Herpes Hour: Toasting to Treatments and Cheers to Complications

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NO FINANCIAL DISCLOSURES

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OVERVIEW

- Cases
- Herpes review
- Evaluation
- Treatment and management
- Differentials

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CASE 1

- Patient referred for a non-healing cornea
- Progressive worsening over the last week
- Pain 9/10
- Wearing an eye patch for comfort
- No recent history of ocular surgery or trauma
- Uncontrolled diabetic
  - A1C > 9.0

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CASE 1

- VAsc: 20/200 OD, 20/25+2 OS
- Pinhole OD: 20/80
- PERRL –APD
- CVF: FTFC
- EOMs: full and smooth, diplopia, (+) pain

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CASE 1

- Gross observation revealed no skin lesions on the face, scalp, or neck
- DED with MGD OU
- **Diffuse 3+ injection of the bulbar and palpebral conjunctiva OD, clear OS**
- **Vertically oriented corneal epithelial defect 6mmx3mm OD**
- **Mild stromal edema surrounding defect OD**
- Anterior chamