Study of Regulatory T-cell Percentages in Peripheral Blood of Patients with Chronic Urticaria

Thesis

Submitted for partial fulfilment of MD. degree in Internal Medicine

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2015

دراسة نسب الخلايا التائية التنظيمية فى المصل لدى مرضى الأرتيكاريا المزمنة

رسالة

توطئة للحصول علي درجه الدكتوراة في الباطنة العامة

مقدمة من

الطبيب / صلاح شعراوى جلال

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جامعة عين شمس

٢٠١٥

سورة البقرة الآية: ٣٢

Acknowledgement

*First of all, thanks are directed to **Allah** for blessing this work until it has reached its end, as a part of generous help throughout my life.*

*I would like to express my deepest sense of Gratitude to my supervisor **Prof. Mohamed Abd-Elrahman El shayeb,** Professor of Internal Medicine, Allergy and Clinical Immunology, Ain Shams University, for his close supervision, valuable instructions, continuous help, patience and guidance. He has generously devoted much of his time and effort for planning and supervision of this study.*

*I wish to express my supreme gratitude to **Dr. Mohamed Nazmy Farres,** Assistant Professor of Internal Medicine, Allergy and Clinical Immunology, Ain Shams University, for his kind assistance, supervision, continuous encouragement and for being kind enough to follow closely every step in the whole work. It was a great honor for me to work under her supervision.*

*I would like to express my deepest gratitude to **Dr. Nermine Abdelnour Melek,** Assistant Professor of Internal Medicine, Allergy and Clinical Immunology, Ain Shams University,for her enthusiastic supervision, continuous support. I am very much grateful for his generous help.*

*Special thanks to **Dr. Eman El sayed Ahmed Khalil,** Lecturer of Internal Medicine, Allergy and Clinical Immunology, Ain Shams University, for her understanding, encouragement and personal attention which have provided a good and smooth basis for my thesis.*

*I take this opportunity to sincerely acknowledge **Dr. Asmaa Saber Moustafa,** Lecturer of Internal Medicine, Allergy and Clinical Immunology, Ain Shams University, for her continuous supervision, guidance, support and patience.*

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ACE	*Angiotensin-converting-enzyme*
ACEI	*Angiotensin-converting-enzyme inhibitor*
ACU	autoimmune chronic urticaria
Ag	Antigen
AITD	Autoimmune Thyroid Disease
AMA ABs	Anti microsomal antibodies
ANA	Anti-nuclear antibody
Anti TgAB	Anti thyroglobulin anti bodies
anti-IgE	Anti Immunoglobulin E
Anti-TPO antibody	Anti thyroperoxidase antibodies
APC	Antigen-presenting cells
ARBS	Angiotensin II Receptor Blockers
ASST	Autologous skin sensitivity test
aTreg	adaptive T-regulatory
Auto Ag	Autoantigen
BAFF	B-cell activating factor
BSACI	British Society for Allergy and Clinical Immunology
C	Complement
C1-INH	C1-esterase inhibitor
cAMP	Cyclic adenosine monophosphate
CAU	Chronic auto immune urticaria
CBC	Complete blood count
CCL	CC chemokine ligand
CCR	C-C motif receptor, beta chemokine receptor
CD	Cluster of differantiation
CIU	Chronic Idiopathic Urticaria
COX	Cyclooxygenase
CRP	C - reactive protein
CSU	Chronic spontaneous Urticaria
CTLA	Cytotoxic T lymphocyte antigen
CU	Chronic Urticaria
CXCR	CXC chemokine receptors

DC	Dentritic cell
DIT	Diiodo-tyrosines
DNA	Deoxyribonucleic acid
ECP	Eosinophilic cationic protein
ELISA	Enzyme linked immunosorbant assay
ESR	Erythrocyte sedimentation rate
FC receptors	(Fragment, crystallizable) region
FceRI	Fc epsilon RI
FITC	Fluorescein isothiocyanate
FKH	Forkhead
Foxo3	Forkhead box O3
Foxp3	Forkhead box P3
FT4	Free T4
GARP	Glycoprotein A repetitions predominant
GATA	Globin transcription factor
GITR	GlucocorticoidinducedTNFR-related protein
GLyCAM	Glycosylation-dependent cell adhesion molecule
HAE	Hereditary angioedema
HBsAg	Hepatitis B surface antibody
HCV Ab	Hepatitis C virus antibody
HDAC	histone deacetylase
HEVs	High endothelial venules
HIF	Hypoxia-inducible factor
HLA-DR	Human leukocyte antigen DR
HPT	Hypothalamic/pituitary/thyroid
H-pylori	*Helicobacter pylori*
HRA	histamine-releasing assays
HSP	Heat shock protein
HTN	Hypertension
ICOS	Inducible T cell co-stimulator
IFN -ɣ	Interferon-gamma
Ig	Immunoglobulin
IGF-1	Insulin-like growth factor I
IL-2Rα	Interleukin-2receptor alpha chain

