

OCULAR MANIFESTATIONS OF SYSTEMIC DISEASES

Objectives:

1. To describe the ocular signs and symptoms associated with systemic diseases and their serious ocular sequelae.
2. To familiarize the student with the important features of diabetic retinopathy and the current screening guidelines
3. To recognize and describe the ophthalmoscopic features of diabetic eye disease
4. To be familiar with the important ocular features of hypertension, thyroid disease, sarcoidosis and inflammatory conditions, malignancy and acquired immunodeficiency syndrome.

Reference:

Chapter 8, Basic Ophthalmology. Frank Berson. Pages: 120-133

Relevance:

Diabetes affects nearly 5% of the population and is the leading cause of new cases of blindness in the working-age population. Several clinical trials have demonstrated that with appropriate referral and treatment the incidence of severe visual loss can be reduced by at least 50%. AIDS is another disease in which more than 75% of patients have some ocular involvement.

Diabetes Mellitus

The most important ocular complication is diabetic retinopathy. The longer a person suffers from diabetes the greater the likelihood of developing retinopathy.

IDDM (insulin dependent):

23% have retinopathy by 5 years after initial diagnosis

80% after 15 years

NIDDM (type 2): similar but lower incidences.

Non-proliferative diabetic retinopathy (NPDR) (graded mild-moderate-severe)

1. Occluded or leaky capillaries: hard exudates (lipid in the nerve fiber layer of the retina)
2. Blood in the retina: flame hemorrhages (nerve fiber layer hemorrhage) and dot and blot hemorrhages (deeper layer of the retina)
3. Microinfarctions of the retina: soft exudates or cotton wool spots

Severe NPDR is marked by increased venous tortuosity, venous beading and IRMA (intraretinal microvascular abnormalities) in addition to the above.

Proliferative diabetic retinopathy (PDR)

Characterized by new abnormal blood vessel formation (neovascularization) of the optic disc or retinal surface. Neovascularization can also occur on the iris leading to severe glaucoma. PDR often remains asymptomatic well beyond the stage of optimal treatment.

If an eye with PDR is not treated, these fragile new blood vessels may bleed into the vitreous causing a vitreous hemorrhage. Fibrous tissue which accompanies the new blood vessels may contract and cause a traction retinal detachment.

Treatment

All patients with retinopathy should be evaluated by an eye care professional. Macular edema may require a focal laser treatment to the areas of leaking blood vessels. This treatment can reduce visual loss by 50%.

PDR is treated by pan-retinal argon laser photocoagulation (PRP). 1000-3000 laser burns are scattered over the entire surface of the retina except for the macula. The treatment is based on the concept that a reduction of the metabolic oxygen requirement of the retina promotes regression of the neovascular tissue. Appropriate PRP can reduce the incidence of severe visual loss by 50-90%.

Studies have shown (Diabetes Control and Complications Trial) that poor glycemic control, hypertension and proteinuria are significant risk factors for the development and progression of diabetic retinopathy.

Hypertension

Chronic changes: Arteriolar sclerosis

Ophthalmoscopic features include:

1. Changes in the arteriolar light reflex

-normal

-Copper wire

-Silver wire

2. Arteriovenous crossing changes

Most significant when located more than 1 disc diameter from the optic nerve head.

Acute changes: Elevated Blood Pressure

-a severe acute rise causes fibrinoid necrosis of the vessel wall which results in lipid exudates, nerve fiber layer infarcts (cotton wool spots), flame shaped hemorrhages and sometimes whitish swelling and edema of the retina. In malignant hypertension, optic disc swelling also occurs.

Thyroid Disease

Grave's disease is an autoimmune disease. Common clinical features include:

1. **Proptosis** or exophthalmos, unilateral or bilateral, may be asymmetric, **is due to extraocular muscle enlargement**

2. **Upper lid retraction**, with upper lid lag in downgaze

3. Thyroid "stare"

4. **Corneal exposure**: ranges from mild dry eye to serious exposure keratopathy with corneal ulceration

5. **Diplopia**- due to a restrictive extra-ocular muscle palsy. Does not follow the pattern of a neurologic muscle palsy

6. **Optic nerve compression:** this optic neuropathy is caused by the enlarged extraocular muscles in the confined retro-orbital space

Treatment ranges from lubricants (artificial tears) for dry eye to orbital decompression surgery with systemic steroids and external beam radiotherapy to treat a vision threatening optic neuropathy. Thyroid orbitopathy tends to “burn out” after about 2 years and most surgery to deal with the eyelid problems and strabismus isn’t done until the quiescent phase.

Auto-immune conditions

Sarcoidosis:

Multi-organ disease characterized by the presence of non-caseating granulomas.

Ophthalmic manifestations: Iritis, iris nodules, lid granulomas, dry eye, retinal vasculitis and choroiditis, inflammatory optic neuropathy

Diagnosis by positive biopsy. Lab evidence: Elevated ACE (angiotensin converting enzyme), anergy, (+) chest x-ray.

Treated with topical or systemic steroids in conjunction with a rheumatologist or respirologist

All of the following may be associated with eye manifestations, especially dry eye and/or anterior uveitis (iritis)

Rheumatoid Arthritis

Juvenile Rheumatoid Arthritis

Behcet’s disease

Reiter’s syndrome (seronegative arthritis and conjunctivitis/urethritis)

Ankylosing Spondylitis

Malignancy

A primary malignancy of the eye is rare. Yet ocular and orbital metastases are present in 5% of cancer patients at autopsy. These usually arise from the breast or lung and infiltrate the choroid, but may also affect the optic nerve or an extraocular muscle.

Lymphoma and leukemia may also occur in the eye with conjunctival or optic nerve infiltration.

AIDS

The most common manifestations are:

1. **Cotton wool spots (AIDS retinopathy)**: present in 50% of patients, due to immune complex microthrombi in the retinal vasculature. No treatment necessary.
2. **CMV retinitis (cytomegalovirus)**: Leading cause of blindness in AIDS patients. “Pizza pie” retina due to hemorrhagic necrosis. Indicative of low to absent CD4 counts. Now treated with Gancyclovir intravitreal implants with improved visual outcomes.
3. **Kaposi’s sarcoma** of the eyelids: Vascular skin malignancy, may also occur on the conjunctiva. Has the appearance of a hemangioma.

Less Common:

1. Zoster Ophthalmicus
2. Herpes Simplex keratitis and retinitis
3. Toxoplasmic or syphilitic uveitis or retinitis

Systemic Infection

Candidiasis may occur in compromised patients with candida growing in blood cultures. Typically involves a seriously ill ICU patient with a central parenteral feeding line. Retinitis and vitreous fungal balls may be seen. Have the appearance of fluffy white infiltrates. Therapy is with systemic antifungals.

Herpes Zoster (Shingles), affecting the 1st division of the trigeminal (Vth) nerve, typically causes a conjunctivitis or keratitis in addition to the characteristic dermatomal dermatitis. The classic presentation is the presence of vesicles on the tip of the nose, implicating the naso-ciliary branch of the Vth nerve. Anterior uveitis and retinitis or optic neuropathy may also occur.

Treatment involves systemic antivirals (Acyclovir 800 mg 5x/day) with proven benefit if started within 72 hours of the onset of the vesicles.

Specific ocular complications are treated with topical medications.