Role of serum prolactin in psoriasis

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قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيم

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LIST OF ABBREVIATIONS

AA	Aminoacids
ACE	Angiotensin-converting enzyme
APC	Antigen presenting cell
CD	Cluster of differentiation
CLA	Cutaneous lymphocyte antigen
Cs-A	Cyclosporine-A
CXC	A chemokine super family in which there are four conserved cystine (C) residues where X is any amino acid.
CXCL	Chemokine ligand
DC	Dendritic cell
ERAP1	Endoplasmic Reticulum Aminopeptidase 1 gene
ESR	Erythrocyte sedimentation rate
GABA	Gamma aminobutyric acid
GAP	Gonadotropin releasing hormone-associated peptide
GH	Growth hormone
GM-CSF	Granulocyte-macrophage colony stimulating factor
HFs	Hair follicles
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
ICAM-1	Intercellular Adhesion Molecule-1
IFIH	Interferon-Induced Helicase gene
IFN-γ	Interferon gamma
Ig	Immunoglobulin
IL	Interleukin
IL28RA	Interleukin 28 Receptor Alpha gene
IP-10	Inducible protein- 10
Jak	Janus kinase
LFA-1	Lymphocyte function associated antigen-1
MAPK	Mitogen-acivated protein kinase
MHC	Major Histocompatibility Complex

LIST OF ABBREVIATIONS (Cont…)

MIG	Monokine induced by interferon gamma
MS	Multiple sclerosis
NFKB	Nuclear factor kappa B
NKT	Natural killer T cell
NSAIDs	Non-steroidal anti-inflammatory drugs
PASI	Psoriasis Area Severity Index
PGA	Physician global assessment
PIF	Prolactin inhibitory factor
PRF	Prolactin releasing factor
PRL	Prolactin
PRLR	Prolactin receptor
PRL-rp	Prolactin releasing peptide
PSORS	Psoriasis susceptibility gene
PUVA	Psoralens and ultraviolet A
RA	Rheumatoid arthritis
RANTES	Regulated upon Activation, Normal T-cell Expressed, and Secreted
REL	Reticuloendotheliosis gene
REM	Rapid eye movement
SLE	Systemic lupus erythematosus
SS	Sjogren's syndrome
SSc	Systemic sclerosis
STAT	Signal transducer and activator of transcription
T-AP interactions	T-cell/APC interactions
T-bet	T-cell associated transcription factor
TBSA	Total body surface area
Tc	T-cytotoxic cell
TGF-β	Transforming growth factor- beta

LIST OF ABBREVIATIONS (Cont…)

Th	T- helper cell
TNF-α	Tumor necrosis factor- alpha
TRAF3IP2	Tumor necrosis factor receptor-associated factors 3 Interacting protein 2
T-reg	T- regulatory cell
TRH	Thyrotropin releasing hormone
TYK2	Tyrosine Kinase 2 gene
UVB	Ultraviolet-B
VCAM-1	Vascular cell adhesion molecule
VEGF	Vascular endothelial growth factor
VIP	Vasoactive intestinal peptide
VLA-4	Very late antigen- 4

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INTRODUCTION

Psoriasis is an inflammatory disease characterized by hyper-proliferation of keratinocytes and accumulation of T cells in the epidermis and dermis of psoriatic lesions. Evidence for the central role of T helper (Th1) lymphocytes comes from both animal models of psoriasis and from trials of treatment with T-cell inhibitors. There is some evidence that psoriasis worsens at ages when hormonal changes such as puberty and menopause are taking place, and may also worsen or improve during pregnancy ***(Gottlieb et al., 2002).***

Prolactin (PRL), a neuropeptide secreted by the anterior pituitary gland, possesses a variety of physiological actions. It has been implicated as an important immunomodulator and exerts a proliferative effect in cultured human keratinocytes via specific receptors ***(Dilmé-Carreras et al., 2011)***.

