RESEARCH COMMUNICATION

Hepatic Angiomyolipoma: Contrast Patterns with SonoVue-enhanced Real-time Gray-scale Ultrasonography

Rui-Xue Wei¹, Wen-Ping Wang¹*, Hong Ding¹, Bei-Jian Huang¹, Chao-Lun Li¹, Pei-Li Fan¹, Jun Hou², Nian-An He³

Abstract

This study was conducted to retrospectively evaluate the pattern of contrast enhancement with SonoVue on gray-scale ultrasonography of hepatic angiomyolipoma (HAML). Imaging features of 33 pathologically proven HAML lesions in 33 patients who underwent baseline ultrasound and contrast-enhanced ultrasonography (CEUS) were assessed retrospectively. All lesions were enhanced in the arterial phase and showed whole-tumor filling in. Thirty-two of 33 (97%) lesions showed early positive enhancement in the arterial phase. Twenty-three of these exhibited isoechoic or hyperechoic features in the portal phase. HAML demonstrate characteristic manifestations with SonoVue-enhanced real-time gray-scale ultrasonography.

Keywords: Contrast agent - hepatic angiomyolipoma - microbubble - ultrasonography

Introduction

Hepatic angiomyolipoma is a rare tumor of the liver. It is composed of three tissue components: blood vessels, smooth muscle, and adipose cells. Preoperative diagnosis of HAML is occasionally very difficult because of the varying proportion of the three components, resulting in the various appearances. Tumor hemodynamic evaluation is important for the differentiation of liver tumors. Contrast agents are used widely to evaluate hepatic tumors in imaging studies (Wilson et al., 2000; Isozaki et al., 2003). SonoVue-enhanced real-time gray-scale ultrasonography is a recently developed ultrasonography (US) technique. Many studies showed that it is useful in the characterization of focal hepatic lesions. With the wide use of CEUS, lots of studies on liver tumors, such as hepatocellular carcinoma (HCC), hemangioma, and focal nodular hyperplasia (FNH), were published (Ding et al., 2005; Fan et al., 2006; von Herbay et al., 2010). To some extent, reports about HAML on CEUS were increasing (Yen et al., 2005; Li et al., 2010; Wang et al., 2010). But, the case number that was included in these studies remains limited. The exact role of CEUS in the diagnosis of HAML, however, remains unclear. Further studies still need to indicate the enhancement pattern of HAML. The aim of our study is to retrospectively evaluate enhancement patterns in HAML on SonoVue-enhanced real-time gray-scale ultrasonography with a relatively large number of cases.

Patients

Between March 2004 and October 2010, 33 cases were collected in our hospital. The patients consisted of 28 women and 5 men, with ages ranging from 18 to 70 years (mean age, 44 years). The tests of serum α-fetal protein were all negative, except for 4 cases with a history of B-type hepatitis. The tumor diameters, as measured on US images, were 9-211 mm (mean, 51 mm). Histopathological diagnosis was obtained by surgical resection in all 33 HAMLs.

Sonography

Because of the long period of patient collection, multiple US systems equipped with real-time low-MI contrast-specific imaging software were used. The equipments consisted of an iU-22 (Philips) (n=14), Technos DU6/DU8 (Esaote Biomedica) (n=18), and Logic E9 (GE) (n=1). Wideband convex array transducers with an MI of 0.07 to 0.12 were used in the contrast-enhanced imaging. The microbubble contrast agent was SonoVue (Bracco), administered with an intravenous bolus injection (1.5-2.4 ml per injection), followed by 5 ml saline flush. Conventional US was performed before the contrast-enhanced imaging was started. After the administration of SonoVue, a real-time contrast scan was performed, focusing on the lesion and the adjacent liver for more than 300 seconds. A timer on the US screen recorded the

¹Department of Ultrasound, ²Department of Pathology, Zhongshan Hospital, Fudan University, Shanghai, ³Department of Ultrasound, Anhui provincial hospital of Anhui Medical University, Hefei, China *For correspondence: puguang61@yeah.net
elapsed time from the bolus injection of contrast agent. All examinations were recorded continuously on digital video disks.

**Image Interpretation**

All observations of the enhancement patterns were totally subjective. Two radiologists were present for each examination, and interpretations were made by consensus at the time of the scan. During the examination, they evaluated the ultrasonographic images by visual inspection, review of cine clips or digital video records. The radiologists determined the diameters and echogenicity of the tumors with conventional ultrasonography. They also evaluated the time delay from injection to the time of tumor enhancement, the washout time (the lesion became hypoechoic relative to the adjacent liver parenchyma), and enhancement patterns of each tumor in different phases. The arterial phase (range, 0-30 seconds, following the beginning of the injection of contrast agent), portal venous phase (range, 31-120 seconds), and late phase (range, 121-300 seconds) appearance was evaluated in terms of relative echogenicity (relative to the adjacent liver parenchyma; hyper-, iso-, or hypoechoic). The filling directions were classified as follows: centrifugal (initial central enhancement that extended to the periphery of the lesion over time), centripetal (initial peripheral enhancement that progressed to the center of the lesion over time), and whole-tumor (enhancement occurred throughout the lesion).

