Endoscopically Obtained Bile Aspirate is an Accurate Adjunct in the Diagnosis of Symptomatic Gallbladder Disease

Kerrey B. Buser, MD

ABSTRACT

Objectives: The experience of a single surgeon in a rural hospital over a 10-year period was analyzed with respect to the utilization of endoscopically obtained bile aspirates as an adjunct in the diagnosis of symptomatic gallbladder disease.

Methods: A retrospective study of the author’s entire cholecystectomy experience over a 10-year period with 641 patients was conducted to evaluate the utility of the bile aspirate in the preoperative selection of operative candidates and with respect to the ultimate pathologic diagnostic accuracy of the test.

Results: Derivation of preoperative diagnosis via traditional standard means was possible in 479 patients. An endoscopically obtained positive bile aspirate was found in 162 additional patients who failed to have positive traditional diagnostic studies (acalculous gallbladder disease). Micro-pathology was determined to be present in 603 patients (94.07%). In 27 of the 38 negatives, there had been positive radiological studies (71%). In 11 of the 38, a positive preoperative bile aspirate had been obtained (28.9%). Of the 162 patients with a positive bile aspirate, 151 (93.21%) of the gallbladder specimens had confirmatory histologic analysis (92.1% confidence interval ± 3.95%).

Conclusion: In patients with symptoms suggestive of clinical gallbladder disease and negative traditional diagnostic studies, the endoscopically obtained bile aspirate has been shown to be a highly reliable tool in establishing the diagnosis and is recommended as an aid in the appropriate selection of candidates who may benefit from cholecystectomy.

Key Words: Acalculous, Endoscopic, Duodenal bile aspirate, Gallbladder disease.

INTRODUCTION

Patients offering symptom complexes and history and physical findings consistent with biliary colic or cholecystitis that have nondiagnostic traditional radiologic studies may represent cases of biliary dyskinesia or acalculous cholecystitis.1,2 Acalculous cholecystitis has been a somewhat controversial entity that accounts for 5% to 22% of cholecystectomies in some series.1,3,4

A high percentage of patients with impaired gallbladder ejection fraction (bile stasis or biliary dyskinesia) will have microcrystals in their gallbladder bile and pathologic evidence of chronic cholecystitis. The data suggest that a spectrum of biliary diseases exists in which bile saturation and gallbladder dysmotility lead to crystal growth, sludge formation, and subsequent chronic inflammation. Biliary pain may be generated at any point in this spectrum.5–7

Acalculous cholecystitis may precipitate disabling and, at times, potentially life-threatening complications, unrelated to macroscopic lithiasis. Acalculous cholecystitis may present at any age, including the pediatric group, which may be much more common than commonly believed and therefore underdiagnosed and insufficiently treated.7–22

Other abnormalities may be present that can be the cause of upper abdominal pain, bloating, nausea, and emesis. Such conditions as gastritis (infectious or nonspecific), pyloric dysfunction, enterogastric reflux, and peptic ulcer disease, among others, may occur individually or in combination with one another and with biliary tract disease. Duodenal bile has been shown to be abnormal in acalculous cholecystitis.13 The diagnostic dilemma can be sorted out via endoscopic examination combined with endoscopically obtained duodenal bile aspirate analysis.23–26 The Meltzer-Lyon test, easily performed in conjunction with the commonly performed esophagogastroduodenoscopy (EGD), is an efficient method to rule out other pathology and accurately diagnose acalculous cholecystitis.26

The microscopic examination of endoscopically obtained duodenal bile is nearly as reliable as microscopic examination of bile that has been aspirated directly from the
gallbladder (being qualitatively similar, but more dilute). 23,27,28

Bile aspirate microscopy has been utilized to assist in establishing the diagnosis of acalculous cholecystitis, and direct microscopy can be regarded as the diagnostic gold standard for biliary sludge. The presence of microcrystals and white blood cells are the essentials of a “positive” duodenal aspirate analysis. 8,15,17,20,25,29–31

Microlithiasis is very rarely found in examined bile from symptomatic postcholecystectomy patients (0.5% frequency), indicating that this is primarily a cholecystic phenomenon. 18,32

Many clinicians look only to radiologic means in diagnosing gallbladder disease. When these modalities are nondiagnostic but the patient’s symptoms suggest a gallbladder cause, the astute clinician should look further. 2,4,24

PATIENTS AND METHODS

The author’s experience as a single surgeon in a small rural hospital over a 10-year period was retrospectively analyzed with respect to the utilization of the endoscopically obtained duodenal bile aspirate as an adjunct in the diagnosis of symptomatic gallbladder disease.

