MANAGING THE ANTENIOR SEGMENT IN SYSTEMIC DISEASE

Carlo J. Pelino, OD, FAAO
cpelino@salus.edu

Joseph J. Pizzimenti, OD, FAAO
pizzimen@nova.edu
I. Rosacea Review

A. Understanding Rosacea
   1. What is rosacea?
   2. Who gets rosacea?
      a) Range of occurrence
   3. What causes rosacea?
      a) Potential causative agents
         (1) “Triggers” of rosacea’s signs and symptoms

II. Recognizing Rosacea

A. Symptoms, Signs, and Stages
   1. Prerosacea
      a) Flushing
      b) Erythema
   2. Stage 1
      a) Prerosacea plus:
         (1) Telangiectasias
   3. Stage 2
      a) Stage 1 plus:
         (1) Edema
         (2) Papules/pustules
         (3) Enlarged pores
   4. Stage 3
      a) Stage 2 plus:
         (1) Tissue hyperplasia
         (2) Rhinophyma

III. Diagnosis and Management

A. Differential diagnoses
   1. Rosacea is a clinical diagnosis; no lab tests necessary
   2. Masqueraders of rosacea

B. Managing the symptoms and Emotions
   1. Medical therapy
   2. Surgical therapy
   3. Counseling
IV. Ocular Rosacea

A. Eye signs are secondary to the inflammatory skin condition
B. Ocular Surface Disease is the main ocular complication of rosacea
C. Etiology is inflammation from Staphlococcus Exotoxins
D. Meibomitis
E. Ophthalmic Work-up
   1. Case examples of ocular rosacea
F. Treatment approaches
   1. Lubricate
   2. Punctal occlusion
   3. Topical meds
      a) Steroids
      b) Cyclosporine
      c) Antibiotics
         (1) Topical azithromycin (AzaSite)
            (a) Has AB and Anti-inflammation Properties
   4. Systemic meds
   5. Dermatology consult
   6. Resources for patients and doctors

Ocular Ischemic Syndrome:

Pathogenesis: Ocular Ischemic Syndrome:

Atheromatous ulceration and stenosis at the bifurcation of the common carotid artery (90% occlusion has to be present )

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<td>&lt; 200 mg/dl</td>
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<td>&gt; 2,500 mg/dl</td>
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“Lipemia Retinalis”

<table>
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<tr>
<th>Cholesterol</th>
<th>Triglyceride</th>
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<td>990 mg/dl</td>
<td>7, 200 mg/dl</td>
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Signs: Ocular Ischemic Syndrome:

- Dilated but not tortuous retinal veins
- Retinal Hemorrhages in mid-peripheral retina (80%) of patients
- Cotton Wool Spots (5%)
- Neovascularization of the Disc (35%)
- Neovascularization of the Retina (8%)
- Rubeosis iridis (65%)
- Uveitis – mild anterior (20%)
- Emboli (retinal)
- Lower IOP – initially

Important Note:

- Leading cause of death = Ischemic heart disease
- Second leading cause of death = Stroke

Work Up:

- Carotid artery evaluation
- Cardiology work up (Echocardiogram)

Treatment:

- Consider carotid surgery if warranted (Endarterectomy)
- Therapeutic approach – Aspirin
- Panretinal photocoagulation (PRP) if neovascularization
- Stop smoking

Side Effects of the Statins:

- Muscle pain
- Renal failure
- Liver enzyme abnormalities
- Myositis
- Rhabdomyolysis
Statins – May cause cataract

- Make sure to check for “Corneal Arcus” – predictor for heart attacks

- Corneal Arcus in patients < 50 years old may be a better indicator than serum cholesterol at showing that they are at risk of having a heart attack

- **Arcus Juvenilis** = Patients younger than 50 years old

**Corneal Arcus**

- Arcus Senilis
- Arcus Juvenilis
- In younger people may lead to MI or cardiovascular disease
- Arcus = “Bow like”
- Hyperlipoproteinemia in younger patients

The Association of Corneal Arcus with Coronary Heart Disease and Cardiovascular Disease Mortality in the Lipid Research Clinics Mortality Follow-up Study (*Am J Public Health* 1990; 80:1200-1204)

