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● *Original Contribution*

CONTRAST-ENHANCED ULTRASOUND IN THE CHARACTERIZATION OF COMPLEX CYSTIC FOCAL LIVER LESIONS

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Abstract—Complex cystic focal liver lesions (FLLs) found at non-contrast ultrasound (US) may turn out to be malignant. In this prospective, monocentric study we investigated the value of contrast-enhanced US (CEUS) in the differential diagnosis of complex cystic FLLs. In the past 3 years, all patients with complex cystic FLLs unclassifiable at US underwent CEUS with low-transmit insonation power. We evaluated 36 consecutive patients with 61 FLLs (1–6/patient, mean = 2). The diameter of the lesions ranged from 1.1 to 7.9 cm (mean = 3.9 cm). Sixteen patients had an extrahepatic malignancy. There were 42 malignant lesions and 19 benign lesions. No lesion had a certain diagnosis at conventional US, whereas 16 FLLs were classified as probable (benign or malignant) and 45 as uncertain. CEUS correctly categorized 95% of the malignant cases. CEUS was not able to differentiate the biliary cystadenoma from its malignant counterpart and misdiagnosed two abscesses. Complete non-enhancement throughout three phases or sustained enhancement in the portal/late phase was exhibited in most benign complex cystic FLLs, except for 1 (of the 3) cystadenomas and in 2 (of the 4) abscesses. On the other hand, all malignant lesions presented a contrast washout with a hypo-enhancing appearance. CEUS may provide added diagnostic value in all complex cystic FLLs found uncertain at conventional US, potentially avoiding the use of more invasive and expensive imaging modalities. (E-mail: An.cor@hotmail.it) © **2015 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Ultrasound, Microbubbles, Liver, Cystic lesions, Contrast agent.**

INTRODUCTION

Cystic liver lesions are increasingly found because of the now frequent use of hepatic imaging. These cystic focal liver lesions (FLLs) are usually benign, without any relevant clinical interest. Nevertheless, cystic FLLs represent a wide spectrum of lesions, including both benign and malignant lesions. Consequently, the radiologist must carefully assess imaging features such as location, size and number and evaluate internal structure and other associated findings (Lin et al. 2009; Vachha et al. 2011).

Because of its advantageous cost/benefit ratio, widespread availability and easy execution, ultrasound (US) is the first-line imaging modality in most countries for the initial liver survey and, consequently, represents the imaging technique that usually detects a complex liver cyst. Unfortunately, given the considerable overlap in appearance of benign and malignant cysts, conventional US has poor diagnostic performance (Mortelé and Peters 2009). Indeed, a complex hemorrhagic cyst may have a solid appearance on US, thus mimicking a malignant lesion, particularly cystic metastasis or biliary cystadenocarcinoma (Zhang et al. 2009). Similarly, solid focal lesions, particularly those with a hypo-echoic appearance in a fatty liver, can be misdiagnosed as cysts at US, especially by an inexperienced radiologist (Liu et al. 2009).

In our institution, US is the imaging technique used first in the study of the liver, and contrast-enhanced ultrasound (CEUS) is usually chosen to characterize FLLs indeterminate on conventional US (Laghi et al. 2010). Until now, CEUS has proven to be extremely useful in the evaluation of both solid liver lesions and complex renal cysts (Ascenti et al. 2007; Bartolotta et al. 2009). However, there is little experience with the role of CEUS in the less common setting of complex liver cysts.

Our single-center, prospective study is an analysis of the imaging findings and diagnostic impact of microbubble injection in the assessment of complex cystic FLLs unclassified at US.

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METHODS

Patients

From January 2010 to December 2012, we enrolled 36 consecutive patients (22 men and 14 women) imaged at our cancer institute. These patients had 61 complex cystic FLLs unclassifiable at conventional US. Eleven patients had a concomitant extrahepatic malignancy, and 13 had a previous history of extrahepatic malignancy. The remaining 12 patients had no history of malignancy, and the lesion represented an incidental finding during an abdominal US examination performed for other reasons. In 30 patients, the cystic lesions were the only finding detected on baseline US examination, whereas in the remaining 6 there were also solid lesions.

