T cell differentiation in autoimmune diseases
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Chapter 7

Prognostic value of Th1/Th2 ratio in rheumatoid arthritis

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Prognostic value of Th1/Th2 ratio in rheumatoid arthritis

Imbalance between proinflammatory T-helper-1 (Th1) and anti-inflammatory T-helper-2 (Th2) cells and, subsequently, their products interferon-γ and interleukin 4, respectively, is believed to be important in the development of autoimmune diseases. Dominance of Th1 over Th2 cells is thought to be important in the pathogenesis of rheumatoid arthritis.\textsuperscript{2,3} We investigated whether the Th1/Th2 ratio in the peripheral blood of patients with rheumatoid arthritis is related to disease severity, measured by response to disease-modifying antirheumatic drugs (DMARDs).

We recruited patients with early rheumatoid arthritis (duration ≤1 year) who had not previously taken DMARDs. We determined disease activity by a modified disease activity score\textsuperscript{4} based on scores for 28 joints. 11 patients with high disease activity (scores ≥6-0, median 6-4 [range 6-0-6-9]) were started on DMARDs; ten on sulphasalazine (2000 mg/day), one on hydroxychloroquine (200 mg/day). We measured Th1/Th2 ratios in peripheral blood by intracellular staining assay with flowcytometric analysis.\textsuperscript{5} The percentages of Th1 and Th2 cells were determined by double staining for CD4 and either interferon-γ or interleukin-4. Data were analysed with Wilcoxon's signed rank test. The median disease activity score decreased to 5-0 (range 3-3-6-9) after 3 months and 4-5 (range 2-9-7-1) after 9 months of therapy. Although activity scores were within a narrow range at baseline, we found large differences in Th1/Th2 ratios between patients. Th1/Th2 ratios did not correlate with disease activity scores or C-reactive-protein concentrations (data not shown). During the first 3 months of therapy, Th1/Th2 ratios increased significantly (median 3-2 vs 6-0, $p=0\cdot001$) because of decreases in Th2 cells (median 5-0 vs 2-3%, $p=0\cdot002$). After 9 months the initial Th1/Th2 ratio did not differ (median 3-2 vs 4-8; $p=0\cdot16$).

This transient increase in the Th1/Th2 ratio during the first 3 months of treatment could have resulted from redistribution of Th1 and Th2 subsets, immunoregulatory effects of the medication, or from a combination of both. The effect, however, seemed to be of no importance to the clinical outcome since changes in the Th1/Th2 ratios and disease activity scores did not correlate after 3 months or 9 months. By contrast, the initial Th1/Th2 ratio correlated significantly with the disease activity score after 9 months (figure).

These data suggest that patients with low Th1/Th2 ratios in the peripheral blood during clinical active phases of rheumatoid arthritis are likely to respond well to the first course of DMARD treatment. The prognostic value of the Th1/Th2 ratio measured by intracellular staining assay in early rheumatoid arthritis needs to be assessed in larger groups of patients for longer times.

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Correlation between Th1/Th2 ratio before treatment and disease activity score after 9 months

References


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