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Comparison of the Enhancement Pattern of Hepatic Hemangioma on Magnetic Resonance Imaging Performed With Gd-EOB-DTPA Versus Gd-BOPTA

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A B S T R A C T

Purpose: To compare magnetic resonance imaging (MRI) findings with gadoxetic acid and gadobenate dimeglumine for the diagnosis of hepatic hemangiomas.
Materials and Methods: In this retrospective study, we included 26 hemangiomas (mean size was 14 mm ± 10 mm) in 19 patients (mean age 60 ± 14 years) scanned with both gadobenate dimeglumine MRI and gadoxetic acid MRI. For each patient, we collected multiple lesion variables including location, number, size and enhancement pattern on arterial, portal venous, 3-minute and hepatobiliary phases with both gadoxetic acid and gadobenate dimeglumine. The enhancement pattern with the two contrast agents was then compared.
Results: The typical enhancement pattern of hepatic hemangiomas was more common—though not statistically significant—with gadobenate dimeglumine compared to gadoxetic acid (57% [15 of 26] vs 42% [11 of 26], respectively; $P = 0.4057$ for both peripheral globular discontinuous enhancement in the arterial phase and centripetal fill-in in the portal venous phase). A significantly higher number of hemangiomas showed centripetal fill-in or hyperintensity in the 3-minute phase with gadobenate dimeglumine compared to gadoxetic acid (88% [23 of 26) vs 58% [15 of 26]; $P = 0.0266$). A pseudo washout sign in the 3-minute phase was detected in one of the 5 flash-filling hemangiomas with gadoxetic acid, but not gadobenate dimeglumine. All hemangiomas were hypointense in the hepatobiliary phase with both gadobenate dimeglumine and gadoxetic acid.
Conclusions: The enhancement pattern of hepatic hemangiomas may vary depending on the hepatobiliary agent, with more frequent lack of the typical pattern with gadoxetic acid compared to gadobenate dimeglumine.

Introduction

Hepatic hemangiomas occur in up to 20% of the general population, most commonly as an incidental asymptomatic finding at cross-sectional imaging.[1] At magnetic resonance imaging (MRI), cavernous hemangiomas—the most common type of hemangiomas—are characterized by well-defined margins and high-signal intensity on T2-weighted images, and show early, peripheral, globular enhancement in the arterial phase, and centripetal enhancement that progresses to uniform filling.[1] Nevertheless, atypical MR imaging features may occur in up to 66% of lesions.[1-4] These atypical MRI features—which may be related to lesion size, presence of calcifications, fibrosis, thrombi, and/or scarring at pathology—may mimic primary liver malignancies (ie, hepatocellular carcinoma and cholangiocarcinoma) or metastases.[1,5,6] In challenging cases, additional work-up may be required for the definitive diagnosis.

Hepatobiliary contrast agents—including gadoxetic acid or gadobenate dimeglumine—are routinely used for detection and characterization of hepatic lesions.[7] Gadoxetic acid has a more robust and earlier hepatobiliary phase compared to gadobenate dimeglumine due to a higher biliary excretion rate (50% and 3%-5%, respectively); however, gadoxetic acid is limited by lower intensity of arterial phase enhancement of vessels and lesions, and lack of a pure delayed phase due to early hepatocellular uptake of this contrast agent.[8,9]

The unique pharmacokinetic features of gadoxetic acid may result in challenges in the characterization of hepatic hemangiomas.[5,10-12] Because the liver enhances sooner and more intensely with gadoxetic acid than with gadobenate dimeglumine, hepatic hemangiomas—which remain hyperintense in comparison to the liver during all vascular phases with gadobenate dimeglumine—may appear to "wash

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out" with gadoxetic acid at 3-minute phase and, after 5-10 minutes, become hypointense. To our knowledge, only one study compared MR imaging features of hepatic hemangioma with gadoxetic acid and gadobenate dimeglumine.[13] This study demonstrated that MRI with gadoxetic acid leads to lower hemangioma-to-liver contrast-to-noise ratio compared to gadobenate dimeglumine during almost all post-contrast phases except the first arterial phase. However, this study included a triple arterial phase sequence and only 3-T MR scanners and was limited by the lack of comparison of the hepatobiliary phase between the two hepatobiliary contrast agents, and, above all, lack of qualitative MRI analysis (eg, type of enhancement) which is the most common diagnostic approach for the characterization of focal hepatic lesions.

The purpose of this study was to compare MRI findings with gadoxetic acid and gadobenate dimeglumine for the diagnosis of hepatic hemangiomas.

