Sensitization To Aeroallergens In Patients With Chronic Urticaria Without Allergic Respiratory Symptoms

Thesis

Submitted for Partial Fulfillment of Master Degree
In Internal Medicine

By

Mayada Moneer Mahmoud EL Khodeery
M.B.B.CH

Under Supervision Of

Prof. Dr./ Maged Refaat
Professor of Internal Medicine,
Allergy and Clinical Immunology
Faculty of Medicine - Ain Shams University

Dr./ Eman Nagib Ossman
Assistant Professor of Internal Medicine,
Allergy and Clinical Immunology
Faculty of Medicine - Ain Shams University

Dr./ Mohmed Nazmy Farris
Lecturer of Internal Medinine,
Allergy and Clinical Immunology
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2009

Contents

Page

Acknowledgement

I humbly submit my sincere gratitude to **Allah**, our creator who has guided me to every success I had in my life.

Special gratitude is offered to ***Prof. Dr./ Maged Mohamed Refaat,*** Professor of Internal Medicine, Allergy and Clinical Immunology, Faculty of Medicine, Ain Shams University, for his support constructive criticism, generous help and encouragement.

Sincere appreciation is extended to ***Dr./ Eman Nagib Osman***, Assistant Professor of Internal Medicine,Allergy and Clinical Immunology, Faculty of Medicine, Ain Shams University.

Special recognition and sincere thanks to ***Dr./ Mohamed Nazmy Faris***, Lecturer of Internal Medicine, Allergy and Clinical Immunology, Faculty of Medicine, Ain Shams University, for giving personal assistance, encouragement and valuable advice.

Special gratitude is offered to ***Dr. Mohamed Youssef***, for being extremely helpful to make this work succeed.

List of Abbreviations

Ach E	: Acetylcholinestrease
AHR	: Airway hyperresponsiveness
APC	: Antigen presenting cells
BHR	: Bronchial hyper-responsiveness
C1INH	: C1 inhibitor
CLD	: Chronic liver disease
CRF	: Chronic renal failure
CU	: Chronic urticaria
DM	: Diabetes
DPU	: Delayed pressure urticaria
EIA	: Exercise induced anaphylaxis
FSU	: Fixed solar urticaria
HAE	: Hereditary angioedema
HD	: House dust
HTN	: Hypertension
IgE	: Immunoglobulin E
IL	: Interlukin
INF	: Interferon
ISHD	: Ischemic heart disease
IVIG	: Intravenous immunoglobulins
MCT	: Mast cell tyrptase
MCTC	: Mast cell tyrptase chymase
MM	: Mixed molds
MP	: Mixed pollens

List of Abbreviations (Cont.)

N	: Number
PG	: Prostaglandin
PIT	: Phagocytic inhibition test
Pt	: Patient
RASP	: Radio-allergiosorbant procedure
RAST	: Radio-allergiosorbant test
SCIT	: Subcutaneous immunotherapy
SD	: Standard deviation
SLIT	: Sublingual immunotherapy
SPT	: Skin prick test
Tcyt	: T cytotoxic
TGF- β	: Transforming growth factor –β
Th1	: T helper cells 1
Th2	: T helper cells 2
TNF	: Tumor necrosis factor
Treg	: T regulatory
TSLP	: Thymic stimulation lymphopoietin
UV	: Urticarial vasculitis
UVB	: Ultraviolet B waves
VEGF	: Vascular Endothelium Growth factor

List of Tables

List of Figures

List of Graphs

Page

Introduction

The etiology of chronic urticaria and angioedema remains uncertain in most of patients. There are several agents and factors including medications, foods, food additives, infections contact ants, physical factors and autoimmunity that are implicated in provoking urticaria symptoms.[227]

In addition, the possible role of inhalant or aeroallergens has been considered in few reports,[228] further more, urticaria as a sole clinical manifestation in inhalants allergy sensitive patients is unusual (airborne urticaria).

A possible association of house dust mite sensitivity with chronic urticaria was described by **Mahesh et al.**[233]. Also, urticaria was statistically significantly associated with sensitization to pollens [252].

Stokli and Bricher[287] described patients with urticaria provoked by tobacco inhalation. The same observation was described by **Heudorf et al.**[288] as a significant association between dermal symptoms and passive smoking in children was found.

In practice, skin test positive to aeroallergens is found in some cases of chronic urticaria, this can be due to concomitant respiratory allergy.[81]

Aim of the Work

The aim of this study is to investigate the possible role of aeroallergens in provoking chronic urticaria in patients without allergic respiratory diseases.