Prospective study of White men (n = 3,930) and women non-hormone users (n = 2139) Followed for an average of 8.4 years

**Results:**

- Corneal Arcus was strongly associated with CHD and CVD mortality only in hyperlipidemic men ages 30-49 years.
- Among 30-49 year old males, corneal arcus was a prognostic factor for CHD independent of hyperlipidemia
Uveitis:

**Symptoms:**
- Pain, photophobia, lacrimation – usually of sudden onset

**Signs:**
- Red eye (Circumlimbal flush)
- Pupillary miosis
- Keratic Precipitates
- Cells in the anterior chamber (WBC)
- Red eye (Circumlimbal flush)
- Pupillary miosis
- Keratic Precipitates
- Flare in the anterior chamber (Protein)

**Granulomatous vs Non-granulomatous**

**Classification:**
- Granulomatous
- Non-Granulomatous

**Anatomic Classification of Uveitis:**
- Anterior Uveitis
  - Iritis
- Iridocyclitis
  - Iritis and Cyclitis
- Intermediate Uveitis (pars planitis)
- Posterior Uveitis
- Panuveitis

**Anterior Uveitis:**
- Most common form of uveitis
- 8 cases per 100,000 population
- Most easily managed form of uveitis
- Accounts for ~ ¾ of cases of uveitis
Treatment:

- Steroid (Pred Forte 1%) q 1-2 hours
- Cycloplegia (Scopolamine or Atropine) BID / TID
- Find the underlying cause

**Dosing Schedule:**

Q 15-30 minutes for the first 6 hours

Q 1 hour for the remainder of the day and day 2

Q 2 hour for day #2

QID x 1 week, TID x 1 week, BID x 1 week, QD x 1 week

**Laboratory Testing:**

- Complete Blood Count (CBC)
- Blood Chemistry (SMA-12)
  - BUN, creatinine, calcium, phosphorus
- Erythrocyte Sedimentation Rate (ESR)

Anti-Nuclear Antibody (ANA)
- Rheumatoid Factor (RF)
- Human Leukocyte Antigen (HLA –B 27)
- Chest X-Ray
- Purified Protein Derivative (PPD)
- Enzyme Linked Immuno-Sorbent Assay
- Angiotensin Converting Enzyme (ACE)

**Uveitis:**

- History is the Key !!!
- Important questions to ask to help find the underlying etiology

Lower back pain ??? ----------- Anklyosing Spondylitis
Wrist/Ankle pain ???----------- Reiter’s syndrome
Knee pain ??? ------------------ Juvenile Rheumatoid Arthritis
Gut pain ??- Crohn’s disease
Discharge ??- Syphilis, Reiter’s
Coughing ??- Tuberculosis, Sarcoid
Rash ??- Syphilis, Lyme, Lupus, Herpes

Who should get a full workup?

- Bilateral, Granulomatous, Child, Recurrent, Recalcitrant, Vitritis
- First time non-granulomatous ??

Common Causes of Anterior Uveitis:

- Idiopathic 33%
- Fuch’s Hetero Iridocyt 6%
- AS 5%
- IBD 1%

Common Causes of Posterior Uveitis:

- Toxoplasmosis 9%
- Intraocular Lymphoma 1%

HLA-B27 Associated Anterior Uveitis with Systemic Disease:

- Ankylosing Spondylitis
- Reiter’s Syndrome
- Juvenile Rheumatoid Arthritis
- Inflammatory Bowel Disease
- Psoriatic Arthropathy
- Whipple’s Disease

Demographic Considerations in Uveitis:

Female ___________ JRA
Male ___________ Ankylosing spondylitis, Sym. Ophthalmia
American black______ Sarcoidosis
Native American _____ VKH
Midwestern __________ Histoplasmosis
Scleritis:
- Nodular Anterior Scleritis
- Necrotizing Anterior Scleritis
- Necrotizing Anterior Scleritis w/o Inflammation (Scleromalacia Perforans)
- Posterior Scleritis

Important Note:
50% of patients with scleritis have an underlying associated systemic disease

