Advances in diagnosis and treatment of macular edema

Essay
Submitted in Fulfillment of M.SC. Degree in Ophthalmology

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Cairo University
2007

Acknowledgement

At first I would like to thank **GOD,** the merciful and the forgiving, for helping me produce this work.

I would like to express my deepest gratitude to ***Prof. Dr. Fadia Mahmoud Samy El Guindy*** for her continuous guide and help in producing this essay.

Also, I would like to express my thanks to ***Assist. Prof. Dr. Heba Tallah Abdel Rahman El- Gendy*** for her great help and valuable advice which guided me throughout the work and for her continuous encouragement and innovative ideas.

I am much thankful and grateful to all my family and to my all colleagues who helped me in producing this work.

Abstract

Macular oedema is the final common pathway of many intraocular and systemic insults. It may develop in a diffuse pattern where the macula appears generally thickened or it may acquire the characteristic petaloid appearance referred to as cystoid macular oedema. Although macular oedema may be associated with underlying conditions, it is most commonly seen following intraocular surgery, venous occlusive disease, diabetic retinopathy, and posterior segment inflammatory disease. As well as clinical suspicion, a wide range of investigations may lead to the diagnosis of macular oedema. Fluorescein angiography and optical coherence tomography provide enhanced visualization of the geometry and distribution of macular oedema. A variety of approaches to the treatment of macular oedema have been attempted, with a variable degree of success. These options have included topical and systemic steroids, topical and oral non-steroidal anti-inflammatory agents and laser photocoagulation treatment. More recently other therapeutic modalities, including immunomodulators, intravitreal injection of triamcinolone, and pars plana vitrectomy have also been employed. Clinical trials are currently looking into the use of anti-VEGFs and steroid slow-release intravitreal device for the management of macular oedema secondary to uveitis and diabetes.

Key words: Macular oedema**,** Cystoid Macular oedema ,Diabetic Macular oedema, Corticosteroids, Triamcinolone, Laser Photocoagulation, Vitrectomy, VEGF, Avastin,

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List of abbreviations

AIDS	: Aquired immunodeficiency syndrome
BAB	: Blood-aqueous barrier
BCVA	: Best corrected visual acuity
BRVO	: Branch retinal vein occlusion
CAIs	: Carbonic anhydrase inhibitors
CCME	: Clinical cystoid macular oedema
Cfz	: Capillary-free zone
CME	: Cystoid macular oedema
CMEA	: Angiographic cystoid macular oedema
CRVO	: Central retinal vein occlusion
cSLO	: Confocal scanning laser ophthalmoscope
DDS	: Drug delivery system
DME	: Diabetic macular oedema
ELM	: External limiting membrane
ERG	: Electroretinogram
ETDRS	: Early Treatment Diabetic Retinopathy Study
FA	: Fluorescein angiography
FDA	: Food and drug adminstration
HAART	: Highly active anti-retroviral therapy
HRT	: Heidelberg retinal tomograph
ICAM-1	: intracellular adhesion molecule-1
ICG	: Indocyanine green
IGF- 1	: Insulin-like growth factor-1
ILM	: Internal limiting membrane
IOP	: Intra ocular pressure
ISPR	: Inner segment photoreceptors
kHz	: kilo Hertz

ME	: Macular oedema
MHz	: Mega Hertz
MMG	: Mild macular grid
Nd:YAG	: Neodymium: yttrium- Aluminum- Garnet
NFL	: Nerve fiber layer
NPDR	: Non-proliferative diabetic retinopathy
NSAIDs	: Non Steroidal Anti-inflammatory Drugs
OCT	: Optical Coherence Tomography
OSPR	: Outer segment photoreceptors
PAF	: Platelet- activating factor
PDR	: Proliferative diabetic retinopathy
PGs	: Prostaglandins
PKC	: Protein kinase C
PPV	: Pars plana vitrectomy
PR	: Photoreceptor
PRP	: Pan retinal photocoagulation
PVD	: Posterior vitreous detachment
RP	: Retinitis pigmentosa
RPE	: Retinal pigment epithelium
SRD	: Serous retinal detachment
SLO	: Scanning Laser Ophthalmoscope
TA	: Triamcinolone acetonide
VA	: Visual acuity
VEGF	: Vascular endothelial growth factor
VMT	: Vitreomacular traction

