Correlation Between Lymphopenia and Clinical Manifestations, Disease Activity and Damage in Systemic Lupus Erythematosus

Thesis
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By

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Abstract:

Objective: SLE is an autoimmune disease characterized by excessive autoantibody production against 'self' antigens and immunocomplex formation, resulting in frequent widespread inflammatory damage to target multiple organ systems. The aim of this study was to determine the association of lymphopenia with the clinical manifestations, serologic abnormalities, disease activity and disease damage as well as drug intake in SLE patients.

Methods: thirty female SLE patients with lymphopenia, fifteen female SLE patients without lymphopenia, and ten healthy females with matched age group served as control. All the patients are fulfilling the ACR criteria of SLE. Disease activity was assessed using SLIDAI. Disease damage was assessed with SLICC/DI**.**

Results: Lymphopenia in SLE was found to be associated with lupus nephritis (P=0.023), leucopenia (P=0.004), disease activity (P=0.03) and organ damage (P=0.02) but was not associated with serological abnormalities or with drug intake (P>0.05).

Conclusion: lymphopenia was associated with lupus nephritis, leucopenia, disease activity and organ damage.

Keywords:

Systemic lupus erythematosus- lymphopenia- disease activity- organ damage

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Contents

List of Abbreviations

aCL	Anticardiolipin
ACR	American College of Rheumatology
ALP	Alkaline phosphatase
ALT	Alanine amino transferase
ANA	Antinuclear antibody
Anti-DNA	Antideoxyribonucleic acid antibodies
Anti-Sm	Anti-Smith
APA	Anti-phopholipid antibody
APCs	Antigen-presenting cells
AST	Aspartate amino transferase
BCR	B cell receptor
C_3	Third component of complement
C_4	Fourth component of complement
CBC	Complete Blood Count
CCL19	CC-chemokine ligand
CCL21	CC-chemokine ligand 21
CCR7	CC-chemokine receptor 7
CD	Cluster of differentiation
CD40-CD40L	CD40-CD40 ligand
CH_{50}	Total hemolytic complement assay
CNS	Central nervous system
CRP	C-reactive protein
CTLs	Cytolytic T lymphocytes
D_H	Diversity of heavy chain
DNA	Deoxyribonucleic acid antibodies
DTH	Delayed type hypersensitivity reaction

DVT	Deep venous thrombosis
ECG	Electrocardiography
ELISA	Enzyme-linked immunosorbent assay
ESR	Erythrocyte sedimentation rate
Fas	Factor of apoptotic signaling
Fc	Fragment crystallizable
H chain	Heavy chain
HB	Hemoglobin
HEVs	High endothelial venules
ICAM-1	Intercellular adhesion molecule 1
ICAM-2	Intercellular adhesion molecule 2
IFN-γ	Interferon-γ
Ig	Immunoglobulin
IL	Interleukin
ISN/RPS	International society of nephrology and renal pathology society
J_H	Joining of heavy chain
L chain	Light chain
LDH	Lactic dehydrogenase
LFA-1	Lymphocyte function-associated antigen-1
LNs	Lymph nodes
MCPs	Metacarpopharyngeal joints
MCV	Mean corpuscular volume
MHC	Major histocompatibility complex
mRNA	Messenger ribonucleic acid
MTPs	Metatarsopharyngeal joints
NK	Natural killer
NK T cells	Natural killer T cells
NO	Nitric oxide

NPSLE	Neuropsychiatric systemic lupus erythematosus
NSAIDS	Nonsteroidal anti-inflammatory drugs
PIPs	Proximal interpharyngeal joints
PLT	Platelet
PNAD	Peripheral node addressin
pre-BCR	Pre-B cell receptor
pre-TCR	Pre- T cell receptor
RAG-1	Recombination activating gene-1
RAG-2	Recombination activating gene-2
RBC	Red cell count
RNA	Ribonucleic acid
ROIs	Reactive oxidative intermediates
SCLE	Subacute cutaneous lupus erythematosus
SD	Standard deviation
SLE	Systemic lupus erythmatosus
SLEDAI	Systemic lupus erythmatosus disease activity index
SLICC/ACR	Systemic lupus lnternational Clinics / America Collage of Rheumatology
SLICC/DI	Systemic lupus international collaborative clinics/damage index
TCR	T cell receptor
T_H cells	T Helper cells
T_H1	T Helper 1
T_H2	T Helper 2
Th-cells	T Helper cells
TIAS	Transient ischemic attacks
TLC	Total leukocyte count
V (D) J	Variable joining diversity

WBC	White blood cell
WHO	World Health Organization
λ5	Lambda 5

List of Tables

List of Figures

Pages

Introduction and Aim of Work

Introduction

SLE is an autoimmune disease characterized by excessive autoantibody production against 'self' antigens and immunocomplex formation, resulting in frequent widespread inflammatory damage to target multiple organ systems. It may affect any organ and produce a broad spectrum of clinical manifestations ***(Yeh et al, 2007)***.

Lymphopenia is a common clinical manifestation and its clinical usefulness has been limited mainly to aid in the diagnosis of SLE because lymphopenia is one of the hematologic criteria according to American College of Rheumatology (ACR) (**Hochberg, 1997**).

Lymphopenia in patients with active SLE is common and may be of pathognomonic significance. However, it may be caused by factors other than SLE. Medications including corticosteroids and cytotoxic agents, infections, and hospital setting can also contribute to reduction in lymphocyte count, which may not be a direct reflection of disease activity ***(Casteleno et al, 1997)***.

Some studies have shown lymphopenia to be associated with particular clinical manifestations of SLE, disease activity and organ damage ***(Vila et al, 2006) (Yu et al, 2007)***.

Aim of Work

The aim of this study was to determine the association of lymphopenia with the clinical manifestations, serologic abnormalities, disease activity (SLEDI) and disease damage (SLICC-DI) as well as drug intake in SLE patients.

Review of Literature

Clinical Features of SLE

Clinical Features of SLE

Constitutional manifestations:

Constitutional symptoms such as malaise, fatigue, fever, and unintentional weight loss are common presenting symptoms of SLE. These symptoms are not specific to just SLE, and diligence should be given to discerning other etiologies such as fibromyalgia, depression, infection, malignancy, endocrinopathy or other connective tissue diseases on initial presentation ***(Lam and Petri, 2005)***.

Mucocutaneous manifestations:

The skin provides one of the best windows through which to view the activity of lupus, both from the patient's perspective in recalling specific features and from the clinician's in establishing the diagnosis or assessing disease activity ***(Edworthy, 2005).***

The skin lesions seen in patients with lupus can be classified into those that are lupus-specific histologically, and those that are lupus non-specific. The lupus-specific lesions may be further divided into those that are acute, subacute and chronic ***(Gladman and Urowitz, 2003)***.