Methods

This retrospective, Health Insurance Portability, and Accountability Act-compliant study was approved by the Institutional Review Board of our Hospital (report N°11/2018, Committee session 10/12/2018), and a waiver of informed consent was obtained.

Study Cohort

Figure 1 portrays the subjects' accrual flowchart following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative guidelines.[14] We retrospectively searched the departmental electronic database at our academic institution looking for MRI reports containing the term hepatic hemangiomas and use of a hepatobiliary contrast agent—either gadoxetic acid (Gd-EOB-DTPA, Eovist/Primovist, Bayer, Leverkusen, Germany) or gadobenate dimeglumine (Gd-BOPTA, Multihance, Bracco, Milano, Italy)—between January 1, 2006 and December 31, 2016.

The initial search yielded 290 MRI exams—140 using Gd-EOB-DTPA and 150 using Gd-BOPTA—in 260 patients. Patients were then excluded based on the following criteria: (1) only MRI exams performed using Gd-EOB-DTPA (n = 114); (2) only MRI exams performed using Gd-BOPTA (n = 127). Whenever more than one MRI exam with gadoxetic acid and/or gadobenate dimeglumine was available in a patient, we chose for the comparison the two MRI exams performed with the shortest time intervals.

MRI Protocol

Dynamic contrast-enhanced liver MRI exams was performed with two different clinical 1.5-T MR systems (Signa Excite, General Electric; Achieva, Philips, Amsterdam, Netherlands) both of them provided with a dedicated abdominal multichannel surface coil. All our MR exams were performed with comparable, clinically appropriate liver protocols, which included single-breath-hold and respiratory-triggered T2-weighted 2-dimensional turbo/fast spin-echo, diffusion weighted images, and T1-weighted 2-dimensional dual gradient-recalled echo MRI. All patients received a weight-based dose of 0.025 mmol/kg of gadoxetic acid or 0.1 mmol/kg body weight of gadobenate dimeglumine, injected by using a power injector (Medrad Spectris Solaris EP MR Injection System; Bayer Healthcare) at a rate of 1 mL/s for gadoxetic acid and 2-2.5 mL/s for gadobenate dimeglumine. Contrast agent administration was followed by 20-mL of 0.9% saline flush at the same injection rate. The MRI parameters are summarized in Table 1. T1-weighted 3-dimensional spoiled gradient-recalled echo breath-hold images were obtained before and after contrast agent injection using a bolus-tracking system. Scanning delays after automatic detection of contrast bolus were 18, 60, and 180 seconds, respectively, for the acquisition of the hepatic arterial, portal venous, and 3-minute phase. Hepatobiliary phases were obtained 120 and 20 minutes after intravenous administration of gadobenate dimeglumine and gadoxetic acid, respectively. The choice of contrast agent was based on clinical indication, availability, and personal preference of the radiologist.

Reference Standard

The reference standard was established by a radiologist (*G.S.*, with 11 years of experience in abdominal imaging), who had access to electronic patient medical records, and all imaging follow-up using the same approach as Gupta RT et al.[13] With the exclusion of 1 hemangioma that reduced in size from 50 mm to 35 mm in a 5-year follow-up but had a typical enhancement pattern for hemangioma, all