**Results**

Compared with the echogenicity of the adjacent liver parenchyma, that of these lesions on baseline image varied widely (Table 1).

All 33 lesions were enhanced in the arterial phase with an initiation time of 10 to 21 seconds (14.5±2.9) after injection of SonoVue. One of 33 (3%) lesions was enhanced and decreased at the same speed and degree with liver parenchyma and maintained isoechoic during the arterial and portal venous phase. Nine of 32 (28.1%) lesions exhibited enhancement defects in the portal phase and late phase (Figure 1). The remaining 23 of 32 (71.9%) lesions exhibited isoechoic or hyperechoic in the portal phase (Figure 2, 3). The washout time of 32 lesions that exhibited hyperechoic in the arterial phase were detailed in Table 1. The dynamic changes of echogenicity of 33 lesions were shown in Table 1.

| Case no. | Diameter(cm) | BUS echogenicity | Arterial phase | Portal venous phase | Late phase | Washout time(sec) |
|----------|-------------|------------------|----------------|---------------------|------------|-------------------|
| 1  | 82 | Mixed | Hetero, Hyper | Hetero, iso | Hetero, hypo | 121-300 |
| 2  | 22 | Bright, homo, hyper | Homo, Hyper | Homo, iso | Homo, iso | No washout |
| 3  | 24 | Bright, homo, hyper | Homo, Hyper | Homo, iso | Homo, iso | No washout |
| 4  | 39 | Homo, hypo | Homo, Hyper | Homo, hypo | Homo, hypo | ~120 |
| 5  | 50 | Mixed | Homo, hyper | Homo, iso | Homo, hypo | 121-300 |
| 6  | 140 | Homo, hypo | Homo, hyper | Homo, hyper | Homo, iso | No washout |
| 7  | 29 | Mixed | Homo, hyper | Homo, hypo | Homo, hypo | ~120 |
| 8  | 24 | Homo, hypo | Homo, hyper | Homo, iso | Homo, hypo | 121-300 |
| 9  | 90 | Mixed | Homo, hyper | Homo, hypo | Homo, iso | 121-300 |
| 10 | 53 | Mixed | Homo, hyper | Homo, hypo | Homo, hypo | ~120 |
| 11 | 211 | Mixed | Homo, hyper | Homo, iso | Homo, iso | No washout |
| 12 | 107 | Homo, hypo | Homo, hyper | Homo, iso | Homo, iso | No washout |
| 13 | 29 | Mixed | Homo, hyper | Homo, iso | Homo, hyp | 121-300 |
| 14 | 31 | Mixed | Homo, hyper | Homo, iso | Homo, hyp | 121-300 |
| 15 | 17 | Homo, hypo | Homo, hyper | Homo, hypo | Homo, hypo | ~120 |
| 16 | 51 | Mixed | Homo, hyper | Homo, iso | Homo, hypo | 121-300 |
| 17 | 26 | Bright, homo, hyper | Homo, hyper | Homo, iso | Homo, iso | No washout |
| 18 | 10 | Homo, hypo | Homo, hyper | Homo, hypo | Homo, hypo | ~120 |
| 19 | 48 | Homo, hypo | Homo, hyper | Homo, iso | Homo, hyp | 121-300 |
| 20 | 17 | Mixed | Homo, hyper | Homo, iso | Homo, hyp | 121-300 |
| 21 | 18 | Mixed | Homo, hyper | Homo, iso | Homo, iso | No washout |
| 22 | 34 | Mixed | Homo, hyper | Homo, iso | Homo, hyp | 121-300 |
| 23 | 53 | Mixed | Homo, hyper | Homo, iso | Homo, iso | No washout |
| 24 | 40 | Homo, hypo | Homo, hyper | Homo, hyp | Homo, hyp | ~120 |
| 25 | 65 | Mixed | Homo, hyper | Homo, hyp | Homo, hyp | ~120 |
| 26 | 9 | Bright, homo, hyper | Homo, hyper | Homo, iso | Homo, iso | No washout |
| 27 | 45 | Mixed | Homo, hyper | Homo, hyp | Homo, hyp | ~120 |
| 28 | 77 | Mixed | Homo, iso | Homo, iso | Homo, iso | No washout |
| 29 | 30 | Mixed | Homo, hyper | Homo, hyp | Homo, hyp | ~120 |
| 30 | 16 | Mixed | Homo, hyper | Homo, iso | Homo, iso | No washout |
| 31 | 60 | Mixed | Homo, hyper | Homo, iso | Homo, hyp | 121-300 |
| 32 | 102 | Mixed | Hetero, hyper | Hetero, hyper | Hetero, hypo | 121-300 |
| 33 | 46 | Mixed | Homo, Hyper | Homo, iso | Homo, hyp | 121-300 |

