Ocular Infection Management-The Next Generation

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UEI
SERIOUS PROBLEMS REQUIRE SERIOUS DOCUMENTATION

THE BIG 6 “I’s”

• INFECTION
• INFLAMMATION
• ISCHEMIA
• INJURY
• IDIOPATHIC
• IATROGENIC (idiopathetic)
Just the facts Mrs. Johnson

• 65 y/o female visiting her friend Madge from Portland, Oregon.

• Madge is one of your favorite long-term patients

• Madge refers patient to you

• Patient is very concerned about her “eye infection”
The Simple Conjunctivitis Case

- 65 y/o female recently in LA to visit son
- Both developed red eyes
- Son told mom he has genital herpes
- and chlamydia
- Mother seen by local ophthalmologist
HX

• My vision is getting worse in my left eye
• It feels very “sore” and itches a lot
• It waters all the time and it feels like my eye is too big for the eye socket
• It’s glued shut every morning and very swollen
• People are afraid to talk to me – they think I’m going to give them “pink eye”
• Am I contagious? Will I lose my vision?
Case : cont’d

• Mom has Hx of trachoma as child and TB in remission. Worked in a TB ward-Was treated years ago

• Mom wears mono-vision CL on OS only. Disposable-wears X wears X 2 weeks. Last worn 9 days ago
Case : Cont’d

• Eye now very painful and vision very bad
• Calif. Dr said the cornea was all “torn up”
• The doctor said the drops he gave me would make it better right-away-it made it worse and I stopped it after a day
• I’ve been using the new drops daily and taking the pills, but it’s just getting worse every day
• Am I going blind?!?
QUESTION:
Differential DX

1. Viral conjunctivitis
2. Chalmydia
3. CL over-wear
4. TB granulomatous uveitis
5. Trachoma
QUESTION: Management?

• 1. Refill and continue the oral tetracycline
• 2. Viroptic 5X/day and oral acyclovir 400mg TID PO
• 3. Topical steroids
• 4. Ciloxan QID
• 5. No TX-send for TB testing (chest X-ray)
Let’s narrow down the differential DX list

- Viral conjunctivitis
- Bacterial keratitis
- Chalmydia
- CL over-wear
- TB granulomatous uveitis
- Trachoma
Most common causes of ACUTE Conjunctivitis

- Toxic or chemical
- Viral
- Chlamydial
- Bacterial
Viral conjunctivitis is the #1 Cause of ACUTE INFECTIOUS Conjunctivitis

- Adenovirus
- Enterovirus
- Herpes FAMILY of Viruses
- Miscellaneous
Adenovirus Family

- DNA Viruses
- At least 35 different serotypes
- Type 8 Classic EKC
- Types 10, 13, 19, and 37 new EKC
- Pharyngoconjunctival fever (PCF) Type 3 and 7
Case #1

: 17 Y/O Female with c/o itching, watering red OD X 4 days associated with flu-like symptoms.

O: “Mixed” conjunctivitis
   Right Pre-Auricular node
   Watery discharge with erythema OU
   Pseudomembrane OD
Differential DX

- H. Simplex
- Allergy
- Vernal/atopic
- GPC
- Bacterial
- Chlamydial
- Molluscum
- Moraxella
- Medicamatosoa
Adenoviral Symptoms

- FB sensation
- Watering
- EKC—Photophobia and Pain
- Blurred vision
- PCF—Pharyngitis and pyrexia
Adenoviral Signs

- Follicular conjunctivitis-Variable most common in lower fornix
- Mild to moderate chemosis
- Lid swelling with mild ptosis
- “Watery” discharge
- Lymphadenopathy in 66%
EKC SIGNS

• Papillary response of upper tarsal conj.
• Subconj. Heme
• Pseudomembrane and conjunctival scarring-Severe form
• Subepithelial infiltrates-Severe form
REMEMBER
ADENOVIRAL DISEASE IS BILATERAL
Traditional Treatments

