IMMUNOLOGIC CONSEQUENCES OF HIV INFECTION

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Abstract

The impact of HIV infection on the immune system has been extensively studied over the past 15 years. We now recognize several important immunopathogenic consequences of HIV infection including CD4+ induced immunodeficiency, immune activation mediated immune dysfunction and cytokine dysregulation. The major target of HIV being the CD4+ helper T cell leads to its depletion and impacts on CD8+ effector, B cell and natural killer cell function. The mechanism of CD4+ cell loss has been proposed to be due to direct depletion of HIV or indirectly by programmed cell death. The loss of CD4+ cell number, although a hallmark feature of HIV infection, is preceded by a loss of CD4+ function. CD4+ functional changes follow a hierarchical loss of antigen, alloantigen and mitogen proliferative activity. Loss of HIV specific antigen reactive CD4+ cells has been proposed to result in a decline of CD8+ effector function. This CD8+ activity has been shown to be mediated by cytotoxic effector cells or CD8+ cells producing factors (i.e., chemokines) capable of suppressing viral replication. The lack of HIV specific T helper function may be a direct effect of HIV on this cell population or indirect effect on antigen presenting cell function. Antigen presenting cells consist of both the macrophage/monocyte and dendritic cell family and are targets for HIV infection based on their CD4 antigen expression. In addition to CD4+ cell depletion, immune activation is a major immunopathogenic consequence of HIV infection. The markers that characterize this activation state include HLA-DR and CD38. The level of expression of these immune activation markers correlates with both CD4+ count (inverse association) and viral load (direct association). In vivo immune activation predisposes CD4+ cells to undergo apoptosis when engaged in antigen specific responses instead of cellular proliferation and IL2 production. Immune activation markers have been extensively studied on CD8+ cells and in vivo quantitative levels of activation antigens on CD8+ T cells have been shown to predict the clinical course of a patient. Another major immunopathogenic factor in HIV infection is cytokine dysregulation. The major category of cytokines involved include proinflammatory cytokines (IL1, IL6, TNF) which directly activate HIV replication, immunity, and chemokines (MIP1 MIP1 RANTES) which can block viral infection by binding to the HIV co-receptor. These cytokines have been shown to be differentially altered in the course of HIV disease both in the blood and lymphoid tissue. In summary this presentation will highlight the immunologic consequence of HIV infection and the immunologic tools that have been developed to evaluate the impact of this virus on the immune system.

*Paper not available.