

# A False-Positive Hepatobiliary Scan: Case Report and Literature Review

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*This case report describes a false-positive hepatobiliary scan in a young woman suspected to have acute cholecystitis who apparently had none of the reasons stated in the literature for a false-positive scan. The literature review shows that the negative predictive value of hepatobiliary scanning for acute cholecystitis is nearly 100 percent, while the positive predictive value is also quite good if conditions known to cause false-positive scans are ruled out. Common causes of positive hepatobiliary scanning, other than acalculus cholecystitis, include chronic cholecystitis, cholecystitis, hepatitis, alcoholism, total parenteral nutrition, pancreatitis, prolonged fasting, and ingestion of food less than one hour prior to scanning. Whether the postpartum state affects the accuracy of hepatobiliary scanning is speculative.*

Many authors consider hepatobiliary scanning to be the diagnostic procedure of choice in patients suspected of having acute cholecystitis.<sup>1,2</sup> Given the appropriate clinical setting, a positive radionuclide biliary scan is highly suggestive of acute cholecystitis,<sup>3,5</sup> and a normal scan can virtually exclude the diagnosis of acute cholecystitis.<sup>3,6-11</sup> Even though primary care physicians are frequently confronted with the differential diagnosis of an acute abdomen, the primary care literature contains relatively little information on this important diagnostic tool. The purpose of this article is to report an unusual case of a false-positive hepatobiliary scan, and to review the literature concerning the clinical usefulness of radionuclide imaging in the diagnosis of acute cholecystitis.

## CASE REPORT

An 18-year-old white woman, six weeks postpartum, presented with a one-week history of right upper quadrant pain that radiated to the right flank and the right scapula. The pain typically was constant, lasted several hours, resolved spontaneously, and was intermittently associated

with food ingestion. There was no history of nausea, vomiting, diarrhea, melena, or hematochezia. The patient had not had a menstrual period since her pregnancy and denied sexual activity since then. She did complain of a nonmalodorous vaginal discharge without pruritus since her pregnancy. She had last eaten about six hours prior to her presentation in the emergency room.

The past history was significant only for a right ovarian cyst, the therapy of which was unclear to the patient. The patient stated that she also had toxemia during her pregnancy.

The patient smoked one pack of cigarettes a day and denied use of alcohol or illicit drugs. She denied allergies and used acetaminophen occasionally for headaches.

On physical examination the patient was in mild distress secondary to abdominal pain. The pulse was 116 beats per minute, the blood pressure was 154/80 mmHg, the respiratory rate was 14/min, and the temperature was 37.7 °C orally. The abdominal examination revealed right upper quadrant tenderness with mild guarding; there was no rebound tenderness, palpable masses, organomegaly, costovertebral tenderness, or surgical scars. Bowel sounds were normal, rectal and pelvic examinations were unremarkable, and the stool was negative for occult blood. The rest of the physical examination was normal.

Admitting laboratory data showed a hemoglobin of 11 mg percent and a hematocrit of 33 percent; the mean cell volume was 83  $\mu^3$ ; the white blood count was  $13.3 \times 10^3/\mu\text{L}$  with 73 percent neutrophils, 1 percent band form, 21 percent lymphocytes, 4 percent monocytes, and 1 percent

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TABLE 1. COMMON CAUSES OF POSITIVE HEPATOBILIARY SCANNING OTHER THAN ACUTE CHOLECYSTITIS

|   |
|---|
| Chronic cholecystitis                               |
| Acalculous cholecystitis                            |
| Hepatitis   |
| Alcoholism  |
| Total parenteral nutrition                          |
| Pancreatitis*                                       |
| Gallstone pancreatitis*                             |
| Prolonged fasting (three or four days)              |
| Food ingestion less than one hour prior to scanning |

\* Controversial

eosinophil. The platelet count was adequate, and the prothrombin time and partial thromboplastin time were normal. Urinalysis showed a specific gravity of 1.022, pH of 7.0, trace acetone, and two to five red cells per high power field as well as occasional white cells. A urine culture later revealed no growth. Serum electrolytes, blood urea nitrogen, creatinine, and glucose were unremarkable. Total serum bilirubin was 0.4 mg/100 mL, the alkaline phosphatase was 164 U/L (normal 57 to 154 U/L), serum glutamic-oxaloacetic transaminase (SGOT) was 20 U/mL (normal 22 to 46 U/L), serum glutamic-pyruvic transaminase (SGPT) was 3 U/L (normal 22 to 46 U/L), and serum amylase was 49 U/L (normal 39 to 116 U/L). A urine pregnancy test was negative.

