CD4 T Lymphocyte Activation in Acute Severe Asthma

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Abstract

The expression of activation molecules on peripheral-blood CD4 and CD8 T lymphocytes and the serum concentrations of two products of activated T lymphocytes [interferon-γ (IFN-γ) and soluble interleukin-2 receptor (sIL-2R)] were measured in patients with acute severe asthma (ASA) and controls. Significantly higher percentages of CD4+ cells from patients with ASA expressed IL-2R, HLA-DR and VLA-1 as compared to controls (p <0.01). In contrast, CD8+ cells from both asthmatics and controls did not express IL-2R and VLA-1, and their expression of HLA-DR in asthmatics was not increased. Serum concentrations of IFN-γ and sIL-2R were significantly elevated in patients with ASA as compared to control groups (p <0.01). Concentrations decreased as the patients improved clinically following therapy. Significant correlations were observed between the improvements in airways obstruction and (1) the decreases in the percentages of peripheral-blood IL-2R+ T lymphocytes and (2) the decreases in serum concentrations of sIL-2R. These observations suggest that CD4 T lymphocyte activation is important in the pathogenesis of ASA.

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part, from activated T lymphocytes. Unstimulated peripheral-blood mononuclear cells (PBMC) from ASA patients were cultured in vitro. Supernatants were tested for NCA using a Boyden chamber technique. PBMC from patients with ASA produced significantly (p < 0.01) greater amounts of NCA than those from controls. NCA release was inhibited by cycloheximide. There was no correlation between NCA and the numbers of contaminating basophils. Separation of monocytes and T cells prior to culture revealed that NCA was produced by both cell types. The NCA produced by PBMC from ASA patients was significantly reduced (p < 0.01) after therapy, to an extent which could be correlated (p < 0.02) with the degree of clinical improvement.

Physicochemical characterization of NCA released exclusively by PBMC from asthmatics indicated that it was associated with proteins of molecular size 12–25 kilodaltons and pi 8.3. It was not inhibited by a monoclonal anti-interleukin-8 antibody which, at the same concentration, completely inhibited the activity of optimal concentrations of human recombinant interleukin-8, suggesting that it is distinguishable from this activity.

Taken together these observations provide evidence that activated CD4 T lymphocytes and monocytes, both of which play a fundamental role in ‘cell-mediated’ inflammation, may be implicated in the pathogenesis of severe asthma.