Visualization of Myocardial Inflammation in Experimental Autoimmune Myocarditis Rats detected by MR Imaging with a Magnetofluorescent Nanoparticles

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Introduction: Clinically, myocarditis is a major cause of sudden death in young adults, and leads to dilated cardiomyopathy in 9% of the cases in a large prospective series. Despite these significant consequences, the poor sensitivity and specificity of traditional diagnostic modalities have hindered the reaching of a consensus on the clinical practice guidelines for its evaluation and treatment. In this study, we investigated whether MNP (magnetic nanoparticle)-contrasted CMR (cardiac magnetic resonance imaging) would be feasible and effective for the detecting the inflammation in a rat model of experimental autoimmune myocarditis (EAM), and whether MNP-contrasted CMR could give a guidance where the biopsy samples should be collected.

Materials and Methods: EAM was induced in forty one 7-week-old male Lewis rats. In this study, we used bifunctional MNPs that enable the detection of both their fluorescence and magnetic properties in cells and tissues. We performed MRI in EAM (n=5) and control rats without myocarditis (n=3) and compared the MR images obtained before and after the intravenous injection of MNPs (12 mg Fe/kg) in order to determine whether the MNPs could provide MRI contrast in the inflamed myocardium. MRI was performed using a 4.7 T MRI system (BioSpec 47/40; Bruker, Germany) with dual ECG and respiratory gating (SA Instruments, Stony Brook, NY, USA). MNPs were intravenously administered (12mg Fe/kg), then we obtained MR images with a gradient-echo (FLASH) sequence (TE/TR = 6/150 ms). Serial CMR was conducted prior and 24 hr after the MNPs injection. We defined regions of interest (ROIs) for numerical analysis; ROIs of myocardium and pectoral muscle from 3 slices in the center of the hearts. From the selected ROIs, the mean SNR values were measured in the myocardium and the pectoral muscle, and they then were compared in control and EAM rats. After in vivo MR imaging, all hearts were stained with hematoxylin and eosin (H&E). The hearts were treated with mouse anti-rat macrophage monoclonal antibody clone ED-1.

Results: On the MR images before and 24 hr after the MNPs injection, there was little SNR change in the pectoral muscle in both the control and EAM rats. In contrast, in the myocardium, there was dramatic change (~75%) in the EAM rats, while it was decreased by ~13% in the control rats (Figure 1). These results support the potential of MNP-combined CMR as a valuable tool in the research and clinical applications. Furthermore, we expect that the MNP-contrast CMR could guide where we biopsy from the heart suspecting myocarditis, which will reduce making an error in diagnosis of human myocarditis.

Conclusion: We demonstrated that the noninvasive imaging of myocardial inflammation is feasible in autoimmune myocarditis rats by using the MNP-contrasted CMR. This CMR approach combined with MNPs provides the feasibility and efficiency to image noninvasively and track myocardial inflammation in EAM rats. These results support the potential of MNP-combined CMR as a valuable tool in the research and clinical applications. Furthermore, we expect that the MNP-contrasted CMR could guide where we biopsy from the heart suspecting myocarditis, which will reduce making an error in diagnosis of human myocarditis.

References