Editorial

Which elements of the criteria for RA are stable over time?

Low seroconversion rate of anti-CCP2 and RF in early inflammatory arthritis


Early diagnosis of RA is increasingly recognized as an essential step towards better patient care. Detection of autoantibodies such as RF and especially ACPA have proved valuable for early identification of patients with early arthritis at risk of developing RA [1]. The presence of ACPA has been shown to be predictive of development of RA [2] and associates with more severe diseases [3], suggesting a possible pathogenic role for these autoantibodies. Functional studies also implicate such a role as ACPA can trigger Fc receptors on inflammatory cells [4] and can activate the complement system [5]. Data derived from mouse studies confirm the hypothesis that ACPA may be pathogenic [6, 7]. Prediction rules and new criteria have been developed to diagnose RA earlier [8, 9]. These prediction rules are based on the 1987 RA criteria [10], which define a phenotype on which most of our pathophysiological studies are based. It has now become clear that this phenotype consists of two syndromes: ACPA-positive and ACPA-negative disease that differ by genetic risk factors, histology, clinical course and response to treatment [11–15]. The new criteria are partly based on the decision to start MTX therapy, which allows the inclusion of a much more heterogeneous phenotype [8]. It is no wonder that the working group that developed the 2010 criteria stressed in their discussion that the patients fulfilling the 2010 criteria are probably less homogeneous and that therefore in clinical trials researchers should document both the proportions of study subjects that fulfil the previous (1987) and new RA classification criteria to enable comparisons. Moreover, the working group warned that the 2010 criteria may probably increase heterogeneity by including different phenotypes, thereby making basic science studies more difficult. Therefore, it is very useful to know which of the individual criteria can change over time. Obviously, the clinical features can change, but recently both the specificity and sensitivity of erosions have been studied [16] and it has become clear that erosions may heal over time [17], indicating that both clinical features and erosions are not stable over time. Therefore, it is very timely to study how often seroconversion can occur. In this issue of Rheumatology, Barra et al. [18] describe a systematic literature review regarding the seroconversion of RF and ACPA (anti-CCP) in patients with early inflammatory arthritis. In this study, they set out to answer the question of what percentage of patients with early inflammatory arthritis undergo seroconversion from negative to positive for RF or ACPA at 1 or 5 years of follow-up [18]. After careful selection of the available data, the authors present data describing a 1.3–8.9% seroconversion rate for RF at 30 months and a 1.9–5.0% seroconversion rate for ACPA at 60 months. Collectively these studies indicate a low seroconversion rate for these autoantibodies in early inflammatory arthritis. These seroconversion rates may even be overestimated a bit because the small studies that use commercial assays show lower seroconversion rates. Also the titre of ACPA and RF is important in this context, since it is likely that these few people that show seroconversion are likely to be of low titre indicating that high titre autoantibodies the seroconversion rate is even lower.

In view of the low and variable baseline positivity for RF and ACPA and the low seroconversion rate, it is interesting to note that in established RA the percentage positivity for RF and ACPA is significantly higher. The authors describe that, as only 7–19% of early inflammatory arthritis patients are diagnosed with RA at follow-up, these data may indicate that most patients that are negative for these autoantibodies will either remit or remain diagnosed as early inflammatory arthritis. These data are in line with previous observations that positivity for ACPA during undifferentiated arthritis predisposes strongly to the development of RA [1]. This systematic literature review now adds to these data that seroconversion of RF and or ACPA does not add significantly to this process.

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