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Does Contrast Enhanced Ultrasound improve the management of liver abscesses? A single centre experience.

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Abstract

Liver abscess is a potentially lethal condition that requires prompt recognition and adequate treatment for a good outcome. The **aim** of this study was to assess the value of contrast enhanced ultrasound (CEUS) in the management of liver abscesses in the clinical practice of a single centre. **Material and methods:** A retrospective analysis was performed including all patients diagnosed with liver abscesses during 5 years (2010-2014) in a tertiary Department of Gastroenterology and Hepatology. The demographic data, the presence of risk factors, the cause of liver abscess, the B-mode conventional US aspect, the CEUS appearance and the patient's outcome were documented and analyzed. **Results:** The study group included 41 patients diagnosed with liver abscesses (17 women and 24 men, mean age 63.3±13.2 years), 16/41 (39%) of them with diabetes mellitus. A single lesion was found in 28 (68.3%) patients, and 13 (31.7%) patients had multiple abscesses. The CEUS study was conclusive for the diagnosis of liver abscess in clinical context in 38/41 cases (92.7%). All conclusive cases presented rim enhancement in the arterial phase and no enhancement in the liquid areas. The honeycomb appearance with septa enhancement was present in 17/41 (41.5%) patients. Washout of the marginal rim was found in 22/41 (53.6%) lesions. **Conclusion:** In our group the most frequent CEUS features found were the rim enhancement in the arterial phase and the presence of no enhancement areas, followed by the honeycomb appearance. CEUS was able to be conclusive for the diagnosis of liver abscess in almost 93% of cases.

Keywords: liver abscess, contrast enhanced ultrasound, drainage

Introduction

Liver abscess is a pus-containing collection, most often caused by bacteria. It is characterized by the presence of viscous fluid surrounded by an inflammatory wall developed as a response of the body against the infectious injury. It is a potentially lethal condition that requires prompt recognition and adequate treatment for a good outcome. The management has changed during the last 40 years. In the past this high morbidity disease was treated either conservatively with antibiotics or by open drainage, with mortality rates ranging from 9-80% [1]. Development of imaging techniques as well as of percutaneous aspiration and drainage has changed all this. Even if the detection and management have greatly benefited from advantages in imaging techniques, the diagnosis may still be difficult due to nonspecific symptoms and variable imaging aspects.

Conventional ultrasound (US) is usually the first imaging technique used in clinical practice for the evaluation of the liver. It is a widespread real time method, with a good accuracy for detecting liver abnormalities, relatively inexpensive, repeatable, accessible, with no radiation, but it lacks the necessary specificity for a positive diagnosis. This disadvantage was overcome by the introduction of ultrasound contrast agents.

Contrast enhanced ultrasonography (CEUS) is also a real-time imaging technique that implies no radiation, with very few side effects, which can be performed even in patients with impaired renal function. Usually, the contrast study follows immediately the standard US examination, thus a positive diagnosis can be obtained in a large number of cases by characterizing the lesions'

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vascular pattern in the arterial, portal and late vascular phases. This technique is accurate in the diagnosis of focal liver lesions as proven by large multicentre studies [2-4] and a meta analysis [5] that showed similar performances to contrast enhanced computer tomography (CT) and magnetic resonance imaging (MRI). The value, indications and limitations of this technique are summarized by the Guidelines and Recommendations concerning the use of CEUS issued in 2004 by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) [6], revised in 2008 [7] and again in 2012, the latter in cooperation with the *World Federation for Ultrasound in Medicine and Biology* (WFUMB) [8].

The conventional US appearance of liver abscesses is variable. A hypoechoic mass with irregular thick wall, with internal septa, sometimes containing gas (bright punctate echoes with dirty shadowing), are the most frequent ultrasound features of these lesions, but not specific. CEUS brings several typical elements that lead to a positive diagnosis, such as: marginal rim enhancement in the arterial phase, with enhancement of the septa (honeycomb appearance), with no enhancement in the liquid areas, and venous hypoenhancement [8-10].

