LEVELS OF SERUM VASCULAR CELL ADHESION MOLECULE-1 IN MEASLES

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Abstract. While the levels of serum vascular cell adhesion molecule-1 (VCAM-1) have been investigated in many diseases, they have not, to our knowledge, been studied in patients with measles. Serum VCAM-1 and creatinine levels were determined in six adolescent and adult Japanese patients with measles in the acute febrile phase and defervescent afebrile phase. Serum VCAM-1 levels were significantly higher in the acute febrile phase than in the convalescent afebrile phase, but no significant difference between the serum creatinine levels was shown in the two phases. Our study revealed that the high serum VCAM-1 level in the acute febrile phase later decreased in the afebrile convalescent phase. The measurement of circulating VCAM-1 may be useful for the assessment of convalescence in patients with measles.

INTRODUCTION

Measles is an acute febrile and eruptive disease caused by infection with the measles virus. Although usually benign, measles may be complicated by numerous illnesses, and no effective drugs to eradicate the virus have yet been developed. Many Japanese adolescents and adults suffer from measles every year (Infections Disease Surveillance Center), most likely due to poor administration of measles vaccine, and the infection has substantial clinical and economic impact in Japan.

Vascular cell adhesion molecule-1 (VCAM-1) is a member of the immunoglobulin superfamily and binds cells expressing the very late antigen 4 ($\alpha1\beta1$) and $\alpha4\beta7$. Serum levels of VCAM-1 are now routinely measured in clinical laboratories and monitored in many diseases. Although serum VCAM-1 has been reported to be elevated in some infectious diseases, *eg*, falciparum malaria (Boehme *et al*, 1994), vivax malaria (Ohnishi, 1999), Q fever (Ohnishi and Kimura, 1999), and septic shock (Gearing and Newman, 1993), to our knowledge, serum VCAM-1 levels have not been investigated in patients with measles. In this study we measured the serum levels of VCAM-1 in the acute febrile and convalescent afebrile phases of measles in adolescent and adult patients.

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PATIENTS AND METHODS

Patients

Levels of serum VCAM-1 and creatinine were measured in the acute febrile and convalescent afebrile phases in six Japanese patients with measles admitted to the Department of Infectious Disease, Tokyo Metropolitan Bokutoh General Hospital. There were 4 male and 2 female patients with age range of 16-39 years old (mean 32 years old). The profiles of the patients are shown in Table 1. All of the patients had contracted the disease in Japan and were diagnosed by confirming the elevation of serum IgM antibody against the measles virus and the presence of characteristic clinical signs, *ie* small maculopapular rash, fever, Koplik's spots, and lymphoadenopathy. None of the patients had evidence of infectious diseases other than measles. Serum creatinine levels were measured immediately and the serum

samples were stored at -80ºC until the assays for VCAM-1.

Informed consent for participation in the study was obtained from all the patients.

Assays

The serum VCAM-1 was measured with commercially available one-step sandwich ELISA kits (R & D System Europe, Abingdon, UK). The assays were performed according to the manufacturer's instructions with the reagents provided. The serum creatinine levels were measured by a creatinine enzyme method (Iatron, Tokyo, Japan): the normal creatinine levels were 0.4~1.1mg/dl.

Statistical analysis

Student's *t*-test was used to assess the differences between values recorded during the acute febrile and convalescent afebrile phases. A level of $p<0.05$ was considered statistically significant.

RESULTS

The levels of serum VCAM-1 in the acute febrile and convalescent afebrile phases are shown in Fig 1. Levels of serum VCAM-1 were significantly higher in the acute febrile phase than in the convalescent afebrile phase.

The level of serum creatinine in the acute febrile and convalescent afebrile phases are shown in Fig 2. The serum creatinine levels of all the patients were in the normal range in both phases, and no significant differences between phases were identified.

DISCUSSION

Although only small numbers were involved, our study revealed that circulating levels of VCAM-1 in measles patients were significantly higher in the acute febrile phase than in the convalecent afebrile phases. While patients with renal failure are well known to have higher serum VCAM-1 level than controls, the elevated serum VCAM-1 levels in our patients

Table 1
Profiles of the patients.

Total number : 6; Man /Woman :4/2
Age : 16~39 years (mean 22.7)
Sampling:
acute febrile phase : 5~8 days of illness
convalescent afebrile phase : 15~20 days of illness

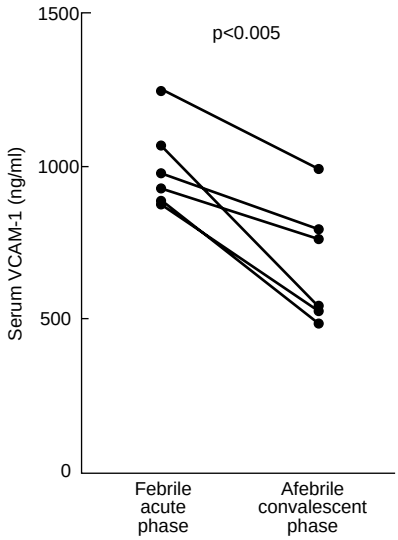

Fig 1–Level of serum VCAM-1 in the acute febrile and convalescent afebrile phases.

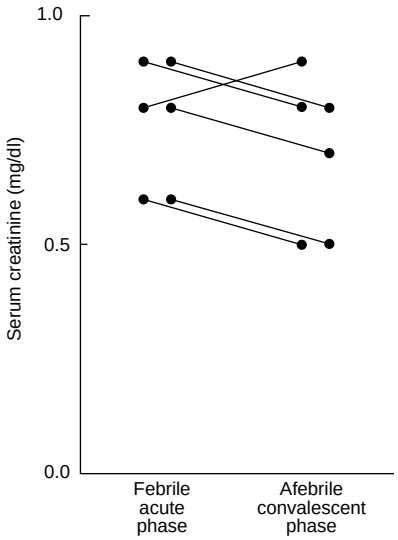

Fig 2–The levels of serum creatinine in the acute febrile and convalescent afebrile phases.

could not be attributed to delayed renal clearance. The normal creatinine levels in our patients, and the absence of any significant difference in creatinine levels between the acute febrile and convalescent afebrile phases, confirmed the absence of renal failure in our study.

We did not investigate the mechanism of VCAM-1 elevation in this study. The measles virus can infect endothelial cells in culture (Cronka *et al*, 1990), and it has been visualized in the vascular endothelial cells of the lung, gut, bile duct and bladder (Moench *et al*, 1988), and in the brain in cases of acute fatal measles (Esoler *et al*, 1995). The elevation of serum VCAM-1 levels may be due to the production of VCAM-1 on the surface of endothelial cells that are infected with measles virus. Although VCAM-1 has been demonstrated *in vitro* in supernatants of TNF-α- and IL-1β-stimulated endothelial cells (Pigott *et al*, 1992), we know that these cytokines may not play an important role in regulating serum VCAM-1 levels in patients with measles because peripheral blood monocytes from patients with measles have been shown to produce normal levels of IL-1β during the acute phase and increased levels of IL-1β during convalescence, whereas TNF-α prodution was decreased in both periods (Ward *et al*, 1991).

In the present study, elevated serum VCAM-1 levels were identified in the acute febrile phase of measles; these levels decreased during the convalescent afebrile phase. Although more studies are needed, particularly on the mechanism underlying elevation of serum VCAM-1 levels during the febrile phase, the measurement of serum VCAM-1 may be of use in the assessment of convalescence in adolescent and adult patients with measles.

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