Hepatic Hemangiomas: Factors Associated with Pseudo Washout Sign on Gd-EOB-DTPA-enhanced MR Imaging

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Purpose: Our study aim was to clarify the characteristics of hemangiomas with pseudo washout sign (PWS) by comparing their features with those of hemangiomas without PWS on gadolinium-ethoxybenzyl-diethylenetriaminepentaacetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance (MR) imaging.

Methods: We evaluated the features of hemangiomas on Gd-EOB-DTPA-enhanced MR imaging of 70 hepatic hemangiomas in 31 patients, investigating the presence of peripheral or central nodular enhancement, diffuse enhancement, and arterioportal shunt during the arterial phase, fill-in enhancement during the portal venous phase, and PWS, which is low signal intensity during the late phase. We visually assessed the intensity of contrast enhancement of the lesion during the arterial, portal venous, late, and hepatobiliary phases using a 4-grade scale and used the Fisher exact and Mann-Whitney U tests to compare hemangiomas with and without PWS.

Results: We observed PWS in 33 (47%) of 70 hemangiomas, which were significantly smaller than the hemangiomas without PWS (17.4 mm ± 20.3 versus 30.1 mm ± 28.5; \( P = 0.005 \)); more frequent diffuse enhancement in hemangiomas with PWS than those without (21.2% versus 2.7%; \( P = 0.026 \)); and no significant differences in nodular enhancement (\( P = 0.231 \)), arterioportal shunt (\( P = 0.403 \)), or fill-in enhancement (\( P = 0.357 \)) between hemangiomas with and without PWS. Visually determined grades of tumor contrast enhancement were significantly lower in hemangiomas with PWS during the portal venous (\( P = 0.007 \)) and late (\( P < 0.001 \)) phases.

Conclusions: Small hemangiomas tend to decrease in signal intensity during the portal venous phase and show PWS during the late phase.

Keywords: gadoxetic acid-DTPA (Gd-EOB-DTPA), hemangioma, liver, magnetic resonance imaging, neoplasms

Introduction

Hepatic hemangioma is the most common benign hepatic neoplasm, with incidence between 0.4 and 7.3% reported in a necropsy series.\(^1\) Their differentiation from malignant liver tumors is important because hepatic hemangiomas usually require no treatment.\(^2\) The utility of enhanced computed tomography (CT) and gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA)-enhanced magnetic resonance (MR) imaging has been reported for the diagnosis of hepatic hemangiomas and their differentiation from malignant liver tumors.\(^3\)-\(^9\) The most common features of hepatic hemangiomas on enhanced CT and Gd-DTPA-enhanced MR imaging are peripheral or central nodular enhancement during the arterial phase, fill-in enhancement during the portal venous phase, and prolonged enhancement during the late phase.\(^3\)-\(^9\)

Gd-EOB-DTPA is a new hepatobiliary contrast agent that has been demonstrated to improve the detection and characterization of focal liver lesions in clinical studies.\(^10\)-\(^14\) Recently, Gd-EOB-DTPA-
enhanced MR imaging has played a very important role in the diagnosis of lesions of the liver. Previous studies of hepatic hemangiomas on Gd-EOB-DTPA-enhanced MR imaging reported that some hepatic hemangiomas might mimic malignant liver tumors; these mimickers do not show the prolonged enhancement during the late phase that is an important finding for the diagnosis of hepatic hemangiomas. This lack of prolonged enhancement has been called the pseudo washout sign (PWS) and is not considered true contrast washout. Its primary cause appears to be the uptake of Gd-EOB-DTPA in the surrounding normal liver parenchyma. Hemangiomas with diffuse enhancement during the arterial phase have been reported to show PWS during the late phase on Gd-EOB-DTPA-enhanced MR imaging, which makes their differentiation from hypervascular hepatocellular carcinomas difficult. However, the characteristics of hemangiomas with PWS have not been fully examined. Therefore, we undertook this study to clarify the characteristics of hemangiomas with PWS by comparing them with features of hemangiomas without PWS on Gd-EOB-DTPA-enhanced MR imaging.