• Cool compresses and ASA
• Lubrication
• Decongestants
• Steroids (infiltrates, membranes, inflammation)
• Membrane removal
• Antibiotics??
• Cycloplegia??
• A CURE?
HOW ABOUT A CURE

• Current topical antiviral agents (Viroptic) are not effective@@@@
• Povidone Iodine 5%: Swish and spit!!@@@@
Is there a Cure for the Common Cold of the eye?
NOT QUITE

• Spit and swish: Povidone 5% ophthalmic solution
• Don’t spare the steroids
Disinfectants and infection

- Broad anti-infective efficacy
- Ionic
- Some stain
- Uncomfortable
- Toxic
- Not all eye approved
- Skin infections
- Pre-op
Enteroviruses

- EHC-Epidemic Hemorrhagic Conjunctivitis
- AHC_Acute hemorrhagic conjunctivitis
- Called Apollo 11 disease after outbreak in Africa from 1969-70
- Enterovirus type 70
EHC Symptoms

- Marked conjunctival hemorrhage
- Bilateral
- Follicular conjunctivitis
- MINIMAL SPK
- PA Nodes common
Herpes Family of Viruses

• Herpes simplex
• Herpes zoster
• Epstein Barr-Infectious mononucleosis
• CMV-Cytomegalovirus
Herpes Simplex

- Type I Above waist-Trigeminal ganglia
- Type II below waist-most severe in eye infection-Saccral ganglia
- 50% reoccurrence within 2 years
- Multiple triggers
- 90% carry antibodies by age 10
Herpes Simplex

• Primary disease
• Recurrent disease
  Conjunctivitis
  Keratitis
• Stromal disease
• Kerato-uveitis
Primary H. simplex

- @@@@
- Pre-auricular node common
- Vesicles
- Follicles
- No dendrite
- Self-limiting disease-BUT-Treat aggressively to prevent recurrence
Recurrent H. simplex

- Pre-auricular node rare
- Virus involves deeper tissues with each episode
- 50% get recurrence within 2 years
- Steroids will exacerbate infectious H. simplex disease
- Contra-indicated in purely infectious disease
QUICK QUIZ

ANYONE THAT WOULD TX HERPES SIMPLEX OCULAR DISEASE WITH TOPICAL STEROIDS WOULD BE CLASSIFIED AS WHAT?

A. A GENIUS
B. A HERO
C. ONLY A PERSON WITH SBS WOULD USE STEROIDS ON HERPES SIMPLEX
Stromal H. simplex-
A whole new ball game

- Mechanism is primarily inflammation
- Stromal infiltrates are the critical sign
- Balanced use of topical steroid (FML) with anti-viral cover
- Consider oral acyclovir at this point in time (HEDS II)
YES, IT CAN GET EVEN WORSE

- H. Simplex kerato-uveitis
- Marked inflammation
- Elevated IOP
- Complex case
HERPES SIMPLEX IS A UNILATERAL DISEASE
Characteristics of Herpes Viruses

- Latency
- Recurrent
TREAT
MECHANISMS
NOT A DIAGNOSIS
Antiviral Therapy
Symptomatic TX

- Cool compresses
- Decongestants
- Cycloplegics
- ASA or tylenol
Idoxuridine

• Indications-H. Simplex
• Problem -Poor ocular penetration
• Dosage:
  YOU MUST BE KIDDING - one drop q 1h daytime and q 2h ATC
  OR
• Every minute X 5 doses every 4H ATC
• Ointment used 5X daily ATC
Idoxuridine dosage forms

- Herplex 0.1%-15cc by Allergan (Also available in the handy 50 gallon economy size)
- Stoxil 0.1% -15cc-SKF
- Stoxcil 0.5% Ophthalmal. Oint 4gm
Adenine arabinoside

- Indications-Herpes simplex
- Caution-May be mutagenic
- Dosage-Instill Ointment 3-5X daily
- Problem-ONLY available as ointment
- VIRA-A 3% 3.5gm tube-PD
Trifluorothymidine