Scleritis:
- Systemic Lupus Erythematous ANA
- Rheumatoid Arthritis Rheumatoid factor
- Ankylosing spondylitis HLA – B27
- Poster Herpes Zoster ophthalmicus
- Syphillis RPR, FTA-ABS
- Gout Uric Acid
- Tuberculosis PPD with anergy panel

Scleritis:
- Nonsteroidal anti-inflammatory drugs (NSAID)
  - Ibuprofen 400-600 mg PO QID for at least 1 week
- Systemic Steroids
  - Prednisone 60-80 mg PO/day for 4-5 days then slow taper
- Immunosuppressive therapy
- Cyclophosphamide

- Subconjunctival steroids are contraindicated in scleritis
- Topical steroids are rarely indicated in scleritis and are not effective

**Episcleritis:**
- Idiopathic (most common)
- Collagen Vascular Disease (RA, SLE, etc.)
- Gout
- Herpes Zoster virus
- Syphilis
- Lyme

**Episcleritis:**
- Topical Steroid (Flarex or Pred Forte)
  QID with taper
- Oral NSAID (Ibuprofen) if topical steroid does not provide relief

Topical steroid will help in the differential diagnosis vs. Scleritis.

**Oral Antiviral Medications:**
Inhibits viral DNA synthesis (Maximally effective within 3 days)
- Acyclovir (Zovirax) 800 mg (PO) 5 x day 7-10 days
- Famcyclovir (Famvir) 500 mg (PO) 3 x day 7 days
- Valacyclovir (Valtrex) 1000 mg (PO) 3 x day 7 days
- Good at reducing pain with Zoster. Famvir has the most bioavailability
• **Common Adverse Effects:** nausea, vomiting, HA, dizziness, abdominal pain

**The Herpetic Eye Disease Study II**

• In the treatment of HSV Epithelial Keratitis, there was **no** benefit from the addition of oral Acyclovir to treatment with topical Viroptic in preventing the development of Stromal Keratitis or Iritis

• **Oral Acyclovir,** reduced by **41%** the probability that any form of herpes of the eye would return in patients who had the infection the previous year. Oral Acyclovir (400mg BID for 12 months)

• Ocular HSV Recurrence Factor Study
  There are no results yet available from this arm of the study

**Tear Film**

• **Lipid Layer** – produced by the meibomian glands
  
• **Aqueous Layer** – made by the main and accessory lacrimal glands

• **Mucous Layer** - made by the goblet cells of the conjunctiva

**Lacrimal gland function:**

• Influenced by sex hormones. Androgens maintain normal glandular functions and suppress inflammation

**Dry Eye**

• Dry eye is multifactorial. A deficiency may occur in any one of the three tear film layers.

• Autoimmune dry eye = lymphocytes and cytokines invade

• Non-autoimmune dry eye = loss of neural tone leads to gland atrophy and immune
**Etiology:**

- Idiopathic
- Collagen Vascular Disease (Sjogren’s, RA, Lupus)
- Diabetes, Reduced levels of androgens (female patients, older age)
- Drugs (BCP, antihistamines, phenothiazines, antihypertensives)
- Lacrimal gland disease (sarcoidosis, lymphoma, tumor, etc.)
- Surgery (Lasik, PRK)
- Environmental (Low humidity, poor air quality, poor ventilation)
- Conjunctival scarring (chemical burn, Stevens-Johnson syndrome)

**Dry Eye:**

Omega – 3 Fatty Acid and Omega 6 Fatty Acid
Metabolic Pathways of Essential Fatty Acids

Alpha-Linolenic Acid (flaxseed oil)

Steridonic Acid

EPA (fish oil)

PGE3 (anti – inflammatory)

LTB 5 (anti – inflammatory)
Dry Eye:

How Omega 3 Fatty Acids Benefit the Dry Eye Patient:
  • Decrease inflammation
  • Alter lipid tear layer
  • They produce lipid layer of tear film
  • Stimulate Tear secretion
  • Prostaglandin E1 increases aqueous production

Omega 3 Sources:
  • Cold water fishes (Salmon, mackerel, tuna)
  • Flaxseed
  • Walnuts
  • Soybean and Canola oil