The results of an ultrasound of the gallbladder on admission were normal. A cholescintigraphic examination using diisopropyl iminodiacetic acid labeled with technetium 99m on the same day of admission showed prompt uptake of the isotope by the liver and rapid excretion into the small bowel without visualization of the gallbladder. No attempt to visualize the gallbladder more than one hour after the intravenous injection of the isotope was made, as very little radioactivity persisted in the liver parenchyma. The medical service made the diagnosis of acute cholecystitis, an impression shared by the surgical service. The patient was started on intravenous cefoxitin and was scheduled for surgery the next morning; no analgesic medication was administered. On laparotomy, the surgeons found no abnormality of the liver, liver capsule, biliary collecting system, or gallbladder. Their evaluation included an intraoperative ultrasound. The only abnormalities noted were some enlarged periportal lymph nodes, which were not biopsied; the gallbladder was not removed.

After a four-day uncomplicated hospital course, the patient was discharged. Save for what seems to be some minor incisional pain, the patient remained asymptomatic to the time of writing.

## DISCUSSION

The normal liver takes up intravenously administered  $^{99m}\text{Tc}$ -labeled derivatives of iminodiacetic acid (IDA) (PIPIDA, HIDA, BIDA, and DISIDA) and excretes it into the bile, providing the physiological basis for cholescintigraphy. The normal gallbladder will concentrate the isotope and excrete it promptly into the small bowel.<sup>5</sup> In patients with acute cholecystitis, the agent will be excreted into the small bowel but will not enter the gallbladder.

Radionuclide imaging of the hepatobiliary system has theoretical advantages over two other commonly used diagnostic tools in the evaluation of acute cholecystitis. As occlusion of the cystic duct is the underlying pathological process in acute cholecystitis, hepatobiliary scanning addresses the specific pathophysiological abnormality. Sonography is an anatomical study that provides circumstantial evidence for acute hepatobiliary disease by demonstration of gallstones or dilation of intrahepatic ducts. Cholescintigraphy is superior to oral cholecystography because of its usefulness in patients in whom the reliable absorption of iopanoic acid tablets is an issue. Finally, radionuclide scanning is useful even in the severely jaundiced patient, as DISIDA scanning has successfully visualized normal gallbladders in patients with serum bilirubin levels as high as 30 mg percent.<sup>10</sup>

The literature pertaining to hepatobiliary imaging by radionuclide cholescintigraphy reports highly accurate results when the test is used properly. Its negative predictive value approaches 100 percent<sup>6-9</sup> and its positive predictive value is also quite good. Many authors argue that a positive scan, that is, one that shows prompt excretion of the radionuclide agent into the small bowel without visualization of the gallbladder, constitutes sufficient evidence for the diagnosis of acute cholecystitis given the appropriate clinical setting.<sup>5,8</sup> Acalculous cholecystitis, seen in postoperative patients and patients with burns, trauma, sepsis, and acquired immunodeficiency syndrome, also results in a positive scan.<sup>12,13</sup>

Despite the high positive predictive value of a positive hepatobiliary scan, however, other conditions that give an abnormal scan must be ruled out (Table 1). Patients with chronic gallbladder disease without acute cholecystitis can have a nonvisualized gallbladder by radionuclide scanning; the rate of false-positive studies reported in the literature varies from 14 to 59 percent.<sup>2,6,11,14</sup> If a positive scan is defined as delayed visualization of the gallbladder (usually longer than one hour postinjection), the incidence of false-positive scanning in patients with chronic cholecystitis will be even higher.<sup>2,3,6,9,11,14-17</sup>

The presence of pancreatitis can be a confounding factor in cholescintigraphy. Many investigators think that the normal gallbladder is visualized in acute pancreatitis,<sup>14,18,19</sup> but many series list pancreatitis as a prominent

cause of false-positive tests.<sup>20-22</sup> Gallstone pancreatitis is an important cause of nonvisualization of the gallbladder,<sup>23-25</sup> but at least one article reports normal scans in patients who had gallstone pancreatitis.<sup>17</sup>

Hepatitis is a well-known cause of false-positive hepatobiliary scanning.<sup>3,19,25</sup> Because the radioisotope agent used in cholescintigraphy competes with the bilirubin in the circulating bloodstream for uptake by the liver, an elevated serum bilirubin can decrease uptake of the radioisotope by the liver and thus detract from the clarity of the images obtained. A patient with a nonvisualizing gallbladder with evidence of hepatitis probably has a false-positive test.<sup>3</sup>

Alcoholism, apparently independent of hepatocellular disease, and total parenteral nutrition are also causes for false-positive tests.<sup>4</sup> These conditions are important because they demonstrate that mechanisms other than cystic duct obstruction may result in the failure of bile to enter the gallbladder. Both of these conditions are associated with decreased bile production, absence of endogenous cholecystikinin stimulation, and increased bile viscosity. These factors diminish stimuli to the gallbladder to contract and refill and therefore compromise the ability of the labeled isotope to enter the gallbladder.<sup>14</sup>

A false-positive hepatobiliary scan in a patient with gastritis and a patient with a liver cyst, both of whom subsequently had normal intravenous cholangiography, are further isolated reported causes of false-positive tests.<sup>26</sup> No clinical details are given for either of these cases.

