Gallbladder Dyskinesia in Children

Humberto L. Lugo-Vicente, MD

ABSTRACT

Background and Objectives: The purpose of this study was to describe clinico-pathological characteristics in a group of children with motility disorders of the gallbladder and correlate the findings with cases receiving surgical treatment for gallstone during the same period.

Methods: Retrospective chart analysis of all cholecystectomies from January, 1990 to June, 1995. Analysis of demographics, symptoms and duration, associated illnesses, diagnostic studies, pathological stratification, length of stay, complications, follow-up and patient satisfaction. Statistical comparison of clinical variables between gallstone and dyskinesia patients was analyzed using chi-square, and analysis of variance (ANOVA).

Results: Twelve children (14%) of 85 underwent laparoscopic cholecystectomy during a 66-month period for gallbladder dyskinesia. Their mean age was 14 ± 3 years (range 7 to 18). Ten patients were female and two were males for a 5:1 ratio. Classic biliary symptoms (RUQ abdominal pain and FFI) predominated for a mean of 48 weeks. A predisposing factor was previous family history of gallstones in five cases (42%). The diagnosis was obtained after gallbladder non-visualization in one child and low ejection fractions after CCK stimulated hepatobiliary scan studies in the remainder. Mean ejection fraction was 16.8%. Ten cases (83%) had mild to moderate chronic cholecystitis, and two children had unremarkable pathologic changes. These changes correlated with the mean duration of symptoms, not with ejection fraction volumes. After a mean follow-up of 17 months, 11 children are free of symptoms, and one continues with intermittent diarrhea. Comparison between calculous and dyskinesia patients showed that biliary dyskinesia children suffer more dyspepsia, undergo more diagnostic studies and have a significant family history of gallstones.

Conclusions: Gallbladder dyskinesia (GD) is a motility disorder causing symptoms similar to those of gallstones, although the clinical picture is more protracted. Diagnosis is confirmed using CCK stimulated hepatobiliary scan ejec-

tion fractions after thorough diagnostic work-up for other gastrointestinal causes. Laparoscopic cholecystectomy is the treatment of choice. Most children present with mild to moderate changes of chronic cholecystitis depending on duration of symptoms. Clinical improvement is seen in most cases after surgery.

Key Words: Gallbladder dyskinesia, Laparoscopic cholecystectomy.

INTRODUCTION

Gallbladder dyskinesia (GD) is a motility disorder of the biliary system characterized by irregular contractility of the gallbladder.¹ The recent use of cholecystokinin (CCK) stimulated hepatobiliary scans in patients with persistent biliary symptoms without gallstone disease has increased the diagnostic awareness of this condition. The therapeutic option has become cholecystectomy in the symptomatic patient after thorough diagnostic work-up excludes other gastrointestinal causes. Its attendant symtomatology, pathological findings and management are less clear in children.

To decide the prevalence of this disorder in the pediatric population, clinical manifestations, predisposing factors, actual management, pathologic findings, and patient satisfaction we elected retrospectively to analyze our experience with children 18 years or less who underwent cholecystectomy for gallbladder dyskinesia as the sole indication. We wanted to determine if a positive CCK simulated hepatobiliary scan for gallbladder dyskinesia in children with biliary manifestations predicted relief of symptoms and correlated with specific pathologic findings after surgical removal.

MATERIALS AND METHODS

The medical charts of all children 18 years or less undergoing cholecystectomy at San Pablo Medical Center (SPMC) during a 5.5 year period were retrospectively analyzed. Children with a diagnosis of biliary dyskinesia underwent retrieval of demographic and clinical characteristics, diagnostic studies, associated illness, type of cholecystectomy, pathologic findings and hospital statistics. A radionuclear study was considered diagnostic of gallbladder dyskinesia if the ejection fraction of the gallbladder content was less than 35% during the heptobiliary scan (DISIDA) stimulated with CCK.²

For purposes of analysis the cases were compared with children undergoing cholecystectomy for gallstone disorders during the same period using student-t-test, analysis of variance (ANOVA) and chi-square. A probability less than 0.05 was considered significant. Results are reported as mean with standard deviation when needed.