Materials and Methods

Patients

From April 1, 2010 to March 31, 2013, 509 consecutive patients underwent Gd-EOB-DTPA-enhanced MR imaging at our institution for the evaluation of suspected liver tumors. Four hundred and seventy-three of the 509 underwent 3-phase enhanced CT examinations, and from them, we selected the patients with hepatic hemangiomas. Diagnosis was based on their typical manifestation as bright signal intensity on T2-weighted MR imaging and was based on their typical manifestation as hypervascular hepatocellular carcinomas (HCC) on enhanced CT examinations, and from them, we selected the patients for this study. Patients were diagnosed by histological examination following surgical resection because of the risk of spontaneous rupture. Twenty-two patients had no history of liver dysfunction. Nine had chronic liver disease, seven cases classified as Child-Pugh A and two classified as Child-Pugh B. The underlying causes of chronic liver disease were hepatitis B (n = 3), hepatitis C (n = 5), and primary sclerosing cholangitis (n = one).

Our ethics review board approved this retrospective study and waived informed consent.

MR imaging technique

MR imaging was performed at 3.0-tesla (Magnetom Trio; Siemens AG, Erlangen, Germany) with a maximum gradient amplitude of 45 mT/m and a slew rate of 200 mT/m/s. The coil had 6 linear elements in a left-to-right direction for both the anterior and posterior components. The standard sequences performed prior to Gd-EOB-DTPA administration were: 2-dimensional T1-weighted gradient-echo (repetition time [TR]/echo time [TE], 110/2.46 and 3.69 ms; flip angle [FA], 70°; thickness, 8 mm; slice gap, 1.6 mm; field of view [FOV], 350 mm; matrix, 320 × 256; slice acceleration factor, 2); T2-weighted turbo spin-echo (TR/TE, 1880/80 ms; echo train length [ETL], 16; slice thickness, 8 mm; slice gap, 1.6 mm; FOV, 350 mm; matrix, 384 × 307; slice acceleration factor, 2); and respiratory-triggered with navigator-echo technique fat-suppressed T2-weighted turbo spin-echo (TR/TE, 2500 to 8600/80 ms; ETL, 10; slice thickness, 8 mm; slice gap, 1.6 mm; FOV, 350 mm; matrix, 512 × 410; slice acceleration factor, 2) sequences.

Dynamic images were obtained using 3-dimensional (3D) fat-suppressed T1-weighted gradient-echo volumetric interpolated breath-hold examination (VIBE) axial series before and after intravenous contrast injection. The image parameters were: TR/TE, 3.06/1.12 ms; FA, 10°; slice thickness, 2 mm; number of partitions, 80; FOV, 350 × 280 mm; matrix, 256 × 224; slice acceleration factor, 2; and acquisition time, 20 seconds. Before dynamic MR imaging, a test dose of one mL of Gd-EOB-DTPA was injected at the rate of one mL/s and followed by 40 mL saline injection through a cubital intravenous line using a power injector. During the test injection, the image at the level of the celiac axis in which the aorta was most enhanced was chosen, and its acquisition time was adopted as the time of peak aortic enhancement. For dynamic MR imaging, 0.025 mmol/kg body weight of Gd-EOB-DTPA was intravenously administered at a flow rate of one mL/s, followed by a 40-mL saline solution flush. Breath-hold 3D fat-
suppressed T₁-weighted VIBE dynamic MR imaging was repeated at 10 s (arterial phase), 50 s (portal venous phase), 160 s (late phase) and 20 min (hepatobiliary phase) after the time of peak aortic enhancement, which was determined by the test injection. In the present study, we evaluated precontrast, arterial, portal venous, late, and hepatobiliary phase T₁-weighted VIBE images.

**Qualitative evaluation**

Two radiologists with 9 and 10 years of experience in abdominal radiology and with knowledge of the diagnosis of hepatic hemangioma independently assessed the following MR imaging features: peripheral or central nodular enhancement, diffuse enhancement, and arterioporal shunt during the arterial phase; fill-in enhancement during the portal venous phase; and PWS (low signal intensity relative to surrounding liver parenchyma without prolonged or fill-in enhancement) during the late phase (Fig. 1).

They visually assessed the degree of contrast enhancement of the enhancing portion of the lesion in relation to that of the liver parenchyma during the arterial, portal venous, late, and hepatobiliary phases using a 4-grade scale (grade 4, clearly higher; grade 3, moderately higher; grade 2, equal; grade 1, lower) (Figs. 2, 3). Any discrepancies were resolved during a third analysis session, in which a decision was reached in consultation with a third radiologist with 10 years of experience in abdominal radiology.

