Ultrasound features of hepatocellular adenoma and the additional value of contrast-enhanced ultrasound

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BACKGROUND: Hepatocellular adenoma (HCA) is a rare benign tumor of the liver. It is of clinical importance to differentiate HCA from other liver tumors, especially hepatocellular carcinoma (HCC). This study aimed to evaluate the characteristic features of HCA by conventional ultrasound and contrast-enhanced ultrasound (CEUS) findings.

METHODS: Twenty-six patients (10 males and 16 females; mean age 36.2±5.0 years) with 26 histopathologically proven HCAs were retrospectively identified. According to the maximum diameter of HCAs, they were divided into three groups: <30 mm, 30-50 mm, and >50 mm. Ultrasound examinations were performed with C5-2 broadband curved transducer of Philips iU22 unit (Philips Bothell, WA, USA). For each lesion, a dose of 2.4 mL SonoVue® (Bracco Imaging Spa, Milan, Italy) was injected as a quick bolus into the cubital vein. Lesions' echogenicity, color-Doppler flow imaging and contrast enhancement patterns were recorded.

RESULTS: Grayscale ultrasound revealed that most of HCAs were hypoechoic (73.1%, 19/26). Spotty calcifications were detected in 26.9% (7/26) of the lesions. Color-Doppler flow imaging detected centripetal bulky color flow in 46.2% (12/26) of the HCAs. CEUS showed that 73.1% (19/26) of the HCAs displayed as rapid, complete and homogenous enhancement, and 53.8% (14/26) showed decreased contrast enhancement in the late phase. There was no significant difference in enhancement patterns among different sizes of HCAs (P>0.05). Centripetal enhancement with subcapsular tortuous arteries was common in larger HCAs.

CONCLUSIONS: CEUS combined with grayscale and color-Doppler flow imaging helped to improve preoperative diagnosis of HCAs. The characteristic imaging features of HCAs included: rapid homogeneous enhancement and slow washout pattern on CEUS; heterogeneous echogenicity on grayscale ultrasound; and centripetal enhancement with subcapsular tortuous arteries in large HCAs.

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KEY WORDS: contrast-enhanced ultrasound; hepatocellular adenoma; ultrasound diagnosis

Introduction

Hepatocellular adenoma (HCA) is a rare benign tumor of the liver, which has a tendency of life-threatening rupture with bleeding or malignant transformation.[1,2] HCA is generally treated with surgery. However, conservative management such as observation may be considered for small HCA.[3] Thus it is of clinical importance to differentiate HCA from other liver tumors, especially hepatocellular carcinoma (HCC).

HCA is often incidentally diagnosed in asymptomatic patients. It is associated with right-upper abdominal pain (80%) and normal liver function.[4] With the development and wide application of various radiological techniques in recent years, the diagnosis rate of HCAs has been increased.[5-7] However, the noninvasive diagnosis of HCAs remains a challenge because of their varied appearances.[8] Contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) are used at present as the principal imaging methods, but they are not safe in patients with renal impairment because of potential contrast-induced nephropathy secondary to iodinated CT contrast or nephrogenic systemic fibrosis associated with gadolinium-chelated MR contrast media.[9]

Grayscale ultrasound and color-Doppler flow imaging (CDFI) are often the firstline imaging modalities for

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hepatic lesions because of the low cost and wide availability.[10] Unfortunately, the reliability of ultrasound and CDFI is limited in diagnosis of focal liver lesion (FLL).[11] Contrast-enhanced ultrasound (CEUS) is reliable for the assessment of FLL.[12] The advantages of CEUS includes relatively lower cost compared to CT or MRI, reduced time of examination, real-time observation over the whole period of enhancement, and lack of ionizing radiation. It has a good sensitivity and specificity in detection and characterization of benign and malignant hepatic lesions.[12-14] Dietrich et al and Kim et al[15, 16] reported the sensitivity and specificity in differentiating HCA from focal nodular hyperplasia (FNH), which ranged from 86% to 95% and from 74% to 79%, respectively. However, only a few reports focused on CEUS findings of HCA with a small number of cases.

