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Case Report

Transient washout of hepatic hemangiomas: Potential pitfall mimicking malignancy

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ABSTRACT

Hemangiomas are the most common tumor of the liver and distinguishing them from malignancy is important. This is a report of 3 hemangiomas in 2 patients that exhibit transient washout of gadoxetate disodium (Eovist), relative to blood pool and liver parenchyma, a characteristic that is used to diagnose hepatocellular carcinoma in at-risk patients. It is important to recognize that high-flow hemangiomas can exhibit transient washout when using a small volume of injected contrast agent. This finding is unlikely to be present on CT examinations because of the larger volume of contrast administered.

Case report

The first case is that of a 52-year-old man with chronic hepatitis C and a suspicious mass on surveillance ultrasound. The patient was asymptomatic, and his alpha-fetoprotein level was within normal limits. Magnetic resonance imaging (MRI) with gadoxetate disodium was performed for further evaluation (Fig. 1) and dynamic 3-dimensional (3D) fat-saturated (FS) fast-spoiled gradient-echo (FSGR) images were obtained before and after the administration of contrast using bolus tracking method triggered off the abdominal aorta at the diaphragm. Images were obtained in the early arterial (time = 0 s), late arterial (time = 15 s), and portal venous (time = 47 s) phases. These sequences show a 2.1-cm mass with rapid continuous peripheral enhancement in the early arterial phase and transient washout relative to both the liver parenchyma and vessels during the portal venous phase. When using the Liver Imaging Reporting and Data System (LI-RADS) criteria, the combination of size greater than 2.0 cm, arterial phase hyperenhancement, and washout appearance would lead to categorization of LI-RADS 5, or definitely hepatocellular carcinoma (HCC). However, extremely high signal on the T2-weighted images and apparent diffusion coefficient (ADC) map favored hemangioma, which was confirmed by contrast-enhanced ultrasound (Fig. 2) and stability on subsequent examinations. All 3D FS FSGR images were obtained with a time to repetition of 4.1 ms and time to echo of 2.0 ms. The precontrast, early arterial phase, and late arterial phase

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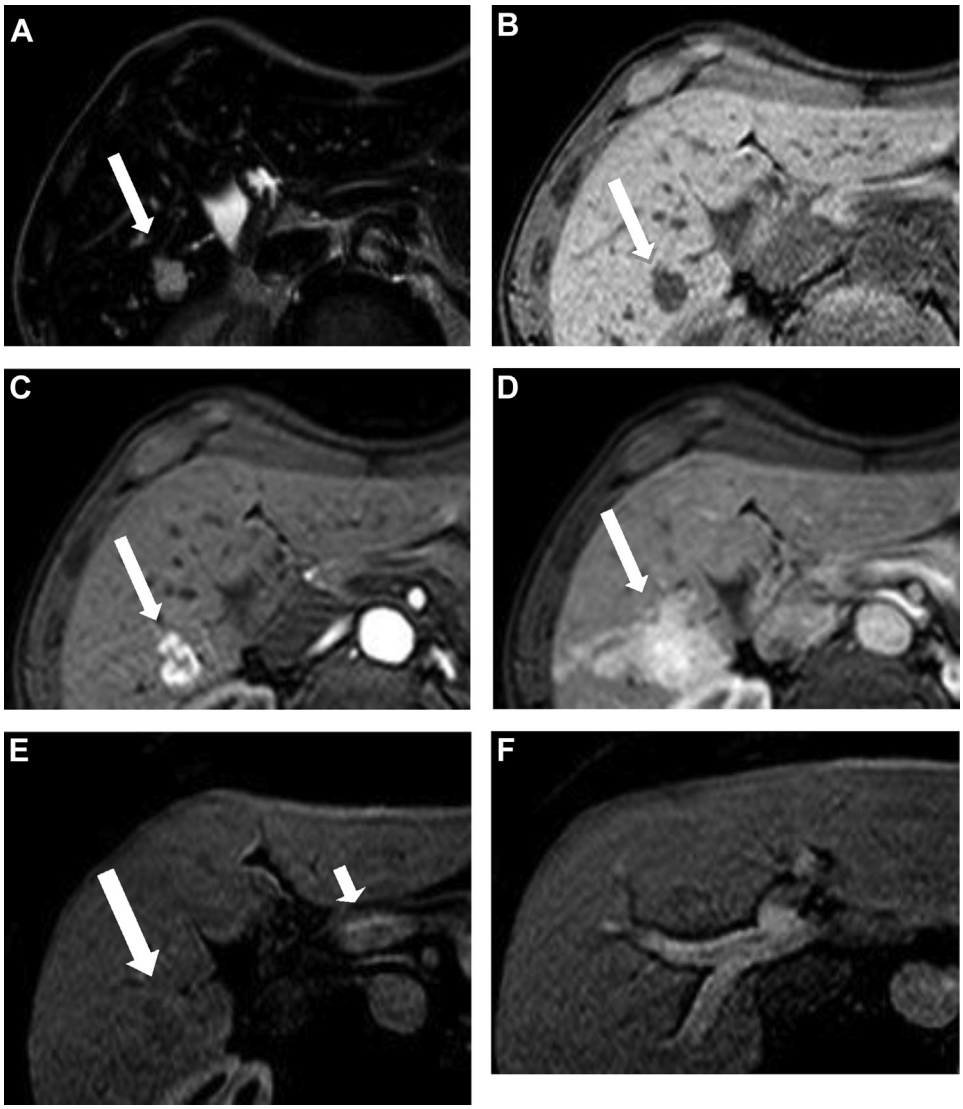

