Original Article

Possible Protective Role of Interleukin-4 in Rheumatoid Arthritis

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Summary:

Background: *Rheumatoid arthritis (RA) is a common chronic inflammatory and destructive asthropathy . Recently , Facus have been deiected to the role of cytokines to play a role in the inflomatory process of this disease , on the top of the list are the IL-4 , IL-1 , and tumor neurosis factions(TNF) Aim of the study : to shed light on the vole of IL – 4 in RA .*
Patieuts & Methods: *the study included 47 patieuts with RA composed with 50 patieuts control (SLE) and 61 healthy controles . Sera of all groups we studied for estimation of IL-4 – level .*
Results: *the study revealed that IL-4 concentration was significantly higher in the normal control group than that in the patients sera (P.<0.001) , More oven there was an inverse association between IL-4 canc. And most of the clinical features .*
Conclusions: *IL-4 cytokine may play an important role in protectin against RA.*

Introduction

Rheumatoid arthritis (RA) is a common chronic inflammatory and destructive arthropathy. It is currently agreed that the inflammatory process in RA is associated with an increased production of a range of cytokines including tumour necrosis factor (TNF)-alpha and interleukin-1 (IL-1), which display potent pro-inflammatory actions that are thought to contribute to the pathogenesis of the disease (Joosten, et.al. 1999).

Interleukin-4 (IL-4) is produced by CD4+ TH2 cells and participates in the differentiation and growth of B cells (Isomaki, 1997), therefore inhibits the activation of TH1 cells, which, in turn, decrease the production of IL-1 and TNF-a, and prohibits cartilage damage (Moore, et.al. 1993). In addition to that, suppresses the production of IL-6 and IL-8 which may play a role in subsiding the inflammation (Sugiyama, et. al., 1995;Chomarat, et. al., 1995). It was noticed that IL-4 inhibits bone resorption through an effect on osteoclasts and pro-inflammatory cytokines in an ex vivo model of bone resorption (Miossec, et. al. 1994). For this reason, there are many trails for application of IL-4 in RA treatment (Chomarat, et. al. 1995; Joosten, et. al. 1999), since immuno-modulation of RA can be achieved by anti-inflammatory T 2 cytokines such as IL-4 (Cottard, et. al. 2000), or IL-10 and IL-13 (Morita, et. al. 2001).

IL-4 level was considered as an indicator for response to treatment in comparison with pro-inflammatory cytokines (Fe cioli, et. al. 1998).

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Patients & Methods:

In this study 47 RA sera samples were studied for IL-4 level in comparison wit 50 patient controls (SLE) and 61 healthy controls. All RA patients were diagnosed according to the revised criteria of the American Rheumatism Association (Arnett, et. al. 1988). Quantitation of IL-4 had been performed using ELISA technique as revised by Diaclone Research Co.

Statistical Analysis:

Mann-Whitney analysis has been applied for differences in median between two groups besides Kruskal-Wallis test for non-normally distributed variables. Univariate analysis has been applied for the data depending on logistic regression and the results were reported as odds ratio (OR), which represented the increased or decreased risk for RA.

Results:

Table 1 showed that IL-4 level in the sera of RA and patient controls was significantly higher than that in the healthy controls (P value < 0001) whereas no significant differences observed between RA and patient controls, though it was higher among SLE sera.

Table 1. IL-4 concentration in pg/ml in the sera of patients in comparison with control groups.

IL-4concentration (pg/ml)	RA patients	Patient controls	Healthy controls
Minimum	2	3	2
Maximum	35	88	67
Mean	7	36.2	8.6
SD	5	8.6	14.6
SE	0.64	0.79	2.3
N	47	50	64
Median	6	10	5
P (Mann-Whitney) for difference between: RA vs. SLE = 0.35 [NS], RA vs. HC= < 0.001; P (Kruskal-Wallis) difference between the three groups = < 0.001.			

Table 2. The correlation between IL-4 concentration (pg./ ml) and the clinical symptoms.

Clinical signs	*Median Negative	Median Positive	SD Negative	SD Positive	SE Negative	SE Positive	Spearman Coefficient
Fever	21 (9)	7 (38)	35.1	71.7	12.9	8.89	-0.155
Joint swelling	28 (6)	9 (41)	35.1	70.4	14.2	8.5	-0.067
Joint stiffness	75 (4)	9 (43)	34.8	68.9	42.09	8.4	-0.177
Mouth ulceration	13 (11)	32(36)	48.2	67.8	15.4	9.3	0.012
Occular Disturbance	21 (19)	30 (28)	70.6	71.2	11.4	10.8	0.042
Occular Sandy	39 (36)	14 (11)	61.2	17.6	8.8	2.9	-0.019
Hair falling	41 (24)	12 (23)	71.7	48.8	14.07	8.9	-0.005
Weight loss	63 (19)	17(28)	56.3	27.4	11.6	10.8	-0.075
Joint effusion	36 (39)	15 (8)	62.2	9.9	8.1	7	0.012
Subcutaneous nodules	72 (30)	32(17)	9.9	61.9	10.3	12.6	-0.039
Skeletal deformity	40 (37)	20 (10)	47.2	29.5	9.6	7.9	-0.113
Total cases	47						

* = Median conc. in (pg./ ml) No. between brackets represents numbers of cases.

