Original Article

Right Upper Quadrant Pain with Normal Hepatobiliary Ultrasound: Can Hepatobiliary Scintigraphy Define the Cause?

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ABSTRACT

Background/Aim: The objective of this study was to assess the value of hepatobiliary scintigraphy (HS) for the diagnosis of right upper quadrant (RUQ) abdominal pain in patients with normal hepatobiliary ultrasound (HU). This is an observational study with a retrospective analysis of data from March 2008 to August 2010. **Materials and Methods:** We reviewed the HS results of 30 patients, aged 29–69 years (average 45.8 years); 12 male and 18 female patients. Patient selection to perform the HS was RUQ abdominal pain, suspected hepatobiliary disorder, and negative HU. All patients had gone through the standard procedure of HS. **Results:** Based on predefined interpretation criteria, HS results were divided into 2 patterns: Normal (*n*=8, 25.8%) and abnormal (*n*=22, 73%): 18 patients (81.8%) having early gallbladder (GB) and common bile duct visualization, and delayed transit to small bowel (SB), which can be seen only after a fatty meal with normal or abnormal GB ejection fraction (GBEF) pattern characteristic of Oddi's sphincter dyskinesia. The remaining 4 patients (8.18%) had acalculous cholycystitis pattern: Delayed GB visualization with activity appearing in SB before GB. **Conclusion:** HS with fatty meal stimulation and GBEF estimation seems to be a reliable test, which may reveal a biliary cause in more than 70% of patients with RUQ abdominal pain and normal HU. Normal results exclude functional biliary cause. The decision for invasive or noninvasive therapeutic approach may depend on the results of HS.

Key Words: Acalculous cholycystitis, hepatobiliary scintigraphy, hepatobiliary ultrasonography, Oddi's sphincter dyskinesia, RUQ abdominal pain

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Recurrent right upper quadrant (RUQ) abdominal pain can be caused by a group of different disease disorders both organic and functional and the workup to determine the cause is a challenge for the treating physician.[1] Organic causes, such as cholelithiasis, peptic ulcer, pancreatitis, gastroesophageal reflux, and tumors, should be excluded before raising the possibility of functional disorders of gallbladder (GB) or Oddi's sphincter (OS). GB and OS functional disorders are not uncommon causes of patients' symptoms presenting with recurrent RUQ abdominal pain and the diagnosis is usually suggested by clinical examination supported by laboratory tests and a negative hepatobiliary ultrasound (HU). However, in some patients the diagnosis lacks enough confidentiality and needs further tests to confirm the functional nature of the disease. Hepatobiliary scintigraphy (HS) has been suggested in this group of patients.[2] Krishnamurthy *et al* used HS with fatty meal for that purpose.[3] The objective of this study was to assess the performance parameters of HS to correctly and confidentially diagnose the etiology of RUQ abdominal pain in patients with normal HU in a university hospital setting.

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MATERIALS AND METHODS

In this observational retrospective study, we reviewed the HS results of 30 patients, age range from 29 to 69 years (average 45.8 years). Twelve males and 18 females; with male to female ratio being 2:3. Patients were referred for HS from different clinics at a university hospital (gastroenterology, primary care, surgery, and emergency) in a period from March 2008 to August 2010. The patient selection criteria to perform the HS was based on clinical presentation with RUQ abdominal pain, negative HU, and

suspected hepatobiliary functional disorder as the cause. All patients had gone through standard procedure of HS. Our routine procedure in performing the HS was as follows: After 2-4 h fasting with patient in supine position, 5–6 mCi (185– 222 MBq) of Tc-99m-trimethylbromo-iminodiacetic acid (Amersham-GE®) is given to the patient intravenously through a previously inserted intravenous line. Acquisition is performed using a large field of view gamma camera (ADAC-Forte®) fitted with low-energy general purpose collimator and with 20% energy window centered on 140 KeV. Caution should be taken to have the upper abdomen in the field of view and the head of gamma camera off centered right to include the entire liver.

