

Indium-111-Leukocyte Imaging in Acute Cholecystitis

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Eleven patients with suspected acute cholecystitis underwent sequential ^{99m}Tc -iminodiacetic derivative (IDA) and ^{111}In -white blood cell (WBC) imaging to determine if ^{111}In -WBCs accumulate within an acutely inflamed hemorrhagic gallbladder wall and, thus, could be employed as a reasonable alternative to ^{99m}Tc -IDA scintigraphy in detecting acute cholecystitis. Seven patients had surgically confirmed acute cholecystitis. Of these cases, five had a true-positive ^{99m}Tc -IDA and ^{111}In -WBC, one an indeterminate ^{111}In -WBC and true-positive ^{99m}Tc -IDA, and one a true-positive ^{111}In -WBC and false-negative ^{99m}Tc -IDA scan. The remaining four patients did not have acute cholecystitis. All visualized their gallbladder within 1 hr after ^{99m}Tc -IDA administration and none had ^{111}In -WBC gallbladder wall uptake. Both ^{111}In -WBC and ^{99m}Tc -IDA scintigraphy accurately detected acute cholecystitis: hepatobiliary scintigraphy demonstrated a cystic duct obstruction and ^{111}In -WBC imaging detected the inflammatory infiltrate within the gallbladder wall. The sensitivity and specificity of each was 86% and 100%, respectively.

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Hepatobiliary scintigraphy is a reliable method to confirm the clinical impression of acute cholecystitis. The sensitivity and specificity of cholescintigraphy in diagnosing acute cholecystitis ranges from 96% to 100% and 81% to 100%, respectively (1-3). False-positive and false-negative studies, however, do occur. False-positive studies have been reported in patients with severe chronic cholecystitis, anorexia, and in patients who have undergone a prolonged fast, total parenteral hyperalimentation or are septic with hepatitis; false-negative examinations in a few patients with acute acalculous cholecystitis also have been reported (4-5). Some previous studies by Datz (6) and Bauman et al. (7) suggest that indium-111-white blood cells (^{111}In -WBCs) accumulate within an inflamed hemorrhagic gallbladder wall and, thus, could be employed as a reasonable alternative to technetium-99m-iminodiacetic derivative (^{99m}Tc -IDA) scintigraphy to detect acute cholecystitis. We performed the following pilot study to compare these two approaches.

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MATERIALS AND METHODS

Eleven patients with a clinical suspicion of acute cholecystitis underwent sequential ^{99m}Tc -IDA/ ^{111}In -WBC scintigraphy to determine: (a) if ^{111}In -WBCs would accumulate within an acutely inflamed hemorrhagic gallbladder wall and (b) the sensitivity and specificity of each agent in detecting acute cholecystitis. All eleven patients were male, ages 43-90 yr (mean 66 yr).

During WBC labeling, each patient (NPO 4 hr) received 5 mCi of either ^{99m}Tc -disofenin or mebrofenin. Anterior 500,000 count standard gamma camera images of the liver and biliary tree were then obtained using a low-energy, all-purpose collimator with a 20% window centered around the 140-keV ^{99m}Tc photopeak at 10-min intervals for 1 hr. Delayed images were obtained up to 4 hr post-radiotracer administration in patients whose gallbladders were not visualized within 60 min. Following this, 500 μCi of the patient's ^{111}In -WBCs were injected and comparable anterior abdominal images were obtained at 4 and 24 hr using a medium-energy collimator with a 20% window centered on the 175- and 247-keV ^{111}In photopeaks. The WBCs were a mixed population and were labeled using the method described in the package insert for ^{111}In -oxyquinoline solution (Amersham) for the radiolabeling of autologous leukocytes with the following modifications:

1. ACD was used as our anticoagulant.
2. Hetastarch was employed in all sedimentation steps.
3. 300 G \times 5 min was used for all centrifugation steps.

A positive ^{99m}Tc -IDA scan demonstrated nonvisualization of the gallbladder up to 4 hr post-radiotracer administration. A positive ^{111}In -WBC scan was one in which ^{111}In -WBC uptake was present within the gallbladder wall. This was manifested by ^{111}In uptake within the gallbladder fossa or below it (i.e., the doughnut sign).

No patients were evaluated in whom liver function was reduced. Acute cholecystitis was present if confirmed histologically by the presence of hemorrhagic necrosis of the gallbladder wall, transmural leukocytic infiltration, or mural edema. Six patients had calculous and one patient had acalculous acute cholecystitis.

RESULTS

Six out of seven patients with acute cholecystitis were ^{111}In -WBC positive, four as early as 4 hr after ^{111}In -WBC administration. One was indeterminate because the location of the gallbladder was unknown, and, thus, we could not determine if ^{111}In -WBC uptake within the inferior portion of the right lobe of the liver was a manifestation of normal hepatic uptake or uptake within an inflamed gallbladder wall. Six patients were ^{99m}Tc -IDA positive and one was negative (Fig. 1A-B).

