CYTOADHERENCE CHARACTERISTICS OF *Plasmodium falciparum* ISOLATES AND CYTOKINE RESPONSE IN PLACENTAL MALARIA INFECTION

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PLASMODIUM FALCIPARUM and the Cytokine Response in Placental Malaria Infection (Cytoadherence Characteristics of Plasmodium falciparum Isolates and Cytokine Response in Placental Malaria Infection)

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Abstract

In the study of cytoadherence of Plasmodium falciparum, the host receptor chondroitin sulfate (CS) A, which is a host receptor for Plasmodium falciparum, was investigated. The chondroitin sulfate A receptor was found in the placenta, and its interaction with Plasmodium falciparum was investigated. The authors found that the cytoadherence characteristics of Plasmodium falciparum isolates varied in placental malaria infection. The cytokine response in placental malaria infection was also studied, and it was found that the cytokine response varied in placental malaria infection. The study concluded that the cytokine response in placental malaria infection is influenced by the host and parasite variability.
In this study, cytoadherence of wild parasite isolates to chondroitin sulfate (CS) A, an important host receptor for Plasmodium falciparum-infected erythrocytes in placenta, and certain aspects of cell-mediated immunity in protection against placental malaria (PM) were investigated.

Differences in the characteristics of parasitized erythrocyte (PE) adhesion with respect to site and ligand domain reflects the heterogeneity of the parasite. In vitro competitive inhibition assays were employed to define structural requirements for adhesion of both wild and laboratory parasite isolates to CSA. Various glycosaminoglycans and polysulfated compounds including certain drugs were used as inhibitors to determine their interference with PE adhesion. The results suggested that disaccharide structure of -4GlcAβ1-3GalNAc-1 and the degree of sulfation are critical for the PE adhesion. We also demonstrated for the first time the variation in the degree of adherence to different chondroitin sulfates among wild isolates. Specific adherence of PE to CSD and CSE as well as heparin interference on CSA-mediated cytoadherence of PE were observed.

In the area cell-mediated immunity, cytokine responses were examined in PM and in relation to human immunodeficiency virus (HIV)/PM co-infection. In vitro cytokine responses by intervillous blood mononuclear cells (IVBMC) from HIV-seropositive and HIV-seronegative women both with and without PM were investigated. In both HIV and HIV/PM co-infection, the severely defective production of interleukin (IL)-12, but not IL-18 and interferon inducible protein (IP)-10, has been suggested to be a critical factor contributing to impaired IFN-γ production, leading to the loss of protection against PM.

Macrophage migration inhibitory factor (MIF) levels were also investigated in the plasma of pregnant women with PM and/or HIV infection. MIF levels in the intervillous blood (IVB) plasma were significantly elevated compared with peripheral and cord plasma. PM, but not HIV, significantly up-regulated MIF levels in IVB plasma. In vitro MIF responses by IVBMC were significantly higher when compared with PBMC. Immunoperoxidase staining showed a consistent pattern of MIF expression in the syncytiotrophoblasts (SCT), extravillous trophoblasts, IVB cells and amniotic epithelial cells (AEC). Cytotrophoblasts, villous stroma, and Hofbauer cells demonstrated focalized staining. AEC and SCT from malaria-infected placenta consistently exhibited strong expression of MIF whereas those from non-infected placenta showed weak expression. Malaria parasites can induce in vitro MIF production in a human trophoblast cell line (BeWo).

Taken together, the results of the study imply that difference in pathogenic processes leading to varying clinical manifestations depend not only on heterogeneity of parasite factors, but also host factors.

KEY WORDS: PLACENTAL MALARIA/ CYTOADHERENCE/ CYTOKINE/ HIV