The **aim** of this study was to assess the value of CEUS in the management of liver abscesses in the clinical practice of a single centre.

Material and methods

Patients

A retrospective analysis was performed including all patients diagnosed with liver abscesses during 5 years (2010-2014) in a tertiary Department of Gastroenterology and Hepatology. In each patient a B-mode conventional ultrasound was performed followed by a CEUS study. The positive diagnosis of liver abscess was established either by ultrasound guided needle aspiration or by a second line imaging technique (contrast enhanced CT or contrast enhanced MRI).

In all patients' demographic data, as well as the presence of risk factors, the cause of liver abscess (if known), the B-mode conventional US aspect, the CEUS appearance and the patient's outcome were documented.

Informed consent for the contrast enhanced study was obtained from every patient. The study protocol was approved by the local Ethical Committee and was in accordance with the Helsinki Declaration of 1975.

Conventional B-mode and contrast enhanced ultrasound

The US studies were performed with a Siemens Accuson S2000™ system (Siemens AG, Erlangen, Germany), using a 3.5 MHz convex transducer. The location, size, number, echogenity and pattern of each lesion were reported.

The CEUS studies were performed in each patient following the conventional US, with the same ultrasound machine, with a convex probe, using a low mechanic index (0.09-0.11) in order to minimize micro bubble disruption.

The same contrast agent was used in all cases: SonoVue® (Bracco SpA, Milan, Italy) – a perfluoro gas containing agent, provided as a sterile, lyophilized powder contained in a septum-sealed vial. For each study 2.4 mL of SonoVue® were injected through a peripheral intravenous cannula of sufficient size, followed by a 10-mL saline flush, as per standard protocol [7,8]. Lesions' vascular enhancement patterns were studied in 3 phases: arterial (10-30 seconds after injection), portal (30-120 seconds) and late phase (>120 seconds), according to the EFSUMB recommendations [7,8]. The contrast study for each patient lasted 5 minutes after bolus injection and was documented by at least 4 video loops no longer than 30 seconds each, containing: B-mode examination, the arterial phase, the portal phase and the late phase. The presence of liver abscesses' typical CEUS features – the marginal rim enhancement in the arterial phase, septa enhancement (honeycomb appearance), no enhancement in the liquid areas, and venous hypoenhancement [7,8] – were documented in the report and followed up in the data analysis. In the specific clinical context and in the presence of the liver abscesses' typical CEUS features, the study was considered conclusive for the positive diagnosis.

Results

During 5 years 2046 CEUS studies were performed in our department for the evaluation of "de novo" focal liver lesions. Out of these only 41/2046 lesions (2%) were liver abscesses.

The study group included 41 patients diagnosed with liver abscesses (17 women and 24 men, mean age 63.3±13.2 years, ranging between 23 and 82 years), 16/41 (39%) of them with diabetes mellitus; 28 (68.3%) patients had a single lesion, while in 13 (31.7%) cases there were multiple abscesses.

The infection spread to the liver in 11/41 (26.8%) cases by arterial seeding in systemic infections (starting from respiratory or urinary infection); in 2/41 (4.9%) cases the infection spread to the liver via the portal circulation (from diverticulitis); while in most cases 23/41 (56.1%) the infection directly spread from a biliary infection. In 5/41 (12.2%) cases the cause of the liver abscess was not established.

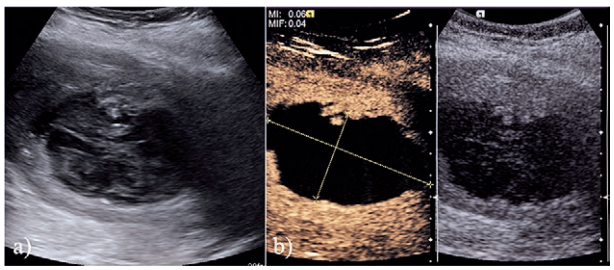

Fig 1. a) Conventional ultrasound aspect in a liver abscess – hypoechoic inhomogeneous lesion with a thick margin; b) CEUS aspect, arterial phase, rim enhancement and unenhanced central area.

