Prognostic Value and Pathophysiologic Significance of the Rim Sign in Cholescintigraphy

Gregory K. Meekin, Harvey A. Ziessman, and R. Scott Klappenbach

Division of Nuclear Medicine, Department of Radiology, Department of Pathology, Georgetown University Medical Center, Washington, DC

This study reviews 27 patients with nonvisualization of the gallbladder on cholescintigraphy. The preoperative diagnosis of acute cholecystitis was confirmed pathologically in 23. A rim of increased hepatic activity (RIHA) adjacent to the gallbladder fossa was seen throughout the study in 35% with acute cholecystitis and in no patients with chronic cholecystitis. Nine patients with "complicated" cholecystitis (defined pathologically as a late stage of the spectrum of acute cholecystitis) had a positive RIHA in contrast to no patients with "noncomplicated acute cholecystitis" ($p < 0.05$). The sensitivity/specificity of the RIHA for "complicated" acute cholecystitis was 45%/100% and the positive/negative predictive value was 100%/39%. Liver tissue that was attached to the gallbladder by adhesions and removed at surgery was reviewed histologically and correlated with the presence or absence of a RIHA. The RIHA seems to be a useful indicator of patients presenting at a later stage of the pathologic spectrum of acute cholecystitis and perhaps at increased risk for complications.

J Nucl Med 28:1679–1682, 1987

Nonvisualization of the gallbladder on technetium-99m (^{99m}Tc) HIDA cholescintigraphy with normal hepatobiliary transit is diagnostic of acute cholecystitis with a sensitivity >95% (*1–3*). The reported specificity is also high, although false-positive studies do occur (*4, 5*). A rim of increased hepatic activity (RIHA) directly adjacent to the gallbladder fossa has recently been described in association with nonvisualization of the gallbladder with a reported incidence of 21% and 60% (*6, 7*). These reports suggest that, although it is not a sensitive sign of acute cholecystitis, it appears to be fairly specific. It has been particularly associated with gangrene and perforation (*8, 9*).

The purpose of our study was to evaluate the frequency and significance of this finding in our patient population, to determine its value for predicting complications of acute cholecystitis, and to investigate its pathophysiologic significance.

Materials and Methods

A retrospective review of 416 consecutive [^{99m}Tc]DISIDA (Tc-disofenin) hepatobiliary studies performed between 1981 and 1985 at GUH revealed 105 with nonvisualization of the gallbladder and normal hepatobiliary transit. Clinical records, pathologic and surgical reports were obtained for 27 patients who underwent surgery; cholecystectomy (*26*), and cholecystotomy (*1*). There were 18 females and nine males whose ages ranged from 21 to 87 yr (mean 61 yr). The other 78 patients either did not undergo surgery or their records were unobtainable.

Cholescintigraphy was performed after an intravenous injection of 5 mCi (185 MBq) [^{99m}Tc]disofenin (2,3-disopropyliminodiacetic acid). All 27 patients had been fasting at least 2 hr but <48 hr prior to the study. None received cholecystokinin. Anterior abdominal images were acquired immediately and at 5, 15, 30, 45, and 60 min after injection for 500,000 counts each on a large field-of-view gamma camera with a low-energy, all purpose parallel hole collimator. The study was considered normal when the gallbladder and small bowel visualized within 60 min. Otherwise the study was continued with delayed images obtained up to 4 hr after injection until there was visualization of these structures or hepatic activity had cleared. Right lateral and left anterior oblique images were obtained as needed. Persistent nonvisualization of the gallbladder with normal hepatobiliary transit was considered to be positive for acute cholecystitis. The hepatobiliary scans were reviewed for the presence or absence of a rim of increased hepatic activity (RIHA) directly adjacent to the gallbladder fossa (Fig. 1).

Pathologic and surgical reports were reviewed in order to

Received Aug. 18, 1986; revision accepted May 11, 1987.

For reprints contact: Harvey A. Ziessman, MD, Georgetown University Hospital, 3800 Reservoir Rd., NW, Washington, DC 20007.

