MEDICAL TREATMENT OF CHOROIDAL NEOVASCULAR MEMBRANE

Essay

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M. Sc. degree in Ophthalmology

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بسم الله الرحمن الرحيم
"قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ"
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Lamyaa Abd El Rahman

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LIST OF ABBREVIATIONS

a-FGF: Acidic fibroblast growth factor.

AMD: Age-related macular degeneration.

ANCHOR: ANti-VEGF antibody for the treatment of predominantly classic CHORoidal neovascular membrane in age related macular degeneration study.

Ang: Angiopoietin.

ARM: Age related maculopathy.

ATP: Adenosine tri-phosphate.

b-FGF: basic fibroblast growth factor.

cm^2: centimeter square.

CME: Cystoid macular edema.

CNV: Choroidal neovascular membrane.

CRT: Central retinal thickness.

DR: Diabetic retinopathy.

ETDRS: Early Treatment of Diabetic Retinopathy Study.

FA: Fluorescein angiography.

FAZ: Foveal avascular zone.

FDA: Food and Drug Administration.

FGF: Fibroblast growth factor.

GLD: Greatest linear dimension.

FOCUS: recombinant humanized Fragment of antibody V٢ in Ocular treatment Combining the Use of visudyne to evaluate Safety.

HDL: High density lipoprotein.

ICAM-١: Intra cellular adhesive molecule-١.

LIST OF ABBREVIATIONS (Cont..)

ICG: Indocyanine green angiography.
IgG: Immunoglobulin G.
IOP: Intraocular pressure.
J: Joule.
kD: kilo Daltons.
kg: kilogram.
m^2: meter square.
MARINA: Minimally classical/ occult trial of the Anti VEGF antibody Ranibizumab In the treatment of Neovascular age related macular degeneration.
MCP: Monocyte chemoattractant protein.
mg: milligram.
ml: milliliter.
mm: millimeter.
MMPs: Matrix metalloproteinases.
MPS: Macular photocoagulation study group.
m-RNA: messenger ribonucleic acid.
mw: mill watt.
ng: nanogram.
nm: nanometer.
NOS: Nitric oxide synthetase.
NV: Neovascularization.
OCT: Optical coherence tomography.
OHS: Ocular histoplasmosis syndrome.

LIST OF ABBREVIATIONS (Cont..)

ONL:	Outer nuclear layer.
PAI:	Plasminogen activator inhibitor.
PDGF:	Platelet derived growth factor.
PDT:	Photodynamic therapy
PED:	Pigment epithelial detachment.
PEDF:	Pigment epithelial derived growth factor.
PJD:	Posterior juxtascleral delivery.
PKC:	Protein kinase C.
RD:	Retinal detachment.
RISC:	Ribonucleic acid induced silencing complex.
RNA:	Ribonucleic acid.
ROP:	Retinopathy of prematurity.
RPE:	Retinal pigment epithelium.
SANA:	Systemic Avastin for Neovascular age related macular degeneration trial.
si RNA:	small interfering ribonucleic acid.
TAA:	triamcinolone acetonide.
TGF:	Transforming growth factor.
TIMP:	Tissue inhibitors of metalloproteinase.
TSP-١:	Thrombospondin-١.
TNF-α:	Tumor necrosis factor alpha.
TrpRS:	Tryptophenyl ribonucleic acid synthetase.
µg:	microgram.
µm:	micrometer.
VA:	Visual acuity.
VEGF:	Vascular endothelial growth factor.
VEGFR:	Vascular endothelial growth factor receptor.
VISION:	VEGF Inhibition Study In Ocular Neovascularization.

INTRODUCTION

The eye contains highly vascularised and completely avascular tissues in close apposition. This specialized anatomy requires tight regulation of the balance between vascular quiescence and vascular growth. Growth normally occurs in ocular embryonic development, but is virtually absent from the eye in adult life. In eye diseases associated with angiogenesis, this delicate balance is disturbed. [١]

Angiogenesis is a tightly controlled process, which involves both endothelial cells and pericytes, and is influenced by numerous agonist growth factors principally vascular endothelial growth factor [VEGF] and inhibiting factors. [٢]

Angiogenesis plays a crucial role in pathogenesis of choroidal neovascular membrane [CNV]. CNV alters the anatomy of the retina through proliferation of new capillaries and enhancement of vascular permeability leading to profound visual loss when it grows under the central part of the retina. [٣]

Researches prompted for medical treatment of CNV based on inhibition of VEGF by aptamers, monoclonal antibodies, and prevention of synthesis and secretion of VEGF by small interfering RNA [si RNA]. Other new modalities in treatment of CNV through modulation of the permeability and adhesion of choroidal endothelial cells by steroids, and inhibition of angiogenesis by endogenous angiogenesis inhibitors like pigment epithelia derived factor [PEDF] and extracellular matrix modulators. [٤, ٥, ٦]

Photodynamic therapy [PDT] is a tissue selective treatment that has demonstrated benefit in patients with subfoveal classic CNV. It is a minimally invasive procedure that can be performed on an outpatient basis. This treatment does not produce a blind spot on the retina. It reduces damage to normal surrounding tissue and allows the treatment to be given again as needed. Recently there has been considerable enthusiasm for potential beneficial effect associated with the use of intravitreal triamcinolone acetonide combined with verteporfin PDT. [٧, ٨]

AIM OF THE WORK

Aim of this work is to review the new modalities of medical treatment of choroidal neovascular membrane.