A rare cause of an abnormal hepatobiliary scan in the western hemisphere is reported from China.<sup>27</sup> Patients with intrahepatic stones, who present with the clinical triad of fever, pain, and jaundice, so-called Oriental cholangitis, often have intrahepatic pooling of the radionuclide isotope, or stasis, that is, delayed appearance of the isotope in the gut.

One study of the use of hepatobiliary scanning in patients with acute abdomen mentions a false-positive scan in a patient subsequently proven at laparotomy to have a normal gallbladder and a colonic lesion.<sup>7</sup> Other conditions reported in the literature to be associated with false-positive scans include liver metastases from a malignant melanoma,<sup>20</sup> uterine cancer with hepatic metastases,<sup>28</sup> cancer of the head of the pancreas,<sup>29</sup> gastric ulcer,<sup>29</sup> and perforated duodenal ulcer.<sup>30</sup>

Extrinsic compression of the cystic duct should constitute another reason for a false-positive radionuclide scan. This condition would prevent filling of the gallbladder even in the absence of cystic duct inflammation, but there are no such documented cases.<sup>31</sup> Congenital absence of the gallbladder would be another reason for a false-positive scan.

Published series that address the accuracy of cholescintigraphy cite occasional scans that are falsely positive for

none of the reasons noted.<sup>32,33</sup> None of these studies gives any clinical or laboratory details that might explain such false-positive results.

Finally, technical considerations can affect the accuracy of the radionuclide biliary scan. Some normal subjects will have a false-positive nonvisualization of the gallbladder if they have eaten less than one hour before the test.<sup>2,3,22,34</sup> Prolonged periods of fasting (greater than three or four days), on the other hand, may be a factor that explains some scans that are falsely positive in the absence of cholecystitis.<sup>34</sup> The length of time after injection of the radioisotope required to define a gallbladder as nonvisualized is also important, and some authors think one hour is insufficient time to detect 100 percent of normal gallbladders.<sup>3,11</sup>

The patient presented in this case report is unlike any in the literature. In the clinical scenario of the case presentation, most authors would agree that the positive predictive value for acute cholecystitis of a positive hepatobiliary scan approaches 100 percent. The patient did not have acute cholecystitis, however, and appeared to have none of the previously reported reasons for a false-positive radionuclide scan. She had a normal serum bilirubin; there was no evidence for pancreatitis, hepatitis, gastritis, perforated duodenal ulcer, gastric ulcer, liver metastases, or hepatic cysts; and she had no evidence of a chronically diseased gallbladder. She had no evidence of a colonic lesion and no indication that she had an intrahepatic stone. The patient was not an abuser of alcohol, was not receiving total parenteral nutrition, and she had neither eaten within an hour of performance of the test nor had she fasted for a prolonged period. Delayed films would not have visualized the gallbladder, as her liver's excretion of the isotope was prompt, and nearly all of the isotope at one hour postinjection was in the small bowel. It is doubtful that intravenous administration of morphine, advocated by some investigators to increase the specificity of radionuclide scanning, would have changed the result on this patient's scan, as this maneuver has been demonstrated to be useful only in situations already known to be associated with false-positive results (for example, chronic cholecystitis).<sup>35</sup>

At laparotomy, the surgical team found periportal adenopathy. As the gallbladder was normal in both size and appearance, extrinsic compression of the common bile duct as a cause for her false-positive scan seems unlikely.

A remote possibility for an explanation of the cause of the false-positive scan described in the patient in this report lies in her postpartum status. As documented by real-time ultrasonography, incomplete emptying of the gallbladder in pregnancy is well described.<sup>36,37</sup> This phenomenon, which is probably related to the high progesterone levels in pregnancy and resulting impairment of smooth muscle contraction, appears to normalize soon after de-

livery, although some of the scant literature on this subject hints that normalization of gallbladder emptying can take months.<sup>37,38</sup> At any rate, any effect that pregnancy or the period of one to two months postpartum has on hepatobiliary scanning is speculative.

While cholescintigraphy is generally a good test of the flow of bile into the gallbladder, the absence of such flow may not indicate cystic duct obstruction. Usually there is an explanation for such a false-positive study. As demonstrated by this case, however, false-positive studies may occur without any apparent reason.

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