as a causative factor for occult gallbladder diseases. Endoscopic ultrasonography (EUS) is potentially far more sensitive than transabdominal ultrasonography (TUS) in visualizing small stones. The aim of this study was to investigate the role of endoscopic ultrasonography (EUS) in the diagnosis of microlithiasis in patients with upper abdominal pain and normal TUS. Thirty-five patients with biliary-type abdominal pain and normal TUS results were prospectively studied. All patients underwent radial EUS by means of a GF UM-20 echoendoscope (Olympus Optical, Tokyo, Japan). Of 35 patients, 33 were revealed to have gallbladder sludge or small stones, and 21 had CBD sludge or microlithiasis. Nine patients were not available for follow-up; of the remaining patients, 13 underwent combined endoscopic biliary sphincterotomy and cholecystectomy, 10 underwent cholecystectomy, and 3 underwent biliary sphincterotomy alone. In a postoperative follow-up at 9.2 months, 25 patients (96.2%) were symptom free. EUS is an important diagnostic tool in patients with unexplained biliary colic. Cholecystectomy with or without EUS is an effective treatment modality in these settings. (J GASTROINTEST SURG 2005;9:961–964)

KEY WORDS: Endoscopic ultrasonography, microlithiasis, transabdominal ultrasonography

Most people with gallstones are clinically asymptomatic. The most common symptom of gallstones is intermittent epigastric or right upper quadrant pain, probably caused by stone impaction in the cystic duct. This biliary pain is generally a steady pain that can last for several hours. Multiple etiologic factors have been proposed for biliary-type abdominal pain. Determining the etiology is of utmost importance because it helps to direct therapy, limits further unnecessary tests, and may improve a patient's long-term prognosis.[1]

Patients with cholelithiasis are more likely to become symptomatic when they have microlithiasis; this is particularly true because they are more likely to develop choledocholithiasis and associated severe complications such as pancreatitis and cholangitis.[2] Microlithiasis is referred to as sludge, biliary sand, biliary sediment, microcrystalline disease, pseudolithiasis, and reversible cholelithiasis.[1] Although prior investigators have raised controversies about the true definition of microlithiasis, most refer to microlithiasis as stones of less than 3 mm in diameter.[3,4]

The sensitivity of transabdominal ultrasonography (TUS) for the diagnosis of microlithiasis is limited to 50%–60%.[1] This may be even less in obese patients and those with an ileus due to acute illness. The gold standard imaging method for diagnosis of common bile duct (CBD) stone is endoscopic retrograde cholangiopancreatography (ERCP), which has the advantage of permitting intervention if stones are

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present,[5] but it is invasive and may cause complications such as pancreatitis. Furthermore, very small stones may be missed on ERCP. Therefore, it is desirable to confirm the presence of CBD stones before embarking upon an ERCP. The two most widely used techniques for detecting microlithiasis are endoscopic ultrasonography (EUS) and bile microscopy. Microscopy of the aspirated bile from the gallbladder or CBD is a relatively invasive procedure, and microscopic examination of duodenal bile for diagnosis of microlithiasis has low sensitivity (~65%).[6] Contrary to bile microscopy, EUS is less invasive and has been shown to have a high positive predictive value for unexplained upper abdominal pain.[7] On the other hand, EUS minimizes the influence of bowel gas or subcutaneous tissue on image quality and produces higher image resolution with a better sensitivity (nearly 95%) for the diagnosis of microlithiasis.[6,8]

The aim of this study was to prospectively evaluate the role of EUS in the diagnosis and management of acute biliary-type upper abdominal pain in patients with clinical diagnosis of microlithiasis but normal TUS results.

PATIENTS AND METHODS

From January 2001 to September 2003, 80 consecutive patients with acute biliary-type abdominal pain were referred to the emergency department of a tertiary referral hospital in Tehran, Iran. Initial evaluation, including a comprehensive history, physical examination, and routine laboratory tests (complete blood cell count, prothrombin time, liver function tests, and blood biochemistry), was performed shortly after admission. Meanwhile, conventional TUS was performed on all patients by expert radiologists with 2- to 4-MHz TUS probes. The initial scan was usually performed during the acute illness; however, if no stones were identified or if unsatisfactory biliary scans were obtained, ultrasonography was repeated once. Of 80 patients, 45 were found to have acute pancreatitis based on acute abdominal pain and a serum amylase level greater than three times the upper limit of normal (normal <110 U/L). They were not included in our study. For the remaining 35 patients in whom our initial evaluation as well as TUS and upper gastrointestinal endoscopy failed to reveal any definite diagnosis, further investigations were requested. These patients were scheduled for radial EUS using a GF UM-20 echoendoscope (Olympus Optical, Tokyo, Japan).