INTRODUCTION TO CHOROIDAL NEOVASCULAR MEMBRANE

Choroidal neovascular membrane [CNV] denotes the pathologic growth of new blood vessels from pre-existing choroidal vessels into the subretinal space (fig. ١). The newly formed vessels lay between the choroid and the retinal pigment epithelium [RPE] or between the native RPE and the neurosensory retina; thus, CNV also referred to as subretinal neovascularization [NV]. [٩]

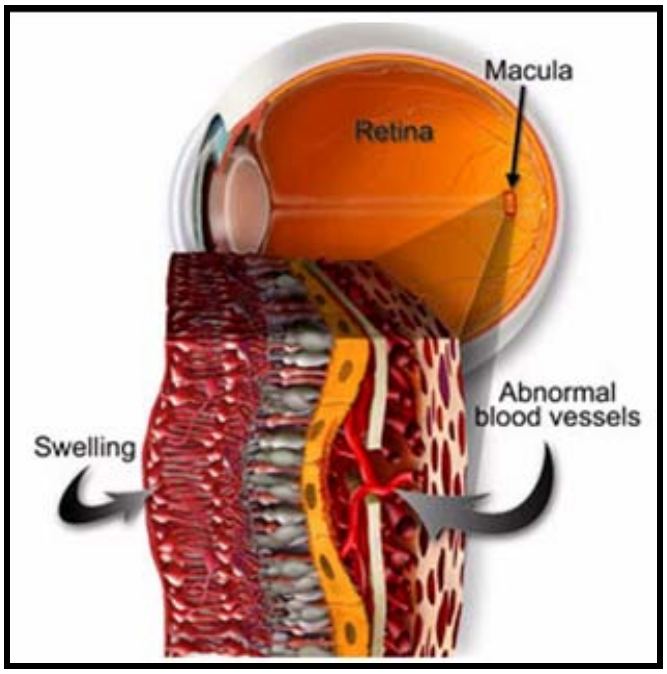

Figure (١): Abnormal leaking new blood vessels. [١٠]

The importance of CNV is that it is the determinant of the disciform process (fig. ٢). The disc-shaped subretinal fibrovascular membrane ultimately progress to cicatrisation and

loss of macular function, which results in rapid progressive decline of vision over a period of (٦-١٢) months.[٩]

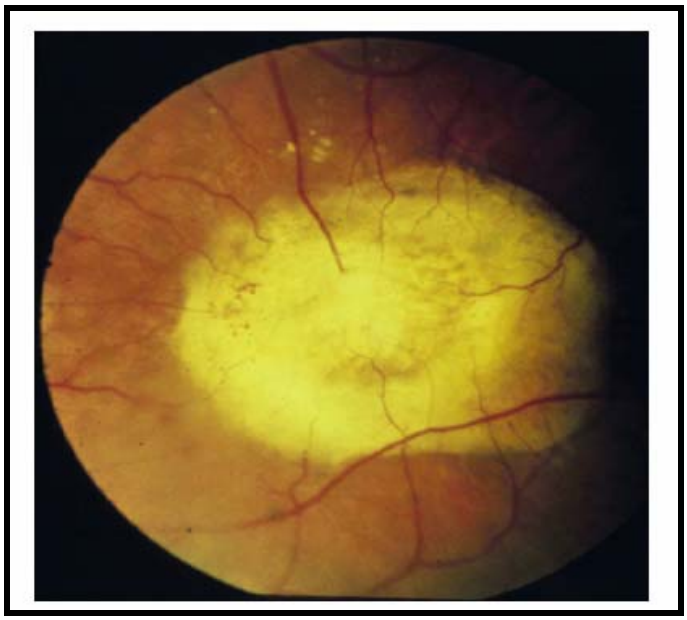

Figure (٢): Disciform subretinal scarring appearing as a white fibrotic scar in a patient with end stage CNV. [١١]

The loss of vision is due to proliferation of new capillaries accompanied by secondary fibrosis and disorganization of the RPE and outer retina (it is somewhat gradual process). Alternatively, secondary alternations in both retinal capillaries and RPE lead to accumulation of serous or serosanguineous fluid beneath RPE, neurosensory retina or within the retina it self and are associated with more active visual dysfunction. [١٢]

A wide range of disorders that affect the integrity of the RPE-Bruch's membrane-choriocapillaris complex result in the development of CNV, a classification of known conditions associated with CNV include [١٣]:

I. ***Degenerative conditions:*** age-related macular degeneration [AMD], myopic degeneration, angiod streaks.

II. ***Inflammatory or infectious conditions:*** ocular histoplasmosis syndrome [OHS], rubella, toxoplasma retinochoroiditis, sympathetic ophthalmia, tuberculosis.

III. ***Trauma:*** choroidal rupture, laser photocoagulation, operating microscopic burn, retinal cryo injury, subretinal fluid drainage, metallic intraocular foreign body.

IV. ***Idiopathic***

V. ***Choroidal tumors:*** malignant melanoma, choroidal nevus, metastatic choroidal tumors, optic glioma.

VI. ***Heredodegenerative (rare):*** vitelliform macular dystrophy, optic nerve drusen.