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Molecular MR imaging of collagen-induced arthritis with endothelial cell-targeted ICAM-1 antibody-conjugated Gd-DTPA

이상용[1], 이상일[2], 최규실[3], 윤권하[3]
전북대학교 의과대학 영상의학교실[1], 경상대학교 의과대학 내과학교실[2],
원광대학교 의과대학 영상의학교실[3]

Purpose: To determine the ability of molecular magnetic resonance (MR) imaging with intercellular adhesion molecule (ICAM)-1 antibody-conjugated gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA-anti-ICAM-1) to provide early detection of synovitis in mouse model of collagen-induced arthritis.

Materials and Methods: Collagen-induced arthritis (CIA) mice were made using type II collagen (CII) and a new specific MR contrast agent was prepared by bioconjugation of Gd-DTPA with anti-ICAM-1 to target angiogenic endothelial cells on synovial blood vessel. The fat-suppressed, coronal MR images were obtained prior to and after intravenous injection of Gd-DTPA as non-targeted and Gd-DTPA-anti-ICAM-1 as targeted contrast agent. For MR imaging, we used a nonarthritic normal mouse, early phase (4 weeks after 1st injection of CII) of CIA mice, and a chronic phase (8 weeks after 1st injection) of CIA mouse. MR images were analyzed quantitatively with regard to signal intensity and correlated with histopathologic and immunohistochemical findings.

Results: The quick T1 enhancement by Gd-DTPA (100 nmoles of Gd/gm of body weight) were shown within 1 minute and nearly disappeared at 80 minutes after injection of contrast agents on MR images of arthritic knees of all CIA mice. However, Gd-DTPA-anti-ICAM-1 (5 nmoles of Gd/gm of body weight) enhanced images displayed significant and more predominant signal enhancement in all arthritic joints of early phase of CIA mice until 24 hours. No significant changes in signal characteristics were shown in the nonarthritic joints of a normal control mouse and chronic phase of CIA mice after injection of Gd-DTPA-anti-ICAM-1. Moreover, MR imaging with Gd-conjugated control antibody (Gd-DTPA-IgG) also showed no significant enhancement until 24 hours. Histopathologic and immunohistochemical examination confirmed the development of synovitis and high expression of ICAM-1 in angiogenic endothelial cells on synovial blood vessel of early phase of CIA mice. MR images were correlated well with those findings.

Conclusion: The molecular MR imaging with Gd-DTPA-anti-ICAM-1 displays specific images targeted to the endothelial cells on synovial blood vessel of CIA in their earlyphase. Therefore, this novel tools will be used to facilitate earlier and more accurate diagnosis and develop new targeted drug delivery system for treatment of rheumatoid arthritis.