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Postcholecystectomy Syndrome

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Recurrence or persistence of pain or other symptoms in the right upper abdominal quadrant following cholecystectomy is an uncommon event, but one which is distressing to both the patient and physician. The cause of postcholecystectomy syndrome may be difficult to establish. One-third of cases will be due to disease outside the biliary tract. Common duct stone, stenosing pappilitis or biliary dyskinesia are often the cause when symptoms arise within the biliary tract. An orderly diagnostic approach, including use of ultrasound and endoscopic retrograde cholangiopancreatography, is outlined. Transpapillary manometry and quantitative cholescintigraphy are newer tests of great promise. A successful treatment, of course, depends on the correct diagnosis.

The term postcholecystectomy syndrome was first used by Womack and Crider¹ to describe complaints of recurrent upper abdominal pain after cholecystectomy. This term now is used to describe a heterogeneous collection of postcholecystectomy complaints.

The symptoms associated with postcholecystectomy syndrome include abdominal pain, usually mild but occasionally severe, and dyspepsia that may be continuous or episodic. When the pain is severe, it often indicates an organic cause of the syndrome. ^{2,3} Patients also may have transient nausea, bloating, and flatulence. In about 5% of patients, the pain is described as similar in intensity and duration to that before cholecystectomy. ⁴

In a review of 5,859 biliary tract operations, 34% of the patients with postchole-cystectomy symptoms had disorders outside the hepatobiliary system,⁵ emphasizing the importance of careful evaluation before cholecystectomy to identify coexisting disease in other organs besides the hepatobiliary system.

ETIOLOGY

The etiology of postcholecystectomy syndrome is not defined fully and probably is not caused by only one factor. The predisposing events may be viewed as intrinsic (hepatobiliary) or extrinsic (nonhepatobiliary). In the intrinsic population, symptoms usually are a result of a common bile duct stone, a retained segment of gallbladder, or an iatrogenic traumatic stricture of the biliary tree. In addition, a cystic duct remnant, stenosing papillitis, and biliary dyskinesia were suggested as intrinsic etiologic factors in postcholecystectomy syndrome.^{6–11} The extrinsic etiologic factors include irritable bowel

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syndrome, peptic ulcer disease, reflux esophagitis, pancreatitis, intraabdominal adhesions, and wound neuroma.

The characteristics of the pain are important in the diagnosis of the underlying etiology. The diagnosis of a retained common bile duct stone is relatively straightforward, whereas the diagnosis of stenosing papillitis and biliary dyskinesia may be difficult. The concept of a "cystic duct stump syndrome," first described by Garlock and Hurwitt¹² in 1951, is controversial. It includes repeated attacks of biliary colic, nausea, vomiting, jaundice, chills, and fever. Although these symptoms probably indicate common duct stones and cholangitis, it has been suggested that the presence of the cystic duct remnant alters pressure in the biliary tract and sphincter of Oddi after a cholecystectomy. 13,14 The findings of others, 7,8 however, suggested that the remnant itself does not cause postcholecystectomy syndrome but that the presence of stones in the remnant may be the genesis of the symptoms. Postoperative biliary distress also was caused by new stone formation, amputation neuroma, and adhesions associated with the cystic duct remnant and leading to kinking of the common bile duct.6,15,16

The term biliary dyskinesia originally was used to describe impaired choledochal motility and abnormal flow of bile from the liver to the duodenum.^{17,18} Whereas biliary dyskinesia is accepted as a clinical entity, intensive research during the past century could not document completely a precise etiology for this malfunction. Others^{19,20} suggested, on the basis of manometric studies of the sphincter of Oddi, that dyskinesia is the result of spasm of the sphincter that increases intraductal pressure and thus produces pain. The role of cholecystokinin in this process is unknown, but it may be a causative agent by paradoxically increasing sphincter tone.²¹

Papillary stenosis was described as a result of acute or chronic inflammation of the papilla of Vater. ²² It was suggested that sten-

osing papillitis is the consequence of chronic passage of gallstones.23 The role of pancreatitis in the inflammatory response is unknown. Histologically, the normal presence of large amounts of collagen in the papilla makes the pathologic diagnosis of inflammatory stenosis difficult.9 Furthermore, several studies showed that there was no conclusive correlation between clinical symptoms and histologic changes in the papilla. 9,23,24 Like biliary dyskinesia, the perceived clinical frequency and importance of papillary stenosis in postcholecystectomy syndrome are controversial, primarily because of the paucity of data to support a specific pathophysiologic mechanism for this disease.

