False-Negative Morphine-Augmented Cholescintigraphy: A Case of Subacute Gallbladder Perforation

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The gallbladder and an infected pericholecystic biloma secondary to subacute perforation were visualized during morphine-augmented cholescintigraphy. Perforation of the gallbladder may relieve cystic duct obstruction and contribute to false-negative visualization in the setting of acute cholecystitis.

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The addition of intravenous morphine sulfate (MS) to conventional hepatobiliary scintigraphy is a frequently utilized pharmacologic manipulation to improve specificity and shorten study time without sacrificing diagnostic accuracy (*1,2*). The use of MS requires an appreciation of its advantages and an awareness of potential pitfalls, as several untoward effects are possible following its administration. Drug-induced increased biliary pressure potentially could lead to perforation of a diseased gallbladder (*3*). In addition, false-negative interpretations could result from either dislodgment of an impacted, obstructing cystic duct calculus which could allow gallbladder filling (*4*) or transient filling of the cystic duct proximal to an obstructing process which could mimic a small contracted gallbladder (*5*).

Spontaneous perforation of the gallbladder is a serious but rare complication of acute cholecystitis (*6*). The diagnosis may not be suspected until surgery because of a lack of specific signs and symptoms. We present the case of a subacute, localized gallbladder perforation with an adjacent pericholecystic biloma detected during morphine-augmented cholescintigraphy (MCS).

CASE REPORT

A 52-yr-old man presented 1 wk earlier with fever and right upper quadrant abdominal pain. At that time, abdominal ultrasonography demonstrated cholelithiasis and a course of oral antibiotics was prescribed. Over the next 4 days, the patient experienced intermittent abdominal pain and low-grade fever. Two days before hospital admission, abdominal pain worsened and nausea, vomiting and high fever developed. Physical examination revealed a toxic-appearing patient; his temperature was 39.5°C and rigors were present. There was minimal right upper abdominal quadrant tenderness without rebound or guarding. The white blood cell count was 7,900/mm^3.

Hepatobiliary imaging with ^{99m}Tc-mebrofenin demonstrated prompt hepatic uptake and normal excretion into the biliary ducts and small bowel. As the gallbladder did not visualize by 60 min, 3.4 mg of MS was administered by slow intravenous push. Twenty minutes later, an abnormal-appearing gallbladder was identified within the gallbladder fossa; it had an irregular contour with a small "nubbin" of activity along its superior margin (Fig. 1). This unusual morphology remained unchanged by 1 hr post-MS. Acute cholecystitis with inappropriate visualization of the gallbladder which communicated with a "walled-off" pericholecystic perforation was considered likely in light of a high clinical suspicion of acute cholecystitis with gram-negative sepsis. On the basis of delayed visualization, the scintigraphic differential diagnosis included chronic cholecystitis with cholelithiasis in a morphologically abnormal gallbladder.

Abdominal ultrasonography performed immediately after MCS showed a distended gallbladder, minimal wall thickening, and a large gallstone with sludge. In addition, a new septated fluid collection abutting the fundus of the gallbladder, not seen on the initial study one week earlier, was present (Fig. 2). This fluid collection corresponded in location to the "nubbin" of activity on MCS and was consistent with a contained perforation.

Emergent surgery disclosed a localized fluid collection at the site of gallbladder perforation and purulent material within the gallbladder. Pathologic examination revealed acute necrotizing cholecystitis with perforation in the fundus; tissue gram stain demonstrated gram-negative rods.

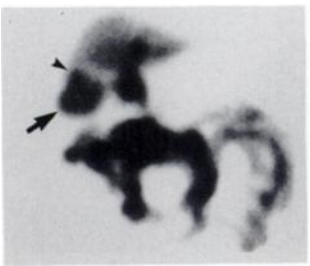

FIGURE 1. Twenty-minute post-MS image with gallbladder activity (arrow) and "nubbin" of activity (arrowhead) superior to the gallbladder, site of the "walled-off" perforation.

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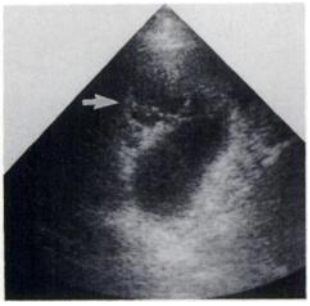

FIGURE 2. Gallbladder ultrasonogram, longitudinal view: septated, pericholecystic fluid collection (arrow) compatible with localized perforation.

DISCUSSION

Perforation of the gallbladder is the most serious complication of acute cholecystitis with an overall incidence of about 10% (*6*). It occurs more frequently in patients with a pre-existing systemic disease such as diabetes mellitus or in those with acalculous cholecystitis, in whom the incidence approaches 40%. Perforation can occur within the first few days of the onset of acute cholecystitis or as late as the second week. Localized perforation with pericholecystic abscess formation, similar to the findings in the current case, is the most common type of perforation.

Spontaneous perforation has been identified during conventional hepatobiliary scintigraphy (*7,8*). A case of gallbladder perforation temporally related to MS administration has also been described, but a causal relationship between the use of MS and the perforation is speculative only (*3*).

The mechanism of action of MS is straightforward: by increasing sphincter of Oddi tone, MS raises intraductal pressure, promoting retrograde gallbladder filling through a patent cystic duct (*1,2,9,10*). Occasionally, the increased intraductal pressure may be sufficient to dislodge an impacted cystic duct stone or overcome a functional cystic duct obstruction secondary to edema, fibrosis or hemorrhage (*4*), or transiently fill the cystic duct proximal to an obstructing process (*5*), giving a false-negative result. Elevated biliary pressure could also cause rupture of weakened, necrotic tissue in a gallbladder with complicated acute cholecystitis (*3*).

The current patient almost certainly had a pre-existing gallbladder perforation prior to MS administration. Perforation in an area of necrosis may have occurred following gallbladder distention and served to relieve partially the cystic duct obstruction characteristic of acute cholecystitis, allowing delayed visualization of the gallbladder. Given this patient's clinical history, the localized pericholecystic collection more likely represented a subacute perforation which occurred within several days prior to the study. If MS had precipitated the perforation, the most likely scintigraphic finding would have been free radioactive bile spillage throughout the abdomen.

Decompression of the gallbladder following perforation may relieve the cystic duct obstruction, permitting inappropriate visualization in the setting of acute cholecystitis. This case report illustrates the potential for false-negative MCS under these conditions.

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