

CASE REPORTS

Cholescintigraphy: Gallbladder Nonvisualization Secondary to Neoplasm

Myron L. Lecklitner, Paul R. Rosen, and Martin L. Nusynowitz

The University of Texas Health Science Center at San Antonio, San Antonio, Texas

Whereas the diagnosis of acute cholecystitis is characterized by nonvisualization of the gallbladder with Tc-99m iminodiacetic acid derivatives, nonvisualization is not specific for acute cholecystitis. The first reported case of nonvisualization of the gallbladder due to neoplasm is added to an expanding list of causes of nonvisualization other than the more frequent causes: acute and chronic cholecystitis.

J Nucl Med 22: 699-700, 1981

The evaluation of the hepatobiliary system by newer Tc-99m-labeled radiopharmaceuticals constitutes the imaging modality of choice for the exclusion of acute cholecystitis. The procedure is useful even in the face of moderate hyperbilirubinemia. However, several conditions besides acute and chronic cholecystitis can result in nonvisualization of the gallbladder. We present a case of such nonvisualization because of primary neoplasm without attendant cholecystitis or cholelithiasis. This case is reported to emphasize the diverse causes of nonvisualization of the gallbladder in hepatobiliary scintigraphic studies and its impact on subsequent clinical decision making.

CASE REPORT

A 49-year-old woman presented with a 6-mo history of nonradiating, intermittent aching and fullness in the right upper quadrant. These bouts were exacerbated by ingestion of spicy and fatty foods. She also reported the use of oral contraceptives for 11 yr before a total hysterectomy performed 5 yr ago. She had been on estrogens for 3 yr after the hysterectomy; these were discontinued because of hypertension.

Physical examination was unremarkable. The patient was afebrile. Laboratory evaluation revealed: total bilirubin 0.3 mg/dl (normal, 0.2-1.2); alkaline phosphatase 165 IU/l (normal, 35-125); LDH 222 IU/l (normal, 20-220); SGOT 37 IU/l (normal, 5-40). Barium enema, upper gastrointestinal series, and two ultrasonic examinations of the right upper quadrant were not helpful. Two oral cholecystograms were reported as showing zero and poor visualization of the gallbladder, respectively. Seventeen days following the second cholecystogram, a hepatobiliary evaluation with Tc-99m para-isopropyl iminodiacetic acid (PIPIDA), 8 mCi, was performed, with informed consent (Figs. 1 and 2). Anterior, right

lateral, and posterior images of the liver acquired in the initial portion of the study were unremarkable, and the gallbladder did not visualize on delayed films. In view of the clinical features, this pattern was consistent with chronic cholecystitis. There was also a suggestion of partial obstruction of the distal portion of the common bile duct, manifested by the duct's dilatation.

The patient was admitted for elective cholecystectomy. Operative findings included a liver of normal contour and texture but appearing yellow. A hepatic biopsy was obtained. The opened gallbladder showed no gallstones or other discrete masses. Hartmann's pouch of the cystic duct was found indurated. An intraoperative cholangiogram was normal; in particular no stones, lucencies, or other abnormalities were found, and there was free flow of contrast medium into the duodenum.



FIG. 1. Hepatobiliary scintigram at 30 min after injection of Tc-99m PIPIDA. There is nonvisualization of gallbladder and dilatation of common bile duct, with some gut activity.

Received Dec. 8, 1980; revision accepted March 13, 1981.

For reprints contact: Myron L. Lecklitner, MD, The Univ. of Texas Health Science Center at San Antonio, 7703 Floyd Curl Dr., San Antonio, TX 78284.



FIG. 2. Hepatobiliary scintigram at 60 min, showing gallbladder and biliary findings as in Fig. 1, with progression of gut activity.

Microscopic examination of the distal portion of the cystic duct revealed a well-differentiated adenocarcinoma of the mucosa extending into the lumen, with no submucosal or serosal involvement. The liver biopsy showed only fatty metamorphosis.

Eleven days after the cholecystectomy, the patient was explored again. The remnant of the cystic duct and the adjacent common bile duct were found to be thickened and were removed. A choledochoduodenostomy was performed. No lymph nodes were identified. Microscopic examination of the common bile duct and cystic duct revealed invasive, well-differentiated adenocarcinoma. It was not clear whether the carcinoma originated in the gallbladder or cystic duct.

The patient's recovery was essentially uneventful. She remains on 5-fluorouracil. Subsequent re-evaluation for metastases by multiple imaging studies has remained negative.

Extensive review of the gallbladder section by two experienced pathologists produced no evidence of acute or chronic cholecystitis or other disease of the gallbladder proper.

