Ocular Manifestations of Systemic Disease

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Objectives

1. To describe the ocular signs and symptoms associated with selected systemic diseases and their serious ocular sequelae.

2. To review the important features of diabetic retinopathy and the current screening guidelines.

3. To be familiar with the important ocular features of hypertension, thyroid disease, sarcoidosis and inflammatory conditions, malignancy and acquired immunodeficiency syndrome.
Introduction

- “The eyes are the window to the soul.”
  --English proverb

- Numerous systemic diseases have ocular manifestations

- Occasionally, the eye findings may be the first indication of underlying systemic disease leading to diagnosis
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Ocular Anatomy
Anatomy: Periocular soft tissues
Anatomy: Lacrimal System
Anatomy: The Globe

- Iris
- Anterior chamber
- Cornea
- Conjunctiva
- Pupil
- Limbus
- Schlemm's canal
- Lens
- Ciliary body
- Sclera
- Choroid
- Retina
- Vitreous cavity
- Optic disc
- Fovea
- Macula
- Central retinal artery and vein
- Optic nerve
- Dura mater
Anatomy: The Retina

The macula = central vision
Examination

- Vision
- External
- Pupils
  - Relative Afferent pupillary defect (RAPD)
- Motility
- Exam of Anterior Segment (Slit Lamp)
- Dilated Ophthalmoscopy
- Visual Fields
Hypertension

- Systolic > 130, Diastolic > 85 mmHg
- 65 million Americans
- Heart, kidneys, brain, & Eye
- May cause damage to retina, choroid, and optic nerve
- Acute & Chronic changes
- Preeclampsia
Hypertension

- **Ocular findings**
  - Arteriolar narrowing & A-V Nicking
  - Cotton Wool spots
  - Retinal hemorrhages
  - Optic nerve swelling (edema)
  - Retinal ischemia & neovascularization

- **May be associated with:**
  - Branch retinal artery occlusion (BRAO)
  - Branch retinal vein occlusion (BRVO)
  - Central retinal vein occlusion (CRVO)
  - Retinal artery macroaneurysm (RAMA)
Hypertensive Retinopathy

Images courtesy of Redatlas.org

Cotton wool spots
Hypertensive Retinopathy

Optic Nerve Edema
Hypertensive Retinopathy

BRAO

CRVO
Diabetic retinopathy (DR) is leading cause of blindness in 20-64yo in US

Duration of DM is directly related to prevalence of retinopathy
- After 20 yrs: **99% of type 1 and 60% of type 2** will have some degree of DR

Pathologic changes include microvascular damage leading to hypoxia, vascular leakage & edema, ischemia, and neovascularization

Prevention & Importance of systemic blood glucose, pressure, & lipid control: DCCT, UKPDS, & ACCORD trials
Diabetic Retinopathy

Classification:

- Non-Proliferative diabetic retinopathy (NPDR)
- Proliferative Diabetic Retinopathy (PDR)

Complications Resulting in Visual Loss

- Macular edema (capillary leakage)
- Macular ischemia (capillary occlusion)
- Sequelae from ischemia-induced neovascularization
Diabetic Retinopathy: Macular Edema
Diabetic Retinopathy:
PDR

NVD

NVE
Diabetic Retinopathy: PDR

NVE
Diabetic Retinopathy: PDR

Vitreous Hemorrhage

Tractional Retinal Detachment
Diabetic Retinopathy: Treatment

- Laser
- Pharmacologic (anti-VEGF meds)
- Surgery

Laser Pan Retinal Photocoagulation

Vitrectomy Surgery
Diabetic Retinopathy: Vitrectomy Surgery

Scar tissue, membranes, & blood on surface of retina

Neovascularization (PDR)
Diabetic Retinopathy: Screening & Prevention

- Screening eye examination for all patients:
  - At time of diagnosis for type 2
  - Within 5 yrs of diagnosis for type 1
  - Pregnancy
- Follow-up exams will be dependent on initial eye findings
- Blood glucose, Blood pressure, and Lipid optimization
- Stop smoking
- Exercise
Carotid Stenosis