Fig. 1 – Case #1, contrast-enhanced MRI of hepatic hemangioma. A 52-year-old man with chronic hepatitis C. MRI demonstrates a 2.1-cm lobulated mass (A, arrow) in the right lobe of the liver with marked hyperintense signal on single-shot fast spin-echo T2-weighted images (time to echo = 210 ms, flip angle = 90°). The lesion is hypointense on precontrast 3D FS FSGR (B, arrow) and on postcontrast images demonstrates peripheral enhancement without distinct nodularity or discontinuity in the early arterial phase (C, arrow) and complete enhancement of the lesion with marked perilesional arterioportal shunting in the late arterial phase (D, arrow). The lesion demonstrates washout appearance on the portal venous phase (E, arrow) compared with the relative hyperintensity of the main portal vein (E, short arrow). Image obtained during the same volume acquisition as image E through the intrahepatic portal vein (F) again demonstrates relative hyperintensity of the portal vessels and liver parenchyma to the lesion.

images were obtained with a flip angle of 10°, and the portal venous phase images were obtained with a flip angle of 20°.

The second case is that of a 71-year-old man with an incidentally noted hepatic lesion seen on CT. MRI with gadoxetate disodium was performed further evaluation (Fig. 3) and dynamic 3D FS FSGR images were obtained before and after the administration of contrast using a fixed time delay. Images were obtained in the early arterial (time = 18 s postinjection), late arterial (time = 30 s postinjection), and transitional phases (time = 4 min postinjection). These sequences show 2 subcentimeter masses that both avidly enhance during the early arterial phase and demonstrate hypointensity during the late arterial phase, relative to both the surrounding parenchyma and blood vessels, that resolved by the transitional phase. Using the LI-RADS criteria, the combination of size under 1.0 cm, arterial phase hyperenhancement, and washout appearance would lead to a categorization of LI-RADS 4, or probably HCC. However, as in the previous case, high signal on the T2-weighted and ADC images favored hemangiomas, which was confirmed by stability on subsequent examinations. All 3D FS FSGR images were obtained using the following parameters: time to repetition = 2.6 ms, time to echo = 1.2 ms, flip angle = 15°.

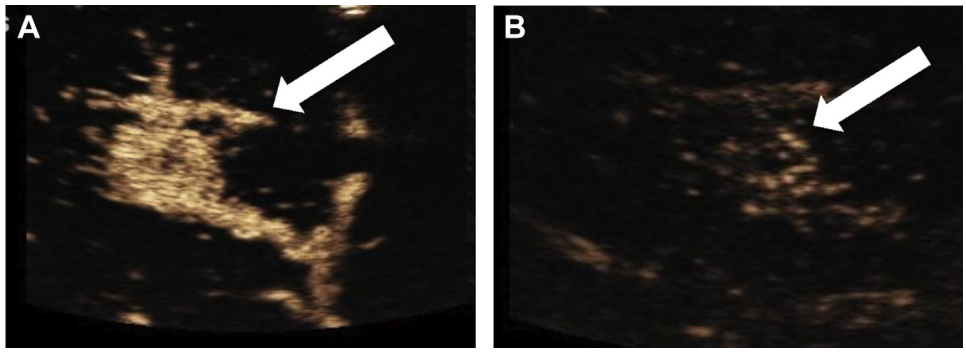

Fig. 2 – Case #1, contrast-enhanced ultrasound confirming hepatic hemangioma. Contrast-enhanced ultrasound demonstrates microbubbles aggregating to the lesion (A, arrow) 26 seconds after injection. The microbubbles do not washout and at 8 minutes and 46 seconds they remain within the lesion (B, arrow), supporting the diagnosis of a hemangioma.