- THE FORMER drug of choice for topical management of Herpes simplex ocular disease.
- Rapid absorption
- Toxicity occurs when used over 21 days
- Dosage-5-8X daily
- Viroptic 1%-7.5cc-Burroughs
ZIRGAN

- Selective Toxicity
- Gel formulation
- Adenoviral effective?
Acycloguanosine (Acyclovir)

• The “Jewish Penicillin” of the anti-viral products
• A pro-drug-minimal side-effects
• Topical agent no more effective than viroptic
• Standard of care for H. Zoster and resistant H. simplex
Zovirax (Burroughs)

• Oral dosage form 200, 400 and 800mg tablets and 200mg/5cc suspension
• H. simplex 400mg 5X/D@@@@
• H. Zoster-”Chickenpox”-200-400mg QID X 10D
• Recurrent-800mg 5 times daily X 10-14 days@@@@
For ALL Herpes It’s the Drug of Choice

- Recurrent or resistant simplex
- All Zoster patients over 50
Famvir
Famcyclovir

- Third generation anti-viral medication
- Pro-drug
- Selective toxicity
- Excellent anti-herpetic activity
- Quite expensive
Famvir
Indications/Dosage forms

• Indications:
  • Resistant ocular simplex or Type II simplex
  • 125-250mg TID
  • Herpes zoster 500mg TID

• Dosage forms:
  • 125/250/500mg tablets
Case 2

S: 54 y/o with red eye X 72H
FB sensation with sticky discharge in AM
O: Mixed conjunctivitis
• No PA Nodes
• Mild chemosis
• Yellow/green discharge
• Min SPK
• No corneal infiltrates
Conjunctivitis-An Ocular Emergency?? Differential DX?

- Environmental
- Viral
- Bacterial
- Other
Tests

- Cultures
- Diff-Quick
- Gram Stain
Diff-Quick Technique
Even a “DIP” Can Do It

Dip 5 times for one second into:

• The fixative
• Solution I
• Solution II
• Rinse in distilled water
• Air dry
Differentiates White Blood Cell Types

- Poly’s: Polymorphonucleocytes (PMN’s): Bacterial infection
- Lymphocytes: Viral infection
- Eosinophils: Allergic disease
Gram Stain

- Differentiates bacteria by differences in cell wall morphology
- Designates bacteria as Gram (+) or (-)
Gram Stain Solutions

- Gram crystal violet: All stain blue
- Gram iodine: All cells stay blue
- Decolorizer: Gram (+) cells “seal” in blue color, Gram (-) cells are colorless with holes in cell wall
- Safranin counterstain: Stains Gram (-) cells red
Culturette Etiquette

• Choose proper culturette: Bacterial vs Viral
• Break solution bulb BEFORE swabbing
• Avoid pus-Dead cells only
• Plate ASAP
Plating Etiquette

- Blood agar: Detects hemolysis: a sign of greater pathogenicity
- Chocolate agar: Heated blood agar: Provides nutrients for Hemophilus growth
- Sabouraud’s: Fungal growth media
- Overlaid E-Coli plate: Culture media for acanthamoeba
Plating Etiquette II
HOW TO LABEL CULTURES

CORNEA
CONJUNC.
LIDS
## Differentiating Characteristics in Conjunctivitis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Bacterial</th>
<th>Viral</th>
<th>Allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge</td>
<td>Purulent</td>
<td>Watery</td>
<td>Stringy</td>
</tr>
<tr>
<td>Itching</td>
<td>Minimal</td>
<td>Minimal</td>
<td>Marked</td>
</tr>
<tr>
<td>Preauricular lymph node</td>
<td>Absent</td>
<td>Common</td>
<td>Absent</td>
</tr>
<tr>
<td>Stain &amp; Smear</td>
<td>Bacteria, PMN</td>
<td>Monocytes, Lymphocytes</td>
<td>Eosinophils</td>
</tr>
</tbody>
</table>
RULE #1
Before you TX Infection-Know the cause
Gram-Positive Organisms