**Quantitative evaluation**

One radiologist with 9 years of experience in abdominal radiology, who attended none of the reading sessions to minimize bias, measured the signal intensities of the 70 hemangiomas, liver parenchyma, and paravertebral muscle in circular regions of interest (ROI) placed over each region on the precontrast, arterial, portal venous, late, and hepatobiliary phases. An attempt was made to place the ROIs over the same regions on successive phase images of each patient. In each hemangioma, the ROI was placed to cover the enhancing portion as much as possible. ROIs of 100 to 200 mm² were placed over the lateral, anterior, and posterior segments of the liver parenchyma at the level of the hilum of the liver with care taken to avoid blood vessels and artifacts, and the obtained intensities were averaged. The ROIs over paravertebral muscle were 100 mm² in size. To evaluate changes in signal intensity in the hemangioma and liver parenchyma, the ratios of the signal intensity of tumor to that of muscle (TMSR) and of the liver to that of muscle (LMSR) during each phase were calculated by dividing in each case the signal intensity of the hemangioma and of the liver by that of the paravertebral muscle.¹³

**Statistical analysis**

Statistical analyses were performed using SPSS
14.0 software for Windows (SPSS version 14.0, Chicago, IL, USA). We used Fisher exact test to analyze categoric variables, including nodular enhancement, diffuse enhancement and arteriportal shunt during the arterial phase, and fill-in enhancement during the portal venous phase; Mann-Whitney U test to analyze continuous variables, including tumor size, visual grades of contrast enhancement of hemangiomas, TMSR, and LMSR during each phase; kappa analysis to determine interobserver agreement for MR imaging features; and weighted kappa analysis to determine interobserver agreement for the visual grades of contrast enhancement of hemangiomas (κ = 0.00 to 0.20, slight agreement; κ = 0.21 to 0.40, fair agreement; κ = 0.41 to 0.60, moderate agreement; κ = 0.61 to 0.80, substantial agreement; and κ = 0.81 to 1.00, almost perfect agreement). We also used the Spearman rank correlation coefficient (Rs) to analyze the relationship between the visual grades of hemangioma contrast enhancement and TMSR and the Fisher exact test to evaluate the difference in MR imaging features between small (<20 mm) and large (≥20 mm) hemangiomas to clarify the association between the MR imaging features and tumor size.

Subgroup analysis for hemangiomas without diffuse enhancement was performed to clarify the characteristics of hemangiomas without diffuse enhancement during the arterial phase, which show PWS during the late phase on Gd-EOB-DTPA-enhanced MR imaging. The data were expressed as mean ± standard deviation, if appropriate. For all
statistical analyses, $P < 0.05$ was considered statistically significant.

**Results**

Table 1 shows the frequencies of the features of hepatic hemangioma on Gd-EOB-DTPA-enhanced MR imaging. Among the 70 hemangiomas, PWS was observed in 33 (47%) during the late phase; nodular enhancement was observed in 56 (80%), diffuse enhancement in eight (11%), and arterioportal shunt in 17 (24%) during the arterial phase; and fill-in enhancement was observed in 57 (81%) during the portal venous phase.

Table 2 compares MR imaging findings between hepatic hemangioma with and without PWS. Hemangiomas were significantly smaller (17.4 ± 20.3 mm) with PWS than without (30.1 ± 28.5 mm) ($P = 0.005$); diffuse enhancement was more frequently

| Table 1. Frequencies of features of all 70 hepatic hemangiomas on Gd-EOB-DTPA-enhanced magnetic resonance imaging |
|---------------------------------------------------------------|
| Appearance | Number (%) of 70 hemangiomas |
| Arterial phase | Nodular enhancement 56 (80.0) |
| | Diffuse enhancement 8 (11.4) |
| | Arterioportal shunt 17 (24.3) |
| Portal venous phase | Fill-in enhancement 57 (81.4) |
| Late phase | Pseudo washout sign 33 (47.1) |
| Note: Data are the number of cases; numbers in parentheses are percentages. Gd-EOB-DTPA, gadolinium-ethoxybenzyl-diethylenetriaminepentaacetic acid |

