Vascular cell adhesion molecule-1 (VCAM-1): A new marker of disease activity in lupus nephritis

Thesis

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By

AbuBakr Abdal Wahab Mohammed Al Hassen

M.B. B.CH

Supervised By

Prof. Dr. Mohamed El-tayeb Nasser

Professor of Internal Medicine and Nephrology

Faculty of Medicine – Ain Shams University

Dr. Sherif Hamdy Maroof

Lecturer of Internal Medicine and Nephrology

Faculty of Medicine – Ain Shams University

Faculty of Medicine

Ain Shams University

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بسم الله الرحمن الرحيم
وَأَنزَلَ ٱللَّهُ عَلَيْكَ ٱلْكِتَٰبَ وَٱلْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُن تَعْلَمُ ۚ وَكَانَ فَضْلُ
ٱللَّهِ عَلَيْكَ عَظِيمًا
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Contents

List of Abbreviations

ARA	The American Rheumatism Association
ACKD	Advanced chronic kidney disease
ACR	American College of Rheumatology
ARB	Angiotensin receptor blockers
ACE	Angiotensin-converting enzyme
ALMS	Asperva Lupus Management Study
ANCA	Anti-neutrophil cytoplasmic antibodies
APS	Antiphospholipid antibody syndrome
BUN	Blood urea nitrogen
BILAG	British Isles Lupus Assessment Group
CXCL-16	Chemokine (C-X-C motif) ligand 16
C	Complement
cDNA	Complementary DNA
CBC	Complete Blood Count
CCL	Chemokine (C-C motif) ligand
CCR	CC chemokine receptors
CRP	C-reactive protein
CXCL	C-X-C motif chemokine
CYC	Cyclophosphamide
CsA	Cyclosporine
DNA	Deoxyribonucleic acid

dsDNA	Double-stranded DNA
ELNT	Euro-Lupus Nephritis Trial
EM	Electron microscopy
ET-1	Endothelial-1
ESRD	End-stage renal disease
GFR	Glomerular filtration rate
HLA	Human leukocyte antigen
IF	Immunofluorescence
ICAM-1	Intercellular adhesion molecule-1
ICs	Immune complexes
IFN	Interferon
IL	Interleukin
ISKDC	International Study of Kidney Disease in Children
ISN	International Society of Nephrology
JAK	Janus kinase
KDOQI	Kidney Disease Outcomes Quality Initiative
KT	Kidney Transplantation
LDH	Lactate dehydrogenase
LM	Light microscopy
LN	Lupus nephritis

MAINTAIN	Mycophenolate Mofetil Versus Azathioprine for Maintenance Therapy of Lupus Nephritis
MHC	Major histocompatibility complex
MBL	Mannose-binding lectin
MCN	Minimal Change nephritis
MCP	Monocyte chemoattractant protein
MMF	Mycophenolate mofetil
MRL	Murine lupus
NPV	Negative predictive value
NIH	National Institutes of Health
PO	Per os
PPV	Positive predictive value
NPV	Negative predictive value
RAAS	Renin–angiotensin–aldosterone system
RANTES	Regulated upon Activation, Normal T-cell Expressed, and Secreted
RNA	Ribonucleic acid
RPS	Renal Pathology Society
RRT	Renal replacement therapy
SD	Standard deviation
SLE	Systemic lupus erythematosus

SLEDAI	Systemic lupus erythematosus disease activity index
SLN	Silent Lupus Nephritis
STAT	Signal transducers and activators of transcription
TGF	Transforming growth factor
TLRs	Toll-like receptors
TMA	Thrombotic microangiopathy
TNF	Tumor necrosis factors
TNFR	Tumor necrosis factor receptor
VCAM-1	Vascular Adhesion Molecules-1
WHO	World Health Organization

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Introduction

Lupus nephritis (LN) is a major complication of systemic lupus erythematosus (SLE) that aggravates both its morbidity and mortality. It is mediated by the glomerular deposition of immune complexes that promote a cascade of inflammatory events leading to severe tissue damage. Anti-dsDNA antibody deposition is an early event in lupus nephritis and is followed by local production of both cytokines and chemokines that trigger glomerular inflammation and ultimately drive the irreversible renal damage ***(Perez et al., 2001).***

A significant number of T cells and macrophages infiltrate the kidneys of patients with lupus nephritis. Chemotactic factors, especially monocyte chemoattractant factor-1 (MCP-1) and adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1) cooperatively facilitate recruitment of mononuclear cells into inflamed tissues ***(Kuroiwa and Lee, 1998).***

Adhesion molecules are a polymorphic family of proteins, produced by endothelial cells, lymphocytes, and polymorphonuclear cells, and includes vascular cell adhesion molecule-1 (VCAM-1), E-selectin, and intercellular adhesion molecule-1 (ICAM-1), among others; all of them play an important role in the activation of the inflammatory process and tissue damage ***(Zaccagni et al., 2004).***