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TECHNICAL NOTE

Evaluation of the changes in signals from the spleen using ferucarbotran

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Abstract
Purpose. Because superparamagnetic iron oxide is actively taken into the reticuloendothelial system, the signal intensity observed on T2-weighted images is reduced not only in the liver but also in the spleen. There is no difference in the reduction in signal intensity in the liver after contrast between the ferumoxides and ferucarbotran, but the reduction in signal intensity in the spleen is considerable. In the present study, we examined the efficacy of T2*-weighted imaging to compensate for the reduction in signal intensity in the spleen by administering ferucarbotran.
Materials and methods. We examined the images obtained from 35 patients who underwent MRI with ferucarbotran. T2-weighted images and T2*-weighted images were obtained before and after administration of ferucarbotran, and the changes in signal intensity in the liver and spleen were then analyzed.
Results. A reduction in signal intensity was observed in the liver by both T2- and T2*-weighted imaging. In the spleen, the signal intensity was reduced on T2-weighted images but was not reduced on T2*-weighted images.
Conclusion. The reduction in signal intensity due to administration of ferucarbotran is low in the spleen. Thus, it was considered necessary to approach the problem of diagnosing ectopic splenic tissue using ferucarbotran with caution.

Key words SPIO · Ferucarbotran · Spleen · MRI

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Introduction

Because superparamagnetic iron oxide (SPIO) is mainly taken up by Kupffer cells in the hepatic reticuloendothelial system, SPIO improves the contrast between normal hepatic tissue with Kupffer cells and malignant tumors without Kupffer cells in the liver.[1–3] SPIO is generally used as a negative contrast medium, as it reduces the signal intensity in normal liver tissue by the strong T2 or T2* shortening effects. Strictly speaking, 80% of SPIO is taken into the hepatic reticuloendothelial system, with the remainder absorbed into the reticuloendothelial system of other organs including the spleen.[4] Therefore, based on studies performed with ferumoxides, the loss of signal intensity in the spleen has been thought to be useful for diagnosing accessory spleen and splenosis.[5,6] However, there have been no studies on the diagnosis of accessory spleen and splenosis using ferucarbotran. Thus, in the present study, we examined the changes in signal intensity in the spleen by administering ferucarbotran.

Materials and methods

The subjects were 35 patients (21 men, 14 women; aged 35–87 years, mean 68 years) who underwent magnetic resonance imaging (MRI) with ferucarbotran between December 2003 and September 2004. The diseases were colon carcinoma in 10 patients, liver cirrhosis in 9 patients, mammary carcinoma in 4 patients, cholangiocarcinoma in 2 patients, liver metastasis in 1 patient, esophageal carcinoma in 1 patient, rectal carcinoma in 1 patient, uterine leiomyosarcoma in 1 patient, cervical cancer in 1 patient, carcinoid in 1 patient, liver abscess

in 1 patient, hepatocellular carcinoma in 1 patient, hepatic hemangioma in 1 patient, and intrapancreatic accessory spleen in 1 patient. Informed consent was obtained from all patients.

Axial T2-weighted fast spin-echo (T2-weighted FSE) images and T2*-weighted gradient-echo (T2*-weighted GRE) images of the entire liver were obtained before administration of ferucarbotran 0.016 ml/kg (Resovist; Schering, Munich, Germany). Axial T2-weighted FSE images or fat suppressed T2-weighted FSE images, and T2*-weighted GRE images, of the entire liver were obtained 10 min after administration of ferucarbotran. Regions of interest were established in the liver and spleen before and after administration of ferucarbotran, and the signal intensity (SI) was measured in each region. The percentage signal intensity change (PSIC) in the liver and spleen before and after administration of ferucarbotran was then determined.

$$PSIC = [(SI_{post\text{-}SPIO} - SI_{pre\text{-}SPIO})/SI_{pre\text{-}SPIO}] \times 100 \quad (1)$$

The T2-weighted FSE and fat suppressed T2-weighted FSE imaging parameters were as follows: TE 100 ms; NEX 4; slice thickness 7 mm; matrix 140–170 × 256; and FOV 350 mm with respiratory triggering. The T2*-weighted GRE imaging parameters were as follows: TR/TE/FA 140–310 ms/7–9 ms/55–60; NEX 1; slice thickness 7 mm; matrix 140–170 × 256; and FOV 350 mm under breath-holding.

