CASE REPORTS

Radionuclide Hepatobiliary Imaging: Nonvisualization of the Gallbladder Secondary to Prolonged Fasting

Mark J. Larsen, William C. Klingensmith III, and Christopher C. Kuni

Veterans Administration Medical Center, and the University of Colorado Health Sciences Center, Denver, Colorado

Radionuclide hepatobiliary imaging demonstrated nonvisualization of the gallbladder in four patients who were studied after fasting from 14 hr to 12 days. Two patients subsequently had normal gallbladders at autopsy, and two gave normal gallbladder visualization on repeat imaging studies after fasts of 2 to 3 hr. These findings suggest that prolonged fasting may be a cause for nonvisualization of a normal gallbladder.

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Radionuclide hepatobiliary imaging is a widely utilized diagnostic test for evaluating hepatic (*1*), gallbladder (*2–6*), and biliary-tract (*7*) function. Nonvisualization of the gallbladder over 4 hr, in combination with normal or relatively normal biliary excretion of the tracer, has a high accuracy in the diagnosis of acute cholecystitis (*2,3*). A number of other causes for nonvisualization have been reported including: (a) chronic cholecystitis (3), (b) the normal, nonfasting state (*6,8–10*), (c) cystic-duct obstruction by tumor (*11*), (d) acute pancreatitis (*12*), (e) alcoholism and total parenteral nutrition (*13*), and (f) physiologic gallbladder distention without specific reference to a fasting state (*14*).

We have studied four patients in whom a prolonged fast was associated with nonvisualization of an otherwise normal gallbladder.

CASE REPORTS

Case 1. A 49-year-old male presented with right upper quadrant abdominal pain. He had a history of peptic ulcer and a partial gastrectomy six years before admission. Liver function tests were normal with the exception of a slightly elevated amylase of 181 IU/l (normal <160), slightly elevated alkaline phosphatase of 87 IU/l (normal <75), and an elevated SGOT of 78 IU/l (normal <20). The oral cholecystogram gave poor visualization of the gallbladder. A Tc-99m diethyl-IDA study yielded normal hepatocyte clearance and transit time, without visualization of the gallbladder through 4 hr (Fig. 1). The patient had been fasting for 12 days. Two days later he had a meal, followed 3 hr later by a second hepatobiliary study. Again there was normal hepatocyte clearance and transit time, but the gallbladder clearly visualized at 1 hr (Fig. 1). Subsequently his symptoms subsided on antacid therapy.

Case 2. A 55-year-old alcoholic male presented with jaundice and weakness of 3 wk duration. Laboratory studies revealed an elevated alkaline phosphatase of 395 IU/l (normal <75), SGOT of 55 IU/l (normal <20), and total bilirubin of 5.3 mg/dl (normal = 0.3–1.3). A Tc-99m trimethyl-bromo-IDA hepatobiliary study showed mildly decreased hepatocyte clearance, normal transit time, and nonvisualization of the gallbladder through 6 hr (Fig. 2). The patient had documented fasting for 14 hr, however, his poor nutritional state suggested a longer period of food deprivation. A repeat Tc-99m di-isopropyl-IDA study 2 days later after a 2.5-hr fast demonstrated normal visualization of gallbladder at 45 min (Fig. 2). The jaundice was judged to be secondary to alcoholic hepatitis, and he improved on detoxification treatment. He never experienced any symptoms of biliary colic. Although two different Tc-99m IDA preparations were used in this patient, their hepatobiliary kinetics are quite similar and should not account for the difference between the two studies (*19*).

Case 3. A 46-year-old quadriplegic male was admitted for complaints of vomiting and diarrhea of 3 days' duration. Oral feeding was stopped and nasogastric suction was begun. On the fourth hospital day, he became febrile and complained of back and abdominal pain. A Tc-99m diethyl-IDA study revealed normal hepatocyte clearance, a normal biliary transit time, and nonvisualization of the gallbladder through 1.5 hr. He had been fasting for at least six days before the hepatobiliary study. A presumptive diagnosis of acute cholecystitis was made; explatory laparotomy revealed a benign-appearing gallbladder. Five months later he died; an autopsy revealed a normal gallbladder with patent bile ducts.

