Soluble vascular cell adhesion molecule-1 is independently associated with soluble tumor necrosis factor receptor 2 in Japanese type 2 diabetic patients

The major clinical consequence of type 2 diabetes is mortality and morbidity from atherosclerotic vascular disease. Although it remains to be clarified which factors are responsible for the evolution of atherosclerosis, the earliest morphological evidence of atherosclerosis is the attachment of monocytes to the cell surface of vascular endothelium. Monocytes attach at the cell surface of adhesion molecules such as vascular cell adhesion molecule 1 (VCAM-1). Jager et al. [1] have shown that increased levels of soluble VCAM-1 are associated with risk of cardiovascular mortality independently of traditional risk factors, homocysteine, and C-reactive protein in type 2 diabetic patients. The mechanisms underlying the development of atherosclerosis, however, are unclear in type 2 diabetic patients.

Along with insulin resistance, tumor necrosis factor (TNF) seems to account for the development of atherosclerosis in type 2 diabetes. Shai et al. [2] demonstrated that soluble TNF receptor 2 (sTNF-R2) is strongly associated with risk of coronary heart disease in type 2 diabetic patients. We recently demonstrated that soluble TNF receptors are not associated with insulin resistance but are associated with albuminuria or aortic stiffness measured by brachial-ankle pulse wave velocity in Japanese type 2 diabetic patients [3–5]. To the best of our knowledge, however, the relationships between VCAM-1 and TNF system activities including soluble TNF receptors were not yet investigated in type 2 diabetic patients. In this regard, the problem is that insulin therapy or the degree of overweight per se affects the concentrations of VCAM-1 and TNF system activities. We therefore recruited insulin naïve type 2 diabetic patients who were not massively obese and investigated the relationships between VCAM-1 and TNF system activity in type 2 diabetic patients.

Fifty-four Japanese type 2 diabetic patients were enrolled. Their age, BMI, fasting glucose, and HbA1c were 62.5 ± 1.7 years (mean ± S.E.M.), 23.6 ± 0.4 kg/m², 137 ± 4 mg/dl, and 6.8 ± 0.1%, respectively. Along with VCAM-1, glucose, insulin, lipids, homocysteine, TNF-α, sTNF-R1, sTNF-R2, high sensitive C-reactive protein (hsCRP), interleukin-6 (IL-6), and leptin were measured in the morning after an overnight fast as described previously in [3,6–8].

With univariate analysis, VCAM-1 was positively correlated with age (r = 0.355, P < 0.01), sTNF-R1 (r = 0.562, P < 0.0001), and sTNF-R2 (r = 0.701, P < 0.0001) in our patients. Serum levels of VCAM-1, however, were not associated with homocysteine, TNF-α, glucose, insulin, BMI, hsCRP, IL-6, or leptin. Multiple regression analyses revealed that VCAM-1 was independently predicted by sTNF-R2 (F = 38.7), which explained 38.2% of the variability of VCAM-1 in our patients.

Thus, it may be suggested that VCAM-1 is associated with TNF system activity in Japanese type 2 diabetic patients.

References


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