Prevalence of thyroid autoimmunity among chronic urticaria patients in comparison to healthy controls

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بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

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Manar Farouk Mohamed Ali Aglan

List of Contents

List of Abbreviations

ARBS	Angiotensin II Receptor Blockers
ACEI	Angiotensin-converting-enzyme inhibitor
AMA ABs	Anti microsomal antibodies
Anti TgAB	Anti thyroglobulin anti bodies
Anti-TPO antibody	Anti thyroperoxidase antibodies
APC	Antigen-presenting cells
ANA	Anti-nuclear antibody
AITD	Autoimmune Thyroid Disease
ASST	Autologous skin sensitivity test
C1-INH	C1-esterase inhibitor
CAU	Chronic auto immune urticaria
CIU	Chronic Idiopathic Urticaria
CU	Chronic Urticaria
CBC	Complete blood count
DM	Diabetes mellitus
DIT	Diiodo-tyrosines
ELISA	Enzyme linked immunosorbant assay
ESR	Erythrocyte sedimentation rate
FceRI.	Fc epsilon RI
FC receptors	(Fragment, crystallizable) region
FT4	Free T4
H-pylori	Helicobacter pylori
HBsAg	Hepatitis B surface antibody
HCV Ab	Hepatitis C virus antibody
HAE	Hereditary angioedema
HEVs	High endothelial venules
HPT	Hypothalamic/pituitary/thyroid
HTN	Hypertension
IGE	Immunoglobulin E
IGF-I	Insulin-like growth factor I
IFN-γ	Interferon-gamma
ILs	Interleukins
KFT	Kidney function test
LPR	Late-phase reaction

List of Abbreviations (Cont.)

LTC4	Leukotriene C4
LFT	Liver function test
MIT	Monoiodo-tyrosines
NSAIDS	Nonsteroidalanti-inflammatorydrugs
RAST	Radio Allegro Sorbent Test
SLE	Systemic lupus erythematosus
TMB	Tetramethylbenzidine
TA	Thyroid autoantibodies
Tg	Thyroid gland
THs	Thyroid hormones
TMA	Thyroid antimicrosomal AB
TPD	Thyroid antiperoxidase
TSH	Thyroid stimulating hormone
TSI	Thyroid stimulating immunoglobulin
TRH	Thyrotropin releasing hormone
TBG	Thyroxine binding globulin
UAS-7	Urticaria activity score -7

List of Figures

List of Figures (Cont.)

List of Tables

List of Tables (Cont.)

Introduction

"Urticaria" is defined as a transient edematous papules, plaque with itching. It is a clinical reaction pattern triggered by many factors causing the liberation of vasoactive substances such as histamine, prostaglandins and kinins. Urticaria is classified according to its duration into acute (<6 weeks duration) and chronic (>6 weeks duration) ***(Shankar et al., 2010).***

Chronic urticaria (CU) is a common skin disorder, affecting 0.1% -1% of the general population. It is characterized by recurrent and transitory (<24 hours) pruritic erythematous wheals that present at least twice weekly for at least 6 weeks ***(Abd El-Azim and Abd El-Azim, 2011).***

Leznoff et al. (1983), suggested an autoimmune basis for the urticaria. This was after the observation that there was an association between thyroid disease and chronic idiopathic urticaria (CIU).

After that ***Gruber et al. (1988),*** detected functional anti-IgE antibodies and proposed that these could be the cause of urticarial wheals. It is now well-established that about 30-50% patients with CU have circulating functional auto antibodies against the high-affinity IgE receptor (FCeRIa) or against IgE ***(Sachdeva et al., 2011).***

There is a growing evidence that some cases of chronic idiopathic urticaria (CIU) are associated with many auto immune diseases as thyroid autoimmunity. The frequency of thyroid antibodies in patients with CIU was 30%, which is higher than that previously reported ***(Najib et al., 2009).***

The autologous serum skin test has proved to be a useful screening in vivo test for autoimmune urticaria ***(Greaves, 2002).***

Patients with a positive ASST are more likely to be , associated with HLADR4, to have autoimmune thyroid disease, a more prolonged disease course and may be less responsive to H1-antihistamine treatment than those with a negative ASST ***(Konstantinou et al., 2009).***

Aim of The Work

The study aims at detecting prevalence of markers of thyroid autoimmunity(thyroid auto antibodies with or without underlying abnormal thyroid functions) among a cohort of ASST positive patients with CU in comparison to ASST negative CU patients as controls, and its correlation with the severity of symptoms.

Allergy

i. Definition:

An **allergy** is a hypersensitivity disorder of the immune system. Allergic reactions occur when a person's immune system reacts to normally harmless substances in the environment. A substance that causes a reaction is called an allergen. These reactions are acquired, predictable, and rapid ***(Lwloar et al., 1995).***

Allergy is one of four forms of hypersensitivity and is formally called *type I* (or *immediate*) hypersensitivity. Allergic reactions are distinctive because of excessive activation of certain white blood cells called mast cells and basophils by a type of antibody called Immunoglobulin E (IgE). This reaction results in an inflammatory response which can range from uncomfortable to dangerous response ***(Lwloar et al., 1995).***

Mild allergies like hay fever are very common in the human population and cause symptoms such as red eyes, itchiness, and runny nose ***(Busse, 2000)*** , eczema, hives, or an asthma attack ***(Schoenwetter, 2000)***.

Allergies can play a major role in conditions such as asthma. In some people, severe allergies to environmental or dietary allergens or to medication may result in life-threatening reactions called anaphylaxis. Food allergies, and reactions to the venom of stinging insects such as wasps and bees are often associated with these severe reactions ***(Kay, 2000).***

A variety of tests exist to diagnose allergic conditions. These include placing possible allergens on the skin and looking for a reaction such as swelling (skin prick test). Blood tests can also be done to look for an allergen-specific IgE (RAST), Total IgE testing, Eosinophil counts ***(Tas, 2009).***

ii. Pathophysiology:

In early phase response:

A type I hypersensitivity reaction against an allergen encountered for the first time and presented by a professional Antigen-Presenting Cell causes a response in a type of immune cell called a T_H2 lymphocyte, which belongs to a subset of T cells that produce a cytokine called interleukin-4 (IL-4). These T_H2 cells interact with other lymphocytes called B cells, whose role is production of antibodies, known as IgE. Secreted IgE circulates in the blood and binds to an IgE-specific receptor on the surface of other kinds of immune cells called mast cells and basophils, which are both involved in the acute inflammatory response. The IgE-coated cells, at this stage are sensitized to the allergen ***(Xystrakis et al., 2006).***

If later exposure to the same allergen occurs, the allergen can bind to the IgE molecules held on the surface of the mast cells or basophils. Cross-linking of the IgE and Fc receptors occurs when more than one IgE-receptor complex interacts with the same allergenic molecule, and activates the sensitized cell. Activated mast cells and basophils undergo a process called degranulation, during which they release histamine and other inflammatory chemical mediators (cytokines, interleukins, leukotrienes, and prostaglandins) from their granules into the surrounding tissue causing several systemic effects, such as vasodilation, mucous secretion, nerve stimulation, and smooth muscle contraction. This results in rhinorrhea, itchiness, dyspnea, and anaphylaxis ***(Brunnée et al., 1997).***

Late-phase response :

After the chemical mediators of the acute response subside, late phase responses can often occur. This is due to the migration of other leukocytes such as neutrophils,