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Gottenberg et al. [1] studied 50 patients with RA: 36% had raised sFLCs with mean values significantly higher than controls (p<0.001) (Figure 35.6), while \( \kappa/\lambda \) sFLC ratios were normal in all but three patients. sFLC concentrations were significantly correlated with IgG (p≤0.04), CRP (p≤0.04), and rheumatoid factor (for \( \kappa \) only; p=0.03), but not with anti-cyclic citrullinated peptide (CCP) antibodies. Significant correlations were observed between disease activity assessed by the Disease Activity Score 28 (DAS28) and both \( \kappa \) (p=0.0004; Figure 35.8) and \( \lambda \) sFLC concentrations (p=0.05; data not shown). Other studies by Ye [2], Djidjik [3] and Garcia de Veas Silva [4] have also identified a correlation between sFLC elevations and disease activity in RA. sFLC concentrations as determined by ELISA were greater in RA patients and correlated with disease activity, whilst the FLC concentrations in synovial fluid were increased, suggesting local production [5]. Further indication of local production was provided by synovial tissue cells staining positively for FLC and CD138 (Syndecan 1; a plasma cell marker) and these findings support the functional relationship between B-cells and disease activity. Interestingly, no correlation was observed between DAS28 and IgG [1]. This may be explained by the longer half-life of IgG (approximately 21 days) compared with sFLCs (2 to 6 hours, Section 35.5). The fast turnover of sFLCs might account for their observed correlation with disease activity.
In a further study including 710 patients with arthritis, Gottenburg et al. [6] found that polyclonal FLCs (and other markers of B-cell activation) were higher in early RA than in undifferentiated arthritis. The authors concluded that B-cell activation is an early pathogenic event in the disease. This was supported by data from the Mayo Clinic: A focused, further analysis of their general population cohort (Section 35.10) revealed increased SFLC concentrations in RA patients (n=270), which were not explained by any differences in eGFR, Deng et al. [7] studied sFLC concentrations in 127 individuals prior to the onset of RA and showed that elevations in SFLC could be recognised 3 to 5 years before RA diagnosis (Figure 35.9). During follow-up, SFLC increased at a rate of approximately 1% per year until RA diagnosis, and 3% per year thereafter. The top decile of SFLC (>47.2 mg/L) was associated with an increased risk of mortality, although this was similar to that reported in the general population cohort (Section 35.10)[8].

In addition to the studies investigating correlations between sFLCs and disease activity, others have assessed the utility of sFLC measurements in assessing response to treatment in RA. Kormelink et al. [5] measured sFLC concentrations at 3 and 6 months following treatment with rituximab (for depletion of CD20-positive cells) and found that they were reduced more significantly in clinical responders than in non-responders, and did not correlate well with intact immunoglobulin measurements. Sellam et al. [9] compared baseline concentrations of various markers in 208 RA patients and found that elevated IgG, presence of rheumatoid factor or anti-CCP antibodies were predictive of response to rituximab, whereas sFLC concentrations were not. Unfortunately, the changes in serum markers in response to treatment were not recorded. A further study of rituximab treatment in 28 RA patients indicated that monitoring changes in sFLC concentrations (and other serum markers) was the most informative way of assessing response to treatment and identifying relapse [10].

Figures

Figure 35.8. Correlation between sFLC concentrations and Disease Activity Score 28 (DAS28) in patients with RA.
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Figure 35.9. FLC concentrations prior to clinical onset of RA and during follow-up.

Red line = trend for RA patients with 95% confidence interval. Black line = trend for general population. (Reproduced with permission from the Journal of Rheumatology)

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References