The patient whose gallbladder visualized after ^{99m}Tc -IDA administration demonstrated a small focus of ^{111}In -

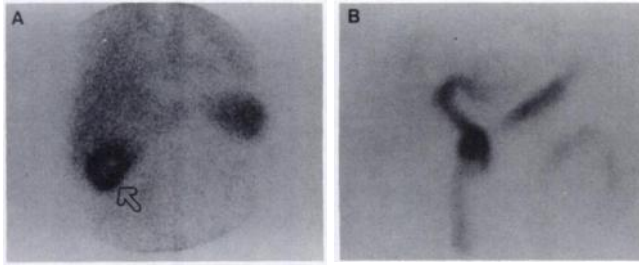


FIGURE 1. (A) Twenty-four-hour anterior ^{111}In -WBC gallbladder scan reveals increased accumulation of ^{111}In -leukocytes (—→) within the gallbladder wall (doughnut sign) of a 67-yr-old man with right upper quadrant pain, nausea, vomiting, and a leukocytosis who postoperatively was found to have acute calculous cholecystitis. (B) Four-hour delayed anterior $^{99\text{m}}\text{Tc}$ -IDA hepatobiliary scan demonstrates nonvisualization of the gallbladder consistent with this patient's acute cholecystitis.

WBCs within the inferior portion of his gallbladder wall corresponding to a site of hemorrhagic necrosis.

Four of eleven patients were treated medically and ultimately were found not to have acute cholecystitis. All had negative $^{99\text{m}}\text{Tc}$ -IDA and ^{111}In -WBC scans (Table 1).

The sensitivity of ^{111}In -WBC scintigraphy in identifying an acutely inflamed hemorrhagic gallbladder wall was 66% at 4 hr and 86% at 24 hr after radiotracer administration. Specificity was 100%. Technetium-99m-IDA scintigraphy identified 86% of patients with acute cholecystitis and excluded it in 100% of those with a patent cystic duct.

DISCUSSION

For patients undergoing intravenous total parenteral hyperalimentation and for anorexic patients who have undergone an extended fast, gallbladders may not visualize despite patent cystic ducts. Reduction in the flow of $^{99\text{m}}\text{Tc}$ -IDA gallbladder tracer with prolonged fasting results in gallbladder atony and increased intraluminal gallbladder pressure from retained bile and sludge due to the absence of endogenous cholecystikinin (4). In this situation, as well as in other conditions known to cause false-positive and/or false-negative (acute acalculous cholecystitis) hepatobiliary scans, it appears that ^{111}In -WBCs may be able to serve as a means of confirming or negating the cholecystigraphic diagnosis. In this pilot study, both indium- and technetium-labeled tracers detected acute cholecystitis

TABLE 1
Results of $^{99\text{m}}\text{Tc}$ -IDA and ^{111}In -WBC Scintigraphy

	IDA		WBC	
	Pos	Neg	Pos	Neg
Surgically positive	6	1	6	1*
Medically negative	0	4	0	4
Sensitivity	86%		86%	
Specificity	100%		100%	

* Patient with indeterminate ^{111}In scintiscan.

with a similar degree of accuracy. Indium-111-WBCs accumulated in 86% of acutely inflamed gallbladder walls 24 hr after radiotracer administration and, in fact, may well have been present in the gallbladder wall of our indeterminate study. Had we performed a $^{99\text{m}}\text{Tc}$ -sulfur colloid liver scan and subtracted it from the ^{111}In -WBC scan, the region of the gallbladder fossa may have become apparent and, thus, the sensitivity of ^{111}In -WBC imaging in detecting an acutely inflamed gallbladder wall may have increased. Indium-111-WBC uptake should not be influenced by intraluminal gallbladder pressure (the major cause of a false-positive hepatobiliary scan) and thus may prevent a misdiagnosis in patients who are critically ill, receiving triphosphopyridine nucleotide, fasting for prolonged periods of time, and in whom false-positive hepatobiliary scans may occur. The initial imaging procedure, however, even in patients with potential false-positive scans should be a hepatobiliary scan in conjunction with or without Sincalide as a premedicate to cleanse a potentially sludge-filled gallbladder of its contents and morphine administration to enhance Sphincter-of-Oddi tone and thus tracer flow to the gallbladder.

Visualization of the gallbladder on $^{99\text{m}}\text{Tc}$ -IDA scintigraphy makes acute cholecystitis highly unlikely and usually results in the search for another explanation for the patient's acute symptomatology. In the uncommon situation where acalculous acute cholecystitis is clinically suspect despite $^{99\text{m}}\text{Tc}$ -IDA gallbladder visualization, ^{111}In -WBCs may also be of value by demonstrating the inflammatory changes occurring within the gallbladder wall, although the cystic duct is patent.

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