Radiographic damage occurs early in rheumatoid arthritis and is predicted by some radiological, clinical and humoral features

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Title: Development of radiographic damage during the first 5-6 years of rheumatoid arthritis. A prospective follow-up study of a Swedish cohort
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Aim: Radiographic damage in rheumatoid arthritis (RA) is the ultimate result of the disease process. A prospective, observational, open study was performed in order to describe the development of radiographic changes in early RA and to search for the predictors of radiographic progression over a period of 5 years. Whether RA displays an erosive pattern and whether early joint damage is a predictor of a poor long-term prognosis in RA patients were other problems addressed in this study.
Methods: Early RA patients (< 24 months from onset) were enrolled a prospective follow-up study: 113 (38 men and 75 women) completed 5 years of follow-up. The patients were examined every 3 or 6 months, depending on their disease activity. Clinical and laboratory data were collected at six-month intervals. The clinical assessment included evaluations of: early morning stiffness (MS); grip strength (GS); the HAQ questionnaire to assess disability; the functional Steinbrocker class (FC); pain and general health during the previous week, measured using a 100 mm visual analogue scale (VAS); active joint counts (AJC); and the Ritchie index (RI).
The laboratory data collected were the erythrocyte sedimentation rate (ESR), haemoglobin level, rheumatoid factor (RF), and analyses for HLA-DRB and DQB alleles. X-rays of the hands and feet were taken at the beginning of the study and each year for 5 years. Articular damage was quantified according to the Larsen method, grading the changes from 0 to 5. The joint damage score (JDS) and the rate of progression were also assessed. For the statistical analysis, a forward stepwise logistic regression model was used.
Results: 113 RA patients (M/F: 38/75) completed the 5-year study. At enrollment the mean disease duration was 11.4 mos.; 71 patients were RF+ (during the follow-up another 8 become RF+); 109 were taking NSAIDS, 1 oral low-dose glucocorticoids and 3 chloroquine. During the follow-up 71 patients were treated with a DMARD for ≥ 6 months. Of 89 patients (84%) carrying the third hypervariable region sequence (HVR 3), 37 (35%) carried the epitope on both alleles. 73 (70%) patients were DRB1*04 positive, 27 (26%) of them homozygous for DRB1*04. 17 patients (16%) had no disease-related allele.
Radiological joint damage occurred early in RA and progressed significantly during the 5-year study period. The rate of progression was most prominent during the first 2 years, decreasing significantly in the 3rd and 4th years (P < 0.01), while the individual rate of progression was highly variable.
At the beginning of the study 60 RA patients (53%) had no detectable erosion, but only 12 (11%) remained non-erosive. 14 patients (26%) with initial erosions showed little or no progression in total JDS over 5 years and did not require aggressive therapy. As a group, compared to the patients with initial erosions, they had a significantly lower ESR and a slower rate of progression during the first year (P 0.009 and 0.0002, respectively). 16 patients developed severe joint damage which eventually required joint replacement. This group at onset had low hemoglobin (P < 0.01) and a high ESR (P < 0.0001).
The patients were divided into two groups: one (33 %) showed a rapid rate of progression, while the other (66%) showed slow to moderate disease progression. After applying a step-wise logistic regression model it was found that severe joint damage during the first year, female gender and a high ESR at baseline could predict 57% of the patients with a high total radiographic progression, and 93% of the patients with low to moderate progression. Age, disease duration, RF, genetic factors, active joint count and erosions had no predictive value.
Conclusions: Radiographic joint damage occurs early in the course of RA, the progression being more rapid in the first 2 years. Early erosions are not always a sign of aggressive disease and the individual rate of progression is variable. Patients with a low to moderate rate of disease progression are easier to identify than those with agressive disease (93% vs 57%) by means of the joint damage during the first year, female gender and a high ESR at baseline.

Comment

In this study the Authors confirm the considerable data in the literature which suggest that the most rapid progression of joint erosion in RA occurs in the first few years of the disease and that persistently high inflammation as defined by high ESR values are prognostic of a poor outcome, but they were unable to demonstrate that RF and DRβ1 positivity may play a role in this mechanism. The weakness of this retrospective study lies in the fact that it raises doubts concerning the role of RF positivity as a prognostic factor for the occurrence of erosions. This prognostic value has been shown by several prospective studies (1, 2). It raises a possible question of the role of DRβ 1 that has been questioned in some recent studies (3). Certainly it offers further support for the use of the area under the curve of an APR (ESR, CRP) as a strong way to predict outcome. These points should be taken into consideration in any future prospective analysis, as well as in future clinical trials.

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