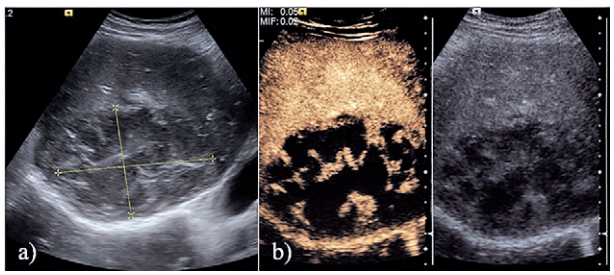

Fig 2. a) Conventional ultrasound aspect in a liver abscess – hypoechoic inhomogeneous lesion; b) CEUS aspect, arterial phase, honeycomb appearance.

The US aspect of liver abscesses included in this study was variable: hypoechoic in 16/41 cases (39%), anechoic in 7/41 (17.1%) cases, hyperechoic in 3/41 (7.3%) patients and inhomogeneous with septa in 15/41 (36.6%) patients. In one patient gas was present inside the lesion.

The CEUS study was conclusive for the diagnosis of liver abscess in the clinical context in 38/41 cases (92.7%). All conclusive cases presented rim enhancement in the arterial phase and no enhancement in the liquid areas (fig 1). The honeycomb appearance with septa enhancement was present in 17/41 (41.5%) patients (fig 2). Washout of the marginal rim was found in 22/41 (53.6%) lesions.

Discussions

Liver abscesses usually develop following diverticulitis, Crohn's disease, appendicitis, ischemic colitis, acute pancreatitis, gastrointestinal tract cancer when the infection subsequently spreads to the liver via portal circulation, or by direct spread from biliary infection, but it can also result from arterial seeding in systemic infections, or secondary to local causes such as acute colecystitis, hematoma, post radio frequency ablation (RFA) or chemoembolization [11]. Patients with diabetes, underlying hepatobiliary or pancreatic diseases or liver transplant have a greater risk to develop this condition [12-15]. Most liver abscesses are polymicrobial and several pathogens can be involved such as: Gram negative bacili – Escherichia coli, Pseudomonas, Klebsiella, Morganella morgani; Anaerobes – Bacteroides, Fusobacterium; Streptococcus; Staphylococcus; Entamoeba histolytica [13].

Even if the clinical signs are nonspecific, a liver abscess should be suspected based on the presence of fever, night sweats, weight loss, abdominal pain, nausea, right hypochondria or abdominal tenderness. The biological tests usually show leucocytosis, inflammatory syndrome, and elevated liver enzymes. But the positive diagnosis is established based on imaging techniques: contrast enhanced CT scan and ultrasound being the modalities of choice (also for guided aspiration of the content).

Conventional ultrasound has a reported sensitivity for detecting pyogenic liver abscesses ranging from 85 to 96% [1,16]. It is a real time examination, relatively inexpensive, accessible, with good accuracy in the evaluation of the biliary system, also in differentiation between cystic and solid structures, all valuable advantages in clinical practice. It is also a dynamic technique and, by repeated examinations, it can demonstrate appearance changes of the lesion during time, which are a characteristic of liver abscesses. But, on the other hand, US is an operator dependent method that needs a good acoustic window, thus being difficult in obese and uncooperative patients. The variable aspect of liver abscesses can also be a challenge in establishing a positive diagnosis. Thus we can find either solid masses with irregular margins, or hypoechoic/anechoic lesion also with irregular thick walls, internal septa, or sometimes the presence of gas inside the lesion. The differential diagnosis with a necrotic tumor, with a hemorrhagic cyst, or with a hematoma can be difficult. Most cases in our study were hypoechoic or inhomogeneous lesions, fewer being anechoic or hyperechoic. The US appearance in an adequate clinical context was suggestive for the diagnosis of liver abscess, but not conclusive.