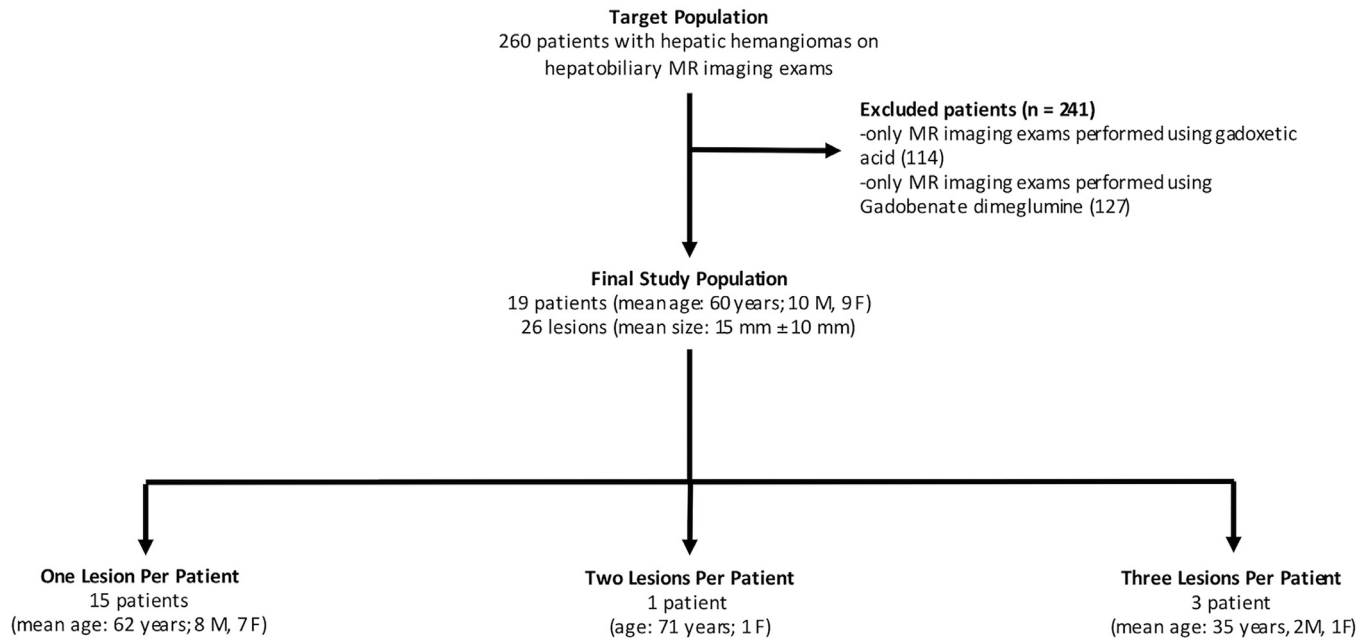

FIG 1. Flowchart shows study enrollment based on recommended Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative guidelines.

TABLE 1
Pulse sequence parameters with the 2 1.5-T MRI scanners. MR1 refers to a Signa Excite, General Electric 1.5-T MR scanner. MR2 refers to an Achieva, Philips Healthcare 1.5-T MR scanner

	T2-w fast-spin echo		T1-w in phase and out-of-phase gradient-recalled-eco		DWI(b0-b50-b800)		T1-w three-dimensional spoiled gradient-recalled-eco	
	MR1	MR2	MR1	MR2	MR1	MR2	MR1	MR2
Matrix	256 × 160	268 × 155	256 × 192	288 × 176	200 × 160	108 × 81	352 × 224	188 × 270
Intersection gap (mm)	1	1	1	1	1	1	2	2
Section thickness (mm)	5-6	6	5-6	7	6	7	4.4	4
Repetition time (ms)	1800	1068	150	182	1800	2195	3.8	4.4
Echo time (ms)	90	80	2.2-4.4	2.3-4.6	58	57	1.2	2.1
Flip angle (degrees)	90	90	80	80	90	90	12	10

the remaining hemangiomas remained approximately stable in size in a median 3-year imaging follow-up (interquartile range: 1.5-3.8 years; min-max: 0.9-9.4 years).

Image Analysis

MR exams were reviewed on a commercial picture archiving and communication system station (PACS - Impax, Agfa-Gevaert, Mortsel, Belgium) by 2 readers in consensus (F.V. and A.B.).

For each patient, the readers documented the following characteristics: (1) number of hepatic hemangiomas; (b) location and size of each hepatic hemangioma; (c) qualitative enhancement features of each lesion on arterial, portal venous, 3 minutes and hepatobiliary phases with both gadoxetic acid and gadobenate dimeglumine. Importantly, the evaluation in the hepatobiliary phase was not performed if the hepatobiliary phase was inadequate. The hepatobiliary phase was defined as adequate when the signal intensity of the hepatic vessels was lower compared to the liver parenchyma.[15] The hepatobiliary phase was defined inadequate when the signal intensity of the vessels was equal or higher compared to the liver parenchyma. Of note, the pattern of enhancement (ie, peripheral globular enhancement, centripetal fill-in) and the degree of enhancement (hypointensity, isointensity, or hyperintensity compared to the surrounding liver and vessels) were noted for each lesion in all postcontrast phases. Specifically, in case of heterogeneous enhancement the signal intensity in the largest component of the lesion was considered.

In addition, the readers assessed the presence of the following signs which have been previously described in contrast enhanced MRI studies:

- "*Pseudo washout*"[6,11]: Lower signal intensity of the hemangioma compared to the surrounding hepatic parenchyma in the 3-minute phase which is caused by gadoxetate disodium uptake by the surrounding hepatic parenchyma as well as a slight decrease of signal intensity of the hemangioma; of note, this sign applies only to lesions that are hyperenhancing on the arterial phase images;
- *Peripheral low intensity rim*[12]: Perilesional rim of hypointensity relative to its center in the hepatobiliary phase.

