Sequential Hepatobiliary Scintigraphy Demonstrating Apparent Transient Biliary Obstruction

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A case of acute acalculous cholecystitis in which sequential hepatobiliary scintigraphy demonstrated apparent transient biliary obstruction is presented. An initial technetium-99m diisopropyliminodiacetic acid ([^{99m}Tc]DISIDA) study in a patient suspected of acute cholecystitis showed persistent hepatic activity, nonvisualization of the gallbladder, and minimal intestinal activity seen only at 24 hr. Following a second injection of [^{99m}Tc]DISIDA administered shortly after the 24-hr image from the first study, the gallbladder and bowel were both visualized within 75 min. At subsequent surgery, acute and chronic cholecystitis were present without evidence of choledocholithiasis or other source of obstruction. Intrahepatic cholestasis following clearance of biliary obstruction may result in late bowel visualization on delayed cholescintigraphic images similar to that seen in partial obstruction. Accurate reflection of the state of hepatobiliary function may require reinjection with [^{99m}Tc] DISIDA.

J Nucl Med 28:1775–1779, 1987

Cholescintigraphy with technetium-99m- (^{99m}Tc) labeled iminodiacetic acid (IDA) derivatives is increasingly used as an adjunct for identifying the presence, degree, and location of extrahepatic biliary obstruction (*1–6*). In patients without underlying liver disease, prompt uptake of the IDA compound by the liver (the so-called hepatocyte phase) is typically followed by delayed (>1 hr) or absent (up to 24 hr postinjection) liver-to-bowel transit in partial or complete obstruction, respectively (*1,4,5,7*). Reported causes of absent or delayed bowel visualization in the absence of extrahepatic biliary obstruction include severe hepatocellular disease (*8–10*), hepatitis (*11*), and intrahepatic cholestasis (*12*). Occasionally, in a patient with cholelithiasis, but with a patent extrahepatic biliary tree at surgery, transient obstruction with subsequent passage of a gallstone has been suggested as the explanation for the variant scintigraphic and surgical findings (*2,4*).

We present here a patient in whom the changing pattern on two hepatobiliary scintiscans performed 1 day apart suggested occurrence and then clearance of a transient biliary tract obstruction. This case suggests the need for caution in interpreting 24-hr delayed hepatobiliary images because of similarities in the scintigraphic patterns of partial and transient biliary obstruction. Repeat hepatobiliary studies may be helpful in the evaluation of possible biliary tract obstruction.

Case Report

The patient is a 65-yr-old white male who was admitted to the hospital 6 hr following acute onset of supraumbilical abdominal pain accompanied by nausea, but no vomiting. A similar episode of pain had occurred 3 mo earlier, accompanied by rigors, fever (T = 102° F), and elevated white blood cell (WBC) count (17,000/cu mm; normal 4.5–11,000/cu mm). Although the pain had resolved spontaneously after several hours on the previous occasion, further evaluation was performed including abdominal ultrasound examination and hepatobiliary cholescintigraphy with ^{99m}Tc-labeled diisopropyliminodiacetic acid (DISIDA), both of which were normal.

Previous medical history was remarkable for similar episodes of abdominal pain 7 and 3 yr earlier, the latter of which ultimately was diagnosed as acute appendicitis, for which an appendectomy was performed. Intraoperative examination of the liver and gallbladder at that time was negative. The patient also had a 6-yr history of mild hypertension that was well controlled on hydrochlorothiazide.

Received Dec. 8, 1986; revision accepted June 15, 1987.

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On admission, the patient was afebrile, and physical examination, initial laboratory studies (including total bilirubin, alkaline phosphatase, and amylase), chest and abdominal x-rays were all within normal limits. On ultrasound examination, the walls of the gallbladder were mildly thickened, there were no stones within the gallbladder, and the common hepatic and common bile ducts were of normal caliber. Technetium-99m DISIDA [3 mCi (111 MBq)) was promptly taken up by the liver, but neither gallbladder nor bowel activity was seen up to 6.5 hr postinjection (Fig. 1A)]. A modest amount of renal activity was apparent on these images.

The next morning, on 24-hr delayed hepatobiliary imaging, a small amount of activity was present in bowel in the right lateral and superior abdomen, although the majority of activity remained in the liver (Fig. 1B). At this time, the patient was asymptomatic, but his temperature was mildly elevated (T = 99.8° F), his total bilirubin, alkaline phosphatase, and transaminase were moderately increased (Fig. 2), and his WBC count was 12,400/cu mm. Repeat sonography was unchanged from the previous day. In an attempt to clarify this somewhat confusing clinical picture, additional hepatobiliary images were obtained following administration of a second dose [^{99m}Tc]DISIDA (1.5 mCi (55.5 MBq)). The gallbladder was visualized by 30 min postinjection, and activity was seen in the duodenum by 75 min (Fig. 3).