- Amaurosis fugax
- Hollenhorst plaque
- Retinal artery occlusion
- Ocular ischemic syndrome (& neovascular glaucoma)
Hollenhorst plaque
Carotid Stenosis: Branch Retinal Artery Occlusion

Retinal whitening due to edema

Emboli
Ocular Ischemic Syndrome

Pain
Red Eye
Loss of vision
Elevated Intraocular Pressure

Patients at risk for ischemic CV disease, stroke, & peripheral Vascular disease
Sickle Cell Disease

- Autosomal Recessive

- Genotype
  - 8% Sickle cell trait (HbAS)
  - 0.4% Sickle cell disease (HbSS)
  - 0.2% SC disease (HbSC)
  - Sickle Thalassemia

- Systemic Complications
  - Crises (painful episodes)
  - Acute chest syndrome
**Sickle Cell Disease: Ocular Complications**

- **Frequency**
  - HbSC (most common) – 33%
  - Sickle Thalassemia – 14%
  - HbSS – less frequently but have more severe systemic complications – 3%

- **Pathogenesis:**
  - Peripheral retinal nonperfusion – ISCHEMIA = Neovascularization
  - Hemorrhage & Tractional Retinal Detachment
Sickle Cell Disease

Capillary nonperfusion in peripheral retina
Sickle Cell Disease

Neovascularization
Sickle Cell Disease: Special Situations

- High Risk for elevated intraocular pressure due to sickling of RBCs
- Require aggressive medical & sometimes surgical Rx to prevent optic nerve damage

Know Sickle Cell Status for patients with Traumatic Hyphema
Giant Cell Arteritis

- AKA: Temporal Arteritis
- Systemic granulomatous vasculitis affecting medium- and large-sized vessels
- Age > 50 yo
- Symptoms
  - Headache
  - Scalp tenderness
  - Jaw claudication
  - Polymyalgia rheumatica
  - Acute vision loss
Giant Cell Arteritis

- Diagnosis:
  - Clinical history
  - Stat ESR &/or CRP
  - Temporal artery biopsy

- Treatment:
  - High-dose systemic steroids (do not defer until after biopsy)
Giant Cell Arteritis

Dilated superficial temporal artery

Scalp Necrosis
Giant Cell Arteritis

Central Retinal Artery Occlusion
Temporal Artery Biopsy

Superficial Temporal artery
Thyroid Eye disease

- May occur with hyper-, hypo-, or euthyroid states

- Hyperthyroidism: goiter, tremor, pretibial myxedema, atrial fibrillation, etc

- Ocular Findings:
  - Proptosis (exophthalmos)
  - Lid Retraction -- **Thyroid stare**
  - Corneal exposure (dry eye, corneal ulcer)
  - Diplopia (due to eye muscle restriction)
  - Optic Nerve compression (optic neuropathy) – 5%
Thyroid Eye Disease: Pathophysiology

- Autoimmune process with cross-reaction against orbital and periorbital soft tissues

Enlargement of ocular rectus muscles
Thyroid Eye disease
Exophthalmos: “Thyroid Stare”
Thyroid Eye disease

Chemosis & Dry Eye
Thyroid Eye disease

- CT scan orbits or Orbital Ultrasound
  - Look for enlargement of eye muscles
- Restrictive myopathy = Double Vision
Thyroid Eye disease:
Orbital Decompression

(For TED-related Optic Neuropathy)
Thyroid Eye disease: Management

- Treatment Considerations:
  - Artificial tears & lubrication
  - Systemic steroids & external beam radiation (if vision threatening)
- Surgery:
  - Orbital decompression
  - Eye muscle surgery
  - Eyelid Surgery
- Stop Smoking
HIV & AIDS

