SERUM LEVEL OF IL 22 IN PSORIATIC PATIENTS AND ITS RELATION TO DISEASE SEVERITY

Thesis

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List of Abbreviations

AMP.....: Anti-Microbial Peptides Antigen
APCs.....: Presenting Cells . Blood Brain Barrier .
BBB.....: Body Surface Area .
Ca2.....: Calcium
CALML5.....: Calmodulin Like 5
CCR.....: Chemokine Receptor
CD.....: Cluster of differentiation
CIA.....: Collagen Induced Arthritis
CLA.....: Cutaneous Lymphocyte-associated Antigen
CNS.....: Central Nervous System
CNVs.....: Copy Number Variations
CRF2.....: Cytokine Receptor Family class 2
CXCL.....: Chemokine Ligand
DCs.....: Dendritic Cells
DLQI.....: Dermatology Life Quality Index
DNA.....: Deoxy Ribonucleic Acid Desmocollin 1
EAE.....: Experimental Autoimmune Encephalomyelitis
FGF.....: Epidermal Growth Factor
ELISA.....: Enzyme Linked Immunosorbent Assay
FDA.....: Food and Drug Administration
FLG.....: Profilaggrin
HBD.....: Human Beta Defensins
HLA.....: Human leukocyte antigen I
IBD.....: Inflammatory Bowel Disease
IFN.....: Interferon
IL-10-TF.....: Interleukin -10-related T cell derived inducible Factor
IL.....: Interleukin
IL-10R2.....: Interleukin-10 Receptor 2
IL-10RB.....: Interleukin-10 Receptor 2 encoding gene
IL-20R1.....: Interleukin -20 Receptor 1
IL-20R2.....: Interleukin -20 Receptor 2

IL-22BP .....: Interleukin -22 binding protein
IL-22R1.....: Interleukin -22 Receptor 1
IL-22RA1.....: Interleukin -22 Receptor 1-encoding gene
JAK.....: Janus Kinase
KCs .....: Kcratinocytes
KDa.....: Kilodalton
KDAP.....: Keratinocyte Differentiation-Associated Protein
KLK7.....: Kallikrein-7
KRT .....: Keratin gene
LCs.....: Langerhans cells
LST .....: Least Significant Difference
mDCs .....: myeloid Dendritic cells
ml.....: Milliliter
MMP.....: Matrix Metalloproteinase
mRNA.....: Messenger ribonucleic acid
MS.....: Multiple sclerosis
NB-UVB.....: Narrow Band UVB
NF- κB .....: Nuclear Factor Kappa B
ng/L .....: Nanograms per litre
NKT .....: Natural Killer T- cells
PAP1 .....: Pancreatitis-Associated Protein 1
PAI-1.....: Plasminogen activator inhibitor 1
PASI.....: Psoriasis Area and Severity Index
pDCs .....: Plasmacytoid Dendritic cells
PIIINP.....: Plasma Procollagen Type III Aminopcptidc
PsA.....: Psoriatic arthritis
PSORS.....: Psoriasis Susceptibility Locus
PUVA.....: Psoralen plus Ultraviolet A
RA .....: Rheumatoid Arthritis
RHE .....: Reconstituted Human Epidermis
RT-PCR.....: Real Time Polymerase Chain Reaction
S100A7.....: Psoriasin
S100A8.....: Calgranulin A

S100A9.....: Calgranulin B
SD.....: Standard Deviation
SNPs.....: Single Nucleotide Polymorphisms
STAT.....: Signal transducers and activator of transcription
TGF.....: Transforming Growth Factor
Th.....: T helper cells
TIMP-1 .....: Tissue-Inhibitor of Metalloprotease-1
TLR .....: Toll Like Receptor
TNF-α .....: Tumor necrosis factor alpha
T-reg .....: Regulatory T cells
UV .....: Ultraviolet
VEGF .....: Vascular Endothelial Growth Factor

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Abstract

Objectives the aim of this study was to detect a relation between serum levels of interleukin – 22 (IL -22) in patients with psoriasis and also to detect a relation of IL-22 with psoriasis area and severity index (PASI). **Background** IL-22 is highly expressed in several different chronic inflammatory conditions, including psoriasis, multiple sclerosis and rheumatoid arthritis. The best studied function for IL-22 is within the skin as it has an inflammatory role during skin inflammation. **Subjects and methods** the study was conducted on 40 patients with psoriasis and 40 age-matched and sex-matched healthy individuals. All patients were subjected to history taking and complete medical examination serum level of IL-22were measured by enzyme-linked immunosorbent assay technique. Serum levels of IL-22 were statistically analyzed in relation to PASI. **Result** the serum levels of IL-22 were elevated in patients with psoriasis compared with healthy people ($p< 0.023$). the serum IL-22 was significantly higher in patients with severe psoriasis as compared with those with mild and moderate psoriasis. There was no statistically signification difference between the serum levels of IL-22 and disease duration. **Conclusion** the significant elevation in the serum level of IL-22 in patients with psoriasis when compared with that of healthy controls and the signification elevation in the serum levels of IL-22 playing a fundamental role in pathogenesis of psoriasis.