| Table 2. Comparison of findings of hepatic hemangioma with and without pseudo washout sign on Gd-EOB-DTPA-enhanced magnetic resonance imaging |
|---------------------------------------------------------------|
| Pseudo washout sign | Yes (n = 33) | No (n = 37) | $P$ |
| Tumor size (mm) | 17.4 ± 20.3 | 30.1 ± 28.5 | 0.005 |
| Magnetic resonance imaging features | | | |
| Arterial phase | | | |
| Nodular enhancement | 24 (72.7) | 32 (86.5) | 0.231 |
| Diffuse enhancement | 7 (21.2) | 1 (2.7) | 0.026 |
| Arterioportal shunt | 10 (30.3) | 7 (18.9) | 0.403 |
| Portal venous phase | | | |
| Fill-in enhancement | 25 (75.8) | 32 (86.5) | 0.357 |
| Visual grades of contrast enhancement | | | |
| Arterial phase | 3.12 ± 0.86 | 2.81 ± 0.84 | 0.084 |
| Portal venous phase | 2.42 ± 0.75 | 2.95 ± 0.78 | 0.007 |
| Late phase | 1.00 ± 0.00 | 2.11 ± 0.31 | < 0.001 |
| Hepatobiliary phase | 1.00 ± 0.00 | 1.00 ± 0.00 | 1.000 |
| Ratio of signal intensity of tumor to that of muscle | | | |
| Precontrast | 0.82 ± 0.20 | 0.78 ± 0.27 | 0.502 |
| Arterial phase | 1.90 ± 0.56 | 1.80 ± 0.72 | 0.420 |
| Portal venous phase | 1.79 ± 0.36 | 2.03 ± 0.51 | 0.048 |
| Late phase | 1.57 ± 0.37 | 1.85 ± 0.46 | 0.002 |
| Hepatobiliary phase | 1.00 ± 0.37 | 1.11 ± 0.41 | 0.232 |
| Ratio of signal intensity of liver to that of muscle | | | |
| Precontrast | 1.28 ± 0.30 | 1.25 ± 0.36 | 0.688 |
| Arterial phase | 1.50 ± 0.30 | 1.62 ± 0.73 | 0.925 |
| Portal venous phase | 1.76 ± 0.25 | 1.76 ± 0.47 | 0.702 |
| Late phase | 1.83 ± 0.25 | 1.77 ± 0.44 | 0.587 |
| Hepatobiliary phase | 1.96 ± 0.46 | 2.04 ± 0.60 | 0.214 |
| Note: Numbers in parentheses are percentages. Gd-EOB-DTPA, gadolinium-ethoxybenzyl-diethylenetriaminepentaacetic acid |

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observed in hemangiomas with PWS (21.2%) than without (2.7%) \((P = 0.026)\); and there were no statistically significant differences in nodular enhancement (72.7 versus 86.5%; \(P = 0.231)\), arterioportal shunt (30.3 versus 18.9%; \(P = 0.403)\), or fill-in enhancement (75.8 versus 86.5%; \(P = 0.357)\) between hemangiomas with and without PWS. Visual grades of tumor contrast enhancement were significantly lower in hemangiomas with PWS than without during the portal venous phase. \(P = 0.007)\) and late \(P < 0.001)\) phases. Interobserver agreement was substantial to almost perfect, with kappa values ranging from 0.66 to 0.86 for interpretation of the MR imaging features and weighted kappa values ranging from 0.80 to 1.00 for visual grade of contrast enhancement.

TMSR was also significantly lower in hemangiomas with PWS than without during the portal venous \(P = 0.048)\) and late phases \(P = 0.002\) but not during the arterial \(P = 0.420)\) and hepatobiliary phases \(P = 0.232)\) (Table 2, Fig. 4). There were no statistically significant differences in LMSR during the arterial \(P = 0.925)\), portal venous \(P = 0.702)\), late \(P = 0.587)\), or hepatobiliary phases \(P = 0.214)\) between hemangiomas with and without PWS. There was a significant correlation between the visual grades of hemangioma enhancement and TMSR (arterial phase: \(Rs = 0.692\), \(P < 0.001)\); portal venous phase: \(Rs = 0.608\), \(P < 0.001); late phase: \(Rs = 0.437\), \(P < 0.001).\)

Table 3 shows a comparison of features of small (\(<20\) mm) and large (\(\geq20\) mm) hepatic hemangiomas on dynamic Gd-EOB-DTPA-enhanced MR imaging. Diffuse enhancement (20.5 versus 0.0%; \(P = 0.007)\) and PWS (64.1 versus 25.8%; \(P = 0.022)\) were more frequently found in small than large hemangiomas. Nodular enhancement (100.0 versus 69.2%; \(P = 0.001)\) and fill-in enhancement (93.5 versus 69.2%; \(P = 0.015)\) were more frequently found in large than small hemangiomas. There was no significant difference in arterioportal shunt between small and large hemangiomas \(P = 0.262)\).

