Tokai J Exp Clin Med., Vol. 23, No. 2, pp.79-80, 1998

Different Plasma Levels of Circulating Cell Adhesion Molecules in Falciparum Malaria Patients According to Disease Severity

Yoshitsugu MATSUMOTO, Toshimitsu NAYA, Christian A. DARKO, Yuko KATAKAI, Shigeyuki KANO*, Mamoru SUZUKI*, Polrat WILAIRATANA**, Sornchai LOOAREESUWAN**, Gary M. BRITTENHAM*** and Masamichi AIKAWA****

School of Agriculture and Life Sciences, University of Tokyo, Tokyo, Japan
**School of Medicine, Gunma University, Gunma, Japan*
***Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*
****Case Western Reserve University, Cleveland, OH, USA*
*****Tokai University, Kanagawa, Japan*

One of the most prominent pathological feature of falciparum malaria is the sequestration of infected red blood cells (IRBCs) in small blood vessels, which is considered to be a major cause of cerebral malaria. It is clear that several different host molecules including intercellular adhesion molecule 1 (ICAM-1) and vascular cell adhesion molecule 1 (VCAM-1) act as receptors for IRBCs *in vitro*. Expression of ICAM-1 on human vascular endothelium can be upregulated by the proinflammatory cytokines, tumour necrosis factor (TNF) and interleukin 1α (IL-1α). These cytokines are present at high levels in the plasma of malaria infected children and elevated levels are related to disease severity. Thus high levels of these cytokines may exacerbate IRBC sequestration by upregulating ICAM-1 expression on endothelium. A direct measurement of expression of adhesion molecules (CAMs) on cell surface is difficult. It has been, however, shown that CAMs expression on the endothelial cells correlates with plasma levels of circulating adhesion molecules (cCAMs) which is shed into the circulation from those cells. Cell adhesion molecules are well known to play an important role during immune resposes. Circulating forms of these molecules have been described pathophysiologically correlated with a variety of inflammatory and infectious diseases (ex. AIDS), graft rejection and autoimmune diseases.

In this study, we examined plasma levels of circulating forms of ICAM-1, ICAM-2, ICAM-3, VCAM-1, and ELAM-1 (cICAM-1, cICAM-2, cICAM-3, cVCAM-1, and cELAM-1 respectively) in patients with complicated or uncomplicated malaria and compared them to uninfected healthy persons. As part of a large scale study on cerebral malaria, plasma samples were obtained from malaria patients who admitted to the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, on the admission day, and Thai volunteers who were not suffering from malaria. Plasma samples were also obtained from Japanese volunteers who had no experience of malaria. Malaria patients were divided into two groups, mild, that is uncomplicated, malaria group and complicated malaria group. The latter was further divided into moderate, severe, and highly severe malaria groups according to the severity of clinical manifestations including central nervous dysfunction, anaemia, hypoglycaemia and so on. All samples were stored frozen at −20℃ until used. Randomly 20 samples from each malaria group (mild, moderate, severe, or highly severe group) and Thai uninfected volunteers and 13 samples from healthy Japanese uninfected volunteers were chosen and examined. Plasma levels of all cCAMs were measured by a quantitative enzyme-linked immunosorbent assay.

Plasma levels of all cCAMs examined were significantly higher in malaria patients compared to uninfected Thai and Japanese persons. The results also show that among malaria patients, cICAM-1 and cELAM-1 lev-

Yoshitsugu MATSUMOTO, Department of Applied Immunology, School of Agriculture and Life Science, University of Tokyo, Yayoi-chou 1-1-1, Bunkyo-ku, Tokyo 113-0032, Japan

els were significantly, and cVCAM-1 was slightly, higher in the complicated malaria groups compared to the uncomplicated malaria groups. No differences between patients with complicated and uncomplicated malaria were observed concerning cICAM-2 and cICAM-3. These results provide evidence that plasma levels of cICAM-1 and cELAM-1 correlate with malaria severity and thus those are involved in the pathophysiology of complicated malaria. In this study we could not differenciate between the plasma levels of cCAMs from patients with cerebral malaria and those with severe malaria without cerebral involvement because of limited numbers of samples. The functional roles of those cCAMs in the disease have remained unsolved. As cCAMs can interfere with intercellular adhesion, the high level of cCAMs in malaria patients could contribute to the impairment of immune responses resulting in progression of the disease. On the other hand, at concentration lower than we have detected in the plasma of malaria patients cICAM-1 has been shown to be enough to inhibit IRBC binding to ICAM-1 in an *in vitro* binding assay. Understanding the pathophysiological function of such cCAMs may give rise to new approaches to the treatment and diagnosis of complications of malaria.