Herpetic Eye Disease

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Intro to me
- Born in Las Vegas - 4/1/1982
- Youngest of 5 kids
- Soccer, volleyball, and singing
- Business Admin at BYU
- Med school at UNR
- Transitional year in Tucson
- 7/12 done with first year here at UVA!!!
Ashley
- 3 years old
- Cutest smile
- Would rather not wear clothes
- Loves being defiant

Matthew
- 11 months
- Unruly hair
- Learning to walk

Learning Points
- Overview of herpes simplex
- Diagnosis and treatment of HSV
- Overview of herpes zoster
- Diagnosis and treatment of HZO

Herpes Simplex
- HSV-1
  - Oral, labial, and ocular
- HSV-2
  - Genital
- Humans only reservoir
- Primary infection through mucosa, then latency in sensory ganglia
- Ocular disease is likely recurrent disease
Viral reactivation due to:
- Psychological stress
- UV light
- Fever
- Other viral infections
- Trauma
- Glucocorticoids

NOTE: these risk factors not documented for ocular disease

HSV Keratitis

- Damage to cornea from active infection, induced inflammation, and immune reaction to past infection.

Corneal Anatomy

- Epithelium
- Bowman's Layer
- Stroma
- Descemet's membrane
- Endothelium
Epidemiology

- Spread by direct contact with infected mucosa
- 90% exposed by age 40 (circulating Ab)
  - >90% of primary infection is asymptomatic
  - Ocular involvement <5% of primary infections
- Usually unilateral
  - Bilateral in 1-12% of cases, especially if patient is atopic or immunocompromised

US: 150 per 100,000
- 20,000 new cases annually
- Recurrence:
  - 1 year = 10%
  - 2 year = 23%
  - 5 year = 40%
  - 10 year = 67%

Signs and Symptoms

- Acute onset
- Pain, decreased vision, watery discharge
- Ciliary flush (peri-limbal conjunctival injection), decreased corneal sensation, dendritic lesions vs. corneal edema/infiltrate
- Clinical diagnosis
  - Can send for serology
  - Can perform scrapings of epithelial lesions

Differential Diagnosis for “red eye”

- Viral conjunctivitis
- Bacterial conjunctivitis
- Viral keratitis
- Bacterial keratitis
- Iritis
- Acute angle closure

NOTE: Even though dendritic pattern typical, other entities with dendritic appearance (HZ, acanthamoeba, recurrent erosion)
Besides keratitis…

- Blepharitis
- Conjunctivitis
- Scleritis
- Iritis
- Iridocyclitis
- Retinitis
- Choroiditis

Skin lesions

Types of Keratitis

- HSV epithelial keratitis
- Stromal keratitis
- Endotheliitis
- Neurotrophic keratopathy
Epithelial Keratitis

- Most common with first episodes
  - Dendritic lesions
    - Granular punctate erosions → vesicles → linear dendrites
    - May ulcerate, but 25% spontaneously heal
    - Worsening with topical steroids
  - Geographic ulcer
    - 22% have dendritic widening into ameboid shape
    - Respond slower to treatment
  - Marginal keratitis (limbitis)
    - Less dendritic, so often mis-diagnosed
    - Neovascularization of underlying stroma common

Stromal Keratitis

- Most common with recurrent disease
- Usually not concurrent with epithelial disease
- Immune (non-necrotizing), i.e. disciform
  - 90% of recurrent stromal keratitis
  - Delayed hypersensitivity to viral antigens
  - Intact epithelium
  - Mild iritis with KP
Stromal Keratitis

- Necrotizing interstitial keratitis
  - Multiple white infiltrates +/- epi defect
  - Stromal inflammation and thinning
  - Iritis, hypopyon, glaucoma
  - Must rule out super-infection

Endotheliitis

- Endothelium primary site of damage
- Corneal edema, KP, and anterior chamber inflammation
- Can have irreversible damage to endothelial cells
- Disciform scarring
Neurotrophic Keratitis

- Degeneration of corneal epithelium due to impaired innervation
  - Lesion in the trigeminal nerve or one of its branches
  - Decreased trophic factors
  - Often with limbal involvement
  - Stages:
    1. non-specific, early corneal irritation, palpebral staining
    2. non-healing ulcer
    3. perforation, stromal melt
  - Can worsen with anti-viral drops
HSV Treatment

- Skin: topical acyclovir 5x/day, warm soaks, add Viroptic gtt 5x/day for eyelid margin involvement for 1-2 weeks
- Conjunctiva: Viroptic or Vidarabine 3% ointment 5x/day
  - Toxicity, especially without intact epithelium
- Cornea
  - Epithelium:
    - Viroptic, cycloplegic, oral acyclovir 400mg 5x/day can be added (if topical toxicity noted), stop steroids, gentle debridement
    - Orals do NOT prevent development of stromal keratitis or uveitis
  - Stromal:
    - cycloplegic, topical steroid, +/-oral acyclovir BID, +/-topical antiviral

NOTE: can recommend long-term prophylaxis with acyclovir 400mg BID in severe, recurrent disease

NOTE: if PK necessary slightly decreased survival rates, due to NV and recurrence
- Improved with oral acyclovir prophylaxis

Herpes Zoster Ophthalmicus

- Varicella-Zoster Virus: 1 of 4 herpes viruses pathogenic to humans (CMV, EBV, HSV)
- Ability to cause acute, chronic, latent or recurrent infection
- VZV is labile, easily destroyed by heat, enzymes and solvents
- More fastidious than HSV and more difficult to culture
- Derivation - (Greek) herpes = to creep
  zoster = belt, girdle, zone
Man is the only reservoir
- Varicella exposure usually by age 9
- Recurrent disease = HZ (shingles)
- HZ = 1% of all skin disease, 20% of adults eventually develop
  - 56% thoracic, 15% HZO
- No sexual, social or racial predilection