Table 4 shows Gd-EOB-DTPA-enhanced MR imaging findings of 62 hepatic hemangiomas without diffuse enhancement during the arterial phase. Hemangiomas were significantly smaller (19.7 mm \(\pm 22.3)\) with PWS than without (30.6 mm \(\pm 28.7)\) \(P = 0.027)\). No statistically significant differences in frequency of nodular enhancement \(P = 1.000)\), arterioportal shunt \(P = 0.373)\), or fill-in enhancement \(P = 0.439)\) were observed between hemangiomas with and without PWS. The visual grades of hemangioma enhancement during the portal venous \(P = 0.015)\) and late phases \(P < 0.001)\) and of TMSR during the portal venous \(P = 0.026)\) and late phases \(P = 0.012)\) were significantly lower in hemangiomas with PWS than without.

**Discussion**

Prolonged enhancement during the late phase on enhanced CT and Gd-DTPA-enhanced MR imaging is an important finding that can be used to diagnose hepatic hemangiomas.24–30 On dynamic enhanced

Table 3: Comparison of features of small (\(<20\) mm) and large (\(\geq20\) mm) hepatic hemangiomas on dynamic Gd-EOB-DTPA-enhanced magnetic resonance imaging

| Magnetic resonance imaging features | Size           | \(n = 39\) | \(n = 31\) | \(P\)    |
|-------------------------------------|----------------|-----------|-----------|---------|
| Arterial phase                      |                |           |           |         |
| Nodular enhancement                | 27 (69.2)      | 31 (100.0) | 0.001     |
| Diffuse enhancement                | 8 (20.5)       | 0 (0)     | 0.007     |
| Arterioportal shunt                 | 7 (17.9)       | 10 (32.3) | 0.262     |
| Portal venous phase                 |                |           |           |         |
| Fill-in enhancement                 | 27 (69.2)      | 29 (93.5) | 0.015     |
| Late phase                          |                |           |           |         |
| Pseudo washout sign                 | 25 (64.1)      | 8 (25.8)  | 0.002     |

Note: Numbers in parentheses are percentages.

Gd-EOB-DTPA, gadolinium-ethoxybenzyl-diethylene-triaminepentaacetic acid.
CT, once the regions in hemangioma enhance during the arterial phase, they also show prolonged enhancement. Choi and associates reported prolonged enhancement of all hemangiomas on enhanced CT, whereas another study indicated no prolongation of enhancement in 63% of hemangiomas during the late phase on Gd-EOB-DTPA-enhanced MR imaging. In the present study, 33 (47%) of 70 hemangiomas showed no prolonged enhancement during the late phase on Gd-EOB-DTPA-enhanced MR imaging. Moreover, 31 (48%) of 64 hemangiomas with nodular or diffuse enhancement during the arterial phase showed no prolonged enhancement during the late phase. This result differed from that on enhanced CT.

It is well known that hemangiomas show various types of enhancement in contrast-enhanced CT and MR imaging, and the possible correlation of the dynamic enhancement pattern of hepatic hemangiomas with the collective size of its constituent vascular spaces has been reported. The vascular spaces of hemangiomas with diffuse enhancement are relatively small compared to those without diffuse enhancement. Hanafusa’s group reported the isoattenuation compared to the surrounding liver parenchyma of approximately half the number of hemangiomas with diffuse enhancement during the portal venous phase on dynamic CT, a pattern also known as high flow hemangioma. Doo and colleagues have reported that hemangiomas with diffuse enhancement during the arterial phase show the pseudo washout sign on Gd-EOB-DTPA-enhanced MR imaging. In the present study, 7 (86%) of 8 hemangiomas with diffuse enhancement during the arterial phase showed PWS during the late phase. The visual assessment of tumor contrast enhancement and TMSR revealed decreased contrast enhancement from the

