RETINAL DIAGNOSIS OF AMD, DIABETES AND OTHER ISCHEMIC VASCULAR DISEASES

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Introduction

- Normal Retinal Histology
- Retinal Ischemic Vascular Diseases
  - Diabetic Retinopathy
  - Hypertensive retinopathy
  - Central and Branch Retinal Artery Occlusion
  - Central and Branch Retinal Vein Occlusion
- Age Related Macular Degeneration (AMD)
Two distinct layers form the inner lining of the posterior two-thirds of the globe:

- The neurosensory retina with 9 distinct histologic layers, derived from the inner layer of the optic cup.
- The retinal pigment epithelium (RPE), a pigmented layer derived from the outer layer of the optic cup.
Sensory Retina

- Transparent layer firmly attached in two areas:
  - Optic disc, and at the ora serrata anteriorly.

- Elsewhere the attachment is weak, maintained by:
  - Intraocular pressure
  - Contacts between the photoreceptor outer segments, the RPE villi, and a mucopolysaccharide-cementing substance

- The retina terminates at the optic disk and the nerve fiber layer increases and is the only structure that continues into the optic nerve.
Retinal Histopathology

- Retina
- Choroid
- Sclera
Retinal Pigment Epithelium

- Single layer of hexagonal-shaped cells with regular arrangement
- The RPE cells vary in size and shape depending on age and location
- Extends from the margin of the optic disk to the ora serrata like the retina
Functions of the RPE

- Maintaining adhesion of the neurosensory retina
- Providing a permeable barrier between the choroid and neurosensory retina
- Phagocytosis of rods and to a lesser extend cones outer segments
- Synthesis of inter-photoreceptor matrix
- Absorption of light and reduction of light scatter within the eye hence improving image resolution
- Transport plus storage of metabolites and vitamins (especially Vitamin A).
The macula or posterior pole is the area bounded by the inferior and superior major temporal vascular archades.

The fovea is a depression in the retina similar in size to the optic disc (1.5 mm).

The foveola is a small red-dish disc in the center of the fovea.
Foveomacular Region

- Area of sharp central vision
- The foveola shows loss of all layers of the sensory retina except for the photoreceptors, the external limiting membrane, the outer nuclear layer, the outer most portion of the outer plexiform layer and a thin internal limiting membrane.

Optical coherence tomography (OCT)
Diabetic Retinopathy
Diabetic Retinopathy

- Leading cause of blindness between the ages of 20-60
- Retinal manifestation of a generalized microangiopathy
- Early in the course the following physiologic abnormalities occur:
  - Impaired regulation of the retinal vasculature
  - Alterations in the retinal flow
  - Breakdown of the blood-retinal barrier
    - Normal BRB is a tight and restrictive physiologic barrier that regulates ion, protein, and water flux into and out of the retina.
- Clinically it is classified as:
  - Non-proliferative
  - Proliferative
## Diabetic Retinopathy Clinical Findings

### Non-Proliferative
- Hemorrhages (dot-blot)
- Cotton wool spots (microinfarcts)
- Hard exudates
- Microaneurysms

### Proliferative
- New blood vessels in the optic disc (NVD)
- New blood vessels in the retina (NVE), vitreous hemorrhage

In the past laser burns used. Anti-vascular endothelial growth factor (VEGF) injections currently used
Diabetic Retinal Capillary Changes

- Histologically the primary changes that occur are:
  - Thickening of the retinal capillary basement membrane
  - Selective loss of capillary pericytes
  - Microaneurysm formation
  - Retinal capillary closure (acellularity)
Microaneurysms, dilated intraretinal telangiectatic vessels (IRMAs) and capillary acellularity
Diabetic Macular Edema

- **Leading cause of blindness from diabetic retinopathy, especially in type 2 diabetes (non-insulin dependent); develops in ½ patients with diabetic retinopathy**

- **Macular edema often seen in combination with lipid deposition and ischemia**
Cotton-wool Spots

- Micro-infarcts in the nerve fiber layer, commonly associated with diseases of microvascular ischemia:
  - Diabetic retinopathy
  - Hypertensive retinopathy
  - Systemic lupus erythematosus

Cytdoid Body: Swollen axonal stumps stuffed with mitochondria appearing as eosinophilic inclusions resembling a cell nucleus
Hard exudates appear as amorphous eosinophilic deposits in the outer plexiform layer.