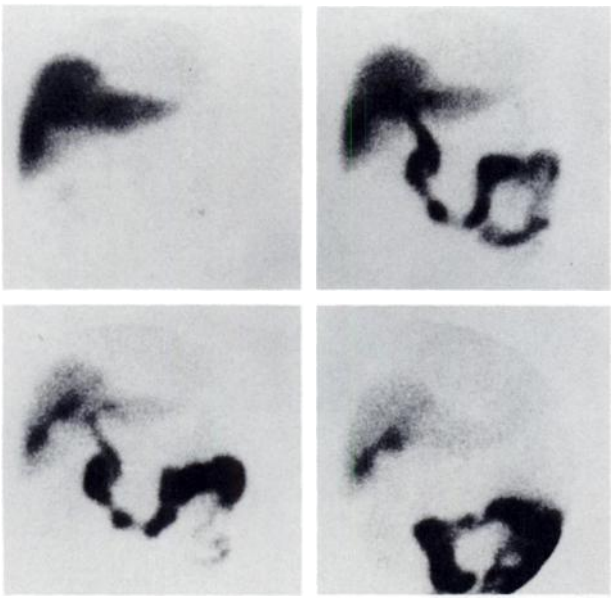

FIGURE 1
Technetium-99m DISIDA images taken at 5, 30, and 60 min and 4 hr postinjection demonstrate a prominent RIHA that is seen throughout the study.

categorize the findings according to the stage of acute cholecystitis and its complications as described by Schein (*10*). For example, evidence at *surgery* of gallbladder edema, dilatation, perforation, empyema, or gangrene or *pathologic* specimens showing cellular infiltration, fibrous exudation, ulceration or necrosis was recorded. "Complicated" acute cholecystitis was defined as the presence of one or more of the following findings: ulceration, necrosis, fibrous exudation, perforation, empyema, or gangrene. These findings were felt to be a late stage of a pathological spectrum of acute cholecystitis representing more serious illness and having the potential for serious clinical manifestations. In contrast, "noncomplicated" cholecystitis was defined as having the surgical and pathologic findings limited to edema, dilatation, and cellular infiltration. The number of studies with and without a RIHA was determined for "complicated" and "noncomplicated" acute cholecystitis and for each surgical or pathologic finding. The sensitivity, specificity, and positive and negative predictive values were then determined.

The microscopic histopathology from 22 patients was reviewed by an experienced pathologist (RSK) for the purpose of studying liver tissue adjacent to the gallbladder that had been removed at the time of surgery.

RESULTS

Nine of 27 studies with nonvisualization of the gallbladder and the preoperative diagnosis of acute cholecystitis had the presence of a RIHA. In all positive studies, the RIHA could be seen throughout the study as a curvilinear band of increased activity along the inferior hepatic edge of the gallbladder fossa (Fig. 1). This RIHA could be seen on the 4-hr delayed images as well. The diagnosis of acute cholecystitis was confirmed by pathologic criteria in 23 patients. The RIHA was seen in eight of 23 (35%). The one additional patient with a RIHA only had a cholecystotomy performed, therefore, no gallbladder tissue specimen was available for pathologic review. At surgery this patient was noted to have a small perforation and intraperitoneal pus. Three patients had a diagnosis of chronic cholecystitis. None had a RIHA.

Eight of nine patients with a RIHA had gallbladders described as dilated at surgery in contrast to six of 18 patients without a RIHA and dilatation at surgery ($p = 0.006$). Only two patients with gallbladder tissue pathology had perforation; neither had a RIHA. One additional patient described above with cholecystotomy and therefore no confirmatory pathology had a small perforation described at surgery.

Twenty patients had "complicated" and seven had "noncomplicated" cholecystitis. Nine of 20 patients with "complicated" acute cholecystitis had a positive RIHA, in contrast to none of seven patients with "noncomplicated" cholecystitis ($p < 0.05$). The sensitivity/specificity of the RIHA for "complicated" acute cholecystitis was 45%/100% and the positive/negative predictive value 100%/39%.