Discussion

Hemangiomas are the most common liver tumor, incidentally found on approximately 5-20% of routine radiologic examinations [1,2]. Differentiating these benign liver lesions from malignant neoplasms is an important and common clinical scenario. Hemangiomas have a characteristic appearance on dynamic contrast-enhanced (DCE) CT and DCE MRI when using a purely extracellular agent. They demonstrate initial discontinuous peripheral globular enhancement with centripetal filling, which expands and persists on delayed-phase imaging,

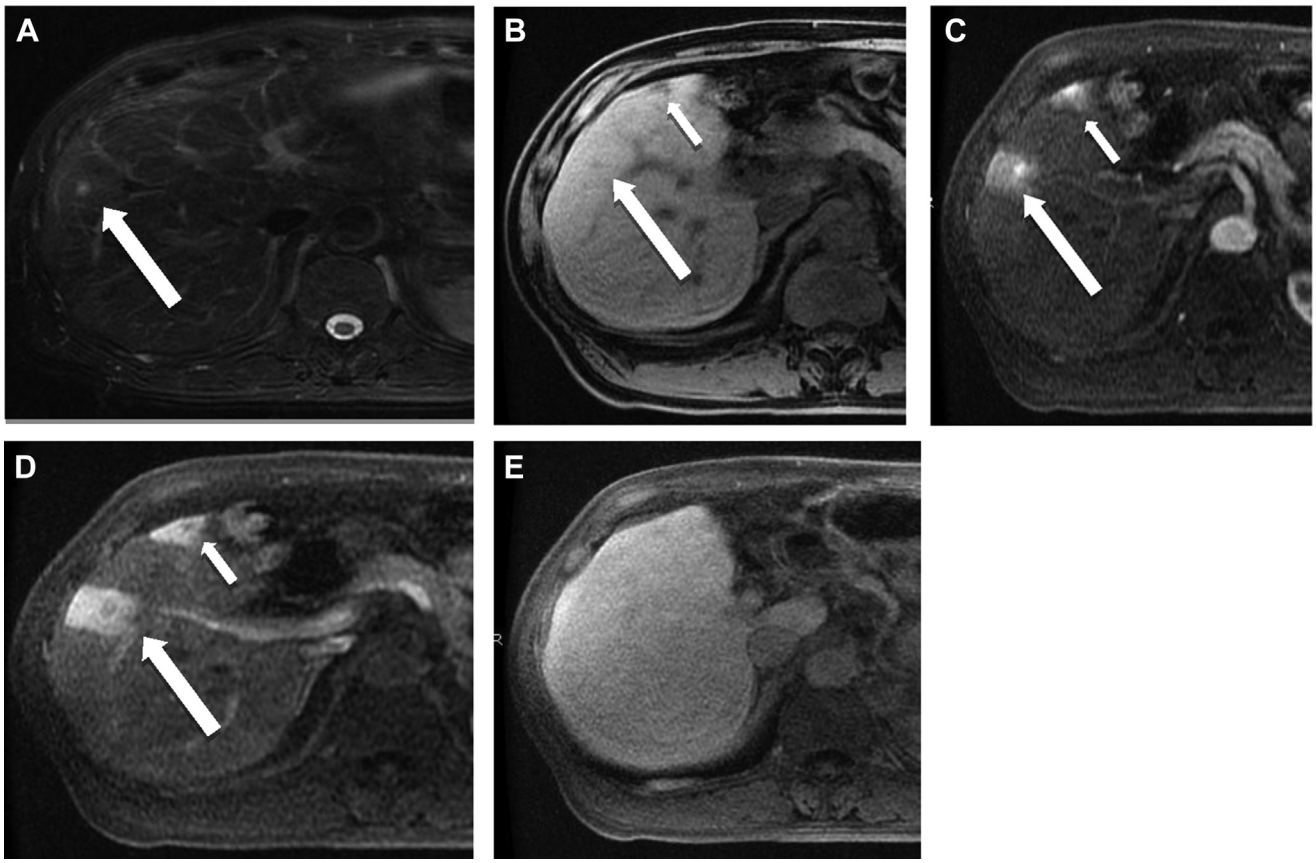

Fig. 3 – Case #2, contrast-enhanced MRI of hepatic hemangioms. A 71-year-old man without significant past medical history with an incidentally noted focal hepatic lesion seen on CT. MRI demonstrates a 0.8-cm mass (A, arrow) in hepatic segment 8 with marked hyperintense signal on fast spinecho T2-weighted images (time to repetition = 10,000 ms; time to echo = 92 ms), no additional lesion is visible. Precontrast 3D FS FSGR images demonstrate that this mass is hypointense (B, arrow) and an additional 0.6-cm hypointense mass at the periphery of segment 8 anterior (B, small arrow). These masses have identical contrast enhancement features and demonstrate complete rapid enhancement in the early arterial phase (C, arrows) and washout relative to surrounding hepatic parenchyma and portal vein on the late arterial phase (D, arrows) with marked perilesional arterioportal shunting in both phases. The washout resolves in the transitional phase (E).

although the rapidity of these sequential changes varies greatly. Attenuation or signal intensity of the enhancing areas should be similar to that of the aorta and other vessels on all phases. DCE kinetics of the aorta is different for CT and MRI owing to the difference in the length of the contrast bolus used. CT uses a relatively long contrast bolus and as a result the first pass of contrast does not have time to redistribute before recirculation of contrast occurs. This leads to the characteristic single peak of enhancement followed by a rapid decrease in enhancement which equilibrates at a low level of enhancement, which then gradually decreases [3,4]. MRI uses a relatively short bolus of contrast, so the first pass of contrast redistributes before recirculation of the contrast can occur. As a result, there is a large first-pass peak, followed by a smaller recirculation peak, followed by equilibration and a gradual decline in signal [5,6]. The sequential enhancement of some hemangiomas is sufficiently rapid that they enhance completely during the arterial phase. These high-flow hemangiomas account for 16% of all hemangiomas and occur much more frequently in smaller lesions, accounting for 42% of hemangiomas <1 cm in diameter [7]. The characteristic DCE MRI appearance of a high-flow hemangioma when using a purely extracellular contrast agent is well-described and consists of arterial-phase immediate homogeneous enhancement with persistant hyperintense signal on the all later phases, similar to those of blood vessels [8,9].