The patient remained asymptomatic thereafter, and his liver function tests gradually returned to normal (Fig. 2). Elective cholecystectomy was performed on the fifth hospital day, with normal common bile duct and intraoperative cholangiogram. No stones were found in the gallbladder, but the serosal surface was slightly thickened, and there were areas of focal hyperemia. These findings were consistent with acute plus chronic cholecystitis.

The patient had an uneventful postoperative course, and was discharged on the twelfth hospital day.

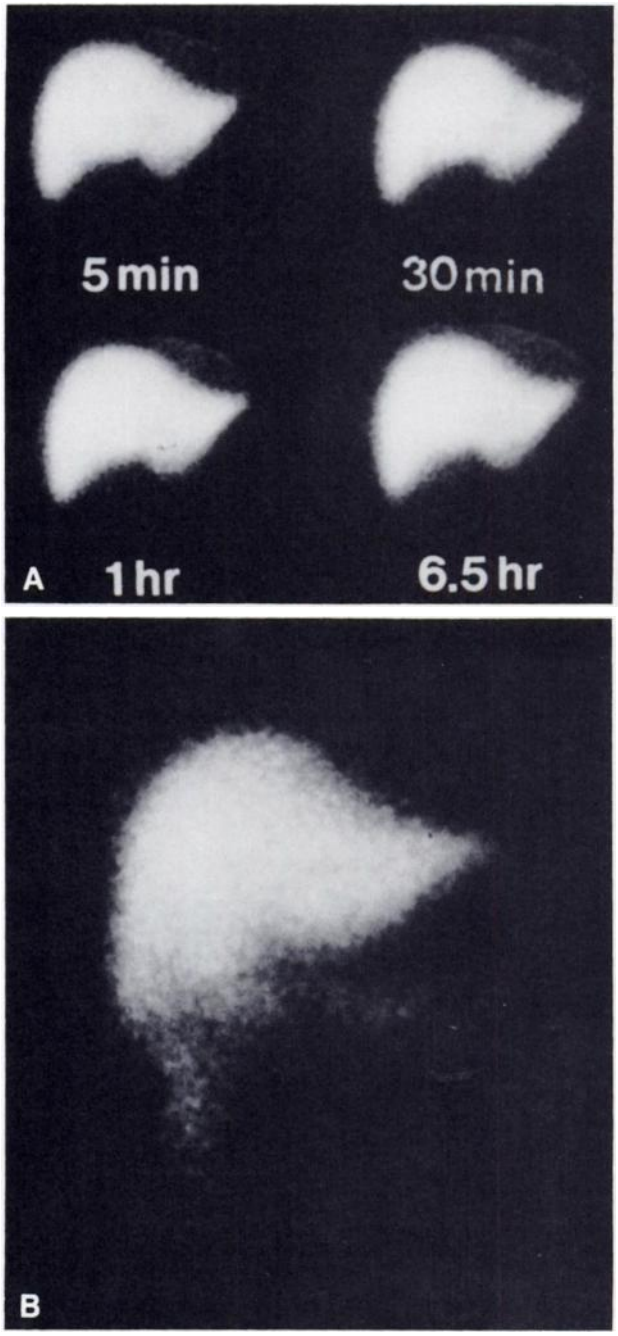

FIGURE 1
Initial [^{99m}Tc]DISIDA cholescintigraphy. Persistent hepatic activity is seen throughout the study, with nonvisualization of the gallbladder and bowel up to 6.5 hr postinjection (Panel A). Faint bowel activity in the right lateral and superior abdomen is seen on the 24-hr delayed image (Panel B).