ILs	Interleukins
IQR	Interquartile range
KAT	Histone acetyltransferase KAT
kDa	Kilo dalton
KFT	Kidney function test
LAP	Leukocyte alkaline phosphatase
LFT	Liver function test
LPR	Late-phase reaction
LTC	Leukotriene C
MAd CAM	Mucosal vascular addressin cell adhesion molecule
MBP	Major basic protein
MC	Mast cell
MIP	Macrophage inflammatory protein
MIT	Monoiodo-tyrosines
MPEC	Long-lived memory cells
NFAT	Nuclear factor of activated T cells
NF-κB	Nuclear factor-κB
NSAIDS	Nonsteroidalanti-inflammatorydrugs
nTreg	naturally occurring T-regulatory
P.B.S.	Phosphate-puffered saline
PBMC	Peripheral blood mononuclear cells
PCR	Polymerase chain reaction
PE	Phycoerythrin
PECy5	Phycoerythrin cytochrome
PLC	Phospholipase C
RANTES	Regulated on activation, normal T cell expressed and secreted
Ras	Rat sarcoma
RAST	Radio Allegro Sorbent Test
RNA	Ribonucleic acid
ROG	Repressor of gata
ROR	Retinoic acid receptor-related orphan receptor
RUNX	Runt-related transcription factor
SHIP	SH2-containing inositol phosphatase
SLE	Systemic lupus erythematosus

SPT	Skin prick test
STAT	Signal transducer and activator of transcription
T conv	Conventional human T-regulatory
TA	Thyroid autoantibodies
TBG	Thyroxine binding globulin
TCR	T cell receptor
Teff	T effector
TF	Transcription factor
TFH	Follicular B Helper T cells
Tg	Thyroid gland
TGF	Transforming growth factor
THs	Thyroid hormones
TLR	Toll receptor
TMA	Thyroid antimicrosomal AB
TMB	Tetramethylbenzidine
TNF	Tumor necrosis factor
TNFR	Tumor necrosis factor receptor
TPD	Thyroid antiperoxidase
Treg	T regulatory
TRH	Thyrotropin releasing hormone
TSH	Thyroid stimulating hormone
TSI	*Thyroid* stimulating immunoglobulin
UAS-7	Urticaria activity score -7
UV	Urticarial vasculitis

Introduction

Chronic urticaria (CU) is a rather common skin disorder characterized by recurrent, transitory, itchy wheals for more than 6 weeks ***(Chen et al., 2008)***.

In 80–90% of patients with CU, no specific underlying cause is found, although there is a subset of these patients in whom autoantibodies to the high-affinity IgE receptor FceRI are found ***(Najib and Sheikh, 2009)***. This subgroup is labelled chronic autoimmune urticaria (CAU). It was later demonstrated that these antibodies stimulated the release of histamine ***(Cherrez et al., 2009)***.

In up to 45% of patients with CU, an immediate wheal and flare response to an intradermal injection of autologous serum (autologous serum skin test, ASST) can be demonstrated ***(Konstantinou et al., 2009)***, suggesting an autoimmune basis for this subset of patients ***(Greaves, 2000)***. The ASST indicates the presence of circulating histamine-releasing IgG autoantibodies directed against the high affinity IgE receptor FcεRIα present on mast cells and basophils and/or IgE ***(Sabroe et al., 1999)***.

Examination of biopsies from urticaria patients demonstrated that most of the infiltrating T cells possessed $CD4^+$ helper phenotype ***(Caproni et al., 2003)***.

The cytokine pattern reported elsewhere showed that skin biopsies of patients with CU resemble the T-helper

cell type 0 (Th0) cytokine profile with increased levels of interleukin-4, interleukin-5 and interferon-gamma messenger (m)RNA+ cells ***(Ying et al., 2002)***.

Alternatively, it is also possible that there is a mixture of Th1/Th2 cell types in the skin of patients with CU. These observations support the notion that T lymphocytes and particularly CD4+ T cells are involved in the pathogenesis of CU ***(Sun et al., 2011)***.

Aim of the work

The present study aims to measure the frequencies of circulating T-regulatory cells ($CD4^+$ $CD25^+$ $Foxp3^+$) in serum among patients with chronic urticaria, as compared to healthy controls. We further aim to assess the possible relation between frequencies of these cells and the severity of chronic urticaria.