Identification and Differentiation of Congenital Gallbladder Abnormality by Quantitative Technetium-99m IDA Cholescintigraphy

Mohammad A. Gad, Gerbail T. Krishnamurthy, and Jerry V. Glowniak

The Veterans Affairs Medical Center and Oregon Health Sciences University, Portland, Oregon

Failure to visualize the gallbladder in its usual location along the right inferior hepatic border suggests many possibilities including acute cholecystitis. The case described here reveals the importance of proper protocol for hepatobiliary imaging with ^{99m}TC-IDA agents, the necessity of quantification of function as an integral part of imaging to enable proper differential diagnosis. A case of bilobed gallbladder presenting as a Valentine heart in an unusual location in the liver is described. The measurement of the CCK-8 induced gallbladder ejection fraction for each lobe facilitated proper diagnosis.

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In recent years, hepatobiliary imaging has gained increasing popularity among physicians, especially since the introduction of the third generation ^{99m}Tc-IDA agents (*1*). The studies are requested either as the initial imaging test or to clarify the findings of other imaging procedures in the diagnosis of various hepatobiliary diseases. Quantification of function is becoming an integral part of imaging in nuclear medicine. The case described here demonstrates the importance of proper imaging and illustrates the role of quantification in the detection of a congenitally abnormal gallbladder.

CASE REPORT

Clinical History

A 37-yr-old black male was admitted to the hospital with a 10-mo history of postprandial colicky right upper quadrant pain and a 3-wk history of fever. Past medical history was significant for non-A, non-B hepatitis, and a right upper lobe needle liver biopsy in May 1989 had revealed pronounced inflammation with multilobular necrosis. Prior to admission, conjugated bilirubin was 0.9 (normal 0–0.4 mg/dl), GGT 1902 (normal 16–74 IU/liter), and amylase 70 (15–110 IU/liter). On admission, the white blood cell count was elevated at 18,600 cells/μl. Liver function tests revealed a total bilirubin of 1.2 (normal 0.1–1 mg/dl) and alkaline phosphatase of 916 (normal 67-213 IU/liter). A CT examination confirmed a multilobulated small liver (Fig. 1) and a small gallbladder with gallstones. Hepatobiliary scintigraphy was obtained to evaluate the liver and gallbladder function.

Scintigraphic Findings

The liver phase of the hepatobiliary study performed with 3 mCi of ^{99m}Tc-mebrofenin (Fig. 2A) revealed markedly inhomogeneous radiotracer uptake by the hepatocytes with very poor uptake in the right upper lobe. The right upper lobe hepatic extraction fraction (HEF) was 47.2% (normal 92%–100%), and the excretion $T_{½}$ was 77.9 min (normal 11–31 min). Duodenal flow of radiotracer was seen at 22 min, and there was no scintigraphic evidence for extrahepatic biliary obstruction (*2,3*). There was no bile collection in the usual gallbladder fossa along the inferior liver border. Instead, bile pooling in the form of a Valentine heart was noted close to the junction of the right and left hepatic ducts suggesting a possible aberrant gallbladder. Repeat ^{99m}Tc-mebrofenin imaging two days later again revealed the Valentine heart-shaped structure in the same location, and the usual gallbladder fossa was again free of any bile accumulation (Fig. 2B). At 45 min, a 10 ng/kg dose of cholecystokinin-8 (CCK-8) was administered intravenously over a 3-min period through an infusion pump. Two regional (Fig. 3A) as well as total ejection fractions of the Valentine gallbladder were calculated. The total ejection fraction was 47.8% (normal >35%).

One day after the hepatobiliary imaging study, the patient had endoscopic retrograde cholangiopancreatography (ERCP), which revealed a bilobed gallbladder (Fig. 3B) and marked marginal serrations consistent with hypertrophied Rokitansky-Aschoff sinuses. Filling of the intrahepatic ducts was difficult and produced pain. The gallbladder contained irregular lucent material suggestive of stones. The small liver associated with the somewhat corkscrew appearance of the bile ducts suggested cirrhosis.

Hospital Course

Ten days later at elective cholecystectomy, the right and left liver lobes showed firm round nodules varying from 2 to 4 cm in size. The gallbladder was found high up in the porta hepatis along the inferior liver surface. The bilobed gallbladder was resected from the inferior hepatic bed. Open liver biopsy of the right and left lobes and an intraoperative cholangiogram were obtained. Surgery was uneventful and the patient was discharged on the fourth postoperative day.

