Grand rounds: A string of anterior segment pearls

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Eyelid abscess vs. Preseptal Cellulitis vs. Orbital Cellulitis

- Preseptal Cellulitis
  - Usually upper eyelid swelling
  - Pain, tenderness, redness
  - Usually caused by adjacent infection (hordeolum, dacryocystitis)

- Orbital Cellulitis
  - All the same signs of preseptal with
  - Proptosis
  - EOM restrictions/pain with eye movements
  - Pupillary involvement
  - Usually an extension from an ethmoid sinusitis

Oral Antibiotic Paradigm

- Penicillins
- Cephalosporins
- Macrolides
- Fluoroquinolones
- Sulfas
- Augmentin: 875mg BID or 500mg TID
- Keflex: 500mg TID
- Zithromax: “Z-pak”
- Levquin or Cipro
- Bactrim DS: 800/160 BID

Preventing Resistance

- Just one organism, methicillin-resistant Staphylococcus aureus (MRSA), kills more Americans every year (~19,000) than emphysema, HIV/AIDS, Parkinson’s disease, and homicide combined
  - most serious MRSA infections, an estimated 85%, are associated with a healthcare exposure, but nearly 14% of the infections are community-associated.
  - Almost 2 million Americans per year develop hospital-acquired infections (HAIs), resulting in 99,000 deaths; the vast majority of which are due to antibiotic-resistant pathogens
  - CDC: Get Smart! Know When Antibiotics Work
    - reaches both the provider and the patient when antibiotics should be used.
  - The IDSA suggests five to seven days is long enough to treat a bacterial infection without encouraging resistance in adults, though children still get the longer course
    - this is different than previous guidelines of treating infections from 10-14 days.

Ocular TRUST 3: Ongoing Longitudinal Surveillance of Antimicrobial Susceptibility in Ocular Isolates

- Background:
- Ocular TRUST is an ongoing annual survey of nationwide antimicrobial susceptibility patterns of common ocular pathogens.
- To date, more than 1,000 isolates from ocular infections have been submitted to an independent, central laboratory for in vitro testing.
- Ocular TRUST, now in its third year, remains the only longitudinal nationwide susceptibility surveillance program specific to ocular isolates.

Ocular Trust 3

- Antimicrobials tested represent six classes of drugs:
  - fluoroquinolones (ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin);
  - dihydrofolate reductase inhibitors (trimethoprim);
  - macrolides (azithromycin);
  - aminoglycosides (tobramycin);
  - polypeptides (polymyxin B); and
  - β-lactams (penicillin).
- Staphylococci were classified as methicillin-resistant (MRSA) or methicillin-susceptible (MSSA) based on susceptibility to oxacillin.
**Ocular Trust 3: Results**

- Most antimicrobials, except penicillin and polymyxin B, continue to be highly active against MSSA (azithromycin shows only moderate activity).
- With the exception of trimethoprim and tobramycin, less than one-third of MRSA strains are susceptible to ophthalmic antimicrobials.
- Susceptibility profiles remain virtually identical for the fluoroquinolones, regardless of methicillin phenotype.
- *S. aureus* is more susceptible to the fluoroquinolones than to macrolides, as represented by azithromycin.

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**Herpes Zoster**

- Nearly 1 million Americans develop shingles each year.
- Ocular involvement accounts for up to 25% of presenting cases.
- Over 50% incur long term ocular damage.

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**Herpes Zoster**

***Varicella-Zoster Virus***

- Herpes DNA virus that causes 2 distinct syndromes.
  1. Primary infection – Chicken pox (Varicella)
     - Usually in children.
     - Highly contagious.
     - Very itchy maculopapular rash with vesicles that crust over after ≈ 5 days.
     - 96% of people develop by 20 years of age.
     - Vaccine now available.