Epidemiology
- More common in elderly- 5th-7th decades
- Annual incidence 1.3/1000 person years
- Majority have no underlying systemic disease
- More severe disease if age > 80 or if immunocompromised
- Young adults- may be a marker for AIDS
- Other triggers- syphilis, TB, XRT, steroid use

Dermatomal Considerations of HZO
- V1 involved 20X more than V2 or V3
- Branches of V1:
  - frontal nerve most often involved
  - lacrimal nerve
  - nasociliary nerve- Hutchinson’s sign, ant ethmoidal branch (side, tip of nose)
  - 50-85% have ocular involvement

Skin
- Vesicular lesions shed virus up to 4 days, crusting 2-4 weeks
- Maculopapular then vesiculopapular
- New lesions may appear for 7 days
- Vesicle fluid starts clear, yellow, purulent as they erupt and crust
Skin

- Hutchinson’s Sign

Dermis involvement leads to scarring, can get superinfection
- Dissemination in 2% of normals, 25% of immunocomp (vesicles >1 dermatome)
  - usually benign process even with visceral dissemination
  - Zoster sine eruption

Other manifestations

- Blepharitis
- Conjunctivitis
- Secondary cellulitis***
  - Pre-septal
  - Orbital
- Episcleritis
- Scleritis – sectoral or diffuse
- Iritis
- Iridocyclitis
  - chronic/recurrant
  - extensive KP, posterior synechiae, hypopyon, hyphema

Other complications

- Cataract
  - Uveitis
- Glaucoma
  - Plugging of TM
  - Posterior and anterior synechiae
- Vitreous debris and hemorrhage
- Optic neuritis
- CN palsy
Retinal complications

- Hemorrhages
- Thrombophlebitis, CRVO
- BRAO, CRAO
- Retinal arteritis
- Retinal detachment
- Macular edema
- Acute retinal necrosis or PORN - retinal and choroidal vascular occlusion, direct viral cytolysis, vitreous traction on the necrotic retina causes RD

Keratitis

- Liesegang(1985) 213 pts at Mayo over a six year period. 94 pts were followed, 61 pts (65%) had corneal involvement - 52 pts (85%) had dermatomal evidence of the nasociliary division involvement

Acute retinal necrosis

- 1-10 days
- Swollen epithelial cells, usually in periphery
- Evidence that these represent active viral replication
- 55% progressed to pseudodendrites

Punctate Epithelial Keratitis

- Liesegang(1985) 213 pts at Mayo over a six year period. 94 pts were followed, 61 pts (65%) had corneal involvement - 52 pts (85%) had dermatomal evidence of the nasociliary division involvement
Pseudodendrites

- 2-15 days
- Coalescence of previous PEK
- Differ from HSV dendrites: no terminal bulbs, and elevation of plaque rather than ulceration***
- 52% progressed to anterior stromal infiltrates

Anterior Stromal Infiltrates

- 6-21 days
- Granular infiltrates under Bowman’s layer
- Single or multiple
- Soluble viral antigen diffusing into stroma

Sclerokeratitis

- 1-3 months
- Stromal infiltration in periphery adjacent to an episcleral or scleral nodule
- w/ or w/o epithelial defect, vascularization, scarring, lipid deposition, or stromal thinning

Keratouveitis/Endotheliitis

- 1-21 days
- Sudden onset folds in Descemet’s w/ stromal and epithelial edema
- May resolve in days or last for years
**Serpiginous Ulceration**
- 2-20 weeks
- Acute stromal edema
- Cellular infiltration with crescent shaped ulcer in periphery
- Smooth edges and grayish base
- Assoc w/ decreased corneal sensation and uveitis
- 75% vascularize, 25% perforate

**Delayed Mucous Plaques**
- 1-16 weeks
- Coarse grayish lesions on the surface of swollen epithelial cells
- Usually assoc w/ neurotrophic keratitis and unstable tear film

**Disciform Keratitis**
- 1-9 months
- Disk-shaped stromal edema w/ minimal infiltrate and intact epithelium
- Delayed hypersensitivity response to viral Ag

**Neurotrophic Keratitis**
- 2-6 months
- Lack of corneal luster, irregular surface, SPK, decreased TBUET, and blink frequency
- Leads to corneal thinning, scarring and perforation
- Delayed epithelial turnover w/ denervation of the cornea
Neurotrophic Corneal Scarring

- 50% had permanent scarring
- 15% visually significant
- 11% significant corneal NV
- 10% lipid deposition

Post-herpetic Neuralgia

- Oral antivirals do not appear to have any effect on preventing PHN
- Oral prednisone is effective, not clear how much or for how long
- Non-narcotic and narcotic analgesia
- Tricyclic antidepressants
- Consult pain specialist

Treatment - summary

- Skin – oral acyclovir or valacyclovir for 7-10 days
- Conjunctiva – ATs, +/- erythromycin ointment
- Corneal pseudodendrite – ATs
- Corneal stromal dz – topical steroid, taper over months to years***
- Uveitis – steroid, cycloplegic, IOP meds
- Neurotrophic – BCL, aggressive lubrication, tarsorrhaphy
- Retinitis, optic neuritis, CN palsy – IV acyclovir, oral prednisone, +/- intraocular antivirals
Changes

- Varicella vaccine to children
- Less "natural boosting"
- Recurrences occurring younger
- Zostavax approved for >60 yo; March 2011 decreased to age 50 yo
  - Reduced risk by 70%