In the present study, we retrospectively analyzed 26 HCAs in an attempt to identify the ultrasound features of HCA and to assess the value of CEUS in preoperative diagnosis.

Methods

Patients

This study was approved by the institutional ethics committee, and requirements for informed consents were waived. Between September 2004 and December 2012, 26 HCAs from 26 patients (10 males and 16 females; mean age 36.2±5.0 years, range 23-63) were retrospectively studied. HCAs with a diameter of at least 10 mm which allows reliable visualization and CEUS analysis were evaluated. In patients with multiple nodules, HCAs suitable for CEUS were those in which biopsies had been performed.

Examination technique

For each HCA, the examination protocol comprised three-steps: ultrasound, CDFI and CEUS. Two experienced physicians performed ultrasound scanning with Philips iU22 unit (Philips Bothell, WA, USA; C5-2 broadband curved transducer, 2-5MHz).

First, conventional ultrasound examinations, including ultrasond and CDFI, were performed. During the grayscale scan, optimized instrument settings were used to find the proper location of lesions and acquire the clear visualization, such as the adjustment of focal zones, depth, time gain compensation and application of harmonic imaging. CDFI was used to evaluate the blood flow signals inside the lesion. Flow parameters were adjusted to the lowest possible pulse repetition frequency (PRF <1000 Hz) and color flow sensitivity was adjusted to better detect the color signals and avoid aliasing.

CEUS was performed using contrast harmonic real-time imaging at a low mechanical index (MI) of 0.05-0.10. Each examination lasted about 5 minutes after the bolus injection of contrast agents. The contrast agent used in the present study was SonoVue® (Bracco Imaging Spa, Milan, Italy). For each lesion, a dose of 2.4 mL of SonoVue® was injected as a quick bolus via a 20-gauge intravenous catheter placed in the cubital vein, and followed by 5 mL of 0.9% normal saline flush. All examinations were digitally recorded. To characterize the lesion, SonoVue® enhancements during the arterial phase (15-30 seconds), portal venous phase (30-120 seconds) and late vascular phase (120-300 seconds) were evaluated.[13]

Image analysis

HCAs were divided into three groups according to the maximum diameter: <30 mm, 30-50 mm and >50 mm. They were evaluated by two independent experienced radiologists in terms of the number, location, maximum diameter, echogenicity (hyperechoic, hypoechoic or isoechoic HCAs; homogeneous or heterogeneous HCAs, which were compared with the intensity of the surrounding liver parenchyma), shape (regular or lobulated), margin (ill- or well-defined appearance) of the lesions in addition to the presence of anechoic region or calcification component. Using CDFI, we observed color flow signals inside the lesion and measured Doppler spectrums and resistance index (RI) of arteries. We also used CDFI to detect whether there is centripetal bulky color flow in the lesion. CEUS revealed patterns of SonoVue® enhancement of the lesion (hypo-enhancement, hyper-enhancement, and iso-enhancement), the homogeneity of enhancement (homogeneous or heterogeneous) and special appearance of enhancement (intra-tumoral hypoechoic non-enhancing areas, subcapsule bulky and tortuous artery) when the arterial, portal venous and late phases were evaluated, as compared with the adjacent liver parenchyma. The time to enhancement, the time of beginning enhancement, the time to peaking, and the time of iso-enhancement and hypo-enhancement were recorded.

Statistical analysis

Data were expressed as mean±standard deviation. Statistical analyses were performed with SPSS 15.0 software package (SPSS, Chicago, IL, USA). The differences between the groups were evaluated using one-way ANOVA. A $P<0.05$ was considered statistically significant. Kappa statistics was used to assess inter-observer agreement. Agreement was reached as $\kappa<0.20$ poor; 0.20-0.39 fair; 0.40-0.59 moderate; 0.60-0.79 substantial; or 0.80-1.00 almost perfect.[17]