In the 22 cases where the microscopic pathology was reviewed, five had liver tissue attached by adhesions to the gallbladder specimen. Four had sufficient liver tissue to review histologically. In one patient with a strongly positive RIHA, the adjacent liver tissue showed inflammatory changes of edema, Kupffer cell hyperplasia, and sinusoidal congestion (Fig. 2). A second patient with a prominent RIHA has lesser changes of Kupffer cell hyperplasia and hepatocyte ischemia. A third patient with a mildly positive RIHA had normal liver pathology. The fourth patient had no RIHA and no liver abnormality. One additional patient in our study with gallbladder necrosis, ulceration, and hemorrhage at pathology was found at surgery to have empyema of the gallbladder with necrotic liver tissue in the gallbladder fossa. No microscopic pathology of the liver was available for our review. The Tc-DISIDA study showed no RIHA.

DISCUSSION

Recent reports have associated the newly described finding of a RIHA with acute cholecystitis and with two particular complications, perforation and gangrenous cholecystitis (*6–9*). The results of our study suggest that the presence of a RIHA associated with nonvisualization of the gallbladder is a clinically useful scintigraphic finding in identifying patients who are at a later stage of the pathologic spectrum of acute cholecystitis and possibly at increased risk for serious complications. Although the sensitivity of the RIHA for "complicated"

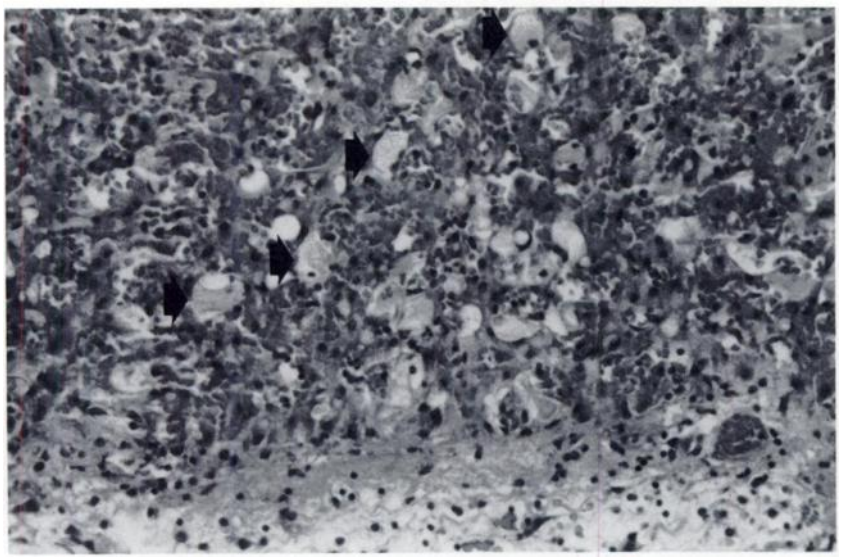

FIGURE 2
In a patient with a positive RIHA, liver parenchyma adjacent to gallbladder shows capsular edema (lower portion of field), sinusoidal congestion, and prominence of Kupffer cells (arrows) laden with bile and lipid material (hematoxylin and eosin ×225).

acute cholecystitis is low, its specificity and positive predictive value are high.

Of particular interest is the mechanism of production of the RIHA. Schein describes three stages of acute cholecystitis following obstruction of the cystic duct; the first being that of edema and congestion, the second a cellular response and the third, vascular and bacterial complications (*10*). These stages are dynamic and follow a relatively predictable time course. It is possible that the RIHA may be associated with a particular stage of acute cholecystitis and that for the sign to be present the scan must be performed during that time frame. In this retrospective study no definite correlation could be found between the time from onset of the patient's symptoms to the time of the hepatobiliary study or surgery with the presence or absence of a RIHA. Clearly other factors may play a role in determining the presence or absence of an inflammatory RIHA, e.g., antibiotics, steroids, and antiinflammatory drugs. Importantly, we found no patient who had "noncomplicated" acute cholecystitis with a RIHA. In addition, the liver pathology found in our patients demonstrates a spectrum of inflammatory changes which suggest a possible etiologic relationship to the RIHA.