CEUS is a proven method that improves the detection and characterization of focal liver lesions [7,8]. The presence of the rim enhancement in the arterial phase, septa enhancement (honeycomb appearance), no enhancement in the liquid areas, and venous hypoenhancement are the most common features of liver abscesses in CEUS [7,8,17]. The rim enhancement in arterial phase is the consequence of perilesional hyperemia. In some cases the surrounding edema can generate a hypoenhancing area in the periphery [18]. CEUS is also helpful for delineating avascular areas inside the abscess [19,20] and identifying 4 possible sonomorphologic stages of the disease: stage I – defined by focal inflammation without necrosis; stage II – by focal clusters of micro-abscesses

appearing to coalesce; stage III – by a single cavity with or without capsule; stage IV – by numerous small abscesses scattered all over the liver [17].

The most frequent CEUS features in our study group were the rim enhancement in the arterial phase and the presence of no enhancement areas, similar with the data presented by other authors. On the other hand CEUS was able to establish the diagnosis of liver abscess in a very large number of cases (92.7%). Even if the number of patients was not very large CEUS proved to be a very useful and reliable method for the diagnosis of these kind of lesions.

The treatment planning of liver abscesses requires the careful assessment of several aspects such as: number of lesions, size, content and extent of the abscess, presence of fistulas. CEUS improves the detection of even small lesions, thus being very useful for the correct evaluation of disease extension. Also, the direct intracavitary injection of contrast agent allows the confirmation of a correct positioning of the needle or catheter, showing possible communication between cavities in complex abscesses, or the presence of fistulas [21,22].

Contrast enhanced CT is also useful for the diagnosis of liver abscesses [23] since it has some advantages over US: no window limitation; it can assess the whole liver; it can distinguish subtle differences in densities, and, in some cases, can also reveal the source of sepsis.

Even if imaging techniques are accurate for the positive diagnosis of liver abscesses, US-guided aspiration with a fine or a larger needle (dependent on the viscosity), can differentiate an abscess from a non-infected fluid collection. It is a rapid, safe and inexpensive procedure that allows a rapid positive diagnosis and also obtains a sample for microbiology [11]. In 45-60% of cases a single microbial pathogen is isolated from the abscess, while in approximately 40% of cases the etiology is polymicrobial. The procedure can be also performed under CEUS guidance, which allows the identification of the best area to be punctured (avascular).

The proper treatment of liver abscesses includes wide-spectrum antibiotics, percutaneous aspiration, percutaneous drainage and surgical drainage [24]. Before the 1970s surgical drainage was considered the treatment of choice for liver abscesses [13] with high mortality rates. Today US-guided percutaneous drainage is the first-line treatment approach, while surgery is reserved only for those cases, where the correct percutaneous treatment failed, or when the cause of the abscess needs urgent surgical treatment [11]. Percutaneous drainage was first described in 1974 [25]. US-guidance is preferred since it offers the advantage of real-time guidance of the needle, allows the monitoring of the course of the needle or the catheter through the tissues and it is also less expensive, while CEUS allows to establish the area that needs drainage and to find the best position for the tip of the drainage. Whenever possible, a transhepatic access route is preferred for direct puncture to avoid pus leakage into the peritoneal cavity. Other complications reported were abscess rupture, pleural contamination due to transpleural passage, liver hematoma [11,26].

A meta-analysis comparing catheter drainage vs. repeated needle aspirations of liver abscesses demonstrated the first to be more effective [27]. Other studies showed good results with repeated needle aspiration in simple abscesses smaller than 5 cm, while in larger abscesses catheter drainage has a better outcome [26].

The limitations of this study are the small number of cases and the fact that it was a retrospective one, but it reflects the clinical practice.

In **conclusion** CEUS is an important tool in the management of liver abscesses. In our group the most frequent CEUS features found were the rim enhancement in the arterial phase and the presence of no enhancement areas, followed by the honeycomb appearance. CEUS was able to be conclusive for the diagnosis of liver abscess in almost 93% of cases.

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Conflict of interest: none

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