

Neurosonologic and Cognitive Evaluation of Systemic Lupus Erythematosus Patients

THESIS

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Mohamed Ibrahim Raslan Hegazy

DEDICATION

To my family and friends

Abstract

Systemic lupus erythematosus (SLE) is a common connective tissue disease that involves almost all organ systems. Involvement of the brain is one of the most important complications of SLE. About 30–70% of SLE patients develop brain involvement, which is manifested as cerebrovascular disease, seizures, cognitive disorders, headaches, and psychosis.

The aim of this study was to investigate whether neuropsychological dysfunction in SLE was associated alterations in CBF.

Total Cerebral Blood Flow Volume (TCBFV) was assessed by measuring flow volume of the extra cranial internal carotid and vertebral arteries using Doppler Ultrasonography and neuropsychological status was assessed by the Mini-Mental State Examination (MMSE), Modified Mini-Mental State Examination (3MS), and General health Questionnaire (GHQ) in 21 SLE patients subgrouped into 10 patients with Antiphospholipid Syndrome (Group Ia) and 11 patients without Antiphospholipid Syndrome (Group Ib) and 10 healthy volunteers.

It was found that CBFV in the Left ICA was significantly lower in patients than in controls (p value=0.05). It was also found that TCBFV was significantly lower in patients with SLE disease activity (p value=0.006). There was no significant difference between patients and controls regarding MMSE, 3MS, or GHQ. There was no significant difference between patient subgroups regarding TCBFV, MMSE, 3MS, or GHQ.

In conclusion, cerebral hypoperfusion measured by Doppler ultrasonography was detected in patients with SLE and is related to disease activity.

Key words: Cerebral Blood Flow Volume; Neuropsychiatric lupus; Cognitive dysfunction; SLE Disease Activity Index (SLEDAI).

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List of abbreviations

aCL	Anti-cardiolipin Antibodies
ACR	American College of Rheumatology
AECA	Anti-endothelial cell antibodies
ANA	Anti-nuclear antibodies
ANCA	Anti-neutrophil cytoplasmic antibodies
anti-b2GP1	Anti-beta 2 glycoprotein 1
anti-dsDNA	Anti-double stranded DNA antibodies
anti-P	Anti-ribosomal P antibody
aPL	Antiphospholipid Syndrome
BACNS	Benign angiopathy of the CNS
c-ANCA	Circulating antineutrophil cytoplasmic antibody
CBF	Cerebral blood flow
CBFV	Cerebral blood flow velocity
CBV	Cerebral blood volume
CNS	Central nervous system
CSF	Cerebrospinal fluid
CSS	Churg–Strauss syndrome
CT	Computed tomography
CTA	Computed tomography angiography
CTDs	Connective tissue disorders
CVDs	Cerebrovascular disorders
CVR	Cerebrovascular resistance
DHEA	Dehydroepiandrosterone
DPTC	Dynamic perfusion computed tomography
DSCPW-MR	Dynamic susceptibility contrast perfusion-weighted magnetic resonance
ECD	Ethyl cysteinyl dimer
EEG	Electroencephalography
ELISA	Enzyme-linked immunosorbent assay
ESR	Erythrocyte sedimentation rate
GACNS	Granulomatous angiitis of the central nervous system
GC	Glucose consumption
HBV	Hepatitis B virus

HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HMPAO	Hexamethyl propylene amine oxime
HSP	Henoch–Schonleinpurpura
ICAM-1	Inter-Cellular Adhesion Molecule 1
γ IFN-	interferon-gamma
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IL-1	interleukin-1
IL-6	interleukin-6
IVIG	intravenous immunoglobulin
LA	Lupus Anticoagulant
LCV	leukocytoclasticvasculitis
MAC	Membrane attack complex
MHC	Majorhistocompatibility complex
MPA	Microscopic polyangiitis
MPO	Myeloperoxidase
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
MS	Multiple Sclerosis
MTT	Mean transit time
NCS	Nerve conduction studies
NIRS	Near-infrared spectroscopy
NPSLE	Neuropsychiatric systemic lupus erythematosus
OC	Oxygen consumption
OEF	Oxygen extraction fraction
PACNS	Primary angiitis of the CNS
PAN	Polyarteritis Nodosa
p-ANCA	Perinuclear antineutrophilcytoplasmic antibody
PCR	Polymerase chain reaction
PET	Positron emission tomography
PMN	Polymorphonuclear leukocytes
PN	Peripheral sensorimotor neuropathy
PNS	Peripheral Nervous System
PR3	Proteinase 3
RCVS	Reversible cerebral vasoconstriction syndrome
SLE	Systemic lupus erythematosus

SLEDAI	Systemic lupus erythematosus Disease Activity Index
SPECT	Single photon emission computed tomography
SS	Sjogren syndrome
TA	Takayasu's arteritis
TCD	Transcranial Doppler ultrasound
α TGF-	Transforming growth factor- alpha
β TGF-	- betaTransforming growth factor
TIA's	Transient ischemic attacks
TM	Transverse myelitis
α TNF-	Tumor necrosis factor -alpha
VCAM-1	Vascular cell adhesion molecule-1
VDRL	Veneral Disease Research Laboratory
WG	Wegener's granulomatosis
XeCT	Xenon-enhanced computed tomography

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INTRODUCTION

AND

AIM OF WORK

Introduction and aim of work

Introduction:

Systemic lupus erythematosus (SLE) is a chronic inflammatory multiorgan disease. It is characterized by a variety of clinical features including abnormalities of the skin, joints, lungs, heart, Kidneys, and the central nervous system (CNS). It has a variable course marked by active and inactive disease periods. The etiology of SLE is unknown, but it is believed to represent a disturbance of the immune system, leading to influence of or damage to various organs. Involvement of the brain – neuropsychiatric SLE (NPSLE) – is one of the most important manifestations, reportedly ranging from 20% to 75% of cases (McCune and Golbus 1988 ;Futrell et al.,1992).

The CNS findings vary from global to focal cerebral dysfunction (Omdal et al., 1989) and the main features are cerebrovascular disease seizures, cerebral atrophy, psychosis, headaches, cognitive abnormalities and mood disorder. Unlike many other organ manifestations, the pathophysiology underlying CNS disease is not clear (van Dam ,1991).The observation of both diffuse and focal CNS involvement in SLE has led to the hypothesis that there are several pathogenetic mechanisms in NPSLE such as microvascular damage, small vessel vasculopathy and autoantibody mediated neuronal cell injury (Devinsky et al.,1988; Hanly et al.,1992).It has been proposed that about two-thirds of neurological manifestations in SLE are not related to the disease itself, but result from associated

causes, such as drugs, infection, and hypertensive and metabolic complications(Kaell et al.,1986

Transcranial color Doppler sonography (TCCD) is a useful tool for intracranial investigation. It provides direct sonographic imaging of intracranial vessels and brain parenchyma. It is also a noninvasive, reproducible and bedside mobile device for evaluating the cerebral hemodynamics, including blood flow direction, flow velocities, and other abnormal vascular lesions (Lin et al., 1995)

Neuropsychological assessment is another method of evaluating brain function (Lezak , 1995 ;Reitan and Wolfson 1993). Neuropsychological testing evaluates the functional capacity of the human brain. Assessing cognitive function has been proposed as a sensitive tool for investigating NPSLE and cognitive dysfunction has been reported in a high proportion of SLE patients (Denburg et al., 1987 ; Hanly et al.,1992; Kozora et al.,1998)

Aim of the work

The purpose of this study was to screen cerebral perfusion by establishing Total Cerebral Blood Flow Volume (TCBFV) by using Doppler Ultrasonography and determining whether a relationship exists between cerebral hypoperfusion, cognitive dysfunction, cumulative tissue damage and the clinical activity of SLE.