Patients with abdominal symptoms suggestive of biliary dyskinesia, but with nondiagnostic traditional radiologic studies were evaluated via endoscopy to rule out other pathologic symptom sources and to obtain a bile aspirate if no other significant disease process was found.

At the time of endoscopy, a suction trap was utilized on the suction port of the endoscope. No suction was applied until the endoscope was in position within the duodenum adjacent to the ampulla of Vater. (This ensures that an accurate duodenal fluid sampling is obtained, without fluid contamination from other areas of the upper intestinal tract. If the duodenum is dry, a washing may be obtained that will provide a diluted but qualitatively accurate specimen).

A retrospective study of the author’s entire cholecystectomy experience between October 1995 and October 2005 with 641 patients was conducted. To evaluate the utility of the endoscopically obtained bile aspirate in the preoperative selection of operative candidates, the ultimate pathologic diagnostic results were correlated.

RESULTS

Derivation of preoperative diagnosis via traditional standard means was possible in 479 patients (74.7%). An endoscopically obtained positive duodenal bile aspirate was found in an additional 162 patients (25.3%), who were symptomatic of biliary disease but who failed to have positive traditional diagnostic studies.

Micropathology was determined to be present in 603 patients (94.07%). In the remaining 38 patients who had negative histologic findings, 27 (71%) had positive preoperative radiologic studies, while 11 (28.9%) had positive preoperative bile aspirates. In this group of negatives, it was more than twice as likely for a patient to have had a positive radiologic test versus a positive bile aspirate, preoperatively.

In the 162 patients with a positive bile aspirate, 151 (93.21%) had confirmatory micropathology (92.1% confidence interval, ± 3.95%). This compares favorably with the 94% positive rate reported in the literature. 2

In comparison, of the 479 patients diagnosed via traditional means, 452 patients had positive micropathology (94.36%), accounting for 75% of the total with proven pathology.

In this series, 151 of the subsequently proven pathologic gallbladders had been missed by traditional diagnostic endeavors, accounting for 23.56% of the 641 initially symptomatic suspects for disease and 25% of the total with proven disease (Figure 1).

Interestingly, 2 patients had negative ultrasonals, negative Hida scans, but positive bile aspirates and positive micropathology. There was even one patient who had a negative ultrasound, a negative Hida scan, a negative CAT scan, but a positive bile aspirate and positive micropathology.

There were 20 patients below the age of 19, (range 11 to 18 years). There was confirmatory micropathology in 17 (85%) of this group. One of the 3 negatives had a positive preoperative ultrasound. One of the remaining 2 negatives had a positive bile aspirate, classic right upper quadrant, and severe postprandial abdominal symptoms that had caused him to miss 3 out of the first 7 weeks of the fall school term. At operation, he was found to have dense adhesions on the gallbladder and a very tightly spiraled cystic duct. He successfully returned to school resuming a normal diet and activity status <1 week after the operation.

DISCUSSION

The literature suggests that patients with symptoms of biliary tract disease, but no gallstones on ultrasonography,
are more common than previously thought. Such patients may benefit from cholecystectomy for acalculous gallbladder disease, with a high degree of patient satisfaction achieved after such surgical therapy.1,2,4,24,25,30,33–37 Early diagnosis and cost containment are advantages of the endoscopically obtained bile aspirate analysis that results in appropriate and timely surgical intervention for what may be otherwise very diagnostically challenging patients.26

Our experience with endoscopically obtained bile aspirate has shown similar results and a high specificity of diagnostic-pathologic accuracy (93.21%). This represents excellent relative specificity for a diagnostic test that has the added value of accurately and simultaneously ruling out other common conditions that may share some symptoms with biliary dyskinesia or nonlithiasic cholecystic disease.

It is therefore felt that in our patients with symptoms suggestive of biliary pain or dyskinesia, but who had negative traditional studies, the duodenal bile aspirate analysis combined with the diagnostic capabilities of the EGD was demonstrated to be a successful and reliable tool in establishing the diagnosis of gallbladder disease, and was important in the selection of candidates for appropriate definitive therapy via cholecystectomy. It was a valuable tool in identifying the nearly 25% of symptomatic patients with provable gallbladder pathology who would have been otherwise missed or treatment delayed due to reliance solely on traditional diagnostic methods.

