

INCREASED IL-18 SERUM LEVELS IN PATIENTS WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS

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Sir - Interleukin-18 (IL-18), formerly called interferon (IFN)- γ -inducing factor, is a proinflammatory novel cytokine related to the IL-1 family that plays an important role in the innate immunity and it has been shown to induce not only Th1 but also Th2 cytokines, among other functions¹. Studies have shown that IL-18 may play a role in the pathogenesis of different pediatric immune mediated diseases and is overexpressed both locally and systemically in adult systemic lupus erythematosus (SLE) patients²⁻⁴. However, the functional role of IL-18 in the pathogenesis of SLE is not yet well understood. We studied 23 consecutive juvenile SLE (JSLE) patients and compared them to 20 controls selected among patients seeking medical care with no signs of ongoing infections or inflammatory diseases. IL-18 was measured in serum samples by a commercially available ELISA kit (Medical & Biological Laboratories Co Ltd, Nagoya, Japan). There were 23 JSLE patients (20 females and 3 males, mean age \pm s.d. of 16.7 ± 2.5 years, range 12-20) and 20 healthy controls (15 females and 5 males, mean age \pm s.d. of 16.4 ± 1.7 years, range 13-20). No statistically significant differences between the ages of JSLE patients and control subjects were seen. The mean duration of the JSLE diagnosis at the time when patients were enrolled was 3.7 ± 2.3 years (range 1-10) for the group as a whole, 4.3 ± 2.3 years (range 1-10) for the JSLE active subgroup and 2 ± 1.2 years (range 1-4) for the inactive JSLE subgroup. The

mean Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score of JSLE patients and active JSLE patients were $9.2 (\pm 10.4)$ and $13.3 (\pm 10.1)$ respectively. Serum levels of IL-18 were higher in JSLE patients when compared to controls (510.4 ± 327.6 pg/ml versus 318.2 ± 74.1 pg/ml – $p < 0.05$) and were higher in active JSLE patients (571.4 ± 377 pg/ml) than in patients with inactive disease (370.9 ± 77.8 pg/ml), but this difference was not statistically significant. Levels of IL-18 showed a positive and significant correlation with SLEDAI ($r = 0.41$, $p < 0.05$). Several studies have reported higher serum levels of IL-18 in adult SLE patients when compared to controls and found a positive correlation between IL-18 levels and disease activity measured by SLEDAI values^{5,6}, although Robak et al⁷ found that higher levels didn't correlate with disease activity. To the best of our knowledge, no study concerning IL-18 levels in JSLE has ever been published. Our study showed higher IL-18 plasma levels in patients with JSLE when compared to healthy controls and also that the elevation of plasma IL-18 levels correlated positively with SLEDAI. Interestingly, our data actually showed higher levels in active JSLE patients although this was not statistically significant when compared to inactive JSLE patients and this could be due to the small number of patients recruited. This study suggests a role for IL-18 also in pediatric SLE pathogenesis. As new therapeutic agents are being currently developed and it's known that IL-18 is overexpressed in active SLE patients^{2,7}, this cytokine may be a target to be controlled in the inflammatory process that starts and maintains activity in these patients.

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