DISCUSSION

The certainty with which the diagnosis of total biliary obstruction can be established from the combination of clinical presentation, hepatobiliary sonography, and cholescintigraphy is dependent to a considerable degree upon the duration of obstruction. Common bile duct obstruction of greater than 1 day is typically characterized by elevated serum bilirubin, alkaline phosphatase, and transaminase levels (*13,14*), sonographic evidence of dilated intra- and extrahepatic biliary radicles (*13*), and nonvisualization of the gallbladder and bowel with scintigraphy (*4,14*). Obstruction of less than one day is usually more difficult to identify; cholescintigraphy has been reported to demonstrate abnormalities earliest with absent bowel activity up to 4 or more hours after injection of the radiopharmaceutical (*7,13*), occasionally in association with normal gallbladder visualization (*2,3*). Even when the results of early noninvasive radiologic imaging are consistent with biliary obstruction, these findings are not always verified at subsequent surgery (*2,4*). When this occurs, clearance of a previous transient obstruction (usually by passage of a gallstone) is most often suggested as the reason that obstruction was not demonstrated at the time of surgery.

Cholescintigraphic evaluation of patients with possible biliary tract obstruction has received considerable attention in recent years, primarily in the context of discriminating between medical and surgical jaundice (*10,11,15*). Although distinguishing between obstruc-

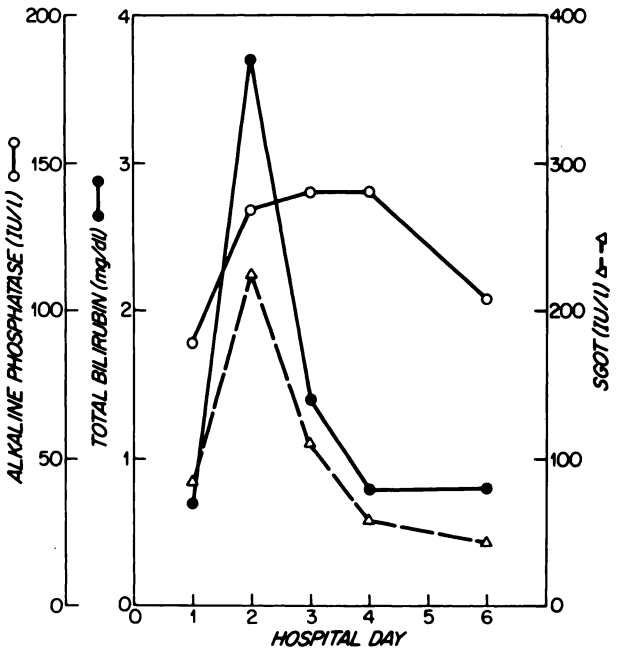

FIGURE 2
Time course of total bilirubin (normal 0.3–1.0 mg/dl), alkaline phosphatase (normal 20–100 IU/1), and serum glutamic oxaloacetic transaminase (SGOT) (normal 10–40 IU/1) during the first six hospital days.

tion and hepatocellular dysfunction is sometimes difficult scintigraphically (*8,16,17*), several recent studies have found prompt uptake of [^{99m}Tc]DISIDA (or BIDA) by the liver, followed by nonvisualization of bowel up to 4 hr postinjection, to be highly sensitive for the detection of biliary tract obstruction (95–100%) in patients without underlying liver disease (*6,11*). Causes of false-positive studies included hepatitis (*6, 10*), primary biliary cirrhosis (*11*), sickle cell crisis (*6*), and drug-induced cholestasis (*11*).

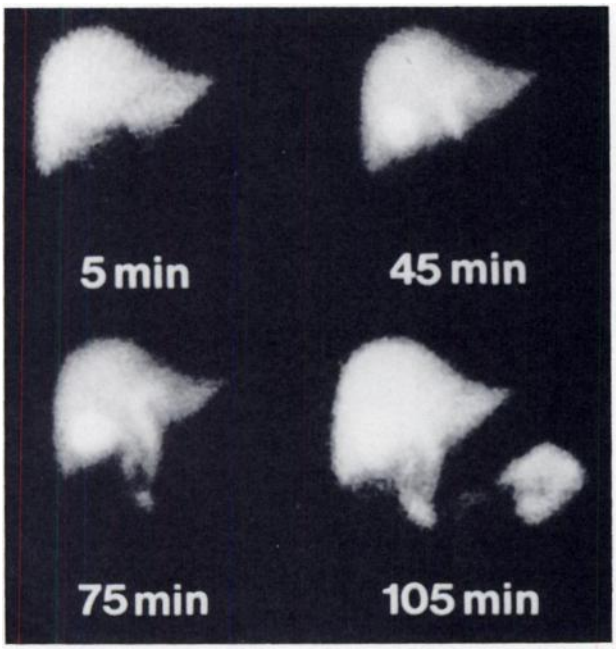

FIGURE 3
Repeat [^{99m}Tc]DISIDA cholescintigraphy injected ~1 hr following 24-hr image shown in Figure 1B. Note normal visualization of gallbladder, and bowel activity within 75 min.