| Findings of Gd-EOB-DTPA-enhanced magnetic resonance imaging of 62 hepatic hemangiomas without diffuse enhancement during the arterial phase: comparison between hemangiomas with and without pseudo washout sign |
|---------------------------------------------------|-------------------|---------|
| Pseudo washout sign                               | Yes (n = 26)      | No (n = 36) | P       |
| Tumor size (mm)                                   | 19.7 ± 22.3       | 30.6 ± 28.7 | 0.027  |
| Magnetic resonance imaging features               |                   |           |        |
| Arterial phase                                    |                   |           |        |
| Nodular enhancement                               | 24 (92.3)         | 32 (88.9) | 1.000  |
| Arterioportal shunt                               | 8 (30.8)          | 7 (19.4)  | 0.373  |
| Portal venous phase                               |                   |           |        |
| Fill-in enhancement                               | 25 (96.2)         | 32 (88.9) | 0.439  |
| Visual grades of contrast enhancement             |                   |           |        |
| Arterial phase                                    | 3.08 ± 0.93       | 2.78 ± 0.83 | 0.135  |
| Portal venous phase                               | 2.38 ± 0.70       | 2.89 ± 0.85 | 0.015  |
| Late phase                                        | 1.00 ± 0.00       | 2.08 ± 0.28 | <0.001 |
| Hepatobiliary phase                               | 1.00 ± 0.00       | 1.00 ± 0.00 | 1.000  |
| Ratio of signal intensity of tumor to that of muscle |                  |           |        |
| Precontrast                                       | 0.79 ± 0.22       | 0.77 ± 0.25 | 0.558  |
| Arterial phase                                    | 1.90 ± 0.60       | 1.78 ± 0.73 | 0.373  |
| Portal venous phase                               | 1.76 ± 0.54       | 2.04 ± 0.51 | 0.026  |
| Late phase                                        | 1.61 ± 0.49       | 1.83 ± 0.46 | 0.012  |
| Hepatobiliary phase                               | 1.04 ± 0.40       | 1.09 ± 0.39 | 0.573  |
| Ratio of signal intensity of liver to that of muscle |                  |           |        |
| Precontrast                                       | 1.27 ± 0.32       | 1.22 ± 0.34 | 0.387  |
| Arterial phase                                    | 1.52 ± 0.36       | 1.62 ± 0.74 | 0.774  |
| Portal venous phase                               | 1.76 ± 0.54       | 1.75 ± 0.48 | 0.753  |
| Late phase                                        | 1.82 ± 0.38       | 1.76 ± 0.44 | 0.363  |
| Hepatobiliary phase                               | 1.97 ± 0.44       | 2.05 ± 0.59 | 0.153  |

Note: Numbers in parentheses are percentages.
Gd-EOB-DTPA, gadolinium-ethoxybenzyl-diehtylenetriaminepenta-acetic acid
arterial to portal venous phases in hemangiomas with PWS and increased enhancement in those without PWS. Therefore, it is suggested that hemangiomas with diffuse enhancement show a more rapid turnover rate of blood flow and less enhancement after the arterial phase because of their small vascular spaces. On Gd-EOB-DTPA-enhanced MR imaging, moreover, the reduced tumor contrast enhancement after the arterial phase is more prominent owing to the uptake of Gd-EOB-DTPA in the surrounding normal liver parenchyma. Hypervascular malignant tumors, such as typical hepatocellular carcinomas or hypervascular metastases, also show marked diffuse enhancement during the arterial phase and washout during the later phase on Gd-EOB-DTPA-enhanced MR imaging. Therefore, the similar enhancement characteristics might make it difficult to differentiate hemangiomas with diffuse enhancement during the arterial phase from the hypervascular malignant tumors on Gd-EOB-DTPA-enhanced MR imaging.

Kato and associates reported the significantly larger mean lesion size of hemangiomas with peripheral enhancement or fill-in enhancement than that of those without. In the present study, we observed peripheral nodular enhancement and fill-in enhancement less frequently in small (<20 mm) than large (≥20 mm) hemangiomas. We observed PWS more frequently in small (<20 mm) hemangiomas. Therefore, small hemangiomas might be difficult to diagnose on Gd-EOB-DTPA-enhanced MR imaging because they do not show important features (peripheral or central nodular enhancement, fill-in enhancement, and prolonged enhancement) for diagnosis.

