EXPRESSION OF TIE2 AND ANG-1 IS RELATED TO THE DEVELOPMENT OF PERSISTENT AND EROSIONAL DISEASE IN PATIENTS WITH EARLY ARTHRITIS

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Methods The authors analysed synovial tissue of 48 DMARD-naïve patients with early arthritis presenting with a diagnosis of RA or undifferentiated arthritis (UA). Disease duration at baseline was <1 year. Patients were prospectively followed and diagnosed after 2 years according to established classification criteria and outcome (self-limiting, persistent or erosive disease). Baseline synovial expression/activation of Ang-1, Ang-2, Tie2, active phospho-Tie2, vascular endothelial growth factor (VEGF) and VEGF receptor (VEGFR) was examined by quantitative immunohistochemistry. Levels of Ang-1, Ang-2 and VEGF in serum of patients, obtained at baseline, were measured by ELISA. X-rays were obtained at baseline and after 2 years of follow-up. Erosion scoring was based on the presence or absence of erosions on x-rays of hands and feet in cases where the modified Sharp–van der Heijde erosion score was ≥1.

Results pTie2 was significantly related to development of erosions in patients with RA (p=0.01) with an explained variance of 50% (Nagelkerke R²=0.502). Tie2, pTie2 and Ang1 (p=0.03) were all significantly related to the development of persistent rather than self-limiting disease in patients with UA at baseline, with a combined explained variance of 69% (Nagelkerke R²=0.69). Serum levels of Ang-1, Ang-2 and VEGF did not correlate with synovial tissue expression of these factors, and serum Ang-1, Ang-2 and VEGF levels and synovial VEGF and VEGFR expression were not related to the development of persistent or erosive disease.

Conclusion Engagement of the Ang-1/Tie2 axis in synovial tissue is related to development of persistent and erosive disease. Targeting this pathway may be useful in improving outcomes in arthritis, and these markers might be useful biomarkers for predicting outcome.

Background Angiogenic growth factors Ang-1 and Ang-2 and their receptor Tie2 are expressed in inflamed synovial tissue and thought to contribute to disease initiation and joint destruction in rheumatoid arthritis (RA). The goal of this study was to examine the predictive value of synovial Ang-1 and Ang-2 expression and Tie2 activation with regard to disease outcome and erosive disease progression in disease-modifying anti-rheumatic drug (DMARD)-naïve patients with early arthritis.