Statistical Analysis

Demographics and MRI data were summarized on an Excel document (Microsoft, Redmond, WA). Categorical variables were summarized as percentage, whereas continuous variables were summarized as mean and standard deviation or median and interquartile ranges. If one or more data was missing, the valid percentages in the available data were calculated. For categorical variables, differences were tested using either the χ^2 test or Fisher's exact test, as appropriate. First, we analyzed the overall study population for demographics and lesion characteristics. Then, we analyzed and compared the enhancement pattern with gadoxetic acid and gadobenate dimeglumine in a per-lesion analysis. All P values were two-tailed. Statistical significance was set at $P < 0.05$.

Results

Patients and Hemangiomas

Our final study population consisted of 19 patients (mean age 60 years ± 14; age range: 35-84 years), including 10 men (mean age 55 years ± 13; age range: 35-73 years) and 9 women (mean age 66 years ± 14; age range: 43-84 years). Characteristics of the study population are summarized in Table 2. Of note, 6 patients had liver cirrhosis.

A total of 26 hemangiomas (mean lesion size was 15 mm ± 10 mm, range 5-50 mm) were included in the study, including a single lesion in 15 patients, 2 lesions in 1 patient, 3 lesions in 3 patients. The median time between gadoxetic acid-enhanced MRI exam and gadobenate dimeglumine-enhanced MRI was 0.9 years (interquartile range: 0.6-1.6 years; min-max 0.2-4.3 years).

Enhancement Pattern on Arterial-, Portal Venous-, and 3-minute Phases

The typical peripheral globular discontinuous enhancement of hepatic hemangiomas was more common—though not statistically significant—with gadobenate dimeglumine compared to gadoxetic acid (Fig. 2) (57% [15 of 26] vs 42% [11 of 26], respectively; $P = 0.4057$; Table 3). Conversely, hypointensity in the arterial phase was more commonly detected with gadoxetic acid compared to gadobenate dimeglumine (38% [10 of 26] vs 27% [7 of 26], respectively; $P = 0.5551$; Table 3). Only one of the 5 flash-filling hemangiomas on gadoxetic acid

TABLE 2
Characteristics of the study population and lesions

Patient characteristics	
Gender, n (%)	
Male	10 (53)
Female	9 (47)
Age (*years*), mean (standard deviation)	60 (14)
Liver disease, n (%)	
Yes	8 (42)
No	11 (58)
Cirrhosis, n (%)	
Yes	6 (32)
No	13 (68)
Lesion characteristics	
Size (*mm*), mean (SD)	15 mm (10)
Size, n (%)	
<10 mm	10 (38)
≥10 mm	16 (62)
Location, n (%)	
Segment II or III	6
Segment IV	3
Segment V, VI, VII or VIII	17

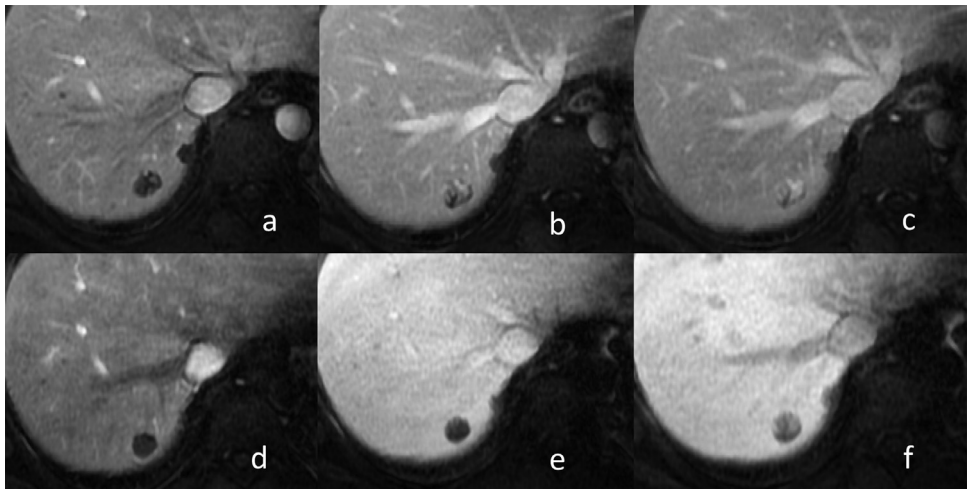

FIG 2. MR imaging exams in a 32-year-old man performed with gadobenate dimeglumine (a, b, c) and gadoxetic acid (d, e, f), show a cavernous hemangioma in the segment VII. At gadobenate dimeglumine enhanced MR the lesion shows peripheral globular discontinuous enhancement in the arterial phase (a), with progressive fill-in in the portal venous (b), and the 3-minute phases (c). At gadoxetic acid enhanced MR, the hemangioma is hypointense in both the arterial (d) and portal venous (e) phases, and shows only minimal centripetal fill-in in the 3-minute phase (f). Notice how the intrahepatic vessels are already hypointense due to contrast uptake. MR, magnetic resonance.

showed a globular discontinuous enhancement with gadobenate dimeglumine, while all the other 4 flash-filling hemangiomas had the same enhancement pattern with the 2 contrast agents.

