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Connective tissue growth factor (CTGF/CCN2): a protagonist in cardiac allograft vasculopathy development?

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Abstract

BACKGROUND:

Connective tissue growth factor (CTGF) has been reported to be upregulated in experimental models of chronic cardiac allograft rejection. We investigated the contribution of CTGF to the development of cardiac allograft vasculopathy (CAV), a surrogate marker for chronic rejection.

METHODS:

This prospective study included 72 adult heart allograft recipients. Genotyping of the rs6918698 polymorphism was performed by sequence-specific primer polymerase chain reaction (PCR). CTGF protein levels were measured in serum. CTGF messenger RNA (mRNA) from myocardial biopsy specimens was quantified by quantitative real-time PCR.

RESULTS:

Recipient genotype was associated with the development of CAV ($p = 0.014$) and the carriers of the C allele (CC and CG genotype) were high-risk recipients for the development of CAV (odds ratio, 3.30; 95% confidence interval, 1.12-9.74; $p = 0.044$). Serum CTGF protein levels could not be associated with the presence of the C allele but were significantly lower in the patients that had developed CAV ($p = 0.038$). This was attributed to the addition of everolimus to their immunosuppression scheme. Myocardial relative CTGF mRNA expression was estimated to be approximately twice as much in the CAV patients than in the patients without CAV ($p = 0.013$).

CONCLUSIONS:

The important role of CTGF during the development of CAV in heart transplantation was supported by the association of CAV with the recipient CTGF-945 CC/CG genotypes. The CAV patients, who were all receiving everolimus treatment, displayed elevated myocardial CTGF mRNA transcription levels, while everolimus has been observed to reduce serum CTGF protein levels.

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