The scanner used was a Gyroscan ACS-NT 1.5T (Philips Medical Systems, Best, The Netherlands).

Results

The PSIC in the liver was reduced in all cases. The mean PSIC in the liver was –61.8% on T2-weighted FSE images and –58.6% on T2*-weighted GRE images. The mean PSIC in the spleen was –44.8% on T2-weighted FSE images, whereas the mean PSIC in the spleen was 0.9% on T2*-weighted GRE images. The PSIC in the spleen was significantly lower on T2*-weighted GRE images than on T2-weighted FSE images ($P < 0.01$) (Fig. 1).

The PSIC in the liver was significantly lower in patients with liver cirrhosis than in those without liver cirrhosis on T2*-weighted GRE images ($P < 0.01$). There was no statistically significant relation of the PSIC in the spleen between T2-weighted FSE and T2*-weighted GRE images with and without liver cirrhosis.

Statistical analysis was performed with Student's *t*-test.

Discussion

Most SPIO administered intravenously is taken into the hepatic reticuloendothelial system, and thus SPIO administration is often performed for diagnosis of metastatic hepatic tumors. Moreover, strictly speaking, 20% of the SPIO administered intravenously is taken into the reticuloendothelial systems of organs other than the liver, including the spleen. Therefore, SPIO is also used for diagnosis of accessory spleen and splenosis, although scintigraphy is more often used for diagnosing accessory spleen and splenosis.[7] Small accessory spleen and splenosis are generally not evaluated using single photon emission computed tomography (SPECT). Furthermore, the diagnosis of ectopic splenic tissue based on splenic inhomogeneity on contrast-enhanced CT[8] may limit detection of small accessory spleen and splenosis.

The signal intensity reduction by SPIO depends on both the number of macrophages and the intracellular cluster size of SPIO. On T2*-weighted GRE images, the signal intensity of the spleen is less decreased than that of the liver, as fine clustered SPIO particles in the spleen produce less susceptibility effect than largely clustered ones in the liver.[9] Nonetheless, the usefulness of SPIO administration for diagnosing accessory spleen and splenosis has been reported.[5,6]

Diagnosis of accessory spleen and splenosis is primarily performed using ferumoxides, and no studies with ferucarbotran have previously been reported. This is partly due to the lower accumulation of ferucarbotran than ferumoxides in the spleen, even though there are no differences in the PSIC in the liver before and after administration of ferumoxides and ferucarbotran, as observed on T2-weighted FSE images.[4] This, in turn, is due to the differences in the particle diameters and doses of ferumoxides and ferucarbotran. The mean particle diameter of ferumoxides is 150 nm, and the dose is 0.56 mg/kg. In contrast, the mean particle diameter of ferucarbotran is 60 nm, and the dose is 0.45 mg/kg. Because particles with larger diameters are physiologically taken into the spleen, less ferucarbotran than ferumoxides is taken into the spleen. Furthermore, because the dose of ferucarbotran is smaller than that of ferumoxides, the PSIC in the spleen is low. Therefore, caution must be exercised when diagnosing accessory spleen and splenosis using ferucarbotran, as the signal intensity reduction in the spleen is lower than with ferumoxides.

With SPIO contrast MRI, the contrast-to-noise ratio on T2*-weighted GRE images at TE 8.4–9.5 ms is good, and T2-weighted FSE images and T2*-weighted GRE images have been reported to be useful for detecting hepatocellular carcinoma.[10] Therefore, these imaging methods with SPIO are routinely used for evaluating