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**Herpes Zoster**

***Varicella-Zoster Virus***

- Herpes DNA virus that causes 2 distinct syndromes.
  1. Primary infection – Chicken pox (Varicella)
  2. Reactivation – Shingles (Herpes Zoster)
     - More often in the elderly and immunosuppressed (AIDS).
     - Systemic work-up if Zoster in someone < 40.
     - Can get shingles anywhere on the body.
     - Herpes Zoster Ophthalmicus (HZO)
       - Shingles involving the dermatome supplied by the ophthalmic division of the CNV (trigeminal)
       - 15% of zoster cases.
Herpes Zoster

• Symptoms:
  – Generalized malaise, tiredness, fever
  – Headache, tenderness, paresthesias (tingling), and pain on one side of the scalp***
    • Will often precede rash
  – Rash on one side of the forehead
  – Red eye
  – Eye pain & light sensitivity

• Signs:
  – Maculopapular rash -> vesicles -> pustules -> crusting on the forehead
  – Respects the midline***
  – Hutchinson sign
    • rash on the tip or side of the nose***
  – Classically does not involve the lower lid
  – Numerous other ocular signs

Herpes Zoster

• Other Eye Disease (Acute):
  – Acute epithelial keratitis (pseudodendrites)
  – Conjunctivitis
  – Stromal (interstitial) interstitial keratitis
  – Endotheliitis (disciform keratitis)
  – Neurotrophic keratitis

• Other Eye Disease (Acute):
  – Episcleritis
  – Scleritis
  – Anterior uveitis
  – IOP elevation
  – Retinitis
  – Choroiditis
  – Neurological complications (nerve palsies)
  – Vascular occlusion

  – Treat the complications just like as if they were primary conditions

Herpes Zoster

• Other Eye Disease (Chronic):
  – Neurotrophic keratitis - 50%
  – Scleritis
  – Mucous plaque keratitis - 5%
  – Eyelid scarring

• Treatment:
  – Treat the complications just like as if they were primary conditions
  – Oral antivirals – must be started within 72 hours of symptoms**
    • Acyclovir 800mg 5x/day x 7-10 days
    • Valtrix 1000mg 3x/day X 7-10 days
    • Famiclovir 500mg 3x/day X 7-10 days
  – Topical ointment to skin lesions to help prevent scarring
    • Bacitracin, erythromycin
Herpes Zoster

• Prevention:
  – Zostivax vaccine
  • Live attenuated herpes virus
  • Only given to people who know they had chicken pox as a child***
  • Only studied in patients > 60 yo
  – 51% reduction in incidence of HZ
  – 60% reduction in symptom severity in those who got HZ
  – 6.5% reduction in post-herpetic neuralgia

• Post-herpetic Neuralgia
  – Constant or intermittent pain that persists for more than one month after the rash has healed
  – Older patients with early severe pain and larger area are at greater risk
  – Can be so severe that it leads to depression & suicide
  – Improves with time
    • Only 2% of pts affected 3 years out
  – Tx:
    • Cool compresses
    • Topical capsaicin ointment or lidocaine cream
    • Analgesics (Tylenol 3, Vicoden)
    • Amitriptyline 25mg PO TID
    • Neurotin (Gabapentin)

Viral conjunctivitis

• Signs:
  – Red eye (conj hyperemia)
  – Watery discharge
  – Follicles in the inferior fornix & conj
  – (+) PA node***
  – Red/swollen eyelids
  – Petechial sub-conj hemes
  – SPK
  – SEI’s (sub-epithelial infiltrates)
  – Pseudomembranes/membranes often seen in EKC

EKC conjunctivitis

• Diagnosis
  – Based on clinical symptoms

• Treatment:
  – Cool compresses
  – Artificial tears
  – “get the red out drops”
  – Vasoconstrictors such as Visine
  – Hygiene***
  – Quarantine/Isolation
  – Betadine 5% solution???
  – Zirgan???
  – Lotemax/Pred Forte QID??? – not until late
Herpes Simplex

- Most common virus found in humans
  - 60-99% are infected by 20 years old
- Double stranded DNA virus
  - HSV type 1 (HSV-1)
  - HSV type 2 (HSV-2)
- Primary infection
  - Occurs in childhood via droplet exposure
  - Subclinical infection in most
- Secondary infection (recurrence)

Herpes Simplex

- Recurrent infection:
  - After primary infection the virus is carried to the sensory ganglion for that dermatome (trigeminal ganglion) where a latent infection is established.
  - Latent virus is incorporated in host DNA and cannot be eradicated
  - Stressors (trauma, UV light, fever, hormonal changes, finals week, etc) cause reactivation of the virus and it is transported in the sensory axons to the periphery - > clinical signs/symptoms
    - Ocular recurrence -> 10% at one year, 50% at ten years

