METASTASIS-INDUCING S100A4 PROTEIN IS ASSOCIATED WITH TREATMENT RESPONSE IN PATIENTS WITH RECENT-ONSET RHEUMATOID ARTHRITIS

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Background/objectives There is increasing evidence that metastasis-inducing S100A4 protein may exert pro-inflammatory and destructive effects in rheumatoid arthritis (RA). The authors have previously demonstrated that S100A4 is significantly up-regulated in RA and correlates with disease activity. Therefore, the authors investigated the relationship between S100A4, disease activity and response to treatment with synthetic disease modifying antirheumatic drugs (DMARDs) in patients with recent-onset RA.

Methods Serum levels of S100A4 protein were determined by ELISA before and after 3 months of initiation of the DMARD treatment in 59 patients with recent-onset RA (symptom duration <6 months). Clinical disease activity (DAS28, swollen joint count) and inflammation (CRP, ESR) were assessed at baseline and after 3 and 12 months. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (ACPA) were analysed at baseline.

Results After initiation of treatment, mean DAS28 (SD) significantly decreased from 5.36 (1.42) at baseline to 3.09 (1.52) at 3 months (n=59) and to 2.69 (1.19) at 12 months (n=40), respectively (p<0.0001). The levels of serum S100A4 protein were significantly higher in patients with recent-onset RA compared with healthy controls (646.60 ± 602.60 vs 46.97 ± 30.12 ng/ml; p<0.001) and significantly decreased after 3 months of treatment (to 388.10 ± 521.00 ; p<0.001). Baseline levels of S100A4 positively correlated with RF (r=0.611; p<0.0001) and ACPA levels (r=0.471; p<0.001), but not with age, symptom duration, disease activity or inflammation. However, the levels of S100A4 corrected for confounders at baseline (r=0.403; p<0.05) as well as at 3 months after treatment (r=0.548; p<0.01) positively correlated with DAS28 after 12 months of treatment in female patients (n=28).

Conclusion S100A4 levels were increased in patients with recent-onset RA and significantly decreased after the treatment. Higher levels of S100A4 in female patients with recent-onset RA were independently associated with disease activity over 12 months. Thus, high levels of S100A4 may have predictive capacity for worse treatment response with synthetic DMARDs in RA.