The typical centripetal fill-in of hepatic hemangiomas in the portal venous phase was more common—though not statistically significant—with gadobenate dimeglumine compared to gadoxetic acid (57% [15 of 26] vs 42% [11 of 26], respectively $P = 0.4057$), while hypointensity in the portal venous phase was more commonly detected with gadoxetic acid compared to gadobenate dimeglumine (Fig. 2), though the difference was only minimal (35% [9 of 26] vs 15% [4 of 26]; $P = 0.1994$); Table 3). Of 9 hemangiomas hypointense in the portal venous phase with gadoxetic acid, one had a globular peripheral enhancement in the arterial phase, while the remaining 8 were also hypointense in the arterial phase. Conversely, all the 4 hemangiomas showing hypointensity in the portal venous phase with gadobenate dimeglumine were also hypointense in the arterial phase.

There was a statistically significant higher number of hemangiomas with homogeneous hyperintensity in the 3-minute phase with gadobenate dimeglumine compared to gadoxetic acid (Fig. 2) (50% [13 of 26] vs 8% [2 of 26], respectively; $P = 0.0016$; Table 3). By adding to this group of hemangiomas, those showing a centripetal fill-in in the 3-minute phase, the difference between the two contrast agents was still significant (88% [23 of 26) vs 58% [15 of 26]; $P = 0.0266$). Conversely, hypointensity in the 3-minute phase was more common—though not

TABLE 3
Enhancement pattern of hepatic hemangiomas on arterial-, portal venous-, 3-minute, and hepatobiliary phases with gadoxetic acid and gadobenate

		Gadoxetic acid MRI	Gadobenate dimeglumine MRI
Hepatic arterial phase			
	Peripheral globular discontinuous enhancement	11 (42.3) 9 patients	15 (57.7) 10 patients
	"Flash filling"	5 (19.2) 5 patients	4 (15.4) 4 patients
	Hypointense	10 (38.5) 7 patients	7 (26.9) 6 patients
Portal venous phase			
	Centripetal fill-in	11 (42.3) 9 patients	15 (57.7) 11 patients
	Hyperintense	3 (11.5) 3 patients	7 (26.9) 7 patients
	Isointense	3 (11.5) 3 patients	0 (0) 0 patients
	Hypointense	9 (34.6) 6 patients	4 (15.4) 4 patients
3-minute phase			
	Centripetal fill-in	13 (50.0) 11 patients	10 (38.5) 8 patients
	Hyperintense	2 (7.6) 2 patients	13 (50.0) 11 patients
	Isointense	4 (15.4) 4 patients	1 (3.8) 1 patients
	Hypointense	7 (26.9) 5 patients	2 (7.6) 2 patients
Hepatobiliary phase			
	Hypointense	23 (100*) 17 patients	14 (100*) 11 patient
	Inadequate phase	3 (–) 2 patients	0 (–) 0 patient
	Not available	0 (–) 0 patients	12 (–) 8 patients

*Only the valid percentages in the available and adequate hepatobiliary phase images were calculated.