Dry Eye:

Important Note:
  • Omega 6 fatty acid is overabundant in the western diet
  • Ideal Omega 6 to Omega 3 ratio is 4:1
  • In the American diet the ratio is 20:1
  • Flaxseed oil may increase the effects of Coumadin and Aspirin
  • Flaxseed oil may increase the risk of certain forms of breast cancer
  • There are no large well controlled studies from the FDA

Dry Eye and Inflammation:
  • Cyclosporine .05% Ophthalmic Emulsion (Immunomodulator) BID
  • Inhibits T lymphocyte activation by inhibiting interleukin-2
  • May take up to 3 months to start having therapeutic effect
  • Burning and stinging are the most common adverse side affects
  • Dietary Omega 3 Fatty Acid Intake
  • TheraTears Nutrition (Taken by mouth 4 Softgel capsules)
  • 2 in the am…2 in the pm
  • Contains flaxseed oil, fish oil, vitamin E
  • Can double the dose for Rheumatoid Arthritis patients
Phlyctenulosis:

Symptoms:
- Pain, tearing, photophobia, blepharospasm

Signs:
- Conjunctival phlyctenule
  Small white nodule on bulbar conj. Near the limbus
- Corneal phlyctenule
  White nodule on the cornea. May have neovascularization

Etiology:
- Inflammation induced by microbial antigens
- Staphylococcus (could be related to blepharitis)
- Tuberculosis, Chlamydia, Candida, Parasites
- Other infections elsewhere in the body
- May accompany acne rosacea or seborrheic blepharitis

Phlyctenulosis:

Differential Diagnosis:
- Inflamed pingueculum / pterygium
- Infectious corneal ulcer

Treatment:
- Topical steroid (Pred Forte 1%) 4-8 times a day
- Topical antibiotic (Polytrim) 4 times a day
- Eyelid hygiene if necessary / Culture the lids

Band Keratopathy:
- May have reduced vision, foreign body sensation
- Calcium in the palpebral fissure area
- Calcium in the basal epithelium and Bowman’s layer
- Begins in the 3 and 9 o’clock positions of the cornea

Etiology:
- Chronic uveitis
- Long standing glaucoma
- Gout
• Sarcoidosis
• Renal Failure
• Paget’s disease
• Juvenile Rheumatoid Arthritis
• Corneal dystrophies
• Hypercalcemia

**Band Keratopathy:**

**Treatment:**

- If the patient has reduced visual acuity
- Intolerable eye irritation
- Cosmetic problem for the patient
- Artificial Tears
- EDTA (Endrate)
- Excimer Laser
- PTK (Photo Therapeutic Keratectomy)

**Chlamydia:**

- Chlamydia trachomatis – obligate intracellular parasite
- Transmitted mainly by sexual contact
- Usually found in young adults (18-35 years of age)
- Acute follicular conjunctivitis

**Signs and Symptoms:**

- Lid swelling, redness, tearing foreign-body sensation
- Unilateral presentation more common than bilateral
- Diffuse **SPK** and **Subepithelial infiltrates**
- Corneal neovascularization and conjunctival scarring

**Treatment:** **Azithromycin 1000 mg single dose ******

- Tetracycline 250-500 mg PO QID for ~3 weeks
- Doxycycline 100 mg PO BID for ~3 weeks
- Erythromycin 500 mg QID for ~3 weeks
**Sexually Transmitted Diseases (STD’s):**
STD that are on the “Ocular-Genital” Axis:
  - Herpes Simplex
    - Phthirus Pubis/ Pediculosis Pubis (“Crabs or Lice”)
      Head and body lice do not attach to the eye – only the pubic louse
  - Syphilis
    Transmitted through direct contact with a syphilis sore
  - Gonorrhea ("The Clap")
    Very mucopurulent discharge in the eye, vagina, or penis

**Subconjunctival Hemorrhage**

**Etiology:**
  - Valsalva
  - Trauma
  - Blood Thinner
  - Uncontrolled High Blood Pressure
  - Idiopathic

**Treatment:**
  - Artificial Tears, Reassure the patient, RTC 2 weeks