RESEARCH COMMUNICATION

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

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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

Asian Pacific J Cancer Prev, **13**, 493-497

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.

Materials and Methods

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

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Table 1. BUS and CEUS Features of the 33 HAML Lesions

Case no.	Diameter(cm)	BUS echogenicity	CEUS			
			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, iso	Homo, hypo	121-300
10	53	Mixed	Homo, hyper	Homo, hypo	Homo, hypo	~120
11	211	Mixed	Homo, hyper	Homo, iso	Hom , iso	No washout
12	107	Homo, hypo	Homo, hyper	Homo, iso	Homo, iso	No washout
13	29	Mixed	Homo, hyper	Homo, iso	Homo, hypo	121-300
14	31	Mixed	Homo, hyper	Homo, iso	Homo, hypo	121-300
15	17	Homo, hypo	Homo, hype	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	Bright, homo, hyper	Homo, hyper	Homo, iso	Homo, iso	No washout
19	48	Homo, hypo	Homo, hyper	Homo, hypo	Homo, hypo	~120
20	17	Mixed	Homo, hyper	Homo, iso	Homo, hypo	121-300
21	18	Mixed	Homo, hyper	Homo, iso	Homo, iso	No washout
22	34	Mixed	Homo, hyper	Homo, iso	Homo, hypo	121-300
23	53	Mixed	Homo, hyper	Homo, iso	Homo, iso	No washout
24	40	Homo, hypo	Homo, hyper	Homo, hypo	Homo, hypo	~120
25	65	Mixed	Homo, hyper	Homo, hypo	Homo, hypo	~120
26	9	Bright, homo, hyper	Homo, hyper	Homo, iso	Homo, iso	No washout
27	45	Mixed	Homo, hyper	Homo, hypo	Homo, hypo	~120
28	77	Mixed	Homo, iso	Homo, iso	Homo, iso	No washout
29	30	Mixed	Homo, hyper	Homo, hypo	Homo, hypo	~120
30	16	Mixed	Homo, hyper	Homo, iso	Homo, iso	No washout
31	60	Mixed	Homo, hyper	Homo, iso	Homo, hypo	121-300
32	102	Mixed	Hetero, hyper	Hetero, hyper	Hetero, hypo	121-300
33	46	Mixed	Homo, Hyper	Homo, iso	Homo, hypo	121-300

Mixed, hyperechoic lesion mixed with hypoechoic area; Homo, homogeneous; Hetero, heterogeneous; Iso, isoechoic; Hyper, hyperechoic; Hypo, hypoechoic

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 hypoechogenicity). 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.

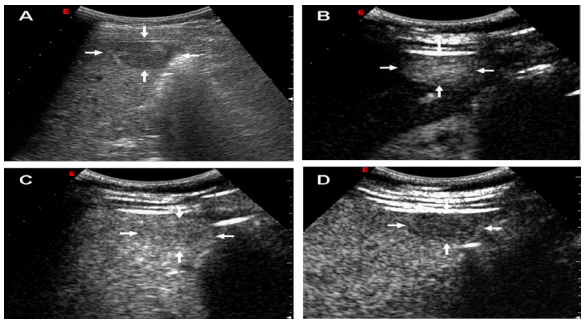

Figure 1. Hepatic Angiomyolipoma in a 38-year-old Woman Shows Washout Early During the Portal Venous Phase. A. Intercostal conventional sonogram shows a hypoechoic lesion in the right lobe, 29 mm in diameter. B. Arterial phase image obtained 17 s after contrast agent administration shows homogeneous 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

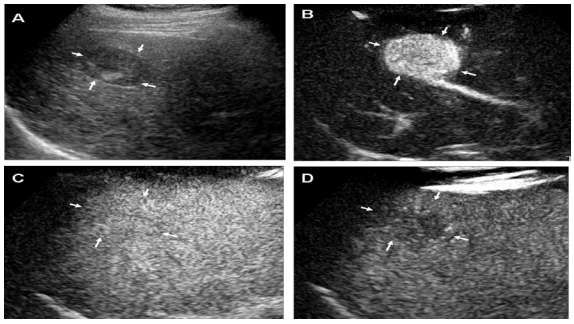

Figure 2. Hepatic Angiomyolipoma in a 50-year-old Woman Shows Washout until Late Phase. A. Oblique subcostal conventional sonogram shows a heterogeneous hypoechoic lesion in the right lobe, 31 mm in diameter. B. Arterial phase image obtained at 14 s after contrast agent administration shows homogeneous enhancement and markedly hypervascular of the lesion. C. Portal phase image obtained at 91 s. The lesion maintains isoechoic relative to the surrounding liver parenchyma. D. Late phase image obtained at 211 s. The nodule becomes 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