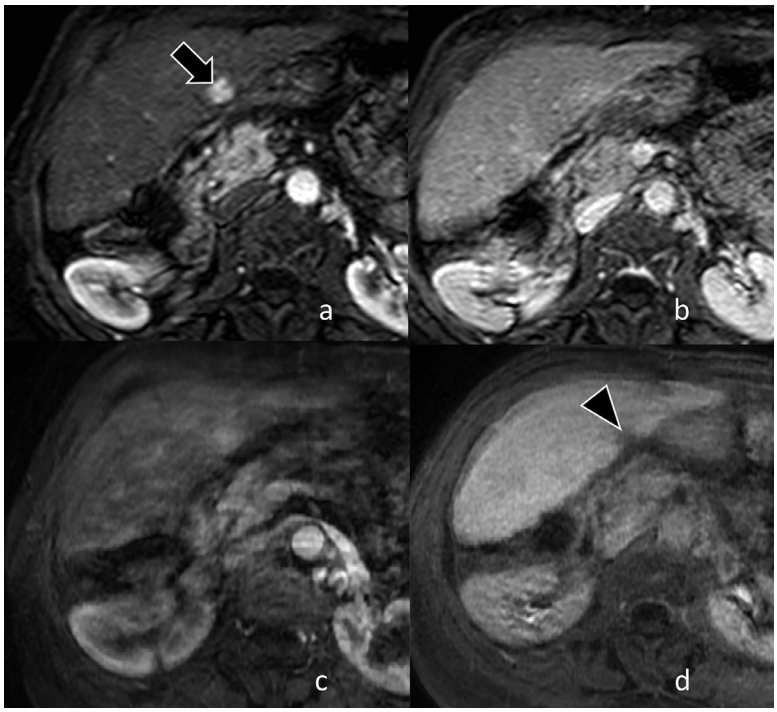

FIG 3. MR imaging exams performed with gadobenate dimeglumine (a, b) and gadoxetic acid (c, d) in an 83-year-old woman with HCV cirrhosis. The flash-filling hemangioma in this patient shows homogeneous enhancement (arrow) in the arterial phase with both gadobenate dimeglumine (a) and gadoxetic acid (c) enhanced MR imaging exams. The hemangioma is slightly hyperintense to the liver in the 3-minute phase with gadobenate dimeglumine (b), and hypointense (arrowhead) in the 3-minute phase with gadoxetic acid (d). The "pseudo washout" sign in this hemangioma refers to the arterial phase hyperenhancement followed by the lower signal intensity of the hemangioma compared to the surrounding hepatic parenchyma in the 3-minute phase. HCV, hepatitis C virus; MR, magnetic resonance.

statistically significant—with gadoxetic acid compared to gadobenate dimeglumine (26.9% [7 of 26] vs 7.6% [2 of 26]; $P = 0.14$; Table 3).

A "pseudo washout" sign was detected with gadoxetic acid—but not with gadobenate dimeglumine—in one of the flash-filling hemangiomas in a cirrhotic patient (Fig. 3). The "pseudo washout" sign was never encountered with gadobenate dimeglumine.

Enhancement Pattern on Hepatobiliary Phase

Hepatobiliary phase images with gadobenate dimeglumine were not available in 8 patients with 12 hemangiomas. Hepatobiliary phase with gadoxetic acid was inadequate in 2 patients with 3 hemangiomas. Therefore, only 11 of 26 hemangiomas in 9 patients were studied with both contrast agents. All the hemangiomas were hypointense with both contrast agents, in the hepatobiliary phase (Table 3). A peripheral low intensity rim in the hepatobiliary phase was detected only in 1 hemangioma with gadoxetic acid MRI (Fig. 4), while this sign was never encountered with gadobenate dimeglumine-MRI.

Discussion

Hepatic hemangioma is the most common benign hepatic tumor.[1] Although the imaging diagnosis of hepatic hemangiomas is oftentimes straightforward, the unique pharmacokinetic features of gadoxetic acid may result in diagnostic challenges. Our results showed that the main differences in the enhancement pattern of hepatic hemangiomas with gadoxetic acid-enhanced MRI compared to gadobenate dimeglumine are noted in the 3-minute phase. This finding is mainly related to the important differences in hepatocellular uptake of these agents (50% with gadoxetic acid and 3%-5% with gadobenate dimeglumine), which lead to agent specific enhancement patterns of focal hepatic lesions.[16] While the different enhancement pattern with the two hepatobiliary contrast agents has been demonstrated for other liver lesions (ie, focal nodular hyperplasia, hepatocellular carcinoma),[17-19] there is only one study comparing these two hepatobiliary agents for the diagnosis of hepatic hemangiomas.[13] This study, however, had many limitations including the lack of qualitative MRI analysis (ie, enhancement pattern—which is the most common diagnostic approach for hepatic hemangiomas—and lack of the 3-minute phase with both agents and of the hepatobiliary phase with gadobenate dimeglumine.

Owing to the rapid parenchymal uptake of gadoxetic acid, in our study population the hepatic hemangiomas were often hypointense compared to liver parenchyma in all postcontrast phases. When comparing the two contrast agents, the relative lower percentage of hemangiomas showing the typical peripheral globular enhancement

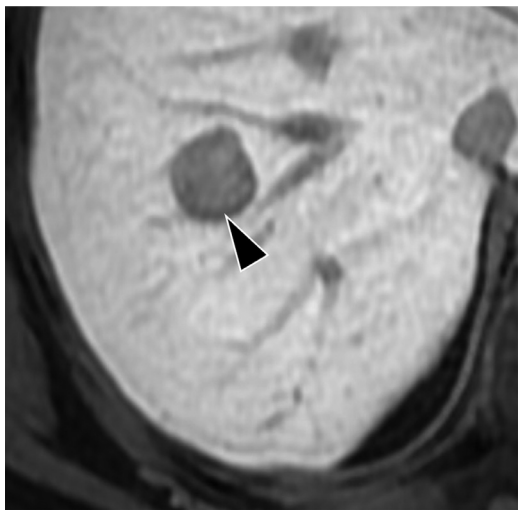

FIG 4. MR imaging exam performed with gadoxetic acid in a 45-year-old man. The hepatobiliary phase in this hemangioma demonstrates a perilesional rim of hypointensity (arrowhead) relative to its center known as peripheral low intensity rim.

