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Modulation of MHC Expression on Human Endothelial Cells by Sera from Patients with Systemic Lupus Erythematosus

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Major histocompatibility complex (MHC) antigen expression on cells is a prerequisite for immune interaction with activated T-cells. This study examined the ability of sera from patients with systemic lupus erythematosus (SLE) to modulate MHC expression on vascular endothelial cells. SLE sera were able to selectively upregulate MHC class I antigen expression on cultured human umbilical venous endothelial (HUVE) cells, without concomitant induction of MHC class II antigen. The stimulation index (SI) for MHC class I expression produced by SLE sera (1.21 ± 0.23) was significantly higher than those for normal controls (1.01 ± 0.10) (P < 0.0001) and non-SLE patients (1.12 ± 0.14) (P < 0.05). Additionally, active SLE patients had higher mean SI than inactive patients (P < 0.001). Preincubation of SLE sera with Protein A-Sepharose beads conjugated with antibodies against tumor necrosis factor-α and interferon-α was able to significantly reduce their ability to upregulate class I MHC expression by HUVE cells, indicating that these cytokines were responsible for the modulatory effect. This could be an important mechanism for the immune-mediated vascular injury seen in SLE.

INTRODUCTION

The vascular endothelial cells are uniquely situated for a primary role both in antigen presentation and as targets for cytotoxic activity. Major histocompatibility complex (MHC) antigen expression on cells is a prerequisite for interaction with T-lymphocytes. There is in vitro and in vivo evidence that activated endothelial cells expressing class II MHC molecules are able to present antigen to CD4+ T-cells (1–5). In addition, CD8+ cytotoxic T-cells recognize their targets in conjunction with MHC class I molecules (6).

Human endothelial cells constitutively express class I but not class II MHC molecules. At sites of inflammation, class II MHC expression has been demonstrated (7). Additionally, class I MHC molecules on endothelial cells are upregulated by various cytokines (8–10), facilitating their participation in the immune reaction.

Systemic lupus erythematosus (SLE) is an autoimmune disorder associated with diffuse vascular injury. This ranges from frank vasculitis to focal endothelial cell necrosis with thrombosis and fibrinoid necrosis leading to gradual vascular scarring and sclerosis. Immune deposits, associated with mononuclear cell infiltration have been demonstrated in the blood vessel walls in this disease. The purpose of this study was to investigate the ability of sera from patients with SLE to modulate MHC expression on human endothelial cells, providing a possible basis for their role in the genesis of the vascular immune injury seen in this disease.

MATERIALS AND METHODS

Patients and Controls

Fifty patients with SLE (mean age 34 years, range 16 to 60 years) were studied. All of them fulfilled the American Rheumatism Association (ARA) criteria for the diagnosis of SLE (11). Classification of disease activity at the time of study was based on the lupus activity criteria count (LACC) as described by Urowitz et al. (12). A LACC score of 2 or more was graded as active SLE. Based on this criteria, 23 patients were graded as active and 27 inactive at the time of study. In addition, 31 healthy controls (mean age 24 years, range 23 to 38 years) and 18 patients with rheumatic disorders other than SLE (non-SLE) (mean age 43 years, range 10 to 57 years) were studied (Table 1). The healthy controls were predominantly young adult females, as the female:male ratio of the SLE patients was 11.5:1. Sera obtained from these patients were stored at −70°C until required.