Case 4. A 63-year-old male was admitted for progressive weakness and numbness in all extremities. Electromyography and studies of nerve conduction velocity revealed a demyelinating polyneuropathy. During his hospitalization he complained of abdominal pain, distention, and left-flank tenderness. Initial labo-

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For reprints contact: Wm. C. Klingensmith III, MD, Div. of Nuclear Medicine, Univ. of Colorado Health Sciences Center, Denver, Colorado 80262.

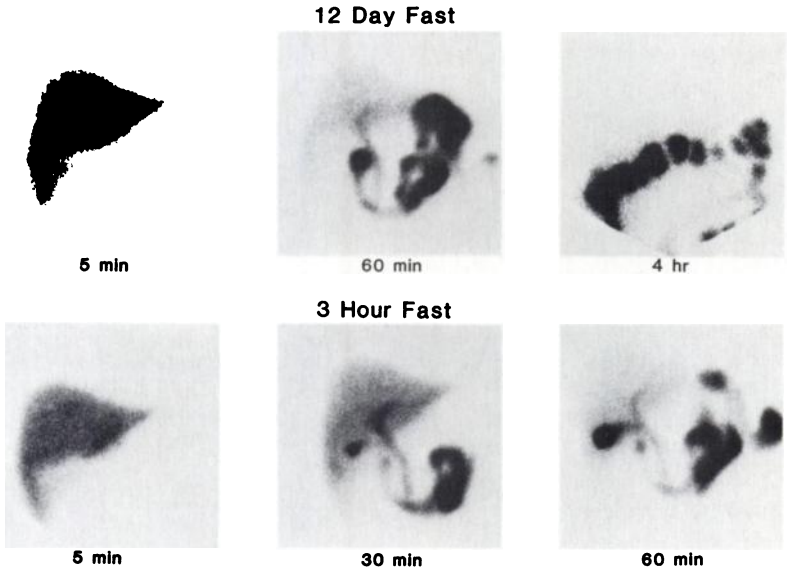

FIG. 1. Following a 12-day fast, hepatobiliary study demonstrates normal hepatocyte clearance and biliary transmit time, without visualization of gallbladder through 4 hr (top). Two days later, repeat study performed 3 hr after a meal demonstrates gallbladder by 30 min (bottom).

ratory studies were normal. Endoscopy showed an antral ulcer, and a saline load test revealed gastric outlet obstruction. Before anticipated surgery, intravenous hyperalimentation was started. When his abdominal pain increased and his laboratory evaluation showed an elevated alkaline phosphatase of 453 IU/l (normal <75) and total serum bilirubin of 5.1 mg/dl (normal = 0.3–1.3), a Tc-99m diethyl-IDA study was performed. Because of the patient's 7-day fast, 1.4 μg of sincalide (the C-terminal octapeptide of cholecystokinin)* was administered intravenously before the study. The gallbladder was not visualized through 24 hr. A presumptive diagnosis of acute cholecystitis was made, but the patient died suddenly of respiratory failure just before scheduled surgery. At autopsy the gallbladder was grossly and microscopically normal.

