Abstract

The aim of this study was to examine whether inhibition of Interleukin (IL)-6 signaling by MR16-1, an IL-6 receptor antibody, attenuates aortitis, cardiac hypertrophy, and arthritis in IL-1 receptor antagonist deficient (IL-1RA KO) mice. Four weeks old mice were intraperitoneally administered with either MR16-1 or non-immune IgG at dosages that were adjusted over time for 5 weeks. These mice were stratified into 4 groups: MR16-1 treatment groups, KO/MR low group (first 2.0 mg, following 0.5 mg/week, n=14) and KO/MR high group (first 4.0 mg, following 2.0 mg/week, n=19) in IL-1RA KO mice, and IgG treatment groups, KO/IgG group (first 2.0 mg, following 1.0 mg/week, n=22) in IL-1RA KO mice, and wild/IgG group (first 2.0 mg, following 1.0 mg/week, n=17) in wild mice. Aortitis, cardiac hypertrophy and arthropathy were histologically analyzed. Sixty-eight % of the KO/IgG group developed aortitis (53% developed severe aortitis). In contrast, only 21% of the KO/MR high group developed mild aortitis, without severe aortitis (P<0.0*1,* vs KO/IgG group). Infiltration of inflammatory cells, such as neutrophils, T cells, and macrophages, was frequently observed around aortic sinus of the KO/IgG group. Left ventricle and cardiomyocyte hypertrophy were observed in IL-1RA KO mice. Administration of high dosage of MR16-1 significantly suppressed cardiomyocyte hypertrophy. MR16-1 attenuated the incidence and severity of arthritis in IL-1RA KO mice in a dose-dependent manner. In conclusion, blockade of IL-6 signaling may exert a beneficial effect to attenuate severe aortitis, left ventricle hypertrophy, and arthritis.

(239 words)