Circulating intercellular adhesion molecule 1 in Kawasaki disease

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要約：

We investigated whether shedding ICAM-1 antigen in sera increases during acute KD patients with and without CAL. Serum ICAM-1 levels found in patients with KD were high during the acute stage of the disease, as compared with those in control subjects. Serum ICAM-1 levels of KD patients with CAL were significantly higher than those found in patients without CAL. Our results suggest that ICAM-1 expression on endothelial cells induced by cytokines does play an important role in the pathogenesis of KD with CAL.

見出し語：Kawasaki disease, intercellular adhesion molecule 1, coronary-artery lesion, giant aneurysm, disseminated intravascular coagulation

Intercellular adhesion molecule 1(ICAM-1) is a member of the immunoglobulin supergene family and functions as a ligand for lymphocyte function associated molecule 1(LFA-1), a member of the integrin family. ICAM-1/LFA-1 mediated adhesion is important in a wide variety of immune reactions, and induction of ICAM-1 expression by cytokines in inflammation appears to be important in regulating leukocyte localization in inflammatory sites. ICAM-1 is strongly induced on epithelial cells, fibroblasts, and endothelial cells by cytokines secreted by monocytes and T lymphocytes including tumor necrosis factor α(TNF-α) and β, interleukin 1α(IL-1α) and β, and gamma interferon(IFN-γ).

It has been reported that the levels of serum cytokines, such as TNF-α, IL-1, IL-2 receptor and IFN-γ levels were increased during the acute stage of Kawasaki disease(KD).[1-3] In addition, peripheral blood mononuclear cells from acute KD patients spontaneously secreted high levels of TNF-α and IL-1.[4,5] Furthermore, we have reported that these levels of serum cytokines in a number of KD patients with coronary-artery lesion (CAL) were higher than those of patients without CAL.[3] These reports suggest that the cytokines play an important role in the exacerbation of vascular damage in KD. In the present study, we investigated whether shedding ICAM-1 antigen in sera increases during acute KD patients with and without CAL.

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The patients in this study met specific diagnostic criteria for KD. We included 16 males and 14 females, aged from one month to four years and seven months(mean, one year and seven months). The day of onset of fever was recognized as the first day of illness. Blood samples were taken for analysis of ICAM-1 levels in serum on the third to the ninth days(mean, 5.5±1.9) of illness before treatment. Two-dimentional echocardiography was used to detect the presence of CAL. In accordance with the KD cardiovascular lesion diagnostic criteria of the Research Committee on Kawasaki Disease, Ministry of Health and Welfare, Japan, coronary arteries with diameters of 4mm or greater were regarded as showing the presence of CAL.[6] The control subjects were 10 healthy children, six males and four females aged from four months to four years and seven months(mean, two years). Serum ICAM-1 levels were measured by a double determinant immunoassay using two monoclonal antibodies, designated HA58 and CL207, each of which recognizes different epitope of ICAM-1 in the F.A.S.T. system as previously reported by us.[7] Results were expressed as units(one unit corresponds to 2ng of purified antigen) calculated from the titration curve of ICAM-1 antigen. During a 30-day period after the onset of the disease, seven KD patients in this study had CAL. A two years and nine month-old KD patient had giant aneurysm of coronary artery with diameters 8mm. An eleven month-old KD patient without CAL was complicated by disseminated intravascular coagulation(DIC) during the acute stage. Figure shows serum ICAM-1 levels during acute KD patients and of control subjects. Serum ICAM-1 levels found in patients with KD were high during the acute stage of the disease(mean±SD, 131.8±84.3), as compared with those in control subjects(64.1±13.2, $p<0.01$). The increased ICAM-1 levels during the acute stage returned to within the normal range during the convalescent stage. In addition, serum ICAM-1 levels of KD patients with CAL were significantly higher than those found in patients without CAL($p<0.01$). It is noted that serum ICAM-1 level as well as TNF-α in a patient with giant aneurysm was markedly elevated during the acute stage of the disease. It is also an interesting that serum ICAM-1 level in a patient complicated by DIC was seen to increase during the acute stage.

It remains unclear that the increased ICAM-1 in sera of acute KD patients may be regulated by shedding on endothelial cells. It has been reported that expression of ICAM-1 on endothelial cells was detected by means of immunoperoxidase staining in skin biopsy samples from acute KD patients.[5] It is therefore likely that the increased ICAM-1 levels in KD patients may reflect the activation of endothelial cells during acute stage of the disease. Our results in the present and previous studies suggest that ICAM-1 expression on endothelial cells induced by cytokines, especially TNF-α, does play an important role in the pathogenesis of KD with CAL.

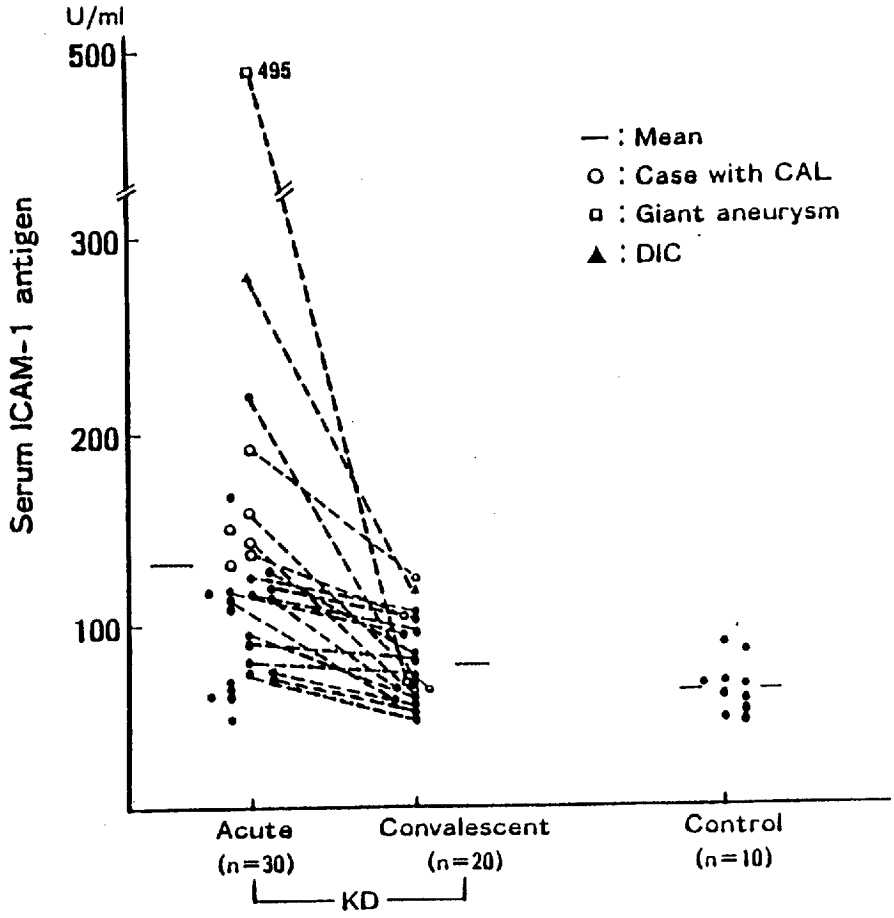

Figure. Serum ICAM-1 levels during acute Kawasaki disease and of control subjects.
ICAM-1=intercellular adhesion molecule 1
CAL=coronary-artery lesion
DIC=disseminated intravascular coagulation

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