DISCUSSION

Carcinoma of the gallbladder occurs in 1-2% of all cholecystectomies (1,2). The diagnosis of gallbladder neoplasm is often made first on histological examination of the gallbladder; in one series this occurred in 32 of 120 patients (27%) (3,4), and this frequency approximates the mean reported in other series.

Scintigraphic nonvisualization of the gallbladder in the setting of a normal liver usually suggests acute or chronic cholecystitis. A visible gallbladder virtually excludes acute cholecystitis except in the rare absence of cystic-duct obstruction (4). Thus, visualization of the gallbladder with acute acalculous cholecystitis is a rare false-negative finding; this entity remains a clinical diagnosis and there is no good test for it. Nonvisualization in the appropriate clinical setting is an excellent indication of acute cholecystitis. Chronic cholecystitis may produce nonvisualization, but other causes have been reported: normal, nonfasting patients (5), acute pancreatitis (6), and, of course, either congenital or surgical absence of the gallbladder.

Visualization of the gallbladder in chronic cholecystitis is

variable; delayed appearance of activity in the area of the gallbladder can occur, and several methods of gallbladder stimulation to induce visualization are available (7,8). If the presence or absence of visualization of the unstimulated gallbladder is used as a criterion, the test is "exceedingly unreliable in identifying patients with chronic gallbladder disease" (9). Fifty-seven percent of pathologically proved chronic cholecystitis did visualize (9). In our experience, on the other hand, whenever liver function is essentially normal, nonvisualization of the gallbladder is an excellent predictor of gallbladder disease of some sort.

Our patient had essentially normal liver function studies, and nonvisualization in our study, plus corroborative oral cholecystography, led to exploratory laparotomy. At surgery, no stones were demonstrated in our patient, nor did she have cholecystitis, but she did have adenocarcinoma at the junction between the gallbladder and cystic duct. The 14-yr history of estrogen administration may have been contributory, since numerous articles have appeared in which oral contraceptives have been incriminated as a cause of hepatobiliary neoplasms (10-12).

The nonvisualization of the gallbladder in this patient cannot be attributed to complete cystic-duct obstruction, since the duct was patent at the initial operation; distal cystic-duct dysfunction may have been due to the tumor.

REFERENCES

1. BLALOCK JB: An analysis of 15 cases of gallbladder carcinoma. *Am Surg* 44:286-289, 1978
2. MELSON GL, REITER F, EVENS RG: Tumorous conditions of the gallbladder. *Semin Roentgenol* 11:269-282, 1976
3. BERGDAHL L: Gallbladder carcinoma first diagnosed at microscopic examination of gallbladders removed for presumed benign disease. *Ann Surg* 191:19-22, 1980
4. ECHEVARRIA RA, GLEASON JL: False-negative gallbladder scintigram in acute cholecystitis. *J Nucl Med* 21:841-843, 1980
5. PAUWELS S, STEELS M, PIET L, et al: Clinical evaluation of Tc-99m-diethyl-IDA in hepatobiliary disorders. *J Nucl Med* 19:783-788, 1978
6. TAAVITSAINEN M, JÄRVINEN H, TALLROTH K: Cholecystigraphy in the diagnosis of acute cholecystitis. *Ann Clin Res* 10:227-234, 1978
7. WEISSMANN HS, FRANK MS, BERNSTEIN LH, et al: Rapid and accurate diagnosis of acute cholecystitis with ^{99m}Tc-HIDA cholescintigraphy. *Am J Roentgenol* 132:523-528, 1979
8. ROSENTHALL L, SHAFFER EA, LISBONA R, et al: Diagnosis of hepatobiliary disease by ^{99m}Tc-HIDA cholescintigraphy. *Radiology* 126:467-474, 1978
9. SUAREZ CA, BLOCK F, BERNSTEIN D, et al: The role of H.I.D.A./P.I.P.I.D.A. scanning in diagnosing cystic duct obstruction. *Ann Surg* 191:391-396, 1980
10. ELLIS EF, GORDON PR, GOTTLIEB LS: Oral contraceptives and cholangiocarcinoma. *Lancet* 1:207, 1978 (Letter to the Editor)
11. LITTLEWOOD ER, BARRISON IG, MURRAY-LYON IM, et al: Cholangiocarcinoma and oral contraceptives. *Lancet* 1:310-311, 1980 (Letter to the Editor)
12. KLATSKIN G: Hepatic tumors: possible relationship to use of oral contraceptives. *Gastroenterology* 73:386-394, 1977