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For reprints contact: G.T. Krishnamurthy, MD, VA Medical Center (115), PO Box 1034, Portland, OR 97207.

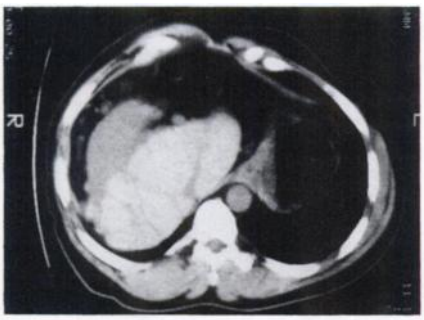

FIGURE 1. Right lateral decubitus CT of the liver shows small multilobulated liver with different tissue densities consistent with cirrhosis.

Pathologic Findings

Intraoperatively opened gallbladder revealed two lobes with several small multifaceted stones ranging in size from 3–8 mm in greatest dimension. Gross pathologic examination revealed a 7.5 × 3 × 1.8 cm gallbladder with an irregular, trabeculated, dark brown mucosa. Microscopic examination did not reveal any specific abnormality of the gallbladder wall.

Right liver lobe biopsy revealed reactive hepatocytes with decreased portal triads suggestive of a regenerating nodule. Left lobe biopsy showed proliferating bile ducts, marked fibrosis, and chronic inflammation. The overall histological changes were compatible with submassive hepatic necrosis and subsequent development of cirrhosis with regenerating nodules. Intraoperative cholangiogram revealed normal common hepatic and common bile ducts without any filling defects.

DISCUSSION

Bile accumulation in an unusual configuration and location and no bile collection in the traditional gallbladder fossa raises many possibilities for differential diagnosis. The most common cause of lack of bile collection in the usual gallbladder fossa is surgical or laparoscopic cholecystectomy, cystic duct obstruction due to acute cholecystitis, or a ^{99m}Tc-HIDA study done immediately after feeding. This patient had no history of previous cholecystectomy and the clinical presentation was suggestive but not strongly indicative of acute cholecystitis. A less frequent cause of gallbladder absence is congenital agenesis occurring in one in 7500 autopsies (*4*). A review of the literature in 1988 found 381 published cases of congenital gallbladder agenesis (*5*). Gallbladder agenesis is attributed to nonvacuolization of the gallbladder primordium during embryonic life (*6*).

The differential diagnosis of a collection of a large quantity of bile along the course of the biliary tree includes:

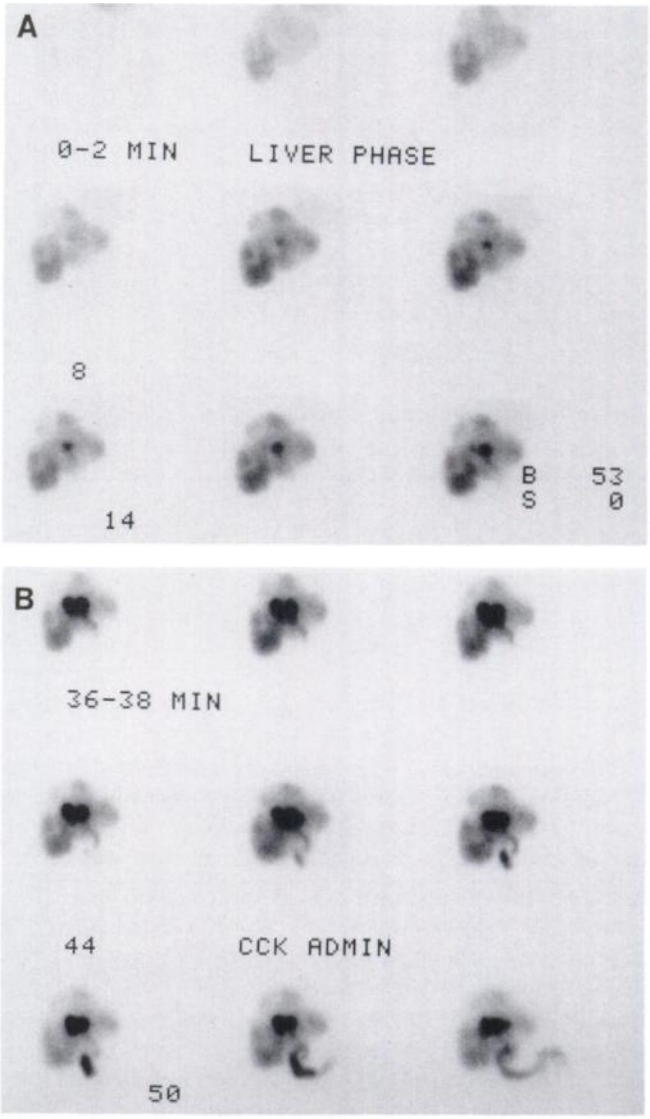

FIGURE 2. Early liver phase images show irregular ^{99m}Tc-mebrofenin uptake over the right lobe corresponding to histologically confirmed cirrhosis (A). Late liver phase images (B) show a Valentine-shaped gallbladder adjacent to the hepatic duct. No bile collection is seen in the traditional gallbladder fossa. The Valentine gallbladder empties following CCK-8 infusion at 44 min.

(a) intrahepatic gallbladder, (b) choledochal cyst, (c) simple or multicystic liver disease with ruptured septum and (d) bilobed or duplicated gallbladder. During the first 2 mo of intrauterine life, the gallbladder is embedded within the

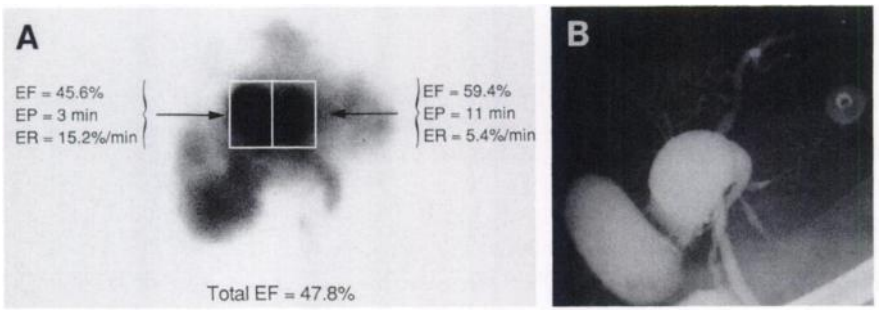

FIGURE 3. The Valentine gallbladder empties in response to CCK-8 with a total ejection fraction (EF) of 47.8%, with slightly different EF values for each lobe (A). EP = ejection period; ER = ejection rate. ERCP confirms the bilobed Valentine gallbladder with a single cystic duct (B).

liver parenchyma. Intrahepatic gallbladder is a congenital anomaly where the caudal projection of the hepatic diverticulum from which the gallbladder develops (*6*) fails to descend and gets embedded within the hepatic parenchyma. An intrahepatic gallbladder may cause a round or pear-shaped filling defect within the liver which fails to contract and empty bile following a meal leading to large residual bile and stone formation. An intrahepatic gallbladder may empty poorly in response to CCK-8 because the wall of the gallbladder is not free to contract and empty bile (*7*). No Valentine-shaped filling defect within the liver in the early liver phase image and a normal emptying response to CCK-8 excluded an intrahepatic gallbladder in our patient. A subhepatic gallbladder may mimic an intrahepatic gallbladder due to the extension of the inferior liver border in front of the gallbladder as was the case in our patient (Fig. 2B).

Choledochal cysts are congenital abnormalities in the vicinity of the common bile duct. They are either of the fusiform or saccular type (Fig. 4). They often act as a substitute bile reservoir and fail to empty following a meal (*8*). The normal gallbladder which is usually present along with the cyst either fills in late or does not fill with bile at all. In 12 patients with choledochal cysts reported by Componovo et al., the gallbladder appeared within 1 hr in one patient, was delayed in two patients, and did not appear at all in nine patients (*9*). The location and shape does not support a choledocal cyst in our patient. Adult-type polycystic kidney disease (PKD) is an autosomal dominant hereditary disease associated with multiple liver cysts (*10*). In patients with PKD, frequency of liver cysts is 20%–40% (*11*). Liver cysts in PKD are seen as filling defects within the liver parenchyma in the hepatic phase of a ^{99m}Tc-IDA study (*12*). The cysts do not fill with bile unless the cyst wall ruptures (*12*).

Gallbladder duplication results from an additional inferior bud on the superiorly advancing ventral biliary tract diverticulum (*6*). When the extra bud fails to regress, two gallbladders are formed, each with an independent cystic duct (Fig. 5). Gallbladder duplication is rare in humans and occurs in 1 out of 4000 cases. However, duplication is common in cats, occurring in 12% (*4*). Other forms of abnormalities are caused by a septum placed either along the long- or the short-axis of the gallbladder. A septum along the long-axis is rare and divides the gallbladder equally into two compartments, where both share a common cystic duct. The septum along the short-axis is relatively more common and is found in 1 of 800 cases (Fig. 5). The short-axis septum divides the gallbladder unequally, often preventing bile emptying from the fundal portion of the gallbladder and thus promoting stone formation only in the distal segment (*4*). Most of the patients with septate gallbladders remain asymptomatic, and their frequent identification is attributed to widespread use of ultrasound for abdominal evaluation.