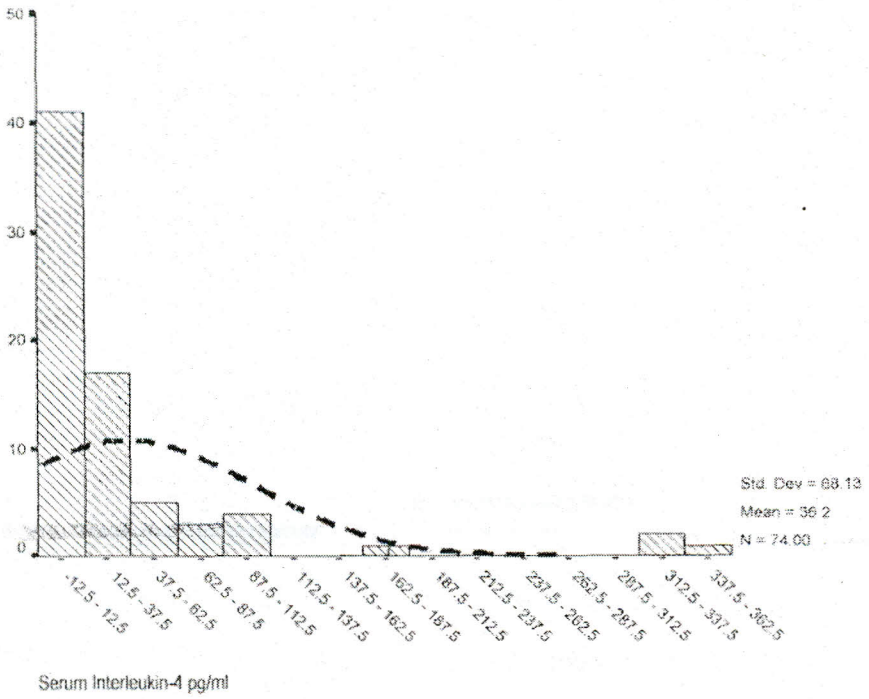

Figure.1 Frequencies of IL-4 concentration in the sera of RA patients

This figure (fig.l) showed the frequencies of IL-4 among patients' sera, which revealed that most the frequencies are in the lower limits [mean 36.2pg. / ml] with only two exceptions which has high cone. While Fig. 2.clearly
demonstrated the variation between normal controls and patients by notice that the majority of frequencies was higher than that for patients [mean 70pg. / ml].

It was clear that there was an association between IL-4 and RP cone, as appeared in Fig. 3 that declared that most of the sero-negative RF cases posses higher IL-4 cone.

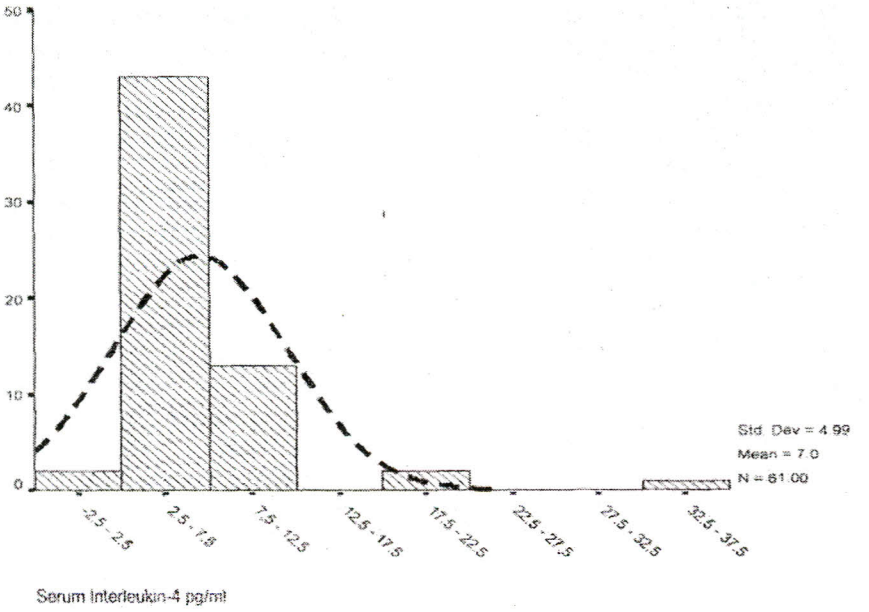

Figure 2- Frequencies of IL-4 concentration in the sera of Patient controls.