10 CYTOKINES IN LUPUS NEPHRITIS, LEVELS OF IL-17 AND IL-23 IN ASSOCIATION TO HISTOPATHOLOGY AND RESPONSE TO TREATMENT

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10.1136/annrheumdis-2011-201230.10

Background and objectives The pathogenesis for lupus nephritis (LN) involves multiple components of the immune system. Recent studies indicate an important role for the T cell subset Th-17, and the associated cytokines IL-17 and IL-23, in LN. Increased knowledge of cytokines in LN may contribute to further understanding of the pathogenesis, identification of new biomarkers and to development of new treatment strategies.

Here the authors aimed to investigate cytokines, previously indicated in LN, in association to histopathological findings and response to therapy.

Methods Fifty-two patients with active lupus nephritis were included. Renal biopsies were performed at baseline and after 6 months of standard induction treatment. Clinical and laboratory data were collected at baseline and at repeated biopsies and serum levels of tumour necrosis factor α (TNFα), IFN-γ, IL-2, IL-4, IL-6, IL-10, IL-6R, IL-17, IL-23 and TGFβ were analysed at both occasions. Biopsies were evaluated regarding WHO-classification and renal disease activity was estimated using the BILAG index. An improvement of at least two grades in renal BILAG was regarded complete response (CR), whereas 1 grade as partial response (PR). Serum samples from 13 healthy volunteers were used as controls.

Results Baseline biopsies showed WHO-class III-IV (n=44) and V (n=8) and all patients had high renal disease activity (BILAG A/B). Follow-up biopsies showed WHO I-II (n=19), III-IV (n=19) or V (n=14). Twenty-two patients were regarded CR, 20 PR and 10 non-responders. At baseline, levels of IL-6, IL-10, IFNγ, IL-17, IL-23 and IL-6R were significantly higher in patients versus controls and TGFβ was significantly lower ($p<0.05$ for all).

Levels of IL-17 at baseline were significantly higher in patients with a persisting active nephritis at follow-up (WHO III, IV or V) versus those with a good histopathological response (WHO I or II) ($p<0.03$). The highest levels of IL-17 were found in WHO class V. BILAG non-responders had significantly higher levels of IL-23 at follow-up versus CR and PR ($p<0.05$), most pronounced among non-responder patients with WHO class V ($p<0.02$).

Conclusions High baseline IL-17 predicted an unfavorable histopathological response, suggesting that patients with high levels of IL-17 may represent a subgroup with more severe disease. BILAG non-responders had high levels of IL-23. This study indicates a role for the IL-23/IL-17 axis in LN regarding response to treatment and suggests that these cytokines may be used as biomarkers and may be targets for future therapies.