Asymmetric diabetic retinopathy and carotid insufficiency: a correlative study

THESIS

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ABSTRACT

Purpose: to detect a correlation between carotid system insufficiency and the presence of asymmetric diabetic retinopathy in diabetic patients.

Subjects and methods: a prospective study of carotid system duplex was conducted on 20 patients with a symmetric diabetic retinopathy.

Results:ipsilateral carotid stenosis to eye with more advanced changes was found in 50% of cases (10 patients), ranging 15-50% with mean 30.5% due to CCA and/or ICA.

Conclusion:asymmetric diabetic retinopathy is considered the exception rather than the rule.Carotid stenosis is a predominant factor in producing it.Its identification is important in early detection of carotid system plaques and prevention of future strokes.

Key words:

(Asymmetric diabetic retinopathy, Carotid stenosis, Carotid plaque)

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List of Abbreviations

ACE	Angiotensis converting enzyme.
AGE	Advanced glycation end products.
ANG	Angiotensin.
BRB	Blood retinal barrier.
CCA	Common carotid artery.
CDDS	Color and duplex Doppler sonography.
CP	Carotid plaque.
CSMO	Clinically significant macular oedema.
DCCT	Diabetic control and complications trial.
DD	Disc diameter.
DME	Diabetic macular edema.
DR	Diabetic retinopathy.
ECA	External carotid artery.
ETDRS	Early treatment diabetic retinopathy study.
FAZ	Foveal avascular zone.
FFA	Fundus fluorescein angiography.
FGF	Fibroblast growth factor.
FOXO	Fork head transcription factor.
GAPDH	Glyceraldehyde phosphate dehydrogenase.
HGF	Hepatocyte growth factor.
HIF	Hypoxia inducible factor.
HDL	High density lipoprotein.
ICA	Internal carotid artery.

IGF	Insulin like growth factor.
ILM	Internal limiting membrane.
IMT	Intima media thickness.
IOP	Intra ocular pressure.
IRMA	Intra retinal microvascular abnormalities.
JAM	Junction adhesion molecule.
LDL	Low density lipoprotein.
MnSOD	Manganese superoxide dismutase.
MAGI	Membrane associated guanylate kinase with inverted domain structures.
mRNA	Messenger riboneucleic acid.
MMP	Matrix metalloproteins.
NPDR	Non proliferative diabetic retinopathy.
NVD	Neovessles at the disc.
NVE	Neovessles elsewhere.
OCT	Ocular coherence tomography.
ODD	Oxygen dependent domain.
PDR	Proliferative diabetic retinopathy.
PDGF	Platelet derived growth factor.
PDGF	Placental derived growth factor.
PKC	Protein kinase C.
PRP	Pan retinal photocoagulation.
PSV	Peak systolic volume.
PVD	Posterior vitreous detachment.
RAS	Renin angiotensin system.
RI	Resistivity index.

RNA	Riboneucleic acid.
ROS	Reactive oxygen species.
RPE	Retinal pigmented epithelium.
TCA	Tricarboxylic acid.
TNF	Tumor necrosis factor.
TSP	Thrombospondin.
UCP	Uncoupling protein.
UKPDS	United Kingdom prospective diabetic study.
VCAM	Vascular cell adhesion molecule.
VEGF	Vascular endothelial growth factor.
VHL	Von HippleLindau factor.
WESDR	Wisconsin epidemiologic study of diabetic retinopathy.
ZO	Zonulaoccludens.

Introduction

Diabetes mellitus is recognized as a group of heterogeneous disorders with the common elements of hyperglycaemia and glucose intolerance due to insulin deficiency, impaired effectiveness of insulin action, or both. The underlying causes for this hyperglycaemia are either an absolute or relative lack of the hormone insulin. This is caused by the pancreas not producing insulin or insufficient insulin action to meet the body's requirements. We are currently witnessing a worldwide epidemic of diabetes with the current prevalence being approximately 200 million people affected around the world. Epidemiological evidence suggests that, without effective prevention and control diabetes will likely continue to increase globally. In fact the prevalence of diabetes is expected to double by 2025.[1]

Diabetic retinopathy can be defined as damage to microvascular system in retina due to prolonged hyperglycemia it is estimated that diabetes mellitus affects 4% of world's population, almost half of whom have some degree of diabetic retinopathy at any given time. Diabetic retinopathy occurs in both type 1 and type 2 diabetes mellitus and has been shown that nearly all type 1 and 75% of type 2 will develop diabetic retinopathy after 15 years duration of diabetes as shown in epidemiological studies. [2,3]

In western population diabetic retinopathy has been shown to be the cause of visual impairment in 86% of type 1 diabetic patients and in 33% of type 2 diabetic patients.[4]

Diabetic retinopathy is primarily classified into Non proliferative diabetic retinopathy (NPDR) formerly termed simple or back ground retinopathy and Proliferative diabetic retinopathy (PDR). Retinopathy progresses from mild characterized by increased vascular permeability to moderate and then severe NPDR characterized by vascular closure and increased risk for the development of PDR, distinguished by the growth of new blood vessels on the retina and posterior surface of vitreous. Visual impairment in diabetic retinopathy occurs due to PDR and diabetic macular edema (DME).

The retinal changes in patients with diabetes result from five fundamental processes: (*i*) formation of retinal capillary microaneurysms, (*ii*) development of excessive vascular permeability, (*iii*) vascular occlusion, (*iv*) proliferation of new blood vessels and accompanying fibrous tissue on the surface of the retina and optic disk, and (*v*) contraction of these fibrovascular proliferations and the vitreous. The clinicopathological lesions of diabetic retinopathy have been well classified. Although a multitude of pathogenic mechanisms have been proposed, the underlying dysfunctional biochemical and molecular pathways that lead to initiation and progression of DR still remains an enigma.[5]

Currently four major biochemical pathways have been hypothesized to explain the mechanism of diabetic eye diseases all starting initially from hyperglycaemia induced vascular injury. These mainly include (*i*) enhanced glucose flux through the polyol pathway, (*ii*) increased intracellular formation of advanced glycation end-products (AGE), (*iii*) activation of protein kinase C (PKC) isoforms and (*iv*) stimulation of the hexosamine pathway. Studies have suggested that these mechanisms seem to reflect a hyperglycaemia induced process initiated by superoxide overproduction by mitochondrial electron transport chain.[6]

Diabetic retinopathy usually develops in a symmetric pattern over a long period of time. Asymmetric diabetic retinopathy is considered to be the exception rather than the rule. So the cause beyond this asymmetry should be revealed. Epidemiological surveys have shown that various risk factors known to be associated with diabetic retinopathy tend to accelerate its course and increase its severity. Systemic factors as hypertension and dyslipidemia, ocular factors as PVD and cataract surgery.

The resultant ocular ischemia caused by carotid stenosis may cause such asymmetry up to neovascularization of retina, iris and in such patients PRP is of little benefit and the outcome is usually less successful.

The presentation of asymmetric diabetic retinopathy should raise the suspicion for urgent investigation of blood supply to head and neck, namely the patency of carotid system. Indeed reversal of carotid stenosis may be most important avenue to maintain or improve vision in such cases and

guard against high morbidity and mortality from both cerebrovascular accidents. Early intervention including carotid endarterectomy may result in improved outcome for these patients.

AIM OF THE WORK

The aim of our study is to detect the relationship between carotid system insufficiency and the presence of asymmetric diabetic retinopathy in diabetic patients.