Four sets of serial digital images are obtained .Starting with flow anterior images (32 frames, 2 s/frame), followed by anterior blood pool for 500 kilo counts, then anterior dynamic images (10 frames, 3 min/frame). That will be followed by static images (right anterior oblique, right lateral, and posterior images for 3 mins each). If the GB is not visualized further delayed images are obtained. However, if GB remains full, fatty meal is given and static images for 3 min each at 5, 10, 15, and 30 min are obtained (30 s each for 15 frames = 8 min). These images are used to calculate the GB ejection fraction (GBEF), which is normally more than 40%.[4] The following parameters are evaluated at the time of study interpretation: (1) liver uptake, (2) GB uptake and GBEF, (3) intra–extra-hepatobiliary bile duct visualization, and (4) transit time of the tracer to the small bowel (SB). The study is considered normal with the following findings: (1) prompt liver uptake, (2) rapid tracer excretion, (3) early GB visualization (<60 min postinjection), (4) early appearance of activity in the SB but after the GB has been seen, and (5) normal GBEF. On the other hand, the study is considered abnormal with one or more of the following observations: (1) delayed liver uptake and clearance, (2) delayed visualization of the GB, (3) activity seen in the SB only after a fatty meal, (4) activity seen in the SB before the GB, and (5) a poor response of the GB to a fatty meal with GBEF < 40%.

RESULTS

Based on the described interpretation criteria, the patients were divided into 2 groups: Group I: (n=8, 27%) with normal scintigraphic pattern [Figure 1] and normal GBEF; and Group II: (n=22, 73%) with abnormal scintigraphic pattern, where we defined 2 subgroups: Group II-a: Characteristic for SO disorder and was seen in 18 patients (81.8%) in which the liver showed normal uptake with early GB visualization (<30 min postinjection) and nonvisualization of SB activity with a hold up in the common bile duct and activity only seen in the SB after administration of a fatty meal administration [Figure 2] whether GBEF was normal 55 ± 7% (n=12) or abnormal 26 ± 5% (n=6), Group II-b: Characteristic pattern of acalculous cholecystitis in the remaining 4 patients (18.2%) in whom the the GB visualization was delayed (≥2 h postinjection) despite a good liver uptake and early appearance of activity in the bile ducts and SB [Figure 3]. In all the four patients GB response to fatty meal was inadequate and was less than 35%.

DISCUSSION

RUQ abdominal pain in the absence of organic causes (eg, cholelithiasis, pancreatitis, and so forth), may be related to a functional disorder of the GB or OS.[1] Patients with RUQ abdominal pain who meet the Rome III symptom-based criteria for functional GB and OS pain should be assessed initially with noninvasive procedures and should undergo conservative treatment. HS has been reported to be a useful

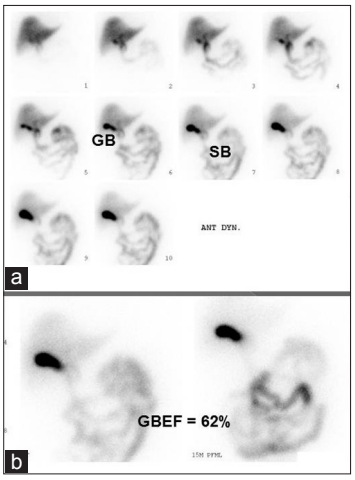

Figure 1: Normal hepatobiliary scintigraphy. (a) Prompt liver uptake and activity seen in bile ducts, gallbladder (GB), and small bowel within 30 min postinjection. (b) Good response of GB to fatty meal with 62% GB ejection fraction

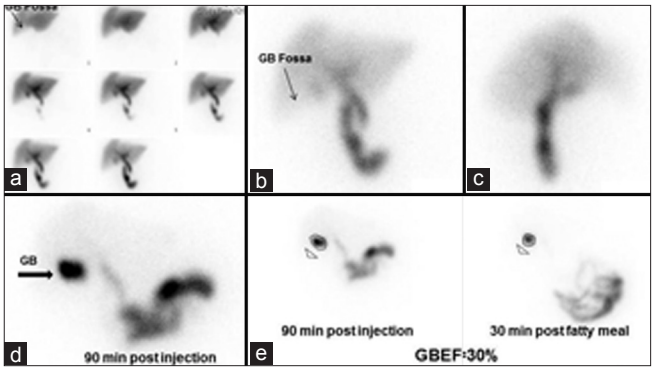

Figure 2: Acalculous cholecystitis. (a) Prompt liver uptake with early appearance of activity in common bile duct and small bowel but not gallbladder (GB) up to 30 min postinjection. (b,c) No GB seen up to 60 min postinjection in the anterior and right lateral images. (d) GB seen 90 min postinjection. (e) Inadequate GB response to fatty meal with GB ejection fraction 30%

