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Citation	The 15th Medical Research Conference (15th MRC), Department of Medicine, University of Hong Kong, Hong Kong, 16 January 2010. In Hong Kong Medical Journal, 2010, v. 16 n. 1, suppl. 1, p. 45, abstract no. 75
Issued Date	2010
URL	http://hdl.handle.net/10722/129840
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The relation of cytokines of IL-17/IL-23 axis to Th1/Th2 cytokines and disease activity in systemic lupus erythematosus

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Introduction: Interleukin (IL)-17 is recently linked to the pathogenesis of systemic lupus erythematosus (SLE) but its relation to disease activity has not been well characterised. The objectives of this study were to examine the relation of serum cytokine levels from the IL-17/IL-23 axis (IL-17, IL-23) to Th1 (IL-12, IFN-γ), Th2 (IL-10, IL-6, IL-4) cytokines and disease activity in SLE patients.

Methods: Serum cytokines were measured by enzyme-linked immunosorbent assays. Disease activity was determined by SLE disease activity index (SLEDAI), anti-dsDNA antibody, C3 and C4 levels.

Results: Serum levels of IL-17, IL-10 and IFN-γ were higher in SLE patients (n=70) compared to age- and sex-matched controls (n=14) [P<0.001]. Higher serum IL-23 level was found in active lupus patients who had cutaneous manifestation (P=0.003) and serositis (P=0.03) compared to those who had not. Serum IL-17 was not different between patients who had active lupus nephritis (n=23), non-renal active lupus (n=13) and inactive disease (n=34) [P=0.23]. However, an inverse correlation between serum IL-17 with proteinuria was found among all SLE patients (r= –0.27, P=0.03). Serum IL-17 level was, otherwise, not related to SLEDAI, glomerular filtration rate, activity or chronicity score and ISN/RPS class among patients with active lupus nephritis and was not found to correlate with serum IFN-γ or IL-10.

Conclusions: Elevated serum IL-23 was found in patients with inflammatory manifestations including cutaneous involvement and serositis. Serum IL-17 level was not shown to correlate with disease activity but demonstrated an inverse correlation with proteinuria suggesting urinary loss of IL-17 and its involvement in lupus renal pathology.

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Serum levels of IL-33 and soluble ST2 and their association with disease activity in systemic lupus erythematosus

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Background: IL-33 has recently been found to be the specific ligand of ST2, an IL-1 receptor family member that is selectively expressed on Th2 cells and mediates Th2 response. This study aimed to measure serum levels of soluble form of ST2 (sST2) and IL-33 in patients with systemic lupus erythematosus (SLE) and to examine its association with disease activity.

Methods: Seventy SLE patients were evaluated for disease activity determined by SLE disease activity index (SLEDAI), serological features (anti-dsDNA antibody, C3 and C4) and 57 patients were evaluated longitudinally on a second occasion. IL-33 and sST2 were measured by sandwich ELISA in the 127 SLE serum samples and compared to 28 age- and sex-matched healthy controls.

Results: Serum sST2 level was significantly higher in SLE patients with active disease (0.51+0.18 ng/mL) compared to those with inactive disease (0.42+0.08 ng/mL) [P=0.006] and to normal controls (0.36+0.13 ng/mL) [P<0.001]. sST2 level correlated significantly and positively with SLEDAI, level of anti-dsDNA antibody and prednisolone dosage and negatively with C3 and remained significantly predictive of active disease after adjustment for prednisolone use in logistic regression analysis (odds ratio=4.6, P=0.01). sST2 level was sensitive to change in disease activity in longitudinal evaluation and not influenced by age, gender, and renal function. Elevated serum IL-33 was comparable in frequency (4.3% vs 7.1%, P=0.62) and levels (P=0.53) between SLE patients and controls.

Conclusion: Elevated serum sST2 level in SLE patients was found to correlate with disease activity and was sensitive to change, suggesting a potential role as surrogate marker of disease activity.