Microemboli as an Etiology of Acute Ischemic Stroke in Watershed zone

Thesis

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By

Nouran Mohamed Salah El-Dein

M.B.B.Ch.

Under supervision of

Prof. Ahmed Abd Elmonem Gaber

Professor of Neurology
Faculty of Medicine - Ain Shams University

Dr. Hossam El-Din Mahmoud Afify

Lecture of Neurology
Faculty of Medicine –Ain Shams University

Dr. Ahmed Mohamed El-Sadek

Lecture of Neurology
Faculty of Medicine –Ain Shams University

Faculty of Medicine
Ain Shams University
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الصمات المتناهية الصغر كمسبب للسكتة الارتوائية في المناطق المستجمعة

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الطبيبة/نوران محمد صلاح الدين

بكالوريوس الطب والجراحة العامة ـ جامعة عين شمس

تحت إشراف

أ.د / احمد عبد المنعم جابر

أستاذ طب المخ والأعصاب

كلية الطب–جامعة عين شمس

د /حسام الدين محمود عفيفي

مدرس طب المخ والأعصاب

كلية الطب–جامعة عين شمس

د / أحمـــد محمد الصادق

مدرس طب المخ والأعصاب

كلية الطب جامعة عين شمس

كليــة الطب

جامعة عين شمـس

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List of Abbreviations

133Xe..... Xenon 133
A.C.A ..... Anterior Cerebral Artery
ACoA..... Anterior Communicating Artery
ACZ ..... Acetazolamide
AEWSI ..... Anterior External Watershed Infarcts
ATP..... Adenosine tri phosphate
BBB..... Blood–brain barrier
BHI ..... Breath-holding Index
BOLD ..... Blood Oxygen Level-Dependent
BZ ..... Border Zone
CA..... Cerebral Autoregulation
CBF..... Cerebral Blood Flow
CBV ..... Cerebral Blood Volume
CO2..... Carbon dioxide
CPP..... Cerebral Perfusion Pressure
CSO ..... Centrum semiovale
CT ..... Computed tomography
CVR..... Cerebral Vasomotor Reactivity
CWS..... Cortical watershed strokes
DM..... Diabetes Mellitus
DWI ..... Diffusion Weighted Image
EEG ..... Electroencephalographic
EWS……External Water Shed
EWSI ..... External Watershed Infarction.
fMRI ..... Functional Magnetic Resonance Imaging

List of Abbreviations (cont.)

FV ..... Flow Velocity.
H+ ..... Hydrogen
HDI ..... Hemodynamic Impairment
HDL ..... High Density Lipoprotein
HTN ..... Hypertension
ICA ..... Internal Carotid Artery
ICP ..... Intracranial pressures
IWS ..... Internal Watershed
IWSI ..... Internal Watershed Infarction.
LDL ..... low density lipoprotein
MAP ..... Mean Arterial blood Pressure
MCA ..... Middle cerebral artery
MES ..... Microembolic signals
MFV ..... Mean flow velocity
NIRS ..... Near-infrared spectroscopy
NO ..... Nitric oxide
NVU ..... Neurovascular unit
OEF ..... Oxygen extraction fraction
Paco2 ..... CO2 partial pressure
PCA ..... Posterior cerebral artery
PCoA ..... Posterior communicating artery
PET ..... Positron emission tomography
PEWSI ..... Posterior External Watershed Infarcts
SPECT ..... Single Photon Emission Computed
TCD…… Transcranial Doppler
TEE ..... Trans-esophageal echocardiography

List of Abbreviations (cont.)

TIA..... Transient Ischemic Attack Tomography
TTE..... Trans Thoracic Echo
VBH …… Velocity Breath Holding
WHO ..... World health organization
WS ..... Watershed
WSI..... Water Shed Infarction

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Introduction

Stroke is a worldwide health problem. It makes an important contribution to the morbidity, mortality and the disability in the developed as well as the developing countries. A WHO collaborative study, which was done in 12 countries, showed that the incidence rates of stroke were 0.2 – 2.5 per 1000 population per year. It is the leading cause of adult disability and the second most common cause of death worldwide. It accounts for 10 – 12% of the total deaths in the developed countries (***Park et al, 2005).***

Disturbances in the cerebral function in stroke are caused by three morphological abnormalities, which include stenosis, occlusion or rupture of arteries, leading to ischemia, infarction and cerebral hemorrhage respectively ***(Bladin et al, 1993)***.

Watershed strokes are named because they affect the distal watershed areas of the brain. The original terminology came from the German literature, which used the analogy of an irrigation system. The German scholars compared the blood flow in distal arterial territories of the brain to the last field on a farm, which was the area with the least supply of water and therefore most vulnerable to any reduction in flow. In a medical context, the term "watershed" refers to those areas of the brain that receive dual blood supply from the branching ends of two large arteries ***(Bladin et al, 1993).***

These events are localized to two primary regions of the brain:

1. Cortical watershed strokes (CWS), or outer brain infarcts, are located between the cortical territories of the anterior cerebral artery (ACA), middle cerebral artery (MCA), and posterior cerebral artery (PCA).

2. Internal watershed strokes (IWS), or sub cortical brain infarcts, is located in the white matter along and slightly above the lateral ventricle, between the superficial systems of the MCA and ACA, or between the deep and the superficial arterial systems of the MCA ***(Momjian et al, 2005).***

The conventional theory implicates hemodynamic compromise produced by repeated episodes of hypotension in the presence of a severe arterial stenosis or occlusion. The lower perfusion pressure found within the border zone areas in this setting confers an increased susceptibility to ischemia, which can lead to infarction. This causal role of severe arterial hypotension has been well described and confirmed by the results of experimental studies in animals ***(Howard et al, 1966)***.

The typical clinical manifestations of syncope, hypotension, and episodic fluctuating or progressive weakness of the hands are also supportive of this theory of hemodynamic failure ***(Bogousslavsky et al, 1993).***

Radiologic studies also support the hypothesis that border zone infarcts distal to internal carotid artery disease are more likely to occur in the presence of a non-competent circle of Willis ***(Masuda et al, 1994)***.

In sharp contrast with this widely prevalent interpretation, several pathologic investigations have emphasized an association between border zone infarction and micro emboli, and embolic material has been found within areas of border zone infarction in autopsy series ***(Masuda et al, 1994).***

Preferential propagation of emboli in the border zone regions also has been found in experimental studies. Border zone infarction may be better explained by invoking a combination of two often interrelated processes: hypo perfusion and embolization ***(Caplan et al, 1998).***

Hypoperfusion, or decreased blood flow, is likely to impede the clearance (washout) of emboli. Because perfusion is most likely to be impaired in border zone regions, clearance of emboli will be most impaired in these regions of least blood flow. Severe occlusive disease of the internal carotid artery causes both embolization and decreased perfusion. Similarly, cardiac disease is often associated with microembolization from the heart and aorta with periods of diminished systemic and brain perfusion. This theory, although it seems reasonable, remains unproved and has been challenged on many accounts ***(Caplan et al, 1998).***