Herpes Simplex Keratitis

- Epithelial Keratitis:
  - Symptoms:
    - Ocular irritation, redness, photophobia, watering, blurred vision
  - Signs:
    - Swollen opaque epithelial cells arranged in a course punctate or stellate pattern
    - Central desquamation results in a dendrite***
      1. Central ulceration
      2. Terminal end bulbs
  - ***Corneal sensation is reduced***

Herpes Simplex Keratitis

- Epithelial Keratitis:
  - Signs (con’t):
    - Mild associated subepithelial haze
    - Elevated IOP***
    - Persistent SPK and irregular epithelium as the ulcer is healing
  - Differential diagnosis:
    - Herpes zoster
    - Healing corneal abrasion
    - Acanthamoeba keratitis
    - Medicamentosa

Herpes Simplex Keratitis

- Epithelial Keratitis:
  - Treatment:
    - Zirgan (ganciclovir gel 0.15%)
      - 5x/day until the dendrite disappears
      - 3x/day for another week
    - Viroptic (trifluridine solution 1%)
      - 9x/day until the dendrite disappears
      - 5x/day for another week
    - Oral antivirals (if topical not well tolerated):
      - Acyclovir 400 mg 5x/day X 7-10 days
      - Valtrex 500 mg 3x/day X 7-10 days
      - Famvir 250 mg 3x/day X 7-10 days
  - Debridement of the dendritic ulcer???
  - Oral antivirals???
  - IOP control
    - Avoid prostaglandins???
  - Steroids???
  - Follow-up
    - Day 1, 4, 7
Herpes Simplex Keratitis

• **Marginal keratitis:**
  – Very rare

  – Looks like a marginal infiltrate...but

  – In HSV marginal keratitis:
    1. Much more pain
    2. Deep neovascularization
    3. No clear zone between infiltrate and limbus

Herpes Simplex Keratitis

• **Immune Stromal Keratitis (ISK):**
  – 2% of initial ocular HSV presentations
  – 20-61% of recurrent disease

  – 88% non-necrotizing
  – 7% necrotizing

  – ***Can be visually devastating***

Herpes Simplex Keratitis

• **Immune Stromal Keratitis:**
  – Symptoms:
    • Gradual blurred vision
    • Halos
    • Discomfort/Pain
    • Redness

  – Signs (non-necrotizing):
    • Stromal haze (inflammation & edema)
    • Neovascularization (deep)
    • Immune ring
    • Scarring and/or thinning
    • Intact epithelium***

  – Signs (necrotizing):
    • All of the above
    • More dense infiltration
    • Often w/ overlying epithelial defect
    • Necrosis and/or ulceration
    • ***high perforation risk***

Herpes Simplex Keratitis

• **Immune Stromal Keratitis:**
  – Treatment:
    • Topical steroids
      – Pred Forte QID-q2H
      – Durezol BID-QID
      – Lotemax QID
    • Topical anti-viral cover
      – Viroptic ( trifluuridine 1%) QID
      – Zirgan (ganciclovir 0.15%) QID

    • Topical cyclosporin (Restasis), AT’s, ung’s to facilitate epithelial healing if ulceration is present

Herpes Simplex Keratitis

• **Endotheliitis:** AKA Disciform Keratitis
  – Not considered a primary form of stromal keratitis
    • Stromal edema is present secondary to endothelial inflammation

  – Symptoms:
    • Blurred vision
    • Halos
    • Discomfort/Pain
    • Redness
Herpes Simplex Keratitis

- **Endotheliitis**: AKA Disciform Keratitis
  - Signs:
    - Central zone of stromal edema often with overlying epithelial edema
    - KP’s underlying the edema
    - AC reaction
    - IOP may be elevated
    - Reduced corneal sensation
    - Healed lesions often have a faint ring of stromal or subepithelial opacification and thinning

Herpes Simplex Keratitis

- **Endotheliitis**: AKA Disciform Keratitis
  - Treatment:
    - Topical steroids
      - Pred Forte QID-q2H
      - Durezol BID-QID
      - Lotemax QID
    - Topical anti-viral cover
      - Viroptic (trifluridine 1%) QID
      - Zirgan (ganciclovir 0.15%) TID
    - Topical cyclosporin (Restasis), AT’s, ung’s to facilitate epithelial healing if ulceration is present