- Eyelids: Kaposi sarcoma, molluscum contagiosum, Herpes zoster ophthalmicus
- Orbit: Cellulitis, B-cell lymphoma
- Cornea: Keratitis (microsporidium, HSV, HZV)
- Keratoconjunctivitis sicca (severe dry eye)
- Anterior uveitis
- HIV retinopathy
- Retinitis (CMV, VZV, toxoplasmosis)
- Choroiditis (pneumocystis, toxoplasmosis)
- B-cell intraocular lymphoma
Kaposi Sarcoma

- Purplish red to bright red highly vascular lesions with surrounding telangiectatic vessels
- Associated with Human Herpes Virus-8 (HHV-8)
- 20-24% of AIDS-related Kaposi sarcoma will involve eye
- Eyelid & Conjunctiva
- Mostly local mass effects – pain, poor eyelid closure, etc
- Treatment: chemotherapy, surgical (if large to debulk)
Kaposi Sarcoma

Photos courtesy of Gary N Holland, MD, University of California, Los Angeles, Department of Ophthalmology, Jules Stein Eye Institute
HIV/AIDS: Molluscum contagiosum

- Typically multiple lesions in HIV or AIDS
HIV/AIDS:
Herpes Zoster

Hutchinson’s sign
AIDS: CMV Retinitis

- Most common intraocular infection with AIDS
- Much reduced incidence since HAART (50% to 10% of pts)
- CD4 count typically < 50 cells/mm³
- Retinal necrosis, exudation, & hemorrhage

Treatment:
- IV ganciclovir/foscarnet
- Intravitreal ganciclovir/foscarnet; Ganciclovir intravitreal implant
AIDS: CMV Retinitis

CD4 < 50
HIV/AIDS:
Toxoplasmosis Retinitis

CD4<100
Syphilis

= Tertiary Syphilis
Need LP
Rx with IV Penicillin G
Tuberculosis

Granulomas = Choroidal Tubercules

Uveitis
Choroidal granulomas
Periphlebitis

Granulomas = Choroidal Tubercules
Septicemia & Endogenous Endophthalmitis

- Hematologic seeding of the eye with infection
- Gram-positive, gram-negative, fungal etiologies
- Candida is most common causative organism
- Immunocompromised or immunosuppressed patients
- Chronic diseases (DM, Renal failure) & indwelling lines or invasive procedures, & intravenous hyperalimentation
- IV Drug Use
- Bilateral in 25%
- Clinical scenarios: Endocarditis, pneumonia, indwelling catheter (fungal), following surgery (cardiac, pulmonary, urologic)
- Treatment: IV Anti-bacterial/fungal
  - Adjunctive: +/- intravitreal antibiotics, Vitrectomy surgery
Septicemia & Endogenous Endophthalmitis

Hypopyon

Pneumonia

Bilateral Endophthalmitis
Septicemia & Endogenous Endophthalmitis

Fungal Endophthalmitis

Vitreous Haze & Debris (Obscures view of retina)
Ankylosing spondylitis

- Spondylarthropathy of the axial skeleton
- Typically affects males (4:1)
- 90% are HLA-B27 (+)
- Presents in early adulthood (15-35 yo) with pain & stiffness in lower back
  - Limitation of spinal flexion
- Juxta-articular osteoporosis & fusion of sacro-iliac joints
- “Bamboo spine”
Ankylosing spondylitis

- **Ophthalmic features:**
  - Anterior uveitis in 30-40%

- **Symptoms**
  - Photophobia
  - Redness
  - Decreased vision

- **Treatment:**
  - Topical corticosteroids
  - Cycloplegia

Fusion of sacro-iliac joints
Ankylosing spondylitis
Behcet’s Disease

- Vasculitis leading to chronic inflammation & ulceration
- Oral aphthaous ulcers
- Genital ulcers
- Skin lesions (e.g. erythema nodosum)
- Eye inflammation (iritis, retinal vasculitis)
Inflammatory Bowel Disease (IBD): Crohn’s Disease & Ulcerative Colitis