MRI characteristics of hemangiomas using hepatocyte-specific gadolinium-based contrast agents have been described as similar during the arterial and early venous phases to those observed using purely extracellular space agents [9–13], although caution has been recommended regarding their enhancement in later phases. In 2009, Doo et al. described the "pseudo washout" sign, whereby a high-flow hemangioma demonstrates relatively decreasing signal intensity during the transitional phase (about 3-5 min after contrast agent injection) as the contrast agent distributes from the vascular space into hepatocytes. This low signal intensity of the hemangioma is not because of actual washout of contrast relative to blood pool, as the hemangioma and blood vessels maintain similar concentrations of contrast agent, and their hypointensity is exaggerated by the increased signal intensity of the surrounding liver and the more rapid blood pool clearance of hepatocyte-specific agents [14]. Subtraction images will demonstrate that the hemangioma has not actually washed out relative to blood vessels.

A separate phenomenon of transient washout during the late arterial or portal venous phases, as a short bolus of contrast material circulates during its first pass after injection, can theoretically occur but has not been previously documented. We report 3 high-flow hemangiomas that demonstrated a transient phase where the concentration of a contrast agent decreased below that of other vessels such as portal vein. This is not expected to happen with CT because of the prolonged bolus length and is more likely to be present when a temporally short bolus is injected, such as with gadoxetate disodium (Eovist) or potentially with more concentrated low-volume purely extracellular agents such as gadobutrol (Gadavist).

The 2014 version of LI-RADS addresses the use of hepatobiliary contrast agents [15]. According to the LI-RADS guidelines, when using gadoxetate disodium, washout should be evaluated during the portal venous phase and not the transitional phase (3-5 min after contrast agent injection). This is because the transitional phase is a dynamic phase during which both hepatocyte uptake and extracellular distribution contribute to the enhancement pattern [16]. Hypointensity in the transitional phase may be due hepatocyte uptake of the surrounding parenchyma, and therefore is different from washout appearance as described when using a purely extracellular agent. This distinction is not applicable to gadobenate (MultiHance), as hepatocyte uptake with gadobenate is delayed until later phases [16].