DIAGNOSTIC EVALUATION

In the process of identifying the cause of postcholecystectomy syndrome, it is important to differentiate between pancreatobiliary diseases and diseases external to the biliary tract. When confronted with a potential postcholecystectomy syndrome, the surgeon always should consider that the cause of the patient's complaints arises from extrabiliary disease. A complete evaluation of both the upper and lower gastrointestinal (GI) tract must be done. It was found that 40% of patients with postcholecystectomy symptoms actually had disease outside the biliary tract (i.e., gastritis or ulcer, functional intestinal diseases, colonic diverticulitis, chronic pancreatitis, or carcinoma of the colon).25

The elimination of an extrahepatobiliary pathologic process should suggest that the patient has either an organic (stone, stricture, or pancreatitis) or a functional (biliary dyskinesia or papillary stenosis) biliary disorder. Patients with a history of acute upper abdominal pain associated with jaundice, fever, and chills usually have a common bile duct stone. By contrast, chronic pain of moderate severity without other associated symptoms generally suggests stenosing papillitis or biliary dyskinesia.

The laboratory evaluation should include a complete blood count and urinalysis, liver function tests, serum amylase, and a test for occult blood in the stool. An important noninvasive test that should be done to exclude organic pancreatic or biliary diseases is ultrasonography.²⁵ To exclude the possibility of gastroesophageal reflux or ulcer disease, the physician should do a barium upper GI series. Endoscopic retrograde cholangiopancreatography (ERCP) often is helpful in the differential diagnosis of postcholecystectomy syndrome, especially in patients with symptoms suggesting obstruction.²⁶

The technique that holds the most promise for the future in the diagnosis of functional disease of the papilla is transpapillary manometry. This test allows the physician to measure and identify high pressure in the sphincter of Oddi. Patients with elevated pressures respond favorably to transendo-scopic papillotomy. 11,20

Quantitative cholescintigraphy recently was shown to be a highly sensitive technique in the diagnosis of papillary stenosis and dysfunction. 22,26 This technique should not replace ERCP but can be used as an initial procedure to differentiate stenosis of the sphincter or other causes of biliary obstruction from nonbiliary causes of postcholecystectomy pain.

In summary, the following steps should be followed in evaluating a patient with postcholecystectomy pain:

- A careful and complete recording of the history, including a review of pre- and postoperative records.
- Exclusion of extrahepatic causes, insofar as possible, by endoscopic and barium examinations of the upper and lower GI tracts.
- 3. Ultrasonography as the initial step in evaluation of the pancreaticobiliary system.
- 4. ERCP in patients with biliary obstructive symptoms.
- Transpapillary manometry for detection of abnormalities of the sphincter of Oddi.

TREATMENT

The treatment of postcholecystectomy syndrome depends on the etiology and may be either nonoperative or interventional. The nonoperative approach is appropriate when the patient has pain of unresolved origin. When the symptoms are thought to be a result of a functional disorder of the sphincter of Oddi (dyskinesia), a trial of a long-acting nitroglycerin preparation or nifedipine (a calcium-channel blocker) may be beneficial. 27,28 Alternatively, spasmolytics and analgesics can be used for the temporary relief of pain. Some physicians treat dyspeptic symptoms with bile acid substitutes or pancreatic enzyme preparations.29 This approach, however, is controversial and frequently fails.