Herpes Simplex Keratitis

- **Neurotrophic Keratitis**:
  - Keratopathy occurs from loss of trigeminal innervation to the cornea resulting in complete or partial anaesthesia
  - The cornea is numb so the pt doesn’t blink
  - Sx’s:
    - Irritation/burning/FB sensation
    - Redness
    - Tearing
    - Decreased vision

Neurotrophic Keratopathy

- **Signs**:
  - Decreased corneal sensation***
  - Interpalpebral SPK
  - **Persistent epithelial defects** in which the epithelium at the edge of the lesion appears rolled and thickened, and is poorly attached
  - Advanced cases may have sterile ulceration, keratitis, and/or corneal melt
  - Pt may be surprisingly asymptomatic**

Neurotrophic Keratopathy

- **Tx**:
  - Find out the cause
  - D/C any meds that may be responsible
  - Lubricate, lubricate, lubricate***
    - Preservative free AT’s, gels, and ung’s q1h-QID
  - Topical Ab drops and/or ung (Polytrim QID, etc)
  - Taping the eyelids at night to ensure adequate closure
  - In severe cases:
    - Patching, tarsorrhaphy, Botox to induce ptosis

Neurotrophic Keratopathy

- **Tx**:
  - Healing an ulcer that won’t heal
    1. Autologous serum
    2. Prokera
      - Amniotic membrane in a CL skirt
    1. Also could use a scleral lens
Autologous Serum

1. Draw 40cc of blood through venipuncture
2. Centrifuge for 5 minutes @ 1500 rpm
3. Centrifuging will divide the blood into its separate components
4. Place 1cc of serum in each bottle
5. Add 4cc of saline to make a concentration of 20% serum eye drops
6. 20% serum eye drop concentration

Herpes Simplex Epithelial Keratitis

• My Regimen:
  – Zirgan 5x/day until the ulcer heals, then 3x/day for one week
  – Oral Valtrex 500 mg 3x/day for 7-10 days
  – Artificial tears
  – L-Lysine 2 grams daily?
  – Debride the ulcer?
• RTC 1 day, 4 days, 7 days

Herpes Simplex Keratitis

• Prophylactic Treatment:
  – Reduces the rate of recurrence of epithelial and stromal keratitis by ≈ 50%
    • Acyclovir 400 mg BID
    • Valtrex 500 mg QD
    • Famvir 250 mg QD
    • L-lysine 1 gram/day
  – Frequent debilitating recurrences, bilateral involvement, or HSV infection in an only eye

Herpes Simplex

• Visual Prognosis:
  – 90% 20/40 or better after 12 years
  – 3% 20/100 or worse after 12 years

Recurrent Corneal Erosions (RCE’s)

• Tendency for minor trauma to cause significant corneal epithelial disturbances
• Pathophysiology
  – Abnormally weak attachment between the basal cells of the corneal epithelium and their basement membrane
• Most common causes of the weak attachment
  – Mechanical trauma**
  – Corneal dystrophy**
  – Corneal surgery

• Severe dry eye patients
• Graft vs. Host Disease
• Filamentary Keratitis
• Neurotrophic keratitis
• Chronic Stainers
Recurrent Corneal Erosions

• Sx’s:
  – Acute, severe pain**
  – Photophobia **
  – Redness
  – Blepharospasm
  – Tearing

***Usually sx’s present first thing in the morning upon opening the eyes.***
And often this is recurrent

Recurrent Corneal Erosions

• Signs:
  – Epithelial defect may be present, usually in the inferior interpalpebral area

Recurrent Corneal Erosions

• Tx:
  – Acutely:
    • Lubrication**
    • Topical Ab (Polytrim QID, erythro or bacitracin ung)
    • Pain control:
      – Cycloplegic (Homatropine BID)
      • Muro 128 drops or ung
    • Bandage lens???
      – Alleviates pain, does not improve healing