- 90% of ocular infections

**Staphylococcus epidermidis**

**S. aureus**

**Streptococcus pneumoniae**

**Coagulase-negative staphylococci, Streptococcus viridans**

Clinical Characteristics
Let’s Start with the Kids: Pediatric conjunctivitis plays by different rules

Don’t treat pediatric conjunctivitis without first:

• Check history
• Check ears
• Check throat
• Check temperature
Kids Conjunctivitis-NO drops alone if.....

- Recurrent or active otitis media
- Fever
- Sore throat
- Generally ill
- Treat with Polytrim/fluoroquinolone and effective oral anti H. Flu
Why treat conjunctivitis:

- Prevent conversion to chronic disease
- Hasten cure
- Prevent spread to other ocular structures or sinus
- Reduce contagion
- Prevent complications
Treatment Agents

- Polytrim
- Fluoroquinolone
- Antibiotic Steroid
- Rarely orals (Exc. Pediatric)
The STYE that Wasn’t

- 32 yowm swollen upper lid
- Very painful
- Warm to touch
- + HX frequent “Styes”
A STYE?
This lesion is best classified as a (an):

1. Stye
2. Dacryocystitis
3. Internal hordeola
4. External Hordeola
5. None of the above
Patient work-up

• NO labs done
• Presumed DX Internal hordeolum of lid
• TX with Oral antibiotic/heat
• Patient calls 24 hours later—much worse
Pre-septal Cellulitis VS ??
The differential dx should include:

1. Dacryocystitis
2. Orbital cellulitis
3. Sinusitis
4. EKC
NOW-How about some tests?

1. CBC
2. Blood culture
3. CT/MRI
4. Temperature (Oral vs rectal)
5. All of the above
6. None of the above are necessary
Proptosis
DON’T Forget Your Differential DX-The Bad Signs

- Decreased Acuity
- Proptosis
- Diplopia-Extraocular paralysis
- Febrile
- Elevated WBC’s
- Get blood cultures
- Consider orbital CT scan
Orbital Cellulitis is a Life/Sight-Threatening Condition

• Patient must be hospitalized
• Parenteral IV therapy is mandatory
• Drug based on culture/sensitivity reports
• HX of trauma or insect bite is common
15 Y/O female presents with mom-C/O red eye-Simple Right??

- Has seen one nurse practitioner
- Has seen Two Optometrists
- Tx with Ciloxan
- Tx with Tobradex
- Mom wonders why nobody can cure her daughter
Chronic Conjunctivitis
Zithromax
Azithromycin

- Broad spectrum activity
- 68 hour 1/2 life
- DOC in penicillin sensitive patients
- Effective in pediatric Hemophilus
- Mild-medium GI side effects
- Excellent compliance (5 day TX) (1 day for chlamydia)
- Moderate cost
- Drug Interactions??
The Killer Conjunctivitis

• Neonatal conjunctivitis is different
• Chemical vs infectious cause
• Chemical: Crede prophylaxis with silver nitrate is no big deal
• Infectious IS A BIG DEAL
Neonatal Conjunctivitis

- Ophthalmia Neonatorum
- Any conjunctivitis in the first month of life
- Chemical vs infectious
- Old TX: Crede prophylaxix used silver nitrate drops to prevent gonorrhea
Neonatal Conjunctivitis

- Always an emergency
- Tx presumptively
- Always culture to R/O gonococci
Neonatal Conjunctivitis
Infectious Types

• Neisseria gonorrhea
• Neisseria meningidis
• Chlamydia trachomatis
• Staph. Aureus
• Strep. Pyogenes
• Strep. pneumoniae
Timeline of Diagnosis