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Introduction and Aim of Work

Anatomically the macula is measured approximately 5.5 mm in diameter and is centered approximately 4 mm temporal to and 0.8 mm inferior to the center of the optic disc ***(Gass, 1997)*.** Macular oedema consists of a localized expansion of the retinal intracellular and/or extracellular space in the macular area. This predilection to the macular region is probably associated with the loose binding of inner connecting fibers in Henle's layer, allowing accumulation of fluid leaking from perifoveal capillaries. The absence of Müller cells in the foveal region is also a contributing factor. ***(Transo et al, 2004)***.

Diabetic macular oedema is one of the common examples of macular oedema secondry to metabolic disorders due to the abnormality of glucose homeostasis resulting in disruption of the blood-retinal barrier ***(Bernard et al, 1995)***.

Cystoid macular oedema could develop following obstructive venous retinopathy. Although it could occasionally be seen in diabetic, aphakic, or pseudophakic macular oedema, yet its occurrence is significantly more common in retinal vein occlusion ***(Jones, 1998)***

In case vitreomacular adhesion is sufficiently dense, prolonged traction may cause CME, degeneration, and detachment of the macula ***(Hikichi et al, 1995)***.

Clinical examination of patients with suspected macular oedema begins with stereoscopic visualization using either the slit lamp and fundus biomicroscopic examination or indirect fundus ophthalmoscopy (***Nussenblatt et al, 1987)***. Furthermore the clinical suspicion of macular oedema can be confirmed with the aid of a wide variety of investigations that can be grouped into three categories according to whether one is

analyzing the underlying pathogenesis, the effect of the macular oedema on the retina, or its impact on visual function ***(Tranos et al, 2004)***.

A variety of approaches to the treatment of macular oedema had been attempted with a variable degree of success. These options have included topical, periocular and systemic steroids, topical and oral non-steroidal anti-inflammatory agents and laser photocoagulation treatment. More recently other therapeutic modalities, including immunomodulators, intravitreal injection of triamcinolone, and pars plana vitrectomy have also been employed. Clinical trials are currently looking into the use of a steroid slow-release intravitreal device for the management of macular oedema secondary to uveitis and diabetes ***(Tranos et al, 2004).***

Recently, Anti-VEGFs were used in treatment of macular oedema. Intravitreal bevacizumab (avastin) is proved to be effective as primary treatment of DME with anatomical and functional improvement and reduced risk of VA loss (***Arevalo et al, 2007)***.The use of intravitreal bevacizumab for BRVO offers significant advantages over triamcinolone and grid-laser treatment ***(Iturralde et al, 2006).***

Aim of Work

A review of different new modalities of diagnosis, methods of investigations and new treatment options in macular oedema.

Anatomy of the macula

Anatomically the macula (macula lutea or central retina) is defined as that portion of the posterior retina that contains xanthophyll and two or more layers of ganglion cells. It measures approximately 5.5 mm in diameter and is centered approximately 4 mm temporal to and 0.8 mm inferior to the center of the optic disc (Fig. 1-1) ***(Gass, 1997)*.**

On the basis of microscopic anatomy, the macular area can be further subdivided into several zones. The fovea (fovea centralis) is a depression in the inner retinal surface in the center of the macula (Fig. 1-1; A). It measures approximately 1.5 mm or one disc diameter in size**.** The central floor of the fovea is called the foveola. It measures approximately 0.35 mm in diameter (Fig. 1-1; *a).* It lies within the capillary-free zone (cfz), which measures approximately 0.5 mm in diameter in most patients (Fig. 1-1; *cfz).*A small depression in the center of the foveola is called the umbo (Fig. 1-1; *u).*The Fovea is surrounded by a 0.5-mm-wide ring zone where the ganglion cell, inner nuclear layer, and outer plexiform layer of Henle are the thickest is called the parafoveal area (Fig. 1-1; *B).* This zone is in turn surrounded by a 1.5-mm zone referred to as the perifoveal area (Fig. 1-1; C) with a max retinal thickness (approximately 0.55 mm) at the foveal margin and minimal thickness (0.13mm) at the umbo ***(Gass, 1997)*.**

