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CTLA-4 and Its Ligands on the Surface of T- and B-Lymphocyte Subsets in Chronic Hepatitis B Virus Infection

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Abstract

Background: During chronic hepatitis B virus (CHB) infection, a number of co-stimulatory, co-inhibitory molecules and theirs ligands play a prominent role in the immune-regulation.
Objective: To compare the number of peripheral-blood mononuclear cells expressing co-inhibitory marker, cytotoxic T lymphocyte associated antigen-4 (CTLA-4) and program cell death ligand-1 (PD-L1) between CHB infected patients and healthy controls.
Material and Method: Peripheral-blood mononuclear cells (PBMCs) from 19 CHB-infected patients and nine healthy controls were stained with specific combinations of the following monoclonal antibodies: CD3-PE/cy5, CD4-APC, CD8-APC, CD152-PE (CTLA-4), CD19PE/Cy5, CD80-FITC (B7-1), CD86-PE (B7-2) and CD274-FITC (B7-H1) according to standard protocol.
Results: The frequencies of B-lymphocyte expressing B7-1, B7-2 and B7-H1 of CHB-infected patients and healthy controls were not shown any statistical differences. The mean percentage of B-lymphocyte with B7-2 molecule was higher than those with B7-1 molecules in both infected- and non-infected groups. In contrast, the frequencies of T-lymphocyte subsets, CD3+, CD4+ and CD8+ expressing CTLA-4 molecules in CHB-infected patients were significantly higher than those in healthy controls with p = 0.04, 0.01 and 0.04 respectively.
Conclusion: An increase in percentage of circulating CD4+/CD152+ (T-cell) was observed in CHB infected patients. A small but significant increase in percentage of CD8+/CD152+ T-cells raises the possibility that CTLA-4 are involved in the development of HBV-specific CD8+ T-cell exhaustion. Overall, CD4+ and CD8+ T-cells presenting CTLA-4 might contribute to the impaired immune response and likely to be a factor influencing in failure of immunological control of the persisting pathogens.

Keywords: Chronic hepatitis B virus, Co-stimulatory molecules, CTLA-4, Ligands, Immune-regulation, Lymphocyte subsets, Flow cytometer

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