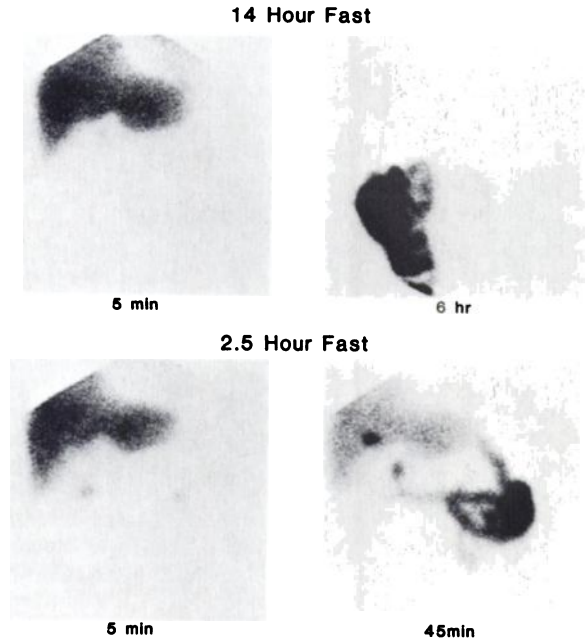

FIG. 2. After a 14-hour fast, hepatobiliary study shows mildly decreased hepatocyte clearance, normal biliary transit time, and nonvisualization of gallbladder through 6 hr (top). Two days later, repeat study following a 2.5-hr fast demonstrates gallbladder by 45 min (bottom).

DISCUSSION

Patients with normal hepatobiliary function who have fasted for 2 to 10 hr show gallbladder radioactivity in hepatobiliary studies by 60 min (*2,3,9*). In the four patients presented here, a prolonged state of fasting (14 hr to 12 days) correlated with nonvisualization of the gallbladder in radionuclide hepatobiliary studies. The presumed mechanism for such failures is that the bile becomes maximally concentrated and the gallbladder wall can no longer transport ions against the high osmotic gradient (*14,15*).

Our findings support a recent report of frequent false-positive diagnoses of cholecystitis in hepatobiliary studies of alcoholic patients and those on total parenteral nutrition (*13*). The authors proposed that bile stasis within the gallbladder inhibits entry of the radiopharmaceutical. They postulated that bile stasis is the result of hepatocyte damage and absence of oral intake, with an associated decrease in bile output and endogenous release of cholecystokinin-pancreozymin. In another report, physiologic gallbladder distention was implicated as a cause for delayed visualization (8 hr) of the normal gallbladder, presumably secondary to a prolonged fast (14), but the duration of the fast was not mentioned. It has been suggested that thick, concentrated bile or sludge within a full gallbladder may prevent easy diffusion of the radionuclide in some cases of chronic cholecystitis (*4*). Again, the fasting state is only implied. The presence of bile sludge can only be suggested by gallbladder nonvisualization, but it can be visualized by ultrasound as a densely echogenic layer in chronically dilated gallbladders (*13,17*).

The problem of a false-positive gallbladder study was recognized in the radiographic literature before the advent of radionuclide hepatobiliary imaging. The phenomenon of "cholecystocholestasis" was thought to account for some false-positive oral cholecystograms (*16*). In one study, a 60-hr fat-free diet resulted in faint visualization or nonvisualization of the gallbladder in normal volunteers, and it was concluded that stasis of bile in the gallbladder was the cause (*16*). This proposed mechanism is quite similar to that proposed for radionuclide studies.

At our institutions we have occasionally encountered a nonvisualized gallbladder in a radionuclide hepatobiliary study in a patient who has fasted for a prolonged period. Because of this experience, we now administer sincalide intravenously 30 min before radionuclide injection in those patients who have fasted longer than 24 hr. Also, we obtain delayed images up to 24 hr, or until the gallbladder is visualized. Some authors feel that 4 hr of imaging is sufficient for the diagnosis of acute cholecystitis (*3*). We feel that

this approach increases the reliability of the study in diagnosing acute cholecystitis.

Occasionally, sincalide may not be effective, as in Case 4. This may represent a problem in dosage or administration of sincalide. A dosage-dependent response of the gallbladder to sincalide has been reported, and the optimum dose found to be 0.02 μg/kg (*18,20*). This is the manufacturer's recommended dosage and the dosage used in our patient. Decreased effectiveness of sincalide in alcoholics and patients on total parenteral nutrition has been observed (*13*).

We tentatively conclude that prolonged fasting may cause nonvisualization of the gallbladder in radionuclide hepatobiliary studies. Our experience, and a review of the literature, support the concept that fasting causes bile stasis in the gallbladder, which may result in false-positive hepatobiliary studies for acute cholecystitis.

FOOTNOTE

* Kinevac, ER Squibb and Sons, Princeton, NJ.

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