DCE images were not obtained during identical phases for cases #1 and #2, because of the different MR imaging protocols used at the 2 different institutions. The dynamic images for case #1 were obtained in the early arterial, late arterial and portal venous phases, and transient washout of the hemangioma was seen in the portal venous phase. The relative signal intensities of the hemangioma, aorta, liver parenchyma, splenic vein, and back muscles were measured during dynamic enhancement and are presented in Figure 4. The aorta demonstrates the typical DCE kinetics of a short bolus injection, with a recirculation peak in the portal venous phase, causing the aorta to have decreased signal intensity in the late arterial phase when compared with the early arterial and portal venous phases. This oscillating signal intensity also occurred in the hemangioma, which temporally lagged behind the aorta and showed decreased signal intensity in the portal venous phase compared with the late arterial phase. From the early arterial phase through the portal venous phase the signal intensities of the liver parenchyma and splenic vein continuously increased and in the portal venous phase the

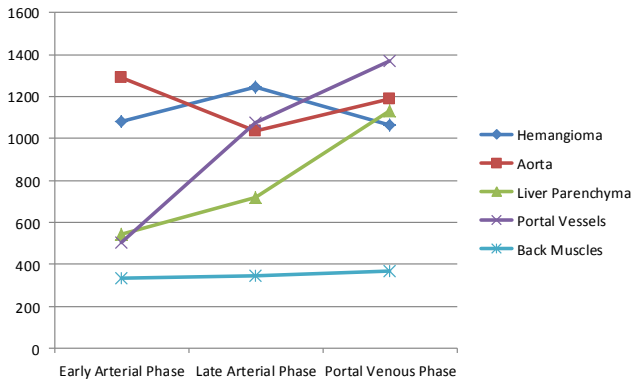

Fig. 4 – Case #1, relative signal intensities illustrating hemangioma washout. Case #1, dynamic-contrast enhancement curves with measurements taken in the early arterial, late arterial, and portal venous phases. The Y-axis represents relative signal intensity. The signal intensity of the back muscles is relatively stable for these time points and acts as an internal control. The signal intensity of the aorta oscillates with decreased signal in the late arterial phase when compared to the early arterial and portal venous phases. The signal intensity of the hemangioma also oscillates but temporally lags behind the aorta. The signal intensity of both the liver parenchyma and splenic vein steadily increase throughout this time period.

liver parenchyma and splenic vein were hyperintense to the hemangioma indicating that the hemangioma experienced true washout. In pseudo washout, the hemangioma would have been hypointense to the liver parenchyma but isointense to the splenic vein. The dynamic images for case #2 were obtained in the early arterial and late arterial phases, with transient washout seen in the late arterial phase.

Transient washout likely depends on several coexisting factors. The bolus of contrast injected must be short and rapid. Both patients received 10 cc of gadoxetate disodium, injected at 1 cc per second for patient #1 and 2 cc per second for patient #2, with a total injection time of only 5-10 seconds, likely shorter than the circulation time and shorter than the image acquisition. There must be rapid flow through the hemangioma, so that a short bolus of contrast will not only enter but also exit rapidly during its first pass. Time-of-flight effects are a separate phenomenon that may cause the intensity of a hemangioma to differ from that of nearby blood vessels. For example, inflow of unsaturated blood into the imaged volume between excitations may increase signal intensity within the aorta, IVC, or occasionally the portal vein, depending on the location of the imaged volume. This was not the case in this situation, as demonstrated by the low signal within the vessels on the unenhanced volumetric images.

Transient washout of a hemangioma is not common, as it depends on a combination of factors, including extremely rapid flow and a short duration bolus of contrast material. We do not intend for our report to invalidate the recommendation in LI-RADS 2014 that gadoxetate disodium portal venous phase images can be used to determine washout and thereby contribute to diagnosis of HCC. However, one must be cognizant that high-flow hepatic hemangiomas can exhibit transient washout during the portal venous phase or late arterial phase and carefully consider other features of hemangiomas to prevent misdiagnosis of HCC in these cases. In particular, extremely high signal on T2-weighted images, high ADC, isointensity to blood vessels more than one minute after contrast agent injection, and marked perilesional arterioportal shunting may suggest high-flow hemangioma as a possible diagnosis. If necessary, further evaluation with multiphasic MRI using extracellular space or blood-pool contrast agent, multiphasic CT, or a contrast-enhanced ultrasound can be performed to prevent mistaking a high-flow hemangioma for malignancy.

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