Approximate Time of Onset of Neonatal Conjunctivitis

- **Chlamydia**
- **Gonococcal**
- **Chemical**

Postnatal Day of Onset:

0 1 2 3 4 5 6 7 8 9 10
Chlamydial Conjunctivitis

- Most common cause of CHRONIC conjunctivitis in all age groups
- STD
- Mother should be checked prior to birth
- Onset in 2nd week post-partum
- Potential conjunctival scarring
- Systemic complications
Chlamydia
Clinical signs

• Moderate mucopurulent discharge
• Papillary conjunctivitis
• Possible pseudomembranes
Chalmydia Treatment

- Both topical and systemic
- Treat parents and friends also
- The family that gets treated together stays together
- Erythromycin ophth. Oint
- Zithromax 10mg/kg/day X 1 day, then 5mg/kg/D X 4 days
- Adults: 1 gm powder packet X 1
Gonococcal Conjunctivitis
Neisseria Conjunctivitis - A TRUE Ocular Emergency

- Onset within first week of life
- HYPER-purulent conjunctivitis
- Marked inflammation of eye and lids
- STD
- Delayed treatment/loss of eye/potentially fatal infection
Neisseria
Lab Work-up

• Labs are mandatory-STAT
• Fastest is gram stain-don’t wait for cultures
• Confirmatory culture
Neisseria Treatment

• Ocular irrigation with antibiotic solutions
• IV Pen or cephalosporin-Dose by weight
• TX parents
• Multiple infections possible with several STD’s
Maternal Herpes simplex-Type II- Genital herpes

• High incidence of infant mortality
• Mother must be pre-tx with oral acyclovir
The “Like-New” 3 year old SCL

- 37 yowf with eye pain—”thinks she scratched her eye
- Wears the “30” day XSCL
- Orders them through the mail
- No local eye doctor
- Current pair 3 years old
- HX of frequent “pink-eye”
Infectious Keratitis

- Herpes Keratitis
- Fungal Keratitis
- Bacterial Keratitis
- Amoebic Keratitis
- Traumatic Keratitis
Treated at Urgent Care

- Urgent care doctor agreed and treated as an abrasion
- Pressure patched X 3 days
- Erythromycin Ointment
- Suffered significant VA loss
- Patient won settlement prior to trial
Culturing: The 1,2,3,4 Rule

• 1: Less than +1 anterior chamber RX
• 2: Less than 2 mm in size
• 3: At least 3mm from optic axis
• 4: Less than 1/4 depth of cornea
Staphylococcus Epidermidis Keratitis
Bacterial Ulcer Guidelines

- Always culture if you have the means
- Patients that get better never sue-those that don’t-DO
- Consider the 1-2-3-4 rule
- Fluoroquinolone mono-therapy is not fool-proof
- Grade the ulcer-Location, location, etc
- Step TX based on cultures
Evolution of the Quinolones

Nalidixic Acid → Norfloxacin → Sparfloxacin
Lomefloxacin → Grepafloxacin → Gatifloxacin
Ciprofloxacin → Levofloxacin → Moxifloxacin

Limited spectrum of activity → Extended spectrum
Enhanced activity against Gram-negative bacteria

Extended spectrum
Enhanced activity against Gram-positives, streptococci, anaerobes, atypical mycobacteria
Improved pharmacokinetic properties

Fourth-Generation Fluoroquinolone Chemical Structures

Gatifloxacin

Moxifloxacin
Potency of Fluoroquinolones
Mather et al, AJO, 2002

MIC's of Fluoroquinolones to 93 Endophthalmitis Isolates

Antibiotic
oflox
cipro
levo
gati
moxi

MIC
0
0.5
1
1.5
2
2.5

Staph epi
Staph aureus
Strep pneumonia
Gram Negatives
The Latest

- **Besivance**: NEW Molecule
- **Moxeza**: Longer duration
- **Zymaxid**: Higher concentration
1st visit to the eye doc: FRIDAY