The examination was performed with the patient in the left lateral decubitus position under mild intravenous sedation with midazolam. The patient was closely monitored during the procedure using pulse oximetry in addition to clinical observation. US images of gallbladder and bile duct were obtained with the instrument placed in the first and second parts of duodenum and at the level of the distal antrum and pylorus. Biliary tract images were obtained at different angles by adjusting the position of the probe. The presence of stones or microlithiasis was noted, as was the presence of other pathologies. Stones were identified as hyperechoic structures casting an acoustic shadow. Hyperechoic, rather mobile images with or without posterior acoustic shadow were considered to be sludge or microlithiasis, based on standard US criteria.[9] The normal range of thickness of the gallbladder wall on EUS was considered to be 3 mm, and the diameter of the CBD, 6 mm or less.

Patients with biliary microlithiasis or gallbladder wall thickness on EUS were offered cholecystectomy. Preoperative ERCP and biliary sphincterotomy was also achieved for patients with dilated CBD, sludge in CBD, or increased level of alkaline phosphatase (ALP). However, in a few patients who refused or were considered unsuitable for cholecystectomy, biliary sphincterotomy was the only therapeutic approach. Cholecystectomy was performed laparoscopically in all except one who underwent open surgery. All patients were closely followed for recurrence of symptoms after the therapy.

Informed consent for the study and the endoscopic procedures was obtained from all patients. The study protocol was approved by the ethics committee of the Digestive Disease Research Center, Tehran University of Medical Sciences.

RESULTS

The study population included 14 males and 21 females with the mean ± SD age of 47.7 ± 13.1 years. EUS was performed successfully in all patients. EUS findings are summarized in Table 1 according to gender.

Table 1. Endosonographic findings in 35 patients with acute biliary-type abdominal pain and normal transabdominal ultrasonography according to gender

Endosonographic findings	Males (n = 14)	Females (n = 21)	Total (n = 35)
Gallbladder sludge/ small stones	12	21	33 (94.3%)
Gallbladder wall thickness	6	18	24 (68.6%)
Common bile duct sludge/small stones	3	18	21 (60%)
Dilated common bile duct (>6 mm)	0	3	3 (8.6%)

Gallbladder sludge and/or microlithiasis was evident in 33 (94.3%) patients as hyperechoic specks of calcification, with or without posterior acoustic shadowing readily distinguishable from the hypoechoic contents of normal gallbladder; among these, 20 patients had also thick-wall gallbladder.

Sludge and/or microlithiasis of the CBD was noted in 21 patients. Among them, 18 patients had normal CBD diameter and in 3, the diameter was greater than 6 mm.

Nine patients were dropped during the follow-up; of the remaining 26 patients (11 males and 15 females) were followed for an average of 9.2 months (range, 3–13 months). Of 26 patients, 4 (15.4%) were found to have elevated serum ALP levels and 3 (11.5%) had elevated aspartate aminotransferase and alanine aminotransferase levels.

Combined endoscopic biliary sphincterotomy and cholecystectomy was achieved in 13 (50%) patients. Ten patients (38.5%) underwent cholecystectomy alone, and 3 (11.5%) underwent biliary sphincterotomy alone.

ERCP with sphincterotomy was performed successfully in all 16 patients. Histology of all removed gallbladders revealed chronic cholecystitis. Meanwhile, cholestrolosis was found in three cases, of which two were verified by EUS prior to the surgery.

At the end of the follow-up, 25 (96.2%) patients remained symptom free. Types of therapeutic procedure and patient outcomes are shown in Table 2.

DISCUSSION

Evaluation of pancreatobiliary diseases continues to evolve as new diagnostic modalities are developed. EUS, a fairly recent development in biliary-tract imaging, has been proved to be a minimally invasive technique with a low morbidity and proven efficacy in the diagnosis of gallbladder and pancreas diseases.

Table 2. Types of therapeutic procedures and treatment outcomes in 26 patients who were followed after treatment

Type of treatment	No. of patients	Mean duration of follow-up ± SD (months)	No. (%) of responding patients*
Cholecystectomy alone	10	10.3 ± 1	10 (100)
Cholecystectomy plus ES	13	8.5 ± 3.2	12 (92)
ES alone	3	8 ± 3.5	3 (100)
Total	26	9.2 ± 2.6	25 (96.2)

ES = endoscopic biliary sphincterotomy.
*Number (%) of patients who became symptom free after the procedure was performed.

Lithiasis of the CBD and gallbladder is a frequent complication. The biochemical abnormalities and symptoms associated with these complications are neither sensitive nor sufficiently specific. The inadequacies of TUS and computed tomography for the diagnosis of microcholedocholithiasis and microcholelithiasis are now well known.[1] EUS, with its high-image resolution and close proximity to the biliary system during the examination, is considered to be superior to TUS for gallbladder imaging.

Patients presenting with recurrent biliary-type abdominal pain in whom conventional TUS is negative present a clinical challenge. These patients frequently undergo a wide range of different examinations in order to exclude choledocholithiasis, biliary dyskinesia, chronic pancreatitis, and peptic ulcer disease. These examinations may not only impose high expenses on the patients and society but also be associated with an increased risk of mortality and morbidity.