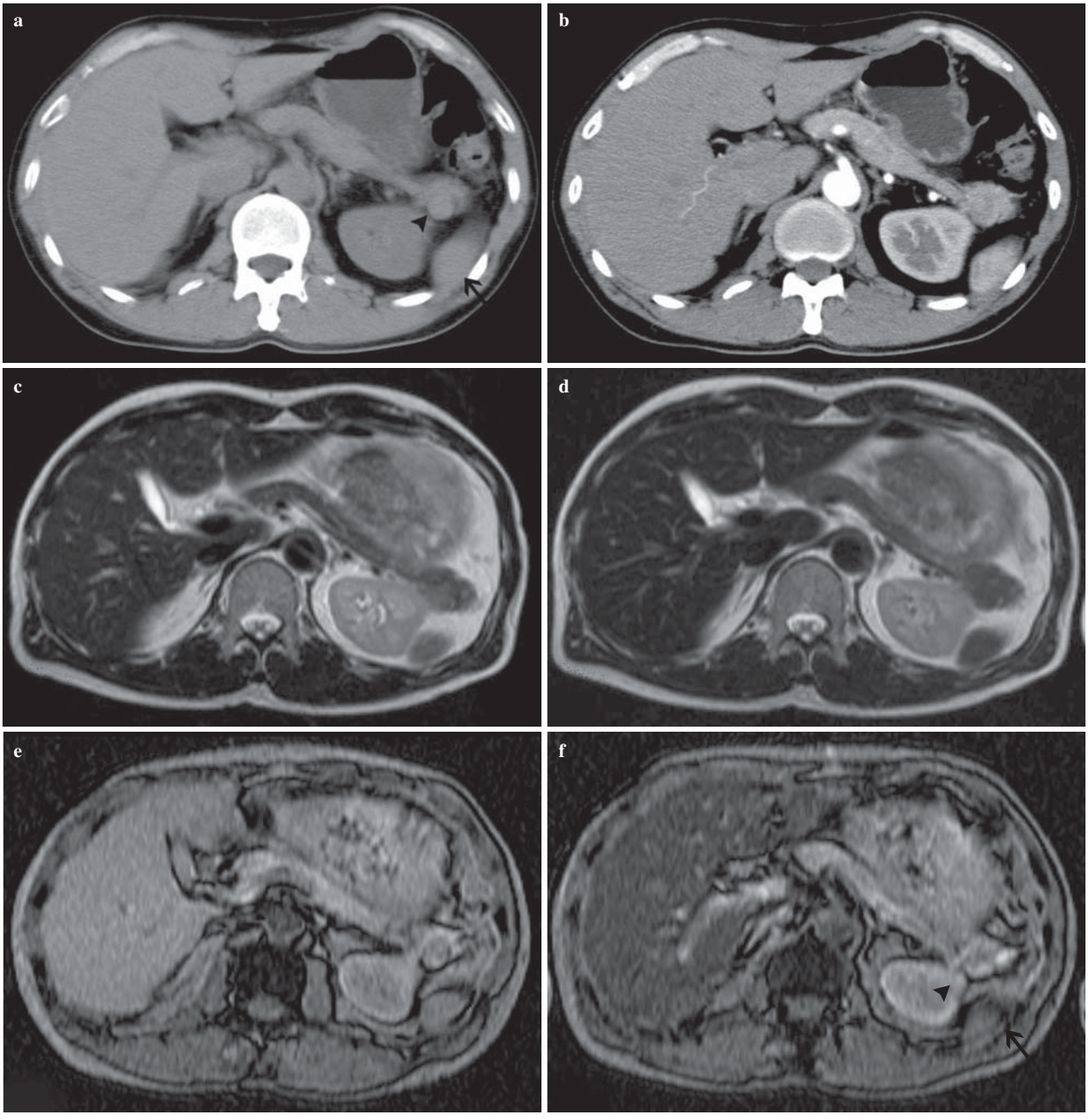

Fig. 1. A 50-year-old man had an intrapancreatic accessory spleen. **a** Computed tomography (CT). **b** Contrast CT. **c** Pre-superparamagnetic iron oxide (pre-SPIO) T2-weighted fast spin-echo (FSE) image. **d** Post-SPIO T2-weighted FSE image. **e** Pre-SPIO T2*-weighted GRE (TE = 9 ms). **f** Post-SPIO T2*-weighted gradient-echo (GRE) (TE = 9 ms). Even after SPIO imaging, the signal reduction in the spleen (*arrow*) and intrapancreatic accessory spleen (*arrowhead*) was low

hepatic disease.[11,12] However, the PSIC in the spleen is low with ferucarbotran. In fact, the diagnosis of accessory spleen is difficult using T2*-weighted GRE images in cases of intrapancreatic accessory spleen (Fig. 1).

Recently, the usefulness of diffusion-weighted imaging in the abdominal region has been documented,[13] and this method is considered to be effective for patients with ferrugination. However, the spatial resolution obtained may not be sufficient for diagnosis of small accessory spleen.

Conclusion

We examined signal changes in the spleen before and after contrast imaging with ferucarbotran. The reduc-

tion in signal intensity is low in the spleen on T2*-weighted GRE images, and so a T2-weighted FSE sequence is necessary for diagnosis of accessory spleen and splenosis when ferucarbotran is used.

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