


IL-6 and some natural inhibitors of chronic human inflammation in RA and SLE

Sir,

The role of IL-6 in chronic inflammation is hotly debated (1). It is thought to be pro-inflammatory in some experimental models of arthritis (2) while in others it seems to be protective (3). One of the ways by which IL-6 may become protective is through the stimulation of the synthesis of some cytokine antagonists, among which TNF R type I (tumor necrosis factor soluble receptor type I-TNF RI) and IL-1 receptor antagonist (IL-1Ra) receptors in systemic lupus erythematosus (SLE), derived from data on serum circulating levels.

We followed 15 patients with rheumatoid arthritis (RA) longitudinally for a period of six months, seeing them at entry into the study, and at months 1, 3 and 6 (60 assays) and tested serum IL-6, TNF RI (p55), IL-1 receptor antagonist (IL-1Ra) and several other parameters. We observed a strong correlation between IL-6 and TNF RI, as well as between IL-6 and CRP (C reactive protein) values. However, no such relationship was seen between IL-6 values and IL-1Ra levels (Fig. 1). Thus, in RA we observed that the higher the initial IL-6 (interleukin 6) response, the stronger appeared to be the synthesis and shedding of soluble TNF RI, but not that of IL-1Ra.

On the other hand, the relationship between IL-6 levels and TNF RI was confirmed in another chronic inflammatory disease, SLE (28 samples: R = 0.42, p < 0.04). No relationship was found between IL-6 and IL-1Ra. In SLE high levels of IL-1Ra were seen (17 patients) while the IL-6 levels were half those usually found in RA (2).

Therefore certain natural inhibitors such as TNF RI seem to be strongly correlated with IL-6 in chronic human inflammatory disorders such as RA and SLE, while others such as IL1 Ra are not. This suggests that IL-6 may act as an inducer of the synthesis and shedding of TNF RI.

The available data in vivo suggest that IL-6 deserves a new look by those studying chronic inflammatory diseases, as a potential indirect antagonist of the tissue damage induced by TNFα through the synthesis and shedding of TNF RI.

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References


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![Fig. 1. Correlations over time between IL-6 (pg/ml) and TNF RI (pg/ml), IL-1 Ra (pg/ml), and CRP levels (mg/L) in rheumatoid arthritis.](image)