Serial microscopic sections of the gallbladder were blindly reviewed by our pathologists and a gradation scale given to each specimen depending on wall involvement:

- Grade 0: Unremarkable–no acute or chronic inflammatory component identified in random portions of the gallbladder wall. Included were flattening of mucosal folds, mucosal congestion and presence of ganglion cells with no hypertrophy.
- Grade 1: Mild cholecystitis–minimal chronic inflammatory changes with slight hyperplastic mucosa.
- Grade 2: Moderate cholecystitis–focal lymphoid aggregates in mucosa or bands of chronic inflammatory cells along muscle coats.
- Grade 3: Severe cholecystitis–full thickness chronic inflammatory changes.

All children or guardians were contacted by phone or in person to determine the outcome of surgery, if symptoms persisted or were relieved.

RESULTS

From January, 1990 through June, 1995, a total of 85 children underwent cholecystectomy in our institution. In 12 patients (14%) the major indication for surgery was biliary dyskinesia and the procedure of choice was laparoscopic cholecystectomy. The mean age of the group was 14.5 years (range 7-18). Ten patients were females and two were males for a 5:1 ratio of female to male. This ratio did not differ from children with gallstone disorders.

Table 1. Most Common Symptoms		
RUQ pain	12 (100%)	
FFI	8 (67%)	
Nausea	5 (42%)	
Vomiting	5 (42%)	
Non-specific abdominal pain	7 (58%)	
Diarrhea	2 (17%)	

These children had histories of biliary symptoms dating 48 \pm 42 weeks (range 4 to 152). **Table 1** illustrates the most common symptoms manifested. As in gallstone disorders, right upper quadrant pain and fatty food intolerance headed the list. Dyspepsia, or vague nonspecific abdominal complaint, was a more significant finding than in children with other gallbladder disorder (p=0.002). Gastritis and/or duodenitis were endoscopic findings in four children (25%), all of whom persisted with symptoms despite the use of medical therapy. None were obese or had abnormal liver chemistry. A positive family history of gallstones was identified in five patients (42%), a finding that proved statistically more significant in GD children (p=0.002).

All cases underwent ultrasonographic study of the abdomen resulting in negative findings. Diagnostic imaging studies comprised one gallbladder series with non-visualization of the gallbladder during the early part of the series, and 11 hepatobiliary scans with abnormally low ejection fractions after CCK stimulation. Mean ejection fraction was 16.8 ± 9 (range 7 to 33). Other studies have included: eight gastro-duodenal endoscopies, one computerized tomography, and one small bowel series.

Management consisted of laparoscopic cholecystectomy in all children with a mean hospital stay of 1.9 ± 0.5 days and no intraoperative complications. Two patients had minor postoperative complications which included emesis and urinary retention. Prophylactic antibiotics were used in half of the cases.

Pathological findings consisted of chronic acalculous cholecystitis in 10 gallbladders (83%) and unremarkable in two. Mild (Grade 1) inflammatory changes were identified in seven specimens (58%), and moderate (Grade 2) changes

Table 2.Correlation of pathologic findings,ejection fraction and symptoms duration.			
Pathologic findings	No patients	Symtoms (wk.)	Ejection fractions
Unremarkable	2	24	11±1
Mild Cholecystitis	7	44	17±5
Moderate Cholecystitis	3	67	20±11

in three (25%). No child had transmural involvement of the gallbladder wall. **Table 2** shows the relationship between pathological findings, mean duration of symptoms and ejection fractions. As is seen, a direct correlation between pathological severity and duration of symptoms was identified. No correlation was found with mean ejection fractions.

After careful interviews and questioning, all children and/or guardians expressed satisfaction and marked improvement of symptoms after the procedure. One child complained of intermittent episodes of diarrhea after surgery. The mean follow-up was 17 months (range 1-31).