Prolactin is well recognised for its role(s) in mammary gland development and function. Moreover, its role in skin biology, including the potent regulation of human hair growth, is becoming clearer. Less widely appreciated, however, is the potential role of PRL in the pathobiology of psoriasis. While the relationship between PRL and psoriasis remains enigmatic, several recent publications on the PRL–psoriasis connection have demonstrated a reawakening of interest in this conundrum. We take the occasion of these reports to underscore the importance of dissecting the role(s) of PRL in the aetiopathology of psoriasis, not least since this may help to identify novel hormonal treatment strategies in its management ***(Langan et al., 2012).***

The presence of PRL or at least a "PRL-like substance" has been reported in human sweat glands. Soon afterwards the PRL receptor was identified on human lymphocytes, and PRL itself was discovered to have local cytokine-like activities. Also,PRL is produced by lymphocytes, promotes the proliferation of B and T lymphocytes, increases the synthesis of the cytokines IFNγ and IL2 in Th1 lymphocytes, and suppresses T lymphocyte apoptosis.Today, it is clear that the human skin and hair follicles (HFs) are not only targets of receptor-mediated PRL bioregulation ,but also the sources of extrapituitary PRL production ***(Langan et al., 2012)*.**

AIM OF THIS WORK

Assess the role of serum prolactin in pathogenesis of psoriasis and its correlation with severity and types of psoriasis.

CHAPTER 1

PSORIASIS

Psoriasis is a common chronic inflammatory, immune-mediated disease that predominantly affects the skin and joints ***(Griffiths and Barker 2007).*** It is characterized by sharply demarcated, red, and scaly symmetrical plaques mainly on the elbow, knee or scalp ***(Christophers, 2001).***

The course of the disease is characterized by relapses and remissions but the condition tends to persist throughout life.

Over years there have been many developments in the understanding of the genetic, molecular and cellular mechanisms that underlie these inflammatory processes and many effective treatments have been developed ***(Mrowietz et al., 2011).***

Epidemiology

Psoriasis is found worldwide, although its frequency varies widely among different ethnic groups. According to published reports, prevalence in different populations varies from 0% to 11.8% (***Icen et al., 2009).*** The highest prevalence, observed in Norway, was obtained by relying on ascertainment by questionnaire without validation of positive responses ***(Gudjonsson and Elder, 2007).***

With the exception of the Norwegian questionnaire study, the highest reported incidences in Europe have been in Denmark (2.9%) and the Faeroe Islands (2.8%), with the average for northern Europe being around 2%***(Gelfand et al., 2005).***

Psoriasis is a disorder with a relatively high prevalence in the general population, mainly as a result of its chronicity and the absence of a cure. ***(Naldi, 2004)***.

It is obvious that mortality among psoriatic patients may be increased as compared with the general population in the late decades of life. The association of psoriasis with smoking and components of the metabolic syndrome may be responsible for such a trend ***(Adams et al.,* 2006**).

Age at onset

Psoriasis may first appear at any age. It is most likely to appear between the ages of 15 and 30 years but its age of onset ranges from birth to the eighth or ninth decade ***(Buntin et al., 1983).***

The age of onset of psoriasis has been used for decades as an appropriate descriptor to define two subpopulations of psoriatic patients (types I and II) according to human leucocytic antigen (HLA) class I antigens ***(Quiero et al., 2013).*** However recently,No significant association was found between HLA-C alleles and family history, clinical findings or severity of the disease ***(bahcetepe et al., 2013).***

Sex ratio

In general, there is no phenotypical difference between both sexes; however, significant female predominance can be seen in the palmoplantar pustular type ***(Griffiths et al., 2004).***

Predisposing factors

1. Genetic factors

There are about ten different psoriasis susceptibility genes; PSORS1-PSORS9 and PSORASI, located on the Human Leukocyte Antigen (HLA) class I allele, specifically HLA-Cw6. PSORS1 and PSORS2 are the major genetic determinant for psoriasis ***(Tiilikainen et al., 1980; Tomfohrde et al., 1994; Capon et al., 2002; Speckman et al., 2003).***