Mixed, hyperechoic lesion mixed with hypoechoic area; Homo, homogeneous; Hetero, heterogeneous; Iso, isoechoic; Hyper, hyperechoic; Hypo, hypoechoic
Figure 1. Hepatic Angiomyolipoma in a 38-year-old Woman Shows Washout Early During the Portal Venous Phase. A. Intercostal conventional sonogram shows a hypoechoic lesion in the right lobe, 29 mm in diameter. B. Arterial phase image obtained 17 s after contrast agent administration shows homogeneous enhancement and markedly hypervascular of the lesion. C. Portal phase image obtained at 31 s. The nodule is slightly hypoechoic relative to the surrounding liver parenchyma. D. Late phase image obtained at 148 s. The nodule becomes obviously hypoechoic relative to the surrounding liver parenchyma.

Whole-tumor filling occurred in all 33 lesions. The whole tumor enhanced rapidly. None of these lesions showed centrifugal or centripetal filling enhancement patterns. Homogeneous enhancement appeared in 31 of 33 lesions in the arterial phase, and the remaining 2 showed heterogeneous enhancement.

Discussion

Hepatic angiomyolipoma is a rare tumor of the liver. Clinically, hepatic angiomyolipoma is more common in women than in men, with a mean age at diagnosis of 49.8 years (Tsui et al., 1999). In our study, 28 cases of 33 patients were women; 5 cases were men. The mean age was 44 years.

Angiomyolipoma is a mixed mesenchymal tumor. Histologically, it is characterized by a mixture of mature fat cells, blood vessels, and smooth muscle cells. The proportion of fatty tissue within the tumor ranges from less than 10% to more than 90%. Preoperative diagnosis of HAML mostly relies on imaging studies, including US, computed tomography (CT), and magnetic resonance imaging (MRI). The imaging features of HAML are diverse as a result of the various proportions of tissue components within the tumor. Therefore, preoperative diagnosis is occasionally very difficult (Takahara et al., 2009). In our study, the echogenicity of 33 lesions on baseline images were variable (Table 1) because of the presence of the multiple ingredients within the lesions. Although a homogeneous or heterogeneous bright hyperechoic area with well-defined margin is the relatively typical appearance of HAML, some cases are difficult to differentiate from hepatic hemangioma. In our study, a bright homogeneous hyperechoic lesion was exhibited in only 5 cases, and 9 of 33 cases showed a hyperechoic lesion mixed with a hypoechoic area. Only 3 of these 14 cases were considered to be HAML, according to appearance on the baseline image. The lesions that appeared to be hypoechoic on the baseline image were usually misdiagnosed as HCC, especially when the patient presented a high risk of HCC.

Tumor hemodynamics can deliver important information for the differentiation diagnosis of liver tumors. Preoperative diagnosis of liver tumors sometimes relies on the enhancement pattern on contrast enhanced imaging (Leslie et al., 1995; Choi et al., 2000). Contrast-enhanced harmonic ultrasonography was demonstrated to be useful in the assessment of tumor vascularization (Isozaki et al., 2003; Trillaud et al., 2009; von Herbay et al., 2010). It has been shown that lots of liver lesions show characteristic enhancement patterns on contrast-enhanced gray-scale ultrasonography. The most common enhancement pattern of hepatic hemangioma on contrast-enhanced harmonic US was peripheral globular enhancement with progressive centripetal fill-in (Kim et al., 2002; Ding et al., 2005). Centrifugal filling was the specific enhancement feature of focal nodular hyperplasia (Kim et al., 2008). In our study, all 33 AML lesions exhibited whole-tumor filling in. Neither centrifugal nor centripetal filling was found in...
of FNHs were isoechic or hypechoic on gray-scale ultrasound (Uggowitzer et al., 1998). On the other hand, sustained enhancement may occur, especially in well-differentiated HCCs (Jang et al., 2007). Therefore, if patients present a risk of HCC, prolonged enhancement should not be considered as a diagnostic feature of a benign lesion (Jang et al., 2007).

Our study still had limitations. For most cases that were incidentally detected by US, contrast-enhanced ultrasonography was recommended for further characterization only when the radiologist found that it was difficult to make a diagnosis. As a result, not all cases of HAML that underwent operation during this period underwent CEUS. So, the imaging features only represent a part of HAML lesions.

In conclusion, hepatic angiomylipoma has several features that are helpful for diagnosis in some cases, such as marked whole-tumor homogeneous enhancement in the arterial phase with prolonged enhancement in the portal or late phase. For other cases, it should be carefully differentiated from other lesions, like HCC, focal nodular hyperplasia, and hemangioma, through employing other imaging modalities or needle puncture biopsy. Further study is necessary to evaluate the role CEUS plays in the diagnosis of HAML.

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