• VA: 20/30 OD      20/20 OS
• SLE: 1mm infiltrate/ epith. Defect/Shallow ulcer
• + 1 FL, + 1 C
• +1-2 Bulbar injec.
• Pain: 7/10
MONDAY

• “DOC-IT’S WORSE”
THE BAD NEWS

• VA CF OD
• Mucopurulent plaque
• Central lesion with satellites
• Hypopion
• Initial lab: + growth-Probable S. aureus
• Patient referred to Univ. cornea specialist
• Scrapped and stained, incl. Gr stain
• DX: Filamentous septate fungi, probably Fusarium
Classic fungal presentation

• VA 20/20 / CF 3 feet  NIPH
• 1- ring infiltrate/(+) C and F
• 2- Hypopion
• 3 – Satellite lesion
• 4 – Suppuration = heavy inflammation
Terms of Endearment-Gone but not forgotten

• Fungal and acanthamoeba-
  Forgotten, but not gone

Index of suspicion is critical-proper DX is mandatory AND it must be “TIMELY”
The Patient at Risk

- Hx of injury from organic material
- “scratched eye with tree branch”, then steroid treated with long term antibiotic/steroid combo
- Immunocompromised-Local vs systemic
- Diabetics/systemic disease
- HIV
- Chemotherapy
- Post-organ transplant
- Oral steroid user
Filamentous VS Yeast Signs

- Filamentous
  - Outdoor activity
  - 24-48 H after injury
  - Mild to severe inflammation
  - Feathery edge with satellites-”scattered lesions represent hyphae in corneal stromal tissue

- YEAST@@@
  - Host is commonly immunocompromised
  - Focal lesion
  - More suppuration
  - Perforation common
  - “Looks more bacterial”
  - No feathery edges or satellites
Natamycin (Pimaricin 5%)  
THE ONLY APPROVED TOPICAL ANTIFUNGAL AGENT@@@@

• Polyene
• Increases cell membrane permeability
• More stable and less toxic than amphotericin
• “Sticks well” to ulcer site-least toxic of all topicals
• Used q 2-4 hours
• Some epithelial toxicity
• Effective against Fusarium, Aspergillus and Candida
The Corneal Abrasion That Wasn’t

- 37 y/o male with eye pain-Hit in eye with hockey stick 24 hours ago
- Wears GP CL’s
- GP CL OD cracked
- VA 20/30 OD
- 20/25 OS
This patient should be cultured?

1. YES

2. NO, That would be ridiculous.
This patient should be immediately referred to a corneal specialist?

1. YES
2. NO, that would be STUPID!!
24 hours later

- Pressure patched
- Erythromycin Ointment X 1 day
- Returns 24 hours, “eye is worse”
- “Dendritic keratitis”
- States he has “sexual herpes”
- VA 20/40 OD
- TX with viroptic 5X/day
Time to refer the patient?

1. YES PLEASE
2. NO, that may not be prudent yet-I think
48 hours-”It’s Worse”

- VA now 20/60
- Infiltrates present
- Referred to corneal specialist
- DX “toxic keratitis”
- No cultures
- Topical steroids
48 hours later-I FEEL BETTER, BUT I’M BLURRY

- Seen by OD that works with corneal specialist
- Looks really bad
- Referred to University specialist
- DC’s steroid for culture
- Eye blows up
- Refers to the BIG Kahuna University specialist
- Eyes is cultured
- Guess what they found?
THE CULTURES

- Bacterial: Negative
- Viral: Negative
- Fungal: Negative
Oh, one other culture....

Positive for acanthamoeba keratitis
THE LAWSUIT

• Patient sues OD and original ophthalmologist
• Claims failure to DX
• Expert witness states DX delayed by “incompetence”
• Claims that it was a “late” DX
Everybody calls it Herpes
Differential DX

- Trauma
- Inflammatory ulcer
- Infection:
  - Herpes
  - Bacteria
  - Fungal
  - Acanthamoeba
THE END