BRIEF COMMUNICATION

Central High Signal in Inflammatory Swollen Lymph Nodes on SPIO-enhanced Interstitial MR Lymphograms: A Mimic of Lymph Node Metastasis

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Introduction

Sentinel lymph nodes (SLNs) are the nodes most often involved in cancer. Previous studies demonstrate that tumor-bearing and inflammatory SLNs are typically differentiated by super-paramagnetic iron oxide (SPIO) or ultra-small SPIO (USPIO)-enhanced interstitial MR lymphography. Tumor-bearing nodes contain areas of high signal, whereas the interior of inflammatory nodes demonstrates a homogeneous low signal, depending on the presence or absence of SPIO- or USPIO-laden macrophages.¹⁻³ However, we recently observed a central area of high signal in inflammatory lymph nodes (LNs) on SPIO-enhanced interstitial MR lymphograms and investigated the pathogenesis.

Materials and Methods

Our institutional committee for animal experimentation approved this protocol. We subcutaneously administered 0.05 mL Freund's complete adjuvant (FCA) into the left foot pad of each of ten 7-to-8-week-old ddY mice to induce lymphadenitis.^{2,4} Two weeks later, we administered 0.17 μmol Fe/foot of ferucarbotran (0.05 mL) into the footpad of each of 6 mice and 0.05 mL normal saline (NS) into the foot pad of 4 mice. Two hours later, we acquired lipid-suppressed T₂-weighted fast-spin-echo images (T₂WI) (repetition time [TR]/effective echo time [TE_{eff}], 4000/60 ms; resolution, 78 × 78 × 1000 μm^3) of the popliteal LNs *in vivo* and *ex vivo*

using a 3.0-tesla whole-body scanner (Signa HDx; GE Healthcare, Milwaukee, WI, USA) with a dedicated radiofrequency (RF) coil for mice. To evaluate nonenhanced areas within the LNs quantitatively, we measured areas of high signal on *in vivo* transverse T₂WIs crossing the center of the LNs. We evaluated iron deposits in the LNs using Prussian blue-stained specimens.

Results and Discussion

The table summarizes results. On *in vivo* T₂WIs, all inflammatory LNs showed central high signals that occupied approximately 30 to 40% of the entire node and peripheral low signals of various shapes, including rim-like, crescent, or wedge shapes (Fig. 1a). The central regions of 3 LNs also showed spotty low signals. Areas of high signal were significantly smaller in mice administered ferucarbotran than those administered normal saline. Histopathologically, no mouse showed obvious necrosis. In 4 cases, more predominant deposition of SPIO-derived iron at the periphery near the LN capsules (Fig. 1c) than at the center (Fig. 1d) may have produced peripheral low and central high signals. We presumed this to result from the arrival of the interstitially administered SPIOs at the periphery of the LNs, where afferent lymph ducts open and there are a large number of macrophages. Our results suggested that central high signals in SLNs on SPIO-enhanced interstitial MR lymphography do not necessarily represent metastatic deposits. However, the imaging findings reported here would be different if the time point of MR imaging acquisition after FCA and SPIO administra-

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Table. Findings of *in vivo* and *ex vivo* magnetic resonance (MR) images and specimens in popliteal lymph nodes involved with lymphadenitis

Contrast agent	<i>In vivo</i> MR Imaging			<i>Ex vivo</i> MR Imaging			Specimen	
	Area of high signal [mm ²]	Distribution of low signal		Distribution of low signal			Distribution of iron*	
		Whole area	Periphery	Whole area	Periphery		Whole area	Periphery
Ferucarbotran	3.9 ± 3.2 [†]	0	6	1	5		2	4**
Normal saline	11.3 ± 1.7 [†]	0	0	0	0		0	0

* We did not include hemosiderin, which is inherently present in lymph nodes (LNs).
** includes one case of several iron deposits at the periphery
[†] statistically significant (*P* = 0.001, *t*-test)

Fig. 1. *In vivo* T₂-weighted images (T₂WI) of the popliteal lymph node (LN) (arrows) involved with lymphadenitis in mice administered (a) super-paramagnetic iron oxide (SPIO) and (b) saline. Bars represent 5 mm. Insets are *ex vivo* magnetic resonance (MR) images of the corresponding LNs. Note the peripheral areas of low and central high signal in the inflammatory LN. Spotty low signals are also seen in the central area. A representative Prussian blue-stained specimen of the popliteal lymph node involved with lymphadenitis. Iron deposits (black dots) accumulate in the lymphatic sinuses at the periphery (c) but are scattered in the paracortical area in the center (d).

tion were changed. Although we chose SPIO in our study because the use of clinically approved contrast material is preferable for the translation of this preclinical research to clinical practice, intravenous USPIO would produce different findings. This point may require further study.

Conclusion: Our experimental study demonstrated that a central high signal in swollen SLNs

on SPIO-enhanced interstitial MR lymphography at a high magnetic field does not always mean the presence of metastatic foci. A central high signal can be observed even in inflammatory SLNs.

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