It has been suggested that the RIHA is the result of an inflammatory process starting in the gallbladder and spreading to the adjacent hepatic parenchyma (*6,8*). The above cases support this hypothesis. The pathophysiologic mechanism explaining the RIHA might be as follows. After obstruction, the gallbladder becomes edematous, congested, and dilated, followed by cellular inflammation. The close proximity of the dilated, increasingly inflamed gallbladder allows the inflammatory process to spread to the adjacent liver. Our findings that eight of nine patients with a RIHA had dilated gallbladders at surgery, but only six of 18 ($p = 0.006$) without a RIHA had dilatation would support this hypothesis. The inflammatory process has been described as greater in the hepatic aspect of the gallbladder than on the free peritoneal edge (*11*) and that the liver edge may show inflammatory changes (*12*). The inflammatory process in the adjacent liver tissue could cause hyperemia, local obstruction of bile canaliculi, extravasation of tracer, and reduced cellular ability to excrete the tracer. With continuing inflammation the liver edge may undergo vascular changes leading to necrosis, the end of the spectrum of inflammatory changes.

It has been suggested that because the RIHA is specific for acute cholecystitis, the study could be concluded at 1 hr, because 2–4 hr delayed images were not necessary to avoid a false-positive study due to chronic cholecystitis (*7*). The positive predictive value of 100% for complicated acute cholecystitis in our study for the RIHA in the setting of nonvisualization of the gallbladder, supports this approach.

In summary, the RIHA appears to be a useful indicator of patients presenting at a later stage of the pathological spectrum of acute cholecystitis and who are perhaps at increased risk for serious complications. Our study suggests that the pathophysiologic mechanism for the RIHA may be related to spread of gallbladder inflammation to adjacent liver and that the stage of inflammation may determine whether or not the sign is present.

ACKNOWLEDGMENTS

The authors thank Martha Witebsky, Sandra Pruitt, and Judy Levy for their help in typing and preparing the manuscript.

REFERENCES

1. Weissmann HS, Badia J, Sugarman LA, et al. Spectrum of ^{99m}Tc-IDA cholescintigraphic patterns in acute cholecystitis. *Radiology* 1981; 138:167–175.
2. Freitas JE, Coleman RE, Nagle CE, et al. Influence of

scan and pathologic criteria on the specificity of cholescintigraphy: concise communication. *J Nucl Med* 1983; 24:876–879.
3. Zeman RK, Burrell MI, Cahow CE, et al. Diagnostic utility of cholescintigraphy and ultrasonography in acute cholecystitis. *Am J Surg* 1981; 141:446–451.
4. Schuman WP, Gibbs P, Rudd TG, et al. PIPIDA scintigraphy for cholecystitis: false positives in alcoholism and total parenteral nutrition. *Am J Roentgenol* 1982; 138:1–5.
5. Kalff V, Froelich JW, Lloyd R, et al. Predictive value of an abnormal hepatobiliary scan in patients with severe intercurrent illness. *Radiology* 1983; 146:191–194.
6. Smith R, Rosen JM, Gallo LN, et al. Pericholecystic hepatic activity in cholescintigraphy. *Radiology* 1985; 156:797–800.
7. Bushnell DL, Perlman SB, Wilson MA, et al. The rim sign: association with acute cholecystitis. *J Nucl Med* 1986; 27:353–356.
8. Brachman MB, Tanasescu DE, Ramanna L, et al. Acute gangrenous cholecystitis: radionuclide diagnosis. *Radiology* 1984; 151:209–211.
9. Smith R, Rosen JM, Alderson PO. Gallbladder perforation: diagnostic utility of cholescintigraphy in suggested subacute or chronic cases. *Radiology* 1986; 158:63–66.
10. Schein CJ. Acute cholecystitis. New York: Harper & Row, 1972: 41–49.
11. Andrews E. Pathological changes of diseased gallbladders. *Arch Surg* 1935; 31:767–793.
12. Noble JF. The relation of hepatitis to cholecystitis. *Am J Path* 1933; 9:473–493.