C-REACTIVE PROTEIN OVEREXPRESSION EXACERBATES PRESSURE OVERLOAD-INDUCED CARDIAC REMODELING THROUGH ENHANCED INFLAMMATORY RESPONSE AND OXIDATIVE STRESS

ACC Poster Contributions
Ernest N. Morial Convention Center, Hall F
Sunday, April 03, 2011, 3:30 p.m.-4:45 p.m.

Session Title: Cardiovascular Complications in Hypertension: Current and Emerging Predictors
Abstract Category: 16. Hypertension
Session-Poster Board Number: 1047-296

Authors: Toshiyuki Nagai, Toshihisa Anzai, Hidehiro Kaneko, Yoshinori Mano, Atsushi Anzai, Yuichiro Maekawa, Tsutomu Yoshikawa, Keiichi Fukuda, Keio university school of medicine, Tokyo, Japan

Backgrounds: Serum C-reactive protein (CRP) elevation predicts the development of cardiovascular disease in patients with hypertension. CRP activates macrophage and enhances oxidative stress. We hypothesize CRP itself has a pathogenic role in the development of pressure overload-induced cardiac remodeling through enhanced inflammatory response and oxidative stress.

Methods: Transgenic mice with human CRP overexpression (Tg) and wild type mice (W) were subjected to transverse aortic constriction (TAC/Tg, TAC/W) and sham operation (Sham/Tg, Sham/W).

Results: One week after operation, TAC mice showed left ventricular (LV) hypertrophy compared with Sham mice, but no significant differences between TAC groups. However, in TAC/Tg, myocardial mRNA levels of interleukin (IL)-6, CD68, glutathione peroxidase-3 (GPx3), 47-kDa 67-subunit of nicotinamide adenine dinucleotide phosphate oxidase (p47phox), collagen I, and the number of infiltrating Mac-2+ macrophages and nuclear factor-kB/p65+ cells were increased than those in TAC/W (all p<0.01). Cardiac fibrosis (% area fraction [AF]) was more prominent in TAC/Tg compared with TAC/W (p<0.05). Four weeks after operation, heart and lung weights were increased in TAC/W than in Sham/W, and these differences were further augmented in TAC/Tg (p<0.01, p<0.05, respectively). LV fractional shortening was lower (p<0.0001) and LV end-diastolic pressure was higher (p<0.05) in TAC/Tg than those in TAC/W. Myocardial mRNA levels of angiotensin type 1 receptor, atrial natriuretic factor, p47phox, GPx3, IL-6 and collagen I, protein level of transforming growth factor-beta1, and the number of infiltrating Mac-2+ macrophages were increased in TAC/Tg than those in TAC/W (all p<0.05). Cardiomyocyte cross sectional area and the AF were greater in TAC/Tg than those in TAC/W (p<0.001, p<0.05, respectively).

Conclusions: Continuous overexpression of human CRP in mice adversely affects pressure overload-induced cardiac remodeling preceded by enhanced inflammation and oxidative stress. CRP plays a pathogenic role in cardiac remodeling and could be a therapeutic target for the treatment of heart failure induced by pressure overload.