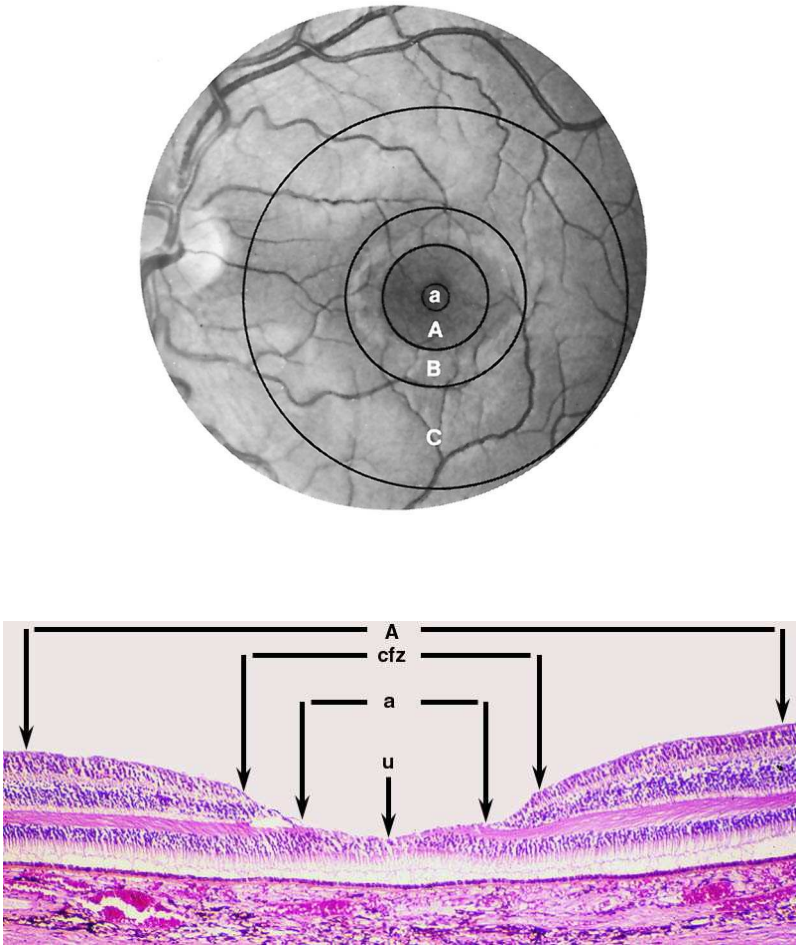

Fig. 1-1 *Normal Macula* ***(Hogan and Alvarado et al, 1971)***

Topographic anatomy *(above)* and histopathology (below) of the macula. **A**, Fovea containing the foveola (a), capillary-free zone (cfz), and umbo (u). **B**, Parafovea. **C**, Perifovea.

Ophthalmoscopically, the anatomic subdivisions of the macula are ill defined. Where, the center of the macula appears as a poorly defined, one-fourth to one disc diameter size zone of greater pigmentation that is maximum in the foveolar area. The foveal reflex appears to lie just in front of the center of the foveola in most normal eyes and therefore overlies the anatomic umbo. There are no consistent ophthalmoscopic landmarks to indicate the margins of either the 0.35-mm diameter foveola or the 1.5-mm diameter fovea. The margins of the capillary-free zone of the retina that in most patients measures approximately 500 μm in diameter angiographically can only be estimated biomicroscopically because the perifoveolar capillary network is not visible***(Fig.1-2, A)***. In younger patients an oval or round halo light reflex at the inner retinal surface may correspond with the foveal margin