- Ulcerative colitis: relapsing, non-transmural, restricted to colon
- Crohn’s disease: relapsing, transmural, affects entire GI tract
- Ocular complications in 10%
  - Uveitis
  - Episcleritis
  - Scleritis
  - Women at higher risk
  - Associated with HLA-B27
Sarcoidosis

- Focal noncaseating granulomas
- AA females, 20-40 yo
- Elevated Calcium, ACE, abnormal CXR
- Lacrimal gland granulomas
- Anterior uveitis
- Retinal inflammation
- Ocular complications: glaucoma, cataract

Hilar Lymphadenopathy
Sarcoidosis

Lacrimal Gland Granuloma
Sarcoidosis

“Mutton fat” KP
(Keratitic Precipitates)
Sarcoidosis

Posterior Synechiae of the iris
Sarcoidosis

Granuloma of optic nerve

Perivascular Inflammation
Rheumatoid Arthritis

- 25% may have ocular findings
- Dry eyes (15-25%)
- Episcleritis
- Scleritis
- Corneal ulcers
- Uveitis
Rheumatoid Arthritis: Scleritis
Multiple Sclerosis: Optic Neuritis

50% of patients with MS will develop Optic Neuritis

20-30% of time will be presenting sign for MS
Metastatic Disease

- Most common intraocular malignancy in adults
- May be asymptomatic
- May produce decreased or distorted vision
- Most common primary: Lung, Breast
- 10% have unknown primary
- No prior history of Cancer in 25%
Metastatic Lung Cancer
Metastatic Breast Cancer

Elevated Amelanotic Mass in Macula

S/p ChemoRx
Myasthenia gravis

- Autoimmune neuromuscular disorder leading to fluctuating muscle weakness & fatiguability
- Circulating antibodies block Ach receptors at post-synaptic NM junction, inhibiting stimulative effect of neurotransmitter Ach
- Ptosis, double vision, problems chewing, talking, and swallowing
- Diagnosis: Tensilon test, single-muscle fiber EMG
- Treatment: Acetylcholinesterase inhibitor (Mestinon)
Myasthenia gravis

Ptosis

Fatiguability
Neurofibromatosis-1

- Autosomal Dominant
- Chromosome 17
- Diagnostic Criteria
  - Café au lait spots
  - Intertrigenous freckle
  - Neurofibroma
  - Optic nerve glioma
  - Lisch nodules
  - Osseous lesions
  - Family history in 1st degree relative
Neurofibromatosis-1

Seen in 90% of cases
Neurofibromatosis-1

S-Shaped Eyelid Neurofibroma
20% with NF-1 will have Optic Nerve glioma

50% of pts with optic nerve glioma have NF-1
Sturge-Weber Syndrome

- Sporadically inherited phakomatoses
- Glaucoma
- Dilated & tortuous episcleral vessels
- Seizures
- CNS angiomas (Leptomeningeal hemangioma)
- Calcification
Sturge-Weber Syndrome

Nevus flammeus (Port Wine Stain)
Sturge-Weber Syndrome: Choroidal Hemangioma
Systemic Medications

- **Benign ocular conditions**
  - Amiodarone – whorl keratopathy

- **Toxic Retinopathies**
  - Thioridazine, chloroquine, hydroxychloroquine, tamoxifen

- **Toxic Optic Neuropathies**
  - Ethambutol, isoniazid
Hydroxychloroquine: Ophthalmic Screening

- Used for rheumatoid arthritis, SLE, etc
- Ocular toxicity rare with usual dose 200 mg bid (5-7mg/kg/day)
- Toxicity related to cumulative dose (>460 g) & duration of use
- Ocular findings: bulls-eye retinopathy
- Recommended screening:
  - Baseline exam & Central VF testing
  - Annual examination & repeat central VF for pts using medicine > 5 yrs
Plaquenil toxicity: Bull’s Eye Maculopathy
Thank You for your Attention

Any Questions???