8 PREDICTING THE EVOLUTION OF INFLAMMATORY ARTHRITIS IN ACPA-POSITIVE INDIVIDUALS: CAN T CELL SUBSET HELP?

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Background and objectives Anticitrullinated protein antibodies (ACPA)+ individuals with musculoskeletal pain are at high risk of developing rheumatoid arthritis (RA). The authors previously demonstrated dys-regulation of T cell subsets in early disease with loss of naïve and regulatory T cell (Treg). The aim of the current study is to evaluate whether T cell subset dysregulation could predict the development of inflammatory arthritis (IA) in ACPA+ individuals with recent onset musculoskeletal pain and no clinical signs of IA.

Methods 50 ACPA+ individuals without clinical synovitis at baseline were followed for up to 42 months. Six colour flow-cytometry was performed. Predictors for the development of IA were frequency of naïve T cell (CD4+CD45RB+CD45RA+CD62L+), Treg (CD4+CD25^{high}Foxp3+) and inflammation related cells (IRC: CD4+CD45RB+CD45RA+CD62L–). Regression was used to determine if any variable had predictive value.

Results Seven patients developed undifferentiated arthritis and 14 RA (1987 American College of Rheumatology criteria) hence 47% patients progressed. 24 patients had other diagnoses including osteoarthritis/mechanical type joint pain. Five patients had <3months follow-up and were excluded. ACPAtitres were similar in both groups. No particular age difference was associated with progression. To look for linear associations with the proportion of patients developing IA, each subset was split into four groups at the quartiles of distribution. Only IRC showed a roughly linear association with frequency of progression from the lowest to highest quartile: 20; 41; 58; 64% respectively. No consistent linear trend was found for naïve T cells (64; 36; 44; 46%) or Treg (46; 31; 55; 56%). Exact logistic regression employing conditional maximum likelihood estimation was used to investigate whether T cell subsets were independently associated with the odds of developing IA. Only comparison between patients in upper quartile for IRC, and those in lower quartile (OR=55.13, p=0.016) reached statistical significance. There was some indication that patients with Treg above the median may also be more likely to develop IA. Loss of naïve T cells was not informative independently of IRC and Treg in this small group of patients. IRC showed promising value and suggest that subclinical inflammation may be detected using this subset. $CD25^{high}$FoxP3+ T cells were previously associated with recently activated T cells despite this phenotype also being associated with regulatory function and may therefore suggest ongoing immune reaction.

Conclusion T cell dys-regulation in ACPA+ individuals with non-specific musculoskeletal pain may be useful in predicting progression towards IA. Our data indicate that to use likelihood binary logistic regression to confirm value of T cell, at least 240 ACPA+ patients should be recruited, assuming around 50% will go on to develop IA.