Recurrent Corneal Erosions

• Tx:
  – After the epithelium heals (recalcitrant RCE’s):
    • Fresh Kote TID (15ml bottle $25)
    • Muro 128 ung qhs (3.5g tube $10)
    • Lotemax QID X 2 weeks, BID X 6 weeks
    • Doxycycline 20-50mg BID
      – Azasite BID (2.5ml bottle $78)

**Avoid chronic long-term AT ung**
Acanthamoeba keratitis

- History of CL wear w/ poor lens hygiene
- Often a history of hot tub/swimming pool/swimming in the river
- Symptoms:
  - Severe pain out of proportion to clinical picture
  - Redness & photophobia
  - All over the course of several weeks
- Signs:
  - Early -> Pseudodendrites
  - Late -> Ring-shaped stromal infiltrate

Acanthamoeba Keratitis

- Sx’s:
  - Severe pain**
  - Redness
  - Tearing
  - Decreased vision
  - Photophobia
  - Minimal discharge

These sx’s tend to develop over a period of weeks.**
H/O CL hygiene problems and swimming in lenses**

Fungal keratitis

- Often a history of vegetative trauma, CL wear
- H/O poor response to topical Ab’s
- Symptoms:
  - Pain, photophobia, tearing, FB sensation
  - Pain often less than what the clinical picture would indicate
- Signs:
  - Stromal infiltrate w/ a feathery border
  - Satellite lesions surrounding the primary infiltrate
**Fungal Keratitis**

- **Sx's:**
  - Gradual onset of pain
  - Irritation/grittiness
  - Photophobia
  - Blurred vision
  - Watery or mucopurulent discharge

- H/O cornea infection diagnosed as bacterial**
- H/O vegetative trauma, CL abuse, chronic steroid use

**Fungal Keratitis**

- **Signs:**
  - Gray-white stromal infiltrate with indistinct “fluffy” or “feathery” borders/margins
  - Often surrounded by fingerlike satellite lesions in the adjacent stroma

**Fungal Keratitis**

- **Signs:**
  - Epithelial defect overlying the ulcer
    - However can be quite small and sometimes is not present
  - Infiltrates may progressively enlarge and extend into deeper tissue
    - Necrosis, thinning and perforation can occur

**Fungal Keratitis**

- **Tx:**
  - Pts may require hospitalization
  - Topical meds:
    - Natamycin 5% (for filamentous fungi)*
    - Amphotericin B 0.15% (for Candida)*
    - Both q1h around the clock initially and then tapered over 6-12 weeks
  - Orals meds:
    - Voriconazole 200 mg BID
    - Itraconazole
    - Fluconazole
    - Cycloplegics (homatropine BID)
    - Surgical (PKP or DALK)

**Fungal Keratitis**

- **Signs:**
  - Epithelial defect overlying the ulcer
    - However can be quite small and sometimes is not present
  - Infiltrates may progressively enlarge and extend into deeper tissue
    - Necrosis, thinning and perforation can occur

**Bacterial Keratitis**

- **Tx:**
  - Hospitalization???
  - No CLs**
  - Pain relief
  - Topical Ab’s: (amount & strength depends on the ulcer)
    - Besivance, Moxeza or Zymaxid q1h around the clock for 24-48 hours & tapering according to clinical progress
    - Fortified Ab’s??? (large ulcers, visual axis, hypopyon)
      - fortified Vancomycin, cephalosporins and/or gentamicin
Ocular Trust 3: Results

- most antimicrobials, except penicillin and polymyxin B, continue to be highly active against MSSA (azithromycin shows only moderate activity)
- with the exception of trimethoprim and tobramycin, less than one-third of MRSA strains are susceptible to ophthalmic antimicrobials
- susceptibility profiles remain virtually identical for the fluoroquinolones, regardless of methicillin phenotype
- S. aureus is more susceptible to the fluoroquinolones than to macrolides, as represented by azithromycin

Bacterial Keratitis

- Tx:
  - Steroids???
    - Reduce inflammation, improve comfort, and minimize corneal scarring...but evidence that they improve final visual outcome is limited
    - Will make herpes, fungal, acanth much worse
    - Epithelialization may be slowed by steroids
    - Can cause corneal thinning (but not usually)
    - DO NOT USE until clinical improvement is seen with Ab’s alone
    - Pred Forte QID
  - Doxycycline or Azasite???
    - Inhibit MMP-9

Thank you for your attention!