Keyword: Interleukin – 22 Psoriasis Psoriasis area and severity index

INTRODUCTION

Psoriasis is one of the most common immune mediated chronic inflammatory skin diseases affecting about 2% of the worldwide population. The etiology and pathogenic mechanisms of psoriasis are still unclear. However, substantial clinical and basic studies indicate that the cellular innate and adaptive immune responses, especially the activation of T cells and release of cytokines by T cells, play critical roles in the pathogenesis of psoriasis ***(Nestle et al., 2009).***

Accumulating evidence suggests that a new subset of T cells, T helper 17 (Th17), may play an important role in the pathology of psoriasis and other immune-mediated inflammatory diseases ***(Pan et al., 2013).***

Interleukin-22 (IL-22) is a cytokine produced by several different cellular sources such as Th17 ***(Liang et al., 2006)*** and Th22cells ***(Trifari et al., 2009),*** and it has been implicated in many chronic autoimmune and inflammatory diseases like systemic lupus erythematous, rheumatoid arthritis, multiple sclerosis, and psoriasis ***(Pan et al., 2012).***

It has been showed that IL-22 could inhibit keratinocyte terminal differentiation and could induce

psoriasis-like epidermis alterations ***(Wolk et al., 2009).*** Additionally, IL-22 mRNA was found significantly elevated in the psoriatic skin lesions ***(Liu et al., 2007).***

In addition, IL-22 can synergize with the other pro-inflammatory cytokines to induce many of the pathogenic phenotypes from keratinocytes and to exacerbate disease progression ***(Ouyang, 2010).*** Due to its crucial roles in inflammation and proliferation cascade, IL-22 may have promise as a potential therapeutic target for psoriasis.

All these findings suggest that IL-22 may be implicated in the pathogenesis of psoriasis. Few studies have evaluated the relation between IL-22 level in psoriatic patients and the severity of the disease. We presume that such relation worth further studies.

Aim of the Work

The aim of this thesis was:

- To evaluate serum level of IL-22 in patients with psoriasis vulgaris in relation to age and sex matched healthy controls
- To correlate serum level of IL-22 in patients with psoriasis with the disease severity according to PASI.

Chapter (1): Psoriasis

Definition:

Psoriasis is a common, chronic, inflammatory skin disease that results from a polygenic predisposition combined with triggering factors, e.g. trauma, infections or medications ***(Roberson and Bowcock, 2010).***

Epidemiology:

Approximately psoriasis affects 2-3% of population worldwide, with prevalence varying according to race and geographic location ***(Tonel and Conrad, 2009).*** The occurrence of psoriasis is more frequent in countries more distant from the equator ***(Parisi et al., 2013).*** Psoriasis is extremely rare to absent in certain ethnic groups, such as Africans, African-Americans, Japanese, Alaskans, Australians, and Norwegians ***(Basko-Plluska and Petronic-Rosic, 2012).***

Men and women are equally affected. All age groups are affected with a peak onset during the second and third decades of life (early onset psoriasis). A second peak of onset occurs during the fifth and sixth decades of life (late onset psoriasis). Psoriasis patients have a natural history of

outbreaks followed by temporary remissions ***(Griffiths and Barker, 2007).***

Clinical Picture:

The important clinical hallmarks are: erythema, thickening and scaling. The plaque type of psoriasis is the most common type ***(Nickoloff and Nestle, 2004).***

The typical history includes itching, skin redness and scaling. Patients may report that their disease worsens in the winter and improves in the summer ***(Lui and Mamelak, 2009).***

The plaques are irregular or oval and most often located on the scalp, trunk, and limbs, with a predilection for extensor surfaces such as the elbows and knees. Smaller plaques may coalesce into larger lesions, especially on the legs and sacral regions. Fissuring within plaques can occur when lesions are present over joint lines or on the palms and soles. Psoriatic plaques tend to be symmetrically distributed over the body. Lesions typically have a high degree of uniformity with few morphologic differences between the two sides. Psoriatic lesions are sometimes surrounded by a pale blanching ring referred to as Woronoff's ring ***(Lui and Mamelak, 2009).***

If the characteristic silvery scales are removed via