with gadoxetic acid enhanced MRI, compounded with hypointensity in the portal venous phase and at 3 minutes, may potentially mimic malignancies, particularly in cirrhotic patients. Our results are in agreement with a recent study by Min JH et al[20] who performed an intraindividual comparison of gadoxetic acid and gadoterate meglumine for the diagnosis of hepatocellular carcinoma in cirrhosis and demonstrated that 9 of 95 (9.5%) hepatocellular carcinomas showed enhancement in the arterial phase with the extracellular agent but not with gadoxetic acid[19]. As in the study by Min JH et al,[20] our results could be explained by the small dosage of gadoxetic acid, which is one-fourth that of gadobenate dimeglumine (0.025 vs 0.1 mmol/kg) and can create difficulty in acquiring the optimal late arterial phase.

In our study population, the "pseudo washout" sign[6,11] was evident only in one of the five flash-filling hemangiomas on gadoxetic acid MRI in a cirrhotic patient. This atypical presentation with arterial phase homogenous enhancement followed by pseudo washout did not permit a confident diagnosis of hepatic hemangioma and mimicked hepatocellular carcinoma. Furthermore, the hypointensity in the portal venous phase with gadoxetic acid in one of the cavernous hemangiomas might suggest that the portal venous could be regarded already as a transitional phase. In challenging lesions, the bright signal intensity on T2-weighted images and the T2-shine through phenomenon may be particularly helpful for the definitive diagnosis.[6] The pseudo-washout sign did not occur with gadobenate dimeglumine.

While prior studies had already highlighted the enhancement pattern of hepatic hemangiomas with gadoxetic acid and gadobenate dimeglumine separately, to our knowledge, this is the first study comparing the two contrast agents in the hepatobiliary phase for the diagnosis of hepatic hemangiomas. In all patients with an adequate hepatobiliary phase, hepatic hemangiomas were hypointense compared to the surrounding liver parenchyma with both contrast agents. However, in 2 patients with 3 hemangiomas the hepatobiliary phase on gadoxetic acid enhanced MRI was inadequate and a reliable evaluation of lesion intensity was not doable. Of note, a peripheral low intensity rim in the hepatobiliary phase—which has been described by Tamada et al[12] as a potential diagnostic pitfall in hepatic hemangiomas on gadoxetic acid enhanced MRI—was detected only in 1 hemangioma with gadoxetic acid MR in our study population, and did not occur with gadobenate dimeglumine.

In addition to the retrospective design and the small sample size of our study, we acknowledge other limitations. First, we did not have pathological proof of the hemangiomas included in this study. While this approach has been widely adopted in previous studies as it reflects the routine practice, we cannot entirely rule out the possibility of misdiagnosis. However, owing to the benignity of this entity, a prospective evaluation with pathology is not conceivable. Another limitation is that the MRI techniques used for this MRI exam may have slightly varied over time or due to the use of different MRI scanners. Indeed, in 4 of the 16 patients, the 2 MRI exams with gadoxetic acid and gadobenate dimeglumine were performed using 2 different 1.5-T MRI scanners. However, all the MRI exams were acquired with comparable, clinically appropriate liver protocols and in our study we only performed a qualitative assessment and not a quantification of signal intensity, which is more affected by MRI acquisition parameters and MRI scanner. Third, contrast enhancement in the liver and lesions was not evaluated by quantitative parameters and indexes. However, qualitative imaging assessment reflects everyday clinical practice. Finally, we acknowledge that the acquisition of the hepatic arterial phase with gadoxetic acid is more affected by transient motion compared to gadobenate dimeglumine. However, all these exams have been judged diagnostic by the radiologists.

In conclusion, our data suggest that the enhancement patterns of hepatic hemangiomas differ between gadobenate dimeglumine and gadoxetic acid-enhanced 1.5-T MRI. Owing to the lower percentage of hemangiomas showing peripheral globular discontinuous enhancement in the hepatic arterial phase, and the higher percentage of hemangiomas showing hypointensity in the portal venous and 3-minute phase with gadoxetic acid compared to gadobenate dimeglumine, gadobenate dimeglumine should be preferred to gadoxetic acid for characterization of hemangiomas.