Yamashita’s group have reported that hemangiomas with diffuse enhancement or peripheral nodular enhancement during the arterial phase have smaller vascular spaces than hemangiomas with fill-in enhancement during the portal venous phase. In the present study, we observed no statistically significant differences in the frequency of peripheral nodular enhancement or fill-in enhancement between hemangiomas with and without PWS.

Characteristics of hemangiomas without diffuse enhancement that show PWS on Gd-EOB-DTPA-enhanced MR imaging have not been examined. In the present study, 26 (42%) of 62 hemangiomas without diffuse enhancement during the arterial phase also showed PWS. Therefore, hemangiomas without diffuse enhancement could also show PWS. Goshima’s group reported the more frequent observation of arterioportal shunt and early peripheral enhancement in hemangiomas than hypovascular metastatic tumors, and these were independent findings suggestive of hemangioma. In our 62 hemangiomas without diffuse enhancement during the arterial phase, 18 without arterioportal shunt and two without peripheral nodular enhancement showed PWS. Moreover, hemangiomas with PWS displayed decreased signal intensity during the portal venous phase that mimicked the intensity of hypovascular metastatic tumors on qualitative and quantitative analysis. Therefore, our results suggest that it might be difficult to differentiate hemangiomas without diffuse enhancement during the arterial phase that show PWS during the late phase from hypovascular metastatic tumors on Gd-EOB-DTPA-enhanced MR imaging.

The finding of bright signal intensity on T2-weighted imaging is important to differentiate hemangiomas from malignant liver tumors when hemangiomas show PWS on Gd-EOB-DTPA-enhanced MR imaging. However, small hemangiomas may not show typical bright signal intensity on T2-weighted imaging because of the partial volume phenomenon. We did not compare the signal intensity on T2-weighted imaging of small hemangiomas with and without PWS because one criterion for the final diagnosis of hemangioma was the lesion’s demonstration of the typical bright signal intensity on T2-weighted MR imaging. Therefore, further investigation is necessary to evaluate the usefulness of T2-weighted imaging for diagnosing small hemangiomas showing PWS on Gd-EOB-DTPA-enhanced images.

Our study has several limitations. First, because hemangiomas are benign lesions and usually do not require invasive procedures, we obtained pathologic proof for only 5 hemangiomas. Therefore, case selection depended solely on imaging findings, with typical findings on enhanced CT and findings of bright signal intensity on T2-weighted MR imaging accepted as diagnostic for hepatic hemangioma. Second, selection bias may have resulted because we did not include atypical hemangiomas, such as low flow and sclerosed hemangiomas, that did not meet the selection criteria. Low flow and sclerosed hemangiomas may be difficult to differentiate from hypovascular malignant tumors because they show hypointensity in all enhanced phases and do not exhibit bright signal intensity on heavily T2-weighted MR imaging. Third, because all the lesions were hemangiomas and we did not include other liver tumors, there might be a bias in the interpretation of findings of Gd-EOB-DTPA-enhanced MR imaging. However, our purpose was to clarify the characteristics of hemangiomas with PWS on Gd-EOB-DTPA-enhanced MR imaging. Fourth, the subtle contrast agent used for test injec-
tion before dynamic study might affect the results in our qualitative and quantitative analyses. Therefore, further investigation will be needed to clarify the characteristics of hemangiomas with PWS on Gd-EOB-DTPA-enhanced MR imaging without use of the test injection technique. Finally, we included 9 patients with chronic liver disease, and severe liver dysfunction may alter the hemodynamics of hemangiomas. However, because we were attempting to clarify the characteristics of hemangiomas with PWS on Gd-EOB-DTPA-enhanced MR imaging, we included as many patients as possible to avoid selection bias from excluding patients with chronic liver disease.

In conclusion, approximately half of the hemangiomas in the present study exhibited PWS during the late phase on Gd-EOB-DTPA-enhanced MR imaging. PWS was predominantly observed if the hemangioma was small or showed diffuse enhancement during the arterial phase. These small hemangiomas tend to have decreased signal intensity during the portal venous phase and can be difficult to diagnose. Knowledge of this finding is important for correct diagnosis of hepatic hemangioma.

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