DISCUSSION

Children with a history of recurrent classic biliary symptoms devoid of gallstones have a higher incidence of acalculous cholecystitis than adults.³⁻⁵ Two-thirds of these cases develop acute abdominal symptoms as a complication of other events such as trauma, sepsis, burns, hypotension, prolonged fasting and need of ventilatory support.⁵⁻¹¹ Gallbladder wall distention is generally present and prompt surgical therapy is needed due to the risk of perforation from gangrenous changes.⁸ Most cases are the result of a combination of mechanical obstruction and local damage caused by imprisoned bile secondary to changes in concentration.⁷ In other instances the child will show biliary symptoms for a protracted period before being considered for surgical therapy.¹²

The diagnosis of cholecystitis is confirmed with ultrasound and hepatobiliary scans. Ultrasonographic findings compatible with gallbladder disorders are marked wall thickness (greater than 3 mm in children), alteration of the acoustic architecture of the wall, increase in size of the lumen, or the presence of intraluminal densities.¹³ Radionuclide scans provided reliable diagnosis of cholecystitis when non-visualization of the gallbladder is associated with prompt visualization of the extrahepatic bile ducts and duodenum.^{4,14} The recent use of cholecystokinin injection during hepatobiliary scanning allows the evaluation of gallbladder contractility and ejection fractions of the isotope emptied.^{15,16} Normal ejection fraction response has been established as those greater than one-third of the gallbladder content.² Below that level the definition of dysmotility of the biliary system pertains.

With the application of modern techniques to study normal biliary motility a composite physiological picture has emerged.¹⁷ The physiology of gallbladder motility is governed by a combination of hepatic secretion, gallbladder contraction and sphincter of Oddi relaxation.¹⁷ This effect is modulated by autonomic (vagal) and hormonal (CCK) mechanisms. Vagal stimulation causes the gallbladder to contract and CCK produces gallbladder contraction and sphincter of Oddi relaxation. Motility disorders of bile flow arise with disruption of this complex interrelationship.18 Biliary dysmotility is believed to be caused by spasm of the sphincter of Oddi associated with either a hypersensitivity of the gallbladder or hyposensitivty of the sphincter of Oddi to CCK. The result is a gallbladder that contracts against a closed biliary drainage system. This increased resistance to flow delaying emptying may predispose to gallstones by increasing the viscosity and altering the solubility of bile salts, cholesterol and phospholipids.

Patients with a history of biliary colic and no radiological evidence of gallstones often have symptoms for an extended period. They undergo extensive work-up, repeated examinations and no demonstrable disease entity.¹⁶ Only a few series have shown that biliary dyskinesia may represent an early phase in the spectrum of calculous biliary tract disease.¹⁶ The presence of cholesterol crystals within the gallbladder bile in patients with biliary dyskinesia attests to this reality.¹ Reproduction of right upper quadrant pain during CCK administration is another useful tool in the diagnosis of dyskinesia. When conventional radiology, ultrasound and upper gastrointestinal endoscopy fail to explain patient symptoms, hepatobiliary scanning is the next step.¹⁹ The diagnosis relies on non-visualization during gallbladder series or low ejection fractions after CCK stimulation tests.

Some authors believe that there is not always an excellent correlation between the presence and absence of symptoms related to biliary dyskinesia and the efficacy of cholecystectomy.¹⁵ Furthermore, the cure rate for biliary type pain has been found greater if stones are documented preoperatively compared with patients with presumptive acalculous cholecystitis.²⁰ Those studies had no correlation with pathological findings or DISIDA-CCK tests. Symptoms in all of our children improved after surgery, and evidence of chronic inflammation was identified in 83% of the specimens studied. Other series have established the success of gallbladder removal in relieving symptoms with a predictive value to an abnormal ejection fraction response of 97%. ^{1,21,22} In our series we established a strong correlation between duration of symptoms and pathological findings using a simple classification of gallbladder wall involvement.

Histologic definition does not always correlate with the clinical picture. Often the typical complaint of chronic cholecystitis remains unrecognized in the child because of a lack of suspicion by the clinician.²³ A plea is made for earlier consideration of biliary dyskinesia as a possible diagnostic entity in children with recurring history of right upper quadrant abdominal pain, vague epigastric discomfort associated with fatty food intolerance and negative ultrasound studies. Laparoscopic cholecystectomy should be offered to appropriately selected children with low ejection fractions after CCK stimulation if thorough work-up fails to show other gastrointestinal disorders. Most cases of biliary dyskinesia are associated with pathological findings of chronic cholecystitis and improvement of symptoms following surgery.