Acute acalculous cholecystitis with transient extrahepatic biliary obstruction, an entity whose existence has been previously suggested (*18*), would seem the most likely explanation for the findings in the present case. The time course of symptoms, liver function tests, and DISIDA imaging was highly suggestive of transient obstruction; there was no evidence of a primary hepatic process such as hepatitis or drug-induced cholestasis, and narcotic analgesia capable of producing apparent common duct obstruction (*19*) had not been administered. Absent or delayed visualization of bowel scintigraphically has been reported in both acute and chronic cholecystitis (*18,20,21*), with mucosal changes and fibrosis in the ampullary region secondary to recurrent inflammation in the adjacent gallbladder (*21*) or extrinsic biliary tract compression (*22*) suggested as possible mechanisms. Cholangitis, of which there was no evidence in this patient, has also been associated with the scintigraphic pattern of common bile duct obstruction (*18,23*). Although passage of a gallstone remains a possible explanation for the progression of events in this patient, objective confirmation of calculous biliary disease is lacking, both from the present and previous hospitalizations.

The 24-hr delayed image from the initial hepatobiliary scan, showing most activity still present in the liver, remains a puzzling aspect of this case. Assuming an obstruction had cleared between the 6.5- and 24-hr images, why had not more of the [^{99m}Tc]DISIDA in the liver been excreted? It is possible that such clearance could have occurred only shortly before the late image, but the location of the activity in the bowel, which appeared to be in the ascending and transverse colon, argues against this hypothesis. Persistent partial obstruction of the common bile duct secondary to edema following passage of a stone could have produced prolonged hepatic retention of the [^{99m}Tc] DISIDA, but the nearly normal excretion of the second dose of DISIDA argues against this possibility as well. More likely, some degree of intrahepatic cholestasis persisted following resolution of the obstruction. This possibility then raises the question of whether the [^{99m}Tc]DISIDA complex retains its physiologic integrity during a period of intrahepatic cholestasis. The renal activity seen during the first study was not excessive, and did not suggest either increased [^{99m}Tc]DISIDA excretion by the kidneys or breakdown of the complex with liberation of free technetium. There was prompt uptake of both doses of [^{99m}Tc]DISIDA, indicating preserved hepatocyte function, although mild hepatic damage was re-

flected in the increased serum bilirubin and alkaline phosphatase. In the absence of obstruction, delayed gallbladder and/or bowel visualization as late as 24 hr postinjection is seen occasionally, indicating that the [^{99m}Tc]DISIDA complex is still effectively excreted by the liver (*20*). Whether such excretion also occurs in cases of transient obstruction is difficult to establish, since sequential studies during an acute obstruction and immediately after it has cleared are not readily obtainable. Late appearance of bowel activity (>1 hr postinjection) has usually been felt to reflect partial biliary obstruction (*1,9,10,12*) rather than possible interval clearance of a complete blockage. To our knowledge, the results of an immediate repeat cholescintigraphic examination in a patient whose initial study appeared to reflect partial obstruction have not been previously reported.

The results of this patient's several [^{99m}Tc]DISIDA scans may reflect different stages in the evolution or resolution of episodes of acute or subacute cholecystitis. The hepatobiliary study performed during the patient's previous hospitalization was begun more than 24 hr following his acute symptoms, and demonstrated normal liver-to-bowel transit (<1 hr), in sharp contrast to the study injected ~8 hr after symptoms started on the present occasion (Fig. 1). During the resolving phase of the acute event, the follow-up DISIDA study showed only slightly delayed bowel visualization (Fig. 3), most likely reflecting the late stages of resolution of the transient obstruction as the patient's acute cholecystitis improved. This would also explain the normal visualization of the gallbladder in this study, which might otherwise be considered a false-negative finding in a patient with proven acute cholecystitis. The exact time in resolving acute cholecystitis at which the gallbladder will be visualized on cholescintigraphy is unknown.

The results of the present case indicate that late delayed cholescintigraphic images should be interpreted cautiously in patients whose early images suggest, but other evidence (clinical, laboratory, or imaging) does not confirm the diagnosis of biliary obstruction. Images obtained following resolution of a transient total obstruction may be indistinguishable from those resulting from persistent partial obstruction with intrahepatic cholestasis. Administration of a second dose of the hepatobiliary agent at 24 hr should be considered if questions remain concerning whether medical or surgical management should be pursued.

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