

Soluble intercellular adhesion molecule-1 levels of patients with acute myeloid leukemia after allogeneic bone marrow transplantation

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Concentrations of serum-soluble intercellular adhesion molecule-1 (ICAM-1) were measured for 10 patients with or without chronic graft versus host disease after allogeneic bone marrow transplantation. Levels of soluble ICAM-1 were higher among patients with chronic graft versus host disease than among those without it, a statistically significant difference. The results indicated that measurement of serum-soluble ICAM-1 is useful for prediction of chronic graft versus host disease. (*J Allergy Clin Immunol* 1997;100:S77-8.)

Key words: Serum-soluble intercellular adhesion molecule-1, bone marrow transplantation, acute myeloid leukemia, chronic graft versus host disease

It is known that intercellular adhesion molecule 1 (ICAM-1, CD54), a 90 kilodalton molecule homologous with the immunoglobulin superfamily, is the principal ligand for leukocyte functional antigen-1 (LFA-1, CD11a/CD18).¹ It has been suggested that evaluation of an 82 kilodalton soluble form of ICAM-1 (sICAM-1) might be useful in the investigation and monitoring of various inflammatory and immune disorders.²⁻⁴ Elevated levels of sICAM-1 are detectable among patients with malignant diseases,⁵ including malignant melanoma,⁶ Hodgkin's disease,⁷ and chronic B-lymphocytic leukemia.⁸ In this study, we measured concentrations of sICAM-1 in serum from patients with acute myeloid leukemia before and after allogeneic bone marrow transplantation.

METHODS

A sandwich ELISA kit (Bender Medsystems, Vienna, Austria) was used in which two antibodies are used to differentiate epitopes of ICAM-1 molecules. A 96-well plate was treated with human anti-sICAM-1 (human) monoclonal antibody, and 100 μ l of the standard solution or the test sample was added, followed by 50 μ l of horseradish peroxidase-labeled anti-sICAM-1 antibody. The reaction was stopped with 4 N sulfuric acid, and absorbance was determined at 450/620 nm with a

Abbreviations used

GVHD:	Graft versus host disease
ICAM-1:	Intercellular adhesion molecule-1
LFA-1:	Leukocyte functional antigen-1
sICAM-1:	Soluble ICAM-1

Titertek Multiskan MCC/340 spectrophotometer (ICN Company). The sICAM-1 concentration in each sample was determined from a standard curve. Ten patients with acute myeloid leukemia who were undergoing bone marrow transplantation participated in the study. All patients received marrow transplants from human histocompatibility leukocyte antigen-identical sibling donors. Serum samples were collected from the patients once a week. The sICAM-1 level before bone marrow transplantation was measured after complete remission had been achieved and before conditioning for bone marrow transplantation.

RESULTS

Healthy persons have low sICAM-1 levels (range, 200 to 260 ng/ml). As shown in Fig. 1, sICAM-1 levels increased in a statistically significant way after bone marrow transplantation among the patients with graft versus host disease (GVHD). In particular, the sICAM-1 level of a patient (patient 5) with grade 4 chronic GVHD was greatly elevated after bone marrow transplantation. In contrast, the patients without GVHD did not have a statistically significant increase in sICAM-1. High serum sICAM-1 concentrations were detectable before the onset of chronic GVHD, indicating that this measurement may be useful in prediction of chronic GVHD. About 2 weeks after sICAM-1 level began to rise, liver dysfunction associated with chronic GVHD was observed among all the patients with GVHD.

DISCUSSION

High serum concentrations of sICAM-1 have been suggested to result from an immune response or inflammation due to chronic GVHD, but the mechanism remains unclear. It has been reported that endothelial cells are activated during allogeneic bone marrow transplantation, mainly in acute GVHD.⁹ Norton et al.,¹⁰ however, reported high expression of ICAM-1 on damaged bile duct epithelial cells of patients with chronic

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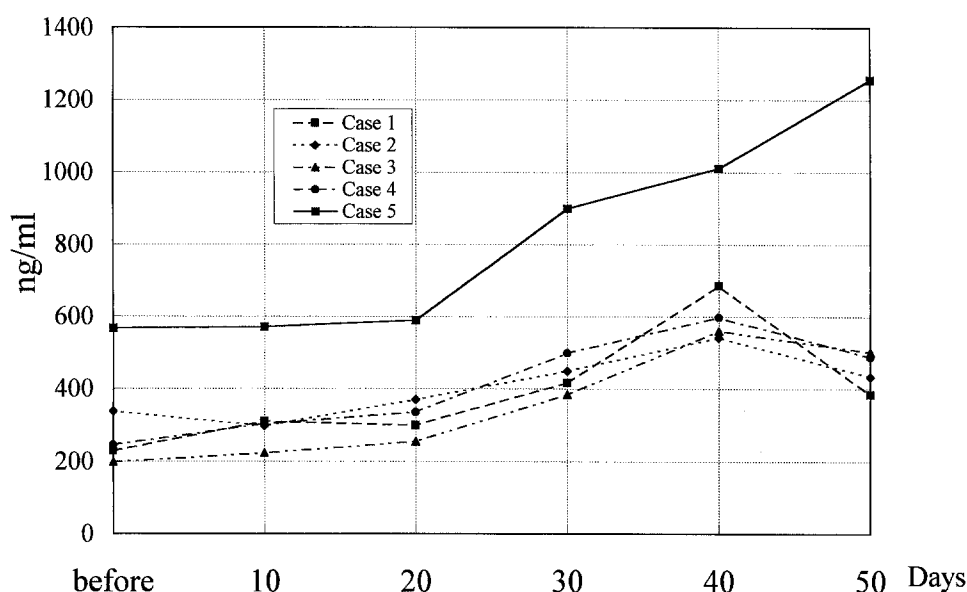


FIG. 1. Levels of serum-soluble intercellular adhesion molecule-1 (sICAM-1) among patients with graft versus host disease. High levels of sICAM-1 were detected after bone marrow transplantation.

GVHD and liver dysfunction. These findings suggest that the high serum levels of sICAM-1 seen after bone marrow transplantation in our study may be derived from endothelial or epithelial cells. Our findings suggest that monitoring of serum sICAM-1 levels may be useful in prediction of chronic GVHD after bone marrow transplantation. It has been reported that interactions between LFA-1 and ICAM-1 play an important role in several immune reactions that require cell-to-cell contact, but the role of sICAM-1 in GVHD is still uncertain. McCabe et al.¹¹ reported that sICAM-1 had some influence on T-cell proliferation or cytokine production in the presence of alloantigens. Binding of sICAM-1 to LFA-1-expressing cells may result in transmembrane signaling and thereby modulate the immune functions of these cells.¹¹ Taken together, these data suggest that elevated sICAM-1 levels induce production of cytokines after bone marrow transplantation, resulting in promotion of GVHD.

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