References:

1. Rescoria FJ, Grosfeld JL. Cholecystitis and Cholelithiasis in Children. *Seminars in Pediatr Surg.* 1992;1(2):98-106.

2. Krishamurthy GT, Bobba VR, Kingston E, et al. Measurement of gallbladder emptying sequentially using a single dose of 99mTclabeled hepatobiliary agent. *Gastroenterology*. 1982;83:773-776.

3. Kirtley JA, Holcomb GW. Surgical management of diseases of the gallbladder and common duct in children and adolescent. <u>AM</u> J Surg. 1966;111:39-56.

4. Pierettu R, Auldist AW, Stephens CA. Acute cholecystitis in children. *SGO*. 1975;140:16-18.

5. Takiff H, Fonkalsrud EW. Gallbladder disease in childhood. *AJDCV*. 1984;138:565-568.

6. Marks C, Espinsa J, Hyman LJ. Acute acalculous cholecystitis in childhood. *J Pediatr Surg.* 1968;3(5):608-611.

7. Ternberg JL, Keating JP. Acute acalculous cholecystitis. <u>Arch</u> Surg. 1975;110:543-547.

8. Holcomb GW, O'Neill JA, Holcomb GW. Cholecytitis, cholelithiasis and common duct stenosis in children and adolescent. <u>Ann</u> <u>Surg.</u> 1980;191(5):626-635.

9. Matolo NM, LaMorte WW, Wolfe BM. Acute and chronic cholecystitis. *Surg Clin North Am.* 1981;61(4):875-883.

10. Nanni G. Acute acalculous cholecystitis in childhood. *Postgraduate Medicine*. 1983;74(5):269-274.

11. Lau GE, Andrassy RJ, Mahour GH. A 30-year review of the management of gallbladder disease at a Childrens Hospital. *Amer Surg.* 1983;49:411-413.

12. Hanson BA, Mahour GH, Woolley MM. Diseases of the gallbladder in infancy and childhood. <u>J Pediatr Surg.</u> 1971;6(3):277-283.

13. McGahan JP, Phillips HE, Stadalnik RC, et al. Ultrasound and radionuclide biliary scanning in acute pediatric abdominal pain. *J Clin Ultrasound.* 1983;11:251-258.

14. Matolo NM, Stadalnik RC, Dixon SM. Value and limitations of scanning of the biliary tract. *SGO*. 1980;150:531-524.

15. Atkins HL, Oster ZH. Asymmetric gallbladder contraction following cholecystokin hepatobiliary imaging. <u>Clin Nucl Med.</u> 1989;14:82-86.

16. Misra DC, Blossom CB, Fink-Bennet D, et al. Results of surgical therapy for biliary dyskinesia. *Arch Surg.* 1991;126: 957-960.

17. Grace PA, Poston GJ, Williamson RCN. Biliary Motility. <u>*Gut.*</u> 1990;31:571-582.

18. Hogan WJ, Geenen JE. Biliary dyskinesia. <u>Endoscopy.</u> 1988;20:179-183.

19. Lennard TWJ, Farndon JR, Taylor RMR. Acalculous biliary pain: diagnosis and selection for cholecystectomy using the cholecystokinin test for pain reproduction. *Br J Surg.* 1984;71:368-370.

20. Fenster LF, Lonborg R, Thirby RC, et al. What symptoms does cholecystectomy cure? Insights from an outcomes measurement project and review of the literature. *Am J Surg.* 1995;169:533-538.

21. Sorenson MK, Francher S, Lang NP, et al. Abnormal gallbladder nuclear ejection fraction predicts success of cholecystectomy in patients with biliary dyskinesia. *Am J Surg.* 1993;166:672-675.

22. Use of cholecystokinin in hepatobiliakry scintigraphy. In Nuclear Medicine syllabus of the Society of Nuclear Medicine. 1988:pp. 81-82.

23. MacMillan RW, Shullinger JN, Santulli TV. Cholelithiasis in childhood. *Am J Surg.* 1974;127:689-692.

Thanks to Dr. Eduardo de León Santoni, San Pablo Medical Center, for reviewing the sugical specimens and developing a stratification of findings.