CONCLUSION

The endoscopically obtained duodenal bile aspirate is a very accurate adjunct in the preoperative diagnosis of symptomatic gallbladder disease and should be a standard part of every surgeon’s diagnostic acumen. Acalculous gallbladder disease remains a clinical diagnosis; however, that requires careful consideration and judgment by the surgeon involved with the care and treatment of this frequently underdiagnosed group of patients.

References

1. Brossenk D, Demetrik J. Laparoscopic cholecystectomy for symptoms of biliary colic in the absence of gallstones. Am J Surg. 2003 Jul;186(1):1–3.
2. Jones DB, Soper NJ, Brewer JD, et al. Chronic acalculous cholecystitis: laparoscopic treatment. Surg Laparosc Endosc. 1996 Apr;6(2):114–122.
3. Gomez NA, Roldos FE, Andrade RA, Rojas JE, Alvarez LR. Biliary sludge: a well defined sonographic entity. Acta Gastroenterol Latinoam. 1998;28(5):327–329.
4. Planells Roig M, Bueno Lledo J, Sanahuja Santafe A, Garcia Espinosa R. Quality of life (GIQLI) and laparoscopic cholecystectomy usefulness in patients with gallbladder dysfunction or chronic non-lithiasic biliary pain (chronic acalculous cholecystitis). Rev Esp Enferm Dig. 2004 Jul;96(7):442–446, 446–451. English, Spanish.
5. Velanovich V. Biliary dyskinesia and biliary crystals: a prospective study. Am Surg. 1997 Jan;63(1):69–74.
6. Lee SP. Pathogenesis of biliary sludge. Hepatology. 1990 Sep;12(3pt2):2008–2038, discussion 2038–2058.
7. Brugge WR, Brand DL, Atkins HL, Lane BP, Abel WG. Gallbladder dyskinesia in chronic acalculous cholecystitis. Dig Dis Sci. 1986 May;31(5):461–467.
8. Flati G, Flati D, Jonsson PE, et al. Role of cholesterol and calcium bilirubinate crystals in acute postoperative acalculous cholecystitis. Ital J Surg Sci. 1984;14(4):333–336.
9. Roslyn JJ, DenBesten L, Thompson JE, Silverman BF. Role of lithogenic bile and cystic duct occlusion in the pathogenesis of acute cholecystitis. Am J Surg. 1980 Jul;140(1):126–130.

