Correlation between sera levels of sVCAM-1 and severity of kidney lesions in patients with lupus nephritis

T. Ilic, I. Mitic, B. Milic and S. Curic

Department of Nephrology, Clinical Center Novi Sad, Serbia and Montenegro

Abstract

We determined sera concentrations of soluble vascular adhesion molecule-1 (sVCAM-1) in group of 80 patients with SLE. Our aim was to investigate correlation between level of sVCAM-1 and degree of disease activity, also severity of lupus nephritis. Using ELISA procedure we determined sera levels of sVCAM-1 in 80 patients with SLE and in group of 27 healthy volunteers. Patients with SLE had significantly higher sera levels of sVCAM-1 comparing healthy controls ($p < 0,001$). Patients with disease in active phase had higher sera levels of this adhesive molecule comparing patients with disease in phase of remission ($p < 0,001$). There was a high positive correlation between sera levels of sVCAM-1 and concentration of anti-ds DNK antibodies in sera of patients with SLE ($r = 0,77$, $p < 0,001$) and there was also negative correlation between sera levels of sVCAM-1 and sera concentrations of C_3 and C_4 component of complement ($r = - 0,64$, $r = - 0,58$). In group of patients with lupus nephritis were detected significantly higher sera concentrations of sVCAM-1 comparing patients without nephritis. Using WHO classification, patients with lupus nephritis were systematized in three categories: class II (5 patients), classes III and IV (18 patients) and class V (7 patients). Patients with class III and class IV of kidney changes had significantly higher levels of sVCAM-1 comparing patients with class II of kidney changes. At the same time, in group of patients with activity index (AI) of kidney changes over 4 sVCAM-1 sera levels were significantly higher comparing group with $AI < 4$. Sera level of sVCAM-1 is reliable parameter in evaluation of autoreactivity degree in SLE. At the same time, sVCAM-1 sera level can be used as reliable marker in evaluation of renal lesion extensivity in SLE.

Key words: SLE, sVCAM-1, lupus nephritis

Introduction

Systemic Lupus Erythematosus (SLE) is chronic, inflamatory connective tissue disease which contains loss of autotolerancy as main immunological disorder accompanied with breakdown of T lymphocytes, collapse of cytokine production and B lymphocite hiperactivity (1). Cytokines are essential regulating factors of immunology response which are included in migration process of inflammatory cells into the place of immunology caused inflammatory tissue reaction, together with adhesive molecules (2). The vascular cell adhesion molecule-1 (VCAM-1) is a member of the immunoglobulin gene superfamily. VCAM-1 supports the adhesion of lymphocytes, monocytes, natural killer cells, eosinophils and basophils through its interaction with leukocyte very late antigen-4 (VLA-4). VCAM-1/VLA-4 interaction mediates firm adherence of circulating non-neutrophilic leukocyte to endothelium. VCAM-1 also participates in leukocyte adhesion outside of the vasculature, mediating presursor lymphocyte adhesion to bone marrow stromal cells and B cell binding to lymph node follicular dendritic cells (3). A soluble form of VCAM-1 (sVCAM-1) has been described. Soluble VCAM-1 levels have been found in the sera of healthy individuals and increased levels of sVCAM-1 can be detected in several diseases including connective tissue diseases (4). Studies have shown that elevated levels of sVCAM-1 are related to disease activity in patients with SLE (5).

The aim of our study was to investigate changes of adhesive molecule sera levels in patients with SLE comparing different phases of disease activity and comparing presence/absence of lupus nephritis. At the same time relation of vascular cell adhesion molecule sera concentrations were analized with concentrations of other disease parameters (titre of ANA, SLED AI, titre of anti-ds DNA antibodies, concentrations of C3 and C4).

Patients and methods

The study was carried out in 80 patients included in crossection study and 10 patients included in longitudinaly study. We used ELISA procedure to determine sVCAM-1 sera levels in 80 patients with SLE and in group of 27 healthy volunteers. An anti-sVCAM-1 monoclonal coating antibody is adsorbed onto microwells. sVCAM-1 present in the sample binds to antibodies adsorbed to the microwells. A mixtureof biotin–conjugated monoclonal anti-sVCAM-1 antibody and Streptavidin–HRP is added. Biotin conjugated anti-sVCAM-1 captured by the first antibody. Streptavidin-HRP binds to the biotin conjugated anti-VCAM-1. Following incubation unbound biotin conjugated anti-sVCAM-1 and Streptavidin – HRP is removed during a wash step and substrate solution reactive with HRP is added to the wells. Acoloured product is formed in proportion to the amount of soluble VCAM-1 present in the sample. The reaction is terminated by addition of acid and absorbance is measured at 450 nm. A standard curve is prepared from six sVCAM-1 standard dilutions and sVCAM-1 sample concentration determined.

Correspodence to: T. Ilic, Department of Nephrology, Clinical Center Novi Sad, Serbia and Montenegro

Results and discussion

Patients with SLE had significantly higher sera levels of sVCAM-1 comparing healthy controls ($p < 0,001$). Patients with disease in active phase had higher sera levels of this adhesive molecule comparing patients with disease in phase of remission ($p < 0,001$). There was high positive correlation between sera levels of sVCAM-1 and concentration of anti-ds DNK antibodies in sera of patients with SLE ($r = 0,77$, $p < 0,001$) and a negative correlation between sera levels of sVCAM-1 and sera concentrations of C_3 and C_4 component of complement ($r = -0,64$, $r = - 0,58$). In group of patients with lupus nephritis a significantly higher sera concentrations of sVCAM-1 were detected comparing patients without nephritis. Using WHO classification, patients with lupus nephritis were systematized in three categories: class II (5 patients), classes III and IV (18 patients) and class V (7 patients). Patients with class III and class IV of kidney changes had significantly higher levels of sVCAM-1 comparing patients with class II of kidney changes. In the same time, in group of patients with activity index of kidney changes (AI) over 4 sVCAM-1 sera levels were significantly higher comparing group with $AI < 4$.

Conclusions

Sera level of sVCAM-1 is reliable parameter in evaluation of autoreactivity degree in SLE. Serial measurements of sVCAM-1 may be helpful for monitoring disease activity in patients with SLE and lupus nephritis. The serum level of sVCAM-1 was correlated with the clinical and histological activity score. Active lupus nephritis (proliferative lupus nephritis, WHO classes III and IV) was associated with significantly elevated sVCAM-1 levels.

References

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