Written informed consent was obtained from all patients, and the study was approved by the ethics committee of the institution.

We included lesions that on US appeared anechoic or markedly hypo-echoic, with absent or moderate posterior enhancement and one or more of the following features: thick and/or irregular walls, internal septa and mural nodules (Fig. 1). Thus, we excluded simple cysts, cysts with coarse wall calcification (more often of hydatid origin) and cystic clusters with thin septa. We also excluded solid lesions with internal necrotic changes, even if extensive, but not having a defined cystic appearance. All lesions included were newly diagnosed, and no patient had previously undergone chemoradiotherapy or percutaneous ablation.

Ultrasound examination

All US and CEUS examinations were performed by four radiologists, who had at least 5 y of experience in liver CEUS. The examiners were blinded to other imaging results, but not to the clinical history. Baseline US was performed with a MyLab 70 XVG GOLD scanner (Esaote, Genoa, Italy) using multifrequency (2.5–5 MHz) convex probes. A preliminary US examination, which included a tissue harmonic imaging mode and a power and color Doppler assessment, was carried out. This allowed us to locate the lesion and to establish the best scanning approach for the subsequent CEUS study. Contrast-enhanced studies were performed with contrast-specific, low-mechanical-index software (CnTI, Contrast Tuned Imaging). The agent employed was SonoVue (Bracco, Milan, Italy), a sulfur hexafluoride-filled microbubble contrast agent. It was injected into the antecubital vein in bolus fashion, followed by a flush of 10 mL of 0.9% normal saline solution. The volume of SonoVue used was 2.4 or 4.8 mL, depending on the radiologist's preference, the patient type and/or the number and distribution of the lesions. In patients with multiple lesions, each lesion was evaluated. In these cases, the single bolus was split into two injections, one for each liver lobe. We waited at least 5 min between the two injections. For both injections we scanned the largest and/or the most suspicious lesion during the arterial phase and then explored the remaining lesions within the same lobe for up to 5 min. We generally used dual-frame real-time mode with the fundamental mode US image on the left side of the monitor and the CEUS mode image on the right. The ultrasound beam was focused at the deeper aspect of the lesion examined. After contrast injection, continuous scanning began immediately and lasted 4–5 min. A low acoustic power setting was used (40–45 kPa derated pressure, expressing a mechanical index of approximately 0.06). A timer on the sonography unit was activated at the moment of injection, and the entire examination movie was archived on the scanner.

Data analysis

The process of CEUS was classified into arterial (10–15 to 25–35 s after injection), portal (30–45 to 120 s),

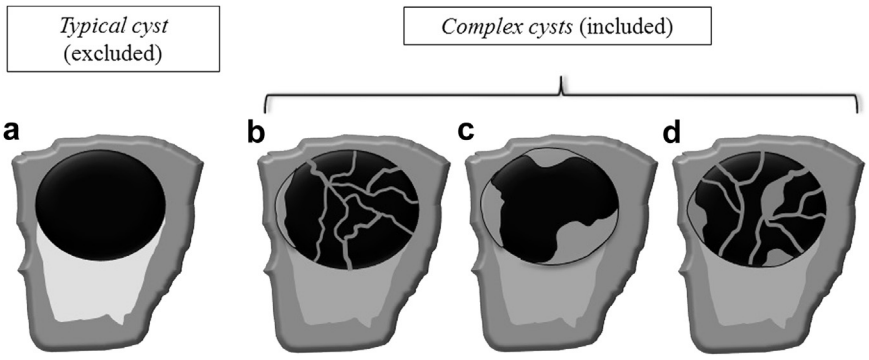

Fig. 1. Ultrasound appearance of complex cystic focal liver lesions. (a) Simple cysts (not included in our series) are defined as well-circumscribed, round or ovoid, anechoic lesions with an increased through-transmission of ultrasound waves. (b) Complex cystic lesion with hairline-thin and a few thick intracystic septa that divide the lesion into multiple compartments, resulting in a multilocular appearance. Coexistent focal mural thickening. (c) Complex cyst with mural nodules. (d) Complex cystic lesion with irregular, thick septa and septal/mural nodules.