Figure 1. Diagnostic/Treatment Pathway Results for 641 Patients Diagnosed with Clinical Gallbladder Disease.
10. Shafer AD, Ashly JV, Goowin CD, Naragas VN, Elliott D. A new look at the multifactorial etiology of gallbladder disease in children. *Am Surg.* 1983 June;49(6):314–319.
11. Frykberg ER, Duong TC, La Fosa JJ, Etienne HB. Chronic acalculous gallbladder disease: a clinical variant. *South Med J.* 1988 Nov;81(11):1353–1357.
12. Tousarskissian B, Kearney PA, Holley DT, Cheung R, Fried A, Strodel WE. Biliary sludging in critically ill trauma patients. *South Med J.* 1995 April;88(4):420–424.
13. Venkataramani A, Strong RM, Anderson DS, Gilmore IT, Stokes K, Hofman AF. Abnormal duodenal bile composition in patients with acalculous chronic cholecystitis. *Am J Gastroenterol.* 1998 Mar;93(3):434–441.
14. Trada M, Garzoli E, Fulzoni PU, et al. Abdominal pain in children: a case of acalculous cholecystitis. *Minerva Pediatr.* 2000 Apr;52(4):231–233.
15. Ponce J, Pons V, Sopena R, Garrigues V, Ponce M, Ortiz V, Pentejo V. Quantitative cholescintigraphy and bile abnormalities in patients with acalculous biliary pain. *Eur J Nucl Med Mol Imaging.* 2004 Aug;31(8):1160–1165.
16. Ko CW, Sekijima JH, Lee SP. Biliary sludge. *Ann Intern Med.* 1999 Feb;130(4 Pt 1):301–311.
17. Shaffer EA. Gallbladder sludge: what is its clinical significance? *Curr Gastroenterol Rep.* 2001 Apr;3(2):166–173.
18. Quallich LG, Stern MA, Rich M, Chey WD, Barnett JL, Elta GH. Bile duct crystals do not contribute to sphincter of Oddi dysfunction. *Gastrointest Endosc.* 2002 Feb;55(2):163–166.
19. Saraswat VA, Sharma BC, Agarwal DK, Kumar R, Negi TS, Tandon RK. Biliary microlithiasis in patients with idiopathic acute pancreatitis and unexplained biliary pain: response to therapy. *J Gastroenterol Hepatol.* 2005 Apr;20(4):399–501.
20. Pazzi P, Gamberini S, Buldrini P, Gullini S. Biliary sludge: the sluggish gallbladder. *Dig Liver Dis.* 2003 Jul;35 Suppl 3:S39–45.
21. Erdogmus B, Yazici B, Safak AA, Ozdere BA. Multiseptate gallbladder with acute acalculous cholecystitis. *J Clin Ultrasound.* 2004 Oct;32(8):423–424.
22. Croteau D, Signer RD, Chaet MS. Acalculus cholecystitis in a two year old. *JSLS.* 2001 Apr–June;5(2):183–185.
23. Realini S, Pertoldi W, Cereda W, Imbugia L. Usefulness of bile analysis collected via endoscopy in the diagnosis of microlithiasis and biliary sludge. *Schweiz Rundsch Med Prax.* 1994 Nov;83(45):1254–1255.
24. Dill JE, Hill S, Callis J, Berkhouser L, Evans P, Morton D, Palmer ST. Combined endoscopic ultrasound and stimulated biliary drainage in cholecystitis and microlithiasis - - diagnoses and outcomes. *Endoscopy.* 1995 Aug;27(6):424–427.
25. Sigman HH, Goldberg N, Niloff PH, Lachance C. Use of biliary drainage in diagnosis of biliary tract disease. *Am J Gastroenterol.* 1977 May;67(5):439–443.
26. Rossi AN, Rossi MB. Meltzer-Lyon test simultaneous with fiberoptic gastroroduodenoscopy. *Surg Gynecol Obstet.* 1983 Oct;157(4):378–379.
27. Agarwal DK, Choudhuri G, Saraswat VA, Negi TS, Kapoor VK, Saxena R. Duodenal bile examination in identifying potential non-responders to bile salt treatment and its comparison with gallbladder bile examination. *Gut.* 1994 Jan;35(1):112–130.
28. Choudhuri G, Agarwal DK, Saraswat VA, Negi TS, Saxena R, Kapoor VK. Is duodenal bile representative of gallbladder bile? A comparative study. *Scand J Gastroenterol.* 1995 Oct;28(10):920–923.
29. Landi K, Sinord J, Cranford JM, Topazian N. Cholesterol crystal morphology in acalculous gallbladder disease. *J Clin Gastroenterol.* 2003 Apr;36(4):364–366.
30. Moskovitz M, Min TC, Gavalier JS. The microscopic examination of bile in patients with biliary pain and negative imaging tests. *Am J Gastroenterol.* 1986 May;81(5):329–333.
31. Brugge WR, Brand DL, Atkins HL, Lane BP, Abel WG. Gallbladder dyskinesia in chronic acalculous cholecystitis. *Dig Dis Sci.* 1986 May;31(5):461–467.
32. Ko CW, Schulte SJ, Lee SP. Biliary sludge is formed by modification of hepatic bile by the gallbladder mucosa. *Clin Gastroenterol Hepatol.* 2005 Jul;3(7):672–678.
33. Adams DB, Tarnasky PR, Haven RH, et al. Outcome after laparoscopic cholecystectomy for chronic acalculous cholecystitis. *Am Surg.* 1998 Jan;64(1):1–5 discussion 5–6.
34. Jagannath SB, Singh VK, Cruz-Correa M, Canto MI, Kalloo AN. A long-term cohort study of outcome after cholecystectomy for chronic acalculous cholecystitis. *Am J Surg.* 2003 Feb;185(2):91–95.
35. Chen PF, Nimeri A, Pham QH, Yuh JN, Gusyjr JR, Chung RS. The clinical diagnosis of chronic acalculous cholecystitis. *Surgery.* 2001 Oct;130(4):578–581, discussion 581–583.
36. Jones-Monahan K, Gruenberg JC. Chronic acalculous cholecystitis: changes in patient demographics and evaluation since the advent of laparoscopy. *JSLS.* 1999 Jul-Sep;3(3):221–224.
37. Dwivedi A, Shetty A, Sanghavi P, Phan T, Lakra Y, Silva Y. Efficacy of laparoscopic cholecystectomy in acalculous gallbladder disease: long term follow-up. *JSLS.* 2004;8(2):119–122.