An important diagnostic procedure, ERCP also can be used as a therapeutic modality. Combined with endoscopic sphincterotomy ERCP is used to remove common bile duct stones and manage papillary dyskinesia. 30-32 Endoscopic balloon dilation of the sphincter of Oddi was used to relieve stenosis of the sphincter, but clinical experience with this technique is limited. 33,34 The complication rate (hemorrhage and perforation) of endoscopic papillotomy was reported to be 5% to 10%. 35

Surgical intervention in these patients has advantages over an endoscopic procedure. Surgical sphincterotomy, sphincteroplasty, 36 and septectomy are procedures with high success rates in treating postcholecystectomy syndromes with biliary causes, especially stenosing papillitis or biliary dyskinesia. The technique of septectomy was introduced in the treatment of postcholecystectomy pain.³⁷ This procedure involves excision of the septum and dividing the common bile duct and the duct of Wirsung, combined with sphincteroplasty. The origin of postcholecystectomy pain was suggested to be obstruction of flow of pancreatic secretions as a result of inflammation and scarring of the ampullary

septum, secondary to repeated passage of gallstones through the papilla of Vater or to cholesterolosis of the ampulla of Vater.³⁷ In support of this hypothesis, it was shown that patients with persistent pain after sphincteroplasty had resolution of their symptoms after septectomy.¹⁰

In patients in whom the pain is associated with a gallbladder remnant, excision of the remnant usually eliminates the symptoms. The possibility that the symptoms of post-cholecystectomy syndrome are associated with a cystic duct remnant in the absence of a demonstrable stone is remote. Therefore, surgical intervention is not warranted even in the presence of a long cystic duct remnant.

It is evident from clinical experience that many patients have pain after cholecystectomy. Resolution needs to be based on developing concrete diagnostic indicators that enable the physician to differentiate between the various organic and functional disorders of the hepatobiliary system. We do not have such reliable diagnostic tests available currently. Therefore we often are forced to continue our reliance on empiric indicators, especially for the diagnosis and treatment of functional biliary disorders.

REFERENCES

- Womack NA, Crider RL. The persistence of symptoms following cholecystectomy. Ann Surg 1947; 126:35.
- Hunt DR, Blumgart LH. latrogenic choledochoduodenal fistula: An unsuspected cause of postcholecystectomy symptoms. Br J Surg 1980; 67:10.
- Ruddell WSJ, Ashton MG, Lincott DJ, Axon AT. et al. Endoscopic retrograde cholangiography and pancreatography in investigation of post-cholecystectomy patients. Lancet 1980; 1:444.
- Bar-Meir S, Halpern Z, Barden E, et al. Frequency of papillary dysfunction among cholecystectomized patients. Hepatology 1984; 4:328.
- Glenn F. Complications following operation upon the biliary tract. In: Artz CP, Hardy JD, eds. Management of Surgical Complications, 3rd ed. Philadelphia: WB Saunders, 1975; 501.
- Bodwell B, Overgaard B. Cystic duct remnant after cholecystectomy: Incidence studied by cholegraphy