Proliferative diabetic retinopathy with neovascularization
Diabetic Ocular Changes

- Iris neovascularization (back arrow)
- Lacy vacuolization of the iris pigment epithelium due to intraepithelial vacuoles containing glycogen (red short arrows)
- Diffuse thickening of the basement membrane of the pigmented ciliary body epithelium (red arrow)
- Corneal epithelium basement membrane thickening
- Increase incidence of cataracts
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Hypertensive Retinopathy

- Systemic hypertension produces changes in retinal, choroidal, and optic disc circulations.
- Arteriolar narrowing precedes the development of hypertension by increasing peripheral vascular resistance.
- Narrowing is due to intimal thickening, medial hyperplasia, hyalinization and sclerosis.
- Severe systemic hypertension results in arteriolar occlusion, retinal hemorrhages (flame-shaped) and retinal ischemia (cotton-wool spots).
Patient with hypertensive retinopathy. Cotton-wool spots and macular star (exudates in Henle’s outer plexiform layer)
Central and Branch Retinal Artery Occlusion

- Usually affects older patients.
- Caused by thrombosis, blockage by an embolus originating in the heart or carotid arteries, localized arteriosclerotic changes or rarely vasculitis.
- Complete occlusion may be preceded by amaurosis fugax (temporary loss of vision in one eye).
- Visual recovery is rare, and patients have reduced life expectancy from vascular disease.
- Histology shows loss of inner two-thirds of the retina.
Cherry Red Spot
Gray edema and ischemia of the neural retina (NFL and GCL) exaggerates the normal redness of the foveal disc

Loss of inner layers of retina with inner ischemic retinal atrophy
Central and Branch Retinal Venous Occlusions

- Commonest retinopathy after DR and AMD
- Changes in the central retinal artery and lamina cribrosa leading to compression of the central retinal vein creating a turbulent flow and predisposing to thrombosis.
- Occurs in two forms:
  - Milder, perfused type with <10 disc areas of nonperfusion
  - More severe, nonperfused/ ischemic type (>10 disc areas)
- Occurs in hypertension, arteriosclerosis, diabetes mellitus and glaucoma.
- Dilatation of the affected vein, blotchy hemorrhages in the territory of the retina drained by the vein, marked retinal edema and retinal ischemia with necrosis (cotton-wool spots).
Typical, widespread hemorrhages in the fundus due to a central retinal vein occlusion.

Intraretinal hemorrhages in inner retinal layers, edema and focal necrosis.
Gliosis, microaneurysms and acellular capillaries develop with time.
Age-Related Macular Degeneration (AMD)
Age-Related Macular Degeneration

- Leading cause of new blindness in adults over 60.
- Genetic and environmental factors are involved.
- Common genes: CFH and ARMS2.
- Risk factors: older age, tobacco use, family history, cardiovascular disease

- There are 2 types of AMD: Dry and Wet.
- Most people develop dry AMD (atrophic AMD).
- Wet AMD (advanced neovascular AMD) is a less common type that usually causes faster vision loss.
- Any stage of dry AMD can turn into wet AMD — wet AMD is always late stage.
First Detectable changes: Drusen

The symptoms of AMD include: hazy vision, difficulty seeing when going from bright light to low light, and a blank or blurry spot in the central vision.

Diffuse drusen – eosinophic material beneath the RPE with soft and hard drusen
Dry Macular Degeneration

- Gradual reduction of the central vision
- Clinically, the retinal damage is limited to the foveo-macular area and causes a gradual and subtle visual loss
- The atrophy of the RPE tends to spread and form well-demarcated borders, called geographic atrophy of macular degeneration

Nutritional supplements found to be beneficial in treating early dry AMD include:
- vitamin C
- vitamin E
- Lutein
- Zeaxanthin
- Zinc Oxide
- Copper (cupric oxide)
Wet Macular Degeneration

- A fibrovascular tissue (star) is present between the retinal pigment epithelium and its basement membrane (Bruch’s membrane) – choroidal neovascularization

There are 2 treatment options that can slow down or stop vision loss from wet AMD:
- Anti-VEGF (vascular endothelial growth factor) injections
- Photodynamic therapy (PDT)
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Picture Sources

- www.oculist.net
The End
Questions?