I - Allergic diseases

The term (allergy) was introduced in 1906 by Von Pirquet, who recognized that in both protective immunity and hypersensitivity reactions, the term (Atopy) (from the greek atopos, meaning out of place) is often used to describe IgE mediated diseases.

The clinical symptoms of allergy are caused by cellular (IgE-triggered) responses to an allergen. Effector cells of allergy include eosinophil and basophil granulocytes, as well as tissue mast cells. Growth and accumulation, as well as IgE-dependent and independent functions of these cells are regulated by distinct proteohormones and peptides.[1]

Cells Involved in Allergic Responses:

Basophil leukocytes and tissue mast cells are inflammatory cells that are found in virtually all human tissues. They appear to be involved in the pathogenesis of such allergic diseases as allergic rhinitis, bronchial asthma, anaphylaxis, atopic and contact dermatitis, chronic urticaria, and hypersensitivity pneumonitis. By releasing a variety of chemical mediators, they could also play a role in the pathophysiology of a wide range of inflammatory disorders of the joints, and of intestine, lung, coronary, and myocardial diseases.[2]

Basophils and mast cells are effecter cells in allergen/IgE-mediated immune responses. They induce type 1

immediate immune response in airway or other organ, resulting in bronchial asthma and other allergic diseases.However, they also play a critical role in host defense against infection with helminthes.[2]

Upon linkage of FcepsilonRI with a complex of allergen and IgE, basophils and mast cells release a large amount of Th2 cytokines and chemical mediators. Therefore these responses are "acquired allergic responses" and induce allergic diseases, such as bronchial asthma.[3]

Although these two cell types are similar in several aspects, striking differences have also been observed. Moreover, human mast cells from different anatomical sites and within an individual tissue synthesize different mediators and have different release mechanisms.[2]

Mast Cells:

Mast cell (or mastocyte) is a resident cell of connective tissue that contains many granules rich in histamine and heparin.[4]

Mast cells were first described by Paul Ehrlich in his 1878 doctoral thesis on the basis of their unique staining characteristics and large granules. These granules also led him to the mistaken belief that they existed to nourish the surrounding tissue, and he named them "Mastzellen" (from the Ancient Greek *masto*, "I feed").[4]

Mast cells are very close to basophil granulocytes (a class of white blood cells) in blood; the similarities between

mast cells and basophils has led many to speculate that mast cells are basophils that have "homed in" on tissues.[4]

However, current evidence suggests that they are generated by different precursor cells in the bone marrow. Nevertheless, both mast cells and basophils are thought to originate from bone marrow precursors expressing the CD34 molecule. The basophil leaves the bone marrow already mature, whereas the mast cell circulates in an immature form, only maturing once in a tissue site. The tissue site an immature mast cell chooses to settle in probably determines its precise characteristics.[4]

Two types of mast cells are recognized, those from connective tissue and mucosal mast cells. The activities of the latter are dependent on T-cells.[5] Immunocytochemical studies have shown the presence within the tissues of two mast cell phenotypes distinguishable by their neutral protease content, the MC T(mast cell tyrptase) phenotype containing only tryptase and the MC TC MC T(mast cell tyrptase chymase) phenotype containing both tryptase and chymase.[6]

IgE Initially, these respective subtypes were suggested to be the equivalents of the “mucosal” and “connective tissue” previously described in experimental animals. However, it is now realized that variable amounts of both mast cell subtypes are present within any given tissue; their relative abundance changes with disease (e.g., in allergy or fibrosis).[6]

However, some rules are becoming apparant, Thus MC T phenotypes appear to be "immune system–related" mast cells with a primary role in host defense, whereas MC TC phenotypes appear to be "non-immune system–related" mast cells with functions in angiogenesis and tissue remodeling rather than immunologic protection. However, it should be remembered that both phenotypes express Fc∈RI and may therefore participate fully in IgE-dependent allergic or parasitic reactions.[6]

The production of a wide range of cytokines by mast cells in response to activation by allergen places the mast cell in the center of the allergic inflammatory response.[7] These cytokines may lead to eosinophil, basophil, and T cell recruitment. Coordinated production of IL-4 and IL-5 by TH2 helper cells enhanced IgE responsivity, thus perpetuating the allergic inflammatory response.[7]

In the asthmatic airways, mast cells may stimulate the release of IL-6 and IL-8 from fibroblasts through the release of various pre-formed and newly generated mediators, and contribute to processes of inflammation and tissue remodeling.[8] Mast cells play a role in Th polarization and that mast cell degranulation leads to more Th2 and less Th1 responses.[9]