- in 500 cases, and significance in 103 reoperations. Ann Surg 1966; 163:382.
- Glenn F, Whitsell JC. The surgical treatment of cystic duct remnant. Surg Gynecol Obstet 1961; 113:711.
- Millbourn E. On the importance of the remnant cystic duct in the development of post-operative biliary distress following cholecystectomy: A study partly based on cholangiography series. Acta Chir Scand 1950; 100:448.
- Acosta JM, Civantos F, Nardi GL, et al. Fibrosis of the papilla of Vater. Surg Gynecol Obstet 1967; 124: 787.
- Moody FG, Berenson MM, McCloskey D. Transampullary septectomy for post-cholecystectomy pain. Ann Surg 1977; 186:415.
- Geenen J, Hogan W, Toouli J, et al. A prospective randomized study of the efficacy of endoscopic sphincterotomy for patients with presumptive sphincter of Oddi dysfunction. Gastroenterology 1984; 86:1086.
- Garlock JH, Hurwitt ES. The cystic duct stump syndrome. Surgery 1951; 29:833.
- Caroli J, Mercadier M. Les Dyskinesies Biliares. Paris: Vigot, 1949; 80.
- Bernhard F. Die klinische bedeutung der gallenbasenneubildung nach cholecystektomie. Chirurg 1943; 15:510.
- Clute HM. Cystic duct stones after cholecystectomy. Surg Clin North Am 1933; 13:603.
- Comfort MW, Walter W. Intermittent jaundice due to neuroma of cystic and common bile duct. Ann Surg 1931; 93:1142.
- Schmieden V, Niessen H. Dyskinesie der gallenwege (cholepathia spastica) and chirurgie. Munchener Medizinische Wochenschrift 1933; 80:247.
- Ivy AC, Sandblom P. Biliary dyskinesia. Ann Intern Med 1934; 8:115.
- Geenen JE, Hogan WJ, Dodds WJ, et al. Intraluminal pressure recording from the human sphincter of Oddi. Gastroenterology 1980; 78:317.
- Toouli J, Roberts-Thomson IC, Dent J, et al. Manometric disorders in patients with suspected sphincter of Oddi dysfunction. Gastroenterology 1985; 88: 1243.
- Hogan WJ, Dodds, WJ, Geenen JE. The biliary tract.
 In: Christensen J, Wingate DL, eds. A Guide to Gastrointestinal Motility. Bristol: Wingate, 1983; 157.
- Shaffer EA, Hershfield NB, Logan K, et al. Cholescintigraphic detection of functional obstruction of the sphincter of Oddi. Gastroenterology 1986; 90: 728.
- 23. Moody FG. The postcholecystectomy syndrome. In: Moody FG, Carey CL, Jones RS, et al., eds. Surgical

- Treatment of Digestive Disease. Chicago: Year Book Medical. 1990: 298.
- Grange TB, Lober PH, Imamoglu K, et al. Stenosis of sphincter of Oddi: A clinicopathologic review of 50 cases. Surgery 1960; 48:304.
- Lasson A. The postcholecystectomy syndrome: Diagnostic and therapeutic strategy. Scand J Gastroenterol 1987; 22:897.
- Zeman RK, Burrell MI, Dobbins J, et al. Post cholecystectomy syndrome: Evaluation using biliary scintigraphy and endoscopic retrograde cholangio-pancreatography. Radiology 1985; 156:787.
- Bar-Meir S, Halpern Z, Bardan E. Nitrate therapy in a patient with papillary dysfunction. Am J Gastroenterol 1983; 78:94.
- Guelrud M, Mendoza S, Rossiter G, et al. Effect of nifedipine on sphincter of Oddi motor activity: Studies in healthy volunteers and patients with biliary dyskinesia. Gastroenterology 1988; 95:1050.
- 29. Bodvall B. The postcholecystectomy syndromes. Clinics in Gastroenterology 1973; 2:103.
- Sivak MV. Endoscopic management of bile duct stones. Am J Surg 1989; 158:228.
- 31. Bickerstaff KI, Berry AR, Chapman RW, et al. Early

- postoperative endoscopic sphincterotomy for retained biliary stones. Ann R Coll Surg Engl 1988; 70:350
- Hawes RH, Cotton PB, Vallon AG. Follow-up 6 to 11 years after duodenoscopic sphincterotomy for stones in patients with prior cholecystectomy. Gastroenterology 1990; 98:1008.
- Siegel JH, Guelrud M. Endoscopic cholangiopancreatoplasty: Hydrostatic balloon dilation in the bile duct and pancreas. Gastrointest Endosc 1983; 29: 99.
- Guelrud M, Siegel JH. Hypertensive pancreatic duct sphincter as a cause of pancreatitis: Successful treatment with hydrostatic balloon dilatation. Dig Dis Sci 1984; 29:225.
- 35. Silvis SE. Current status of endoscopic sphincterotomy. Am J Gastroenterol 1984; 79:731.
- Antrum RM, Hall R. Transduodenal sphincteroplasty: An analysis of 118 consecutive cases. Br J Surg 1984; 71:446.
- Moody FG, Becker JM, Potts JR. Transduodenal sphincteroplasty and transampullary septectomy for post-cholecystectomy pain. Ann Surg 1983; 197: 627.