For patients with acute recurrent pancreatitis, the role of EUS for diagnosing microlithiasis of the gallbladder or CBD is obviously established.[10,11] Although the role of microlithiasis as a cause of acute recurrent pancreatitis[1,9,12] or idiopathic acute cholangitis[13] has been well established, to our knowledge there is only one study that has shown that EUS can identify biliary microlithiasis in patients with biliary-type pain and normal TUS.[8]

In the present study, EUS revealed microlithiasis or sludge in gallbladder in 33 of 35 examined patients. Choledocholithiasis was found in 20 patients. Following the therapeutic approaches, 96% of the patients became symptom free, a figure similar to the previous study regarding biliary pain due to microlithiasis.[8] Our study clearly supports the great value of EUS in the detection of cholelithiasis and choledocholithiasis in patients with negative TUS results.

Microscopic examination of bile also has been suggested for the diagnosis of microlithiasis. Bile microscopy is a relatively invasive procedure with an overall sensitivity of 65%–90%.[1] Its diagnostic yield varies with respect to the site of bile aspiration—greatest when bile is collected from the gallbladder and lowest when it is collected from the duodenum. In contrast to bile microscopy, EUS is less invasive and can accurately diagnose biliary microlithiasis. Thus, we believe that EUS is the best diagnostic method in patients who have biliary-type pain with normal TUS results and suspected microlithiasis.

Some critical points should be considered regarding our study. First, there may be a possible bias in selecting the patients. Another possibility of bias is that the EUS is an operator-dependent procedure.

Our small sample size should be kept in mind, but the major limitation probably is the fact that it was an uncontrolled trial. On the other hand, 13 patients underwent combined endoscopic biliary sphincterotomy/cholecystectomy, and it is unclear whether cholecystectomy alone was sufficient for these patients. However, despite these critical points, the high rate of response to the therapeutic procedures is in agreement with the effectiveness of our approach.

In summary, EUS seems to be a promising diagnostic modality in patients with a clinical suspicion of cholelithiasis and choledocholithiasis and a normal TUS results. Larger, long-term, controlled prospective studies are needed to form a better understanding of the role of EUS in detecting pathogenesis, clinical significance, and optimum form of therapy for patients with microlithiasis. In conclusion, in patients with biliary type abdominal pain and normal transabdominal ultrasonography, EUS is a useful diagnostic modality and it can influence the management plan.

REFERENCES

1. Levy MJ. The hunt for microlithiasis in idiopathic acute recurrent pancreatitis: should we abandon the search or intensify our efforts? Gastrointest Endosc 2002;55:286–293.
2. Janowits P, Kratzer W, Zemmler T, et al. Gallbladder sludge: spontaneous course and incidence of complications in patients without stones. Hepatology 1994;20:291–294.
3. Houssin D, Castaing D, Lemoine J, et al. Microlithiasis of the gallbladder. Surg Gyn Obstet 1983;157:20–24.
4. Sharma BC, Agarwal DK, Dhiman RK, et al. Bile lithogenicity and gallbladder emptying in patients with microlithiasis: effect of bile acid therapy. Gastroenterology 1998;115:124–128.
5. Venu RP, Geenen JE, Toouli J, et al. Endoscopic retrograde cholangiopancreatography. Diagnosis of cholelithiasis in patients with normal gallbladder x-ray and ultrasound studies. JAMA 1983;249:758–761.
6. Dahan P, Andant C, Levy P, et al. Prospective evaluation of endoscopic ultrasonography and microscopic examination of duodenal bile in the diagnosis of cholecystolithiasis in 45 patients with normal conventional ultrasonography. Gut 1996;38:277–281.
7. Dill JE, Dill BP. Quality of life outcomes following endoscopic ultrasound for dyspepsia/unexplained upper abdominal pain. Acta Endosc 2000;30:231–235.
8. Dill JE, Hill S, Callis J, et al. Combined endoscopic ultrasound and stimulated biliary drainage in cholecystitis and microlithiasis diagnosis and outcomes. Endoscopy 1995;27:424–427.
9. Ros E, Navarro S, Bru C, et al. Occult microlithiasis in idiopathic acute pancreatitis: prevention of relapses by cholecystectomy or ursodeoxycholic acid therapy. Gastroenterology 1991;101:1701–1709.
10. Liu CL, Lo CM, Chan JK, et al. EUS for detection of occult cholelithiasis in patients with idiopathic pancreatitis. Gastrointest Endosc 2000;51:28–32.
11. Frossard JL, Sossa-Valencia L, Amouyal G, et al. Usefulness of endoscopic ultrasonography in patients with idiopathic acute pancreatitis. Am J Med 2000;109:196–200.
12. Lee SP, Nicholls JF, Park HZ. Biliary sludge as a cause of acute pancreatitis. N Engl J Med 1992;326:589–593.
13. Ko CW, Sekijima JH, Lee SP. Biliary sludge. Ann Intern Med 1999;130:301–311.