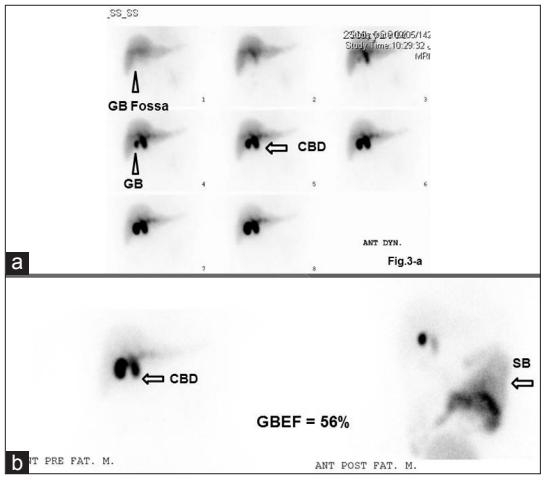

Figure 3: Oddi's sphincter (OS) dysfunction. (a) Activity seen in gallbladder (GB) and common bile duct (CBD) but not in small bowel (SB) (lower CBD obstruction vs or OS dysfunction). (b) Normal post–fatty GB ejection fraction = 56% and activity seen in SB excluding the lower CBD obstruction

noninvasive imaging tool for the diagnosis and management of patients who present RUQ abdominal pain and normal HU.[2] It has been considered an excellent test to determine the cystic duct patency and presence or absence of acute or chronic, acalculous cholecystitis and measurement of GBEF. The sensitivity of HS has been reported to range from 86% to 97% and specificity from 73% to 100%.[3]

A GBEF > 33% post–fatty meal is considered normal and not different from the lower limit of normal sinclaide-stimulated GBEF (> 35%).[4]

Most published data have defined gallbladder dysfunction as an ejection fraction less than 35–40%. GBEF of less than 35% is usually associated with acalculous cholecystitis in 95% of patients with RUQ abdominal pain and normal HU.[5,6] HS with fatty meal stimulation may be a good alternative to sinclaide stimulation and is a useful modality for the diagnosis of chronic acalculous cholecystitis.[7] This filtering approach permits the selection of the small nonresponders group who will require further invasive procedures, such as cholecystectomy, manometry, and sphincterotomy.[3] Our results revealed that HS has the potential to clearly separate the normal from the abnormal group. The American College of Radiology has published appropriateness criteria on the use of different imaging modalities in patients with RUQ abdominal pain and reported that it may be appropriate to use HS in patients with equivocal HU or in hospitalized patients with suspected acalculous cholecystitis and equivocal HU.[2] This criteria probably was one of the reasons for the limited number of patients included in our study. A normal HS with fatty meal stimulation and normal GBEF excludes functional disorders of the GB or OS dysfunction as a cause of RUQ abdominal pain. Twenty-seven percent of our patients with RUQ abdominal pain and negative HU had normal HS and thereafter the treating physician investigated nonbiliary cause for the patients' symptoms. OS dysfunction is a functional disorder of biliary tract leading to RUQ abdominal pain and can be observed in both pre- or post-cholecystectomy patients. HS has been used to investigate the OS dysfunction and showed very good correlation with manometry and the sensitivity of the test was reported to be more than 90%.[8] HS with or without cholecystokinin (CCK) has been reported to provide useful and reliable information in patients with RUQ abdominal pain and guiding the physician in designing the management plan whether to go for OS manometry if the HS is positive or to be more conservative if it was negative.[9] Eighty-two percent of our patients with abnormal HS had characteristic features of OS dysfunction; 66% of them with normal GBEF, and 34% had inadequate response to fatty meal with abnormal GBEF. These findings had an important impact on the treating physicians' management plan for each patient, and hence patients with motility disorder of OS who present with biliary-like symptoms should have OS manometry to confirm the diagnosis and it may lead to sphincterotomy, which has been reported to relieve the symptoms in 80% of patients.[10]

Acalculous cholecystitis forms about 2–5% of acute cholecystitis, and chronic acalculous cholecystitis is also not common (about 5–10%) compared with chronic cholecystitis.[11,12]

Gallbladder dysfunction was seen only in 4 patients (18%) with GBEF less than 35%. The sensitivity of HS in acute acalculous cholecystitis has been reported to be between 60% and 92.5%.[13]

CONCLUSION

HS with fatty meal stimulation and GBEF estimation seems to be a reliable test, which may reveal a biliary cause in more than 70% of patients with RUQ abdominal pain and normal HU. Normal results exclude functional biliary cause and will re-direct the investigation for other disorders. The results of HS will influence the decision of the treating physician for invasive or noninvasive therapeutic approach in this group of patients.

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