“Sarcoidosis in a Patient with Rheumatoid Arthritis Treated with Etanercept: The Critical Role of the CD4+ Cell Dependent Type 1 Helper T Response”

Key words: sarcoidosis, etanercept, rheumatoid arthritis, TNF-α, interferon-γ, CD4+ cell


To the Editor

We read with interest the case report “Development of Sarcoidosis during Etanercept Therapy” by Ishiguro et al (1). We believe that this case can highlight the importance of the CD4+-cell-dependent type 1 helper T (Th1) response in sarcoidosis and we would like to add several studies of interest to their discussion. Prior to the advent of highly active antiretroviral therapy, new-onset sarcoidosis occurred only rarely in HIV-infected patients. Morris et al (2) noted that the sarcoid response appeared to depend on the preservation or restoration of the peripheral CD4+ lymphocyte count, and in most cases it was not seen at counts of less than 200 cells per cubic millimeter. These associations illustrate, in an unusual experiment of nature, the pivotal role of CD4+ T cells in sarcoidosis and HIV infection.

Type 1 and type 2 T cells play a significant regulatory role in rheumatoid arthritis (RA). van Roon et al. (3) have shown that in RA the cytokine pattern of blood T cells shows relative predominance of interleukin (IL)-4 over interferon-γ (IFN-γ). This suggests that the potency of T1 over T2 cell activity is lower in the blood of RA patients than in healthy controls. Likewise, an inverse relationship between serum tumor necrosis factor-alpha (TNF-α) levels and the ratio IFN-γ: IL-4 production of peripheral blood T cells was observed. In this study of van Roon et al., IFN-γ production decreased whereas IL-4 production increased with increasing joint damage, and a decrease in IFN-γ was correlated with an increase in TNF-α and C-reactive protein.

On the other hand, sarcoidosis can complicate treatment with interferon alfa (4). In vitro, interferon alfa causes T cells to produce large amounts of IFN-γ and limited amounts of IL-4 and IL-5, suggesting that interferon alfa favors the development and enhancement of type 1 helper responses. In another study of interest (5), phenotypic analysis of peripheral blood T cell subsets was performed on blood from RA patients before and after treatment with monoclonal anti-TNF-α antibody. In that study (5), an increase in the number of CD4+ T cells expressing the homing receptor CD49d in high density was observed after treatment, and the number of IFN-γ-producing T cells was significantly increased after treatment with monoclonal anti-TNF-α antibody. It resulted in a significant rise in the Th 1: Th 2 ratio.

These studies support the second hypothesis proposed by Ishiguro et al in the discussion of their case report.

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References