The diagnosis of various gallbladder abnormalities by ^{99m}Tc-IDA scintigraphy require utilization of both morphologic and quantitative physiologic parameters. All of the findings collectively are consistent with a bilobed Valentine subhepatic gallbladder, which was verified at surgery. The pattern of markedly abnormal liver function tests associated with patchy ^{99m}Tc-IDA uptake was consistent with non-A, non-B hepatitis progressing to cirrho-

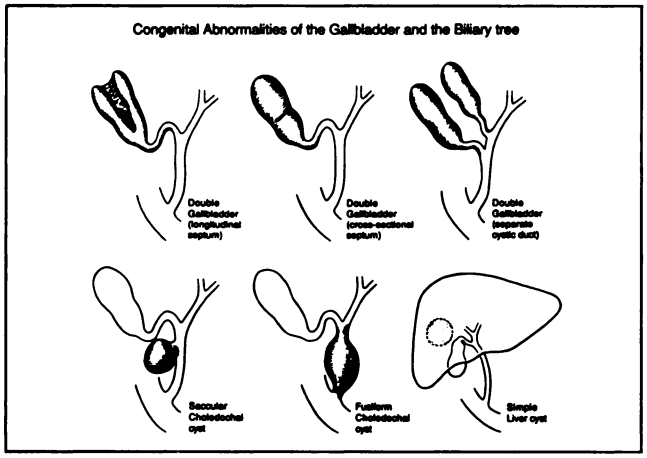

FIGURE 4. Various types of congenital anamolies of the gallbladder (see text for details).

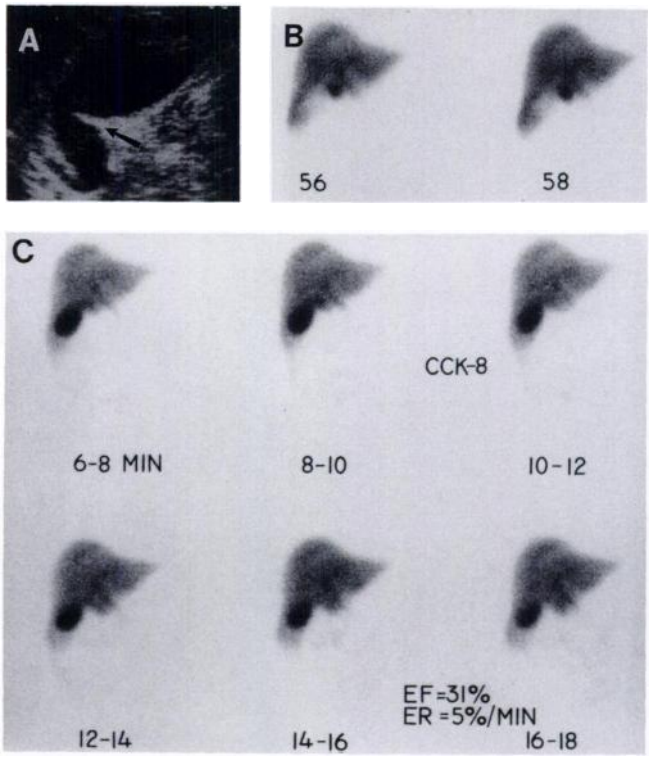

FIGURE 5. In another patient, a transverse septum (arrow) well visualized on US divides the gallbladder into two portions (A). The portion connected to the cystic duct fills with bile at 56–58 min (B) and the portion towards the fundus fills 2 hr later (C). Following injection of CCK-8, the fundal portion empties poorly, but the portion connected to the cystic duct empties much better with an ejection fraction (EF) of 31% (C). ER = ejection rate.

sis. Low hepatic extraction fractions and prolonged hepatic excretion $T_{½}$ on hepatobiliary scintigraphy were consistent with moderate to severe hepatocellular disease without any evidence for common bile duct obstruction. This patient points out the importance of being prepared to address unexpected findings during hepatobiliary imaging with ^{99m}Tc-IDA agents in solving the problems encountered by the patient and the referring physicians.

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