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References

1. Vilgrain V, Boulos L, Vullierme MP, et al. Imaging of atypical hemangiomas of the liver with pathologic correlation. Radiographics 2000;20:379–97.
2. Jang HJ, Kim TK, Lim HK, et al. Hepatic hemangioma: Atypical appearances on CT, MR imaging, and sonography. Am J Roentgenol 2003;180:135–41.
3. Semelka RC, Brown ED, Ascher SM, et al. Hepatic hemangiomas: A multi-institutional study of appearance on T2-weighted and serial gadolinium-enhanced gradient-echo MR images. Radiology 1994;192:401–6.
4. Szurowska E, Nowicki T, Izycka-Swieszewska E, et al. Is hepatotropic contrast enhanced MR a more effective method in differential diagnosis of hemangioma than multi-phase CT and unenhanced MR? BMC Gastroenterol 2011;11:43.
5. Goshima S, Kanematsu M, Watanabe H, et al. Hepatic hemangioma and metastasis: Differentiation with gadoxetate disodium-enhanced 3-T MRI. Am J Roentgenol 2010;195:941–6.
6. Doo KW, Lee CH, Choi JW, et al. "Pseudo washout" sign in high-flow hepatic hemangioma on gadoxetic acid contrast-enhanced MRI mimicking hypervascular tumor. Am J Roentgenol 2009;193:W490–6.
7. Seale MK, Catalano OA, Saini S, et al. Hepatobiliary-specific MR contrast agents: Role in imaging the liver and biliary tree. Radiographics 2009;29:1725–48.
8. Tamada T, Ito K, Yamamoto A, et al. Hepatic hemangiomas: Evaluation of enhancement patterns at dynamic MRI with gadoxetate disodium. Am J Roentgenol 2011;196:824–30.
9. Pietryga JA, Burke LM, Marin D, et al. Respiratory motion artifact affecting hepatic arterial phase imaging with gadoxetate disodium: Examination recovery with a multiple arterial phase acquisition. Radiology 2014;271:426–34.
10. Tateyama A, Fukukura Y, Takumi K, et al. Gd-EOB-DTPA-enhanced magnetic resonance imaging features of hepatic hemangioma compared with enhanced computed tomography. World J Gastroenterol 2012;18:6269–76.
11. Kim B, Byun JH, Kim HJ, et al. Enhancement patterns and pseudo-washout of hepatic haemangiomas on gadoxetate disodium-enhanced liver MRI. Eur Radiol 2016;26:191–8.
12. Tamada T, Ito K, Ueki A, et al. Peripheral low intensity sign in hepatic hemangioma: Diagnostic pitfall in hepatobiliary phase of Gd-EOB-DTPA-enhanced MRI of the liver. J Magn Reson Imaging 2012;35:852–8.
13. Gupta RT, Marin D, Boll DT, et al. Hepatic hemangiomas: difference in enhancement pattern on 3T MR imaging with gadobenate dimeglumine versus gadoxetate disodium. Eur J Radiol 2012;81:2457–62.
14. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. J Clin Epidemiol 2008;61:344–9.
15. Agnello F, Dioguardi Burgio M, Picone D, et al. Magnetic resonance imaging of the cirrhotic liver in the era of gadoxetic acid. World J Gastroenterology 2016;22:103–11.
16. Dahlqvist Leinhard O, Dahlström N, Kihlberg J, et al. Quantifying differences in hepatic uptake of the liver specific contrast agents Gd-EOB-DTPA and Gd-BOPTA: A pilot study. Eur Radiol 2012;22:642–53.
17. Gupta RT, Iseman CM, Leyendecker JR, et al. Diagnosis of focal nodular hyperplasia with MRI: multicenter retrospective study comparing gadobenate dimeglumine to gadoxetate disodium. Am J Roentgenol 2012;199:35–43.
18. Park Y, Kim SH, Kim SH, et al. Gadoxetic acid (Gd-EOB-DTPA)-enhanced MRI versus gadobenate dimeglumine (Gd-BOPTA)-enhanced MRI for preoperatively detecting hepatocellular carcinoma: An initial experience. Korean J Radiol 2010;11:433–40.
19. Tirkes T, Mehta P, Aisen AM, et al. Comparison of dynamic phase enhancement of hepatocellular carcinoma using gadoxetate disodium vs gadobenate dimeglumine. J Comput Assist Tomogr 2015;39:479–82.
20. Min JH, Kim JM, Kim YK, et al. Prospective intraindividual comparison of magnetic resonance imaging with gadoxetic acid and extracellular contrast for diagnosis of hepatocellular carcinomas using the liver imaging reporting and data system. Hepatology 2018;68:2254–66.