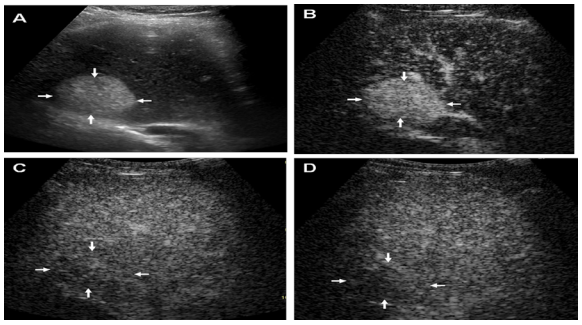

Figure 3. Hepatic Angiomyolipoma in a 54-year-old Woman Shows no Washout up to 300s. A. Oblique subcostal conventional sonogram shows a heterogeneous hypoechoic lesion in the right lobe, 46 mm in diameter. B. Arterial phase image obtained at 26s after contrast agent administration shows homogeneous enhancement of the lesion. C. Portal phase image obtained at 78 s. The lesion maintains isoechoic relative to the surrounding liver parenchyma. D. Late phase image obtained at 130 s. Notte persistent isochoic relative to the surrounding liver

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

these lesions. Li R et al. (2010) reported that no peripheral nodular arterial enhancement, centripetal filling, or spoke wheel-like enhancement pattern was depicted in their study of 18 patients with 19 HAML lesions. The finding is in accordance with our study.

Conventionally, the wash-in and washout time is usually used as an important standard for the differentiation of benign and malignant liver tumors on enhanced CT, MRI, and US (Ogawa et al., 2006; Burns et al., 2007). According to the relevant literature (Ding et al., 2005; von Herbay et al., 2010), the typical hemodynamic pattern of HCC on contrast-enhanced US was the whole-lesion enhancement or mosaic enhancement in the arterial phase with an enhancement defect in the portal venous phase.

In our group, all 33 HAMLs 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 showed isoechoic during the whole enhancement process. The other 32 of 33 (97%) lesions showed early positive enhancement in the arterial phase, indicating that AML was a hypervascular tumor. Nine of 32 (28.1%) lesions exhibited enhancement defects in the portal phase (washout time was less than 120 seconds) and late phase. This group of lesions was liable to be confused with HCC. However, intratumoral necrosis was found frequently in primary liver carcinoma pathologically; it was correlated with the irregular defect areas on contrast-enhanced imaging (Ogawa et al., 2006). Ding et al. (2005) reported that 35.6% of primary liver carcinomas showed mosaic enhancement in the arterial phase of low-MI real-time ultrasonography (Ding et al., 2003). In our study, all 9 hyperenhancing lesions showed homogeneous enhancement, including 4 cases larger than 30 mm in diameter. This may help the differentiation with HCC. There were 2 cases that were larger than 80 mm in diameter that showed heterogeneous enhancement during the whole process because of the intratumoral hemorrhage. To some extent, that appearance was similar to the enhancement pattern of HCC. But one of them showed hyperechoic, and the other showed isoechoic during the portal venous phase. The remaining 23 of 32 (71.9%) lesions exhibited isoechoic or hyperechoic in the portal phase. Twelve of 23 lesions became hypoechoic during the late phase (washout time between 121-300 seconds), and the remaining 11 lesions maintained isoechoic in the late phase with no washout visible up to 300 seconds. Wang et al. (2010) reported that 8 of the 23 lesions exhibited hyperenhancement in the arterial phase and showed slight hyperenhancement or isoenhancement in the portal phase and late phase. Li et al. (2010) performed real-time SonoVue-enhanced ultrasonography in 18 patients with 19 tumors. In their study, hyperenhancing pattern in the arterial phase and prolonged hyperenhancement during the portal and late phase were detected in 17 tumors. Yan et al. (2002) described CT findings of 12 AML lesions. Their result showed that 8 HAML lesions enhanced markedly in the arterial phase and remained persistently in the portal phase. The extended enhancement was suggestive of benign liver lesions (Burnes et al., 2007; Von Herbay et al., 2010). Most FNHs showed sustained portal venous phase enhancement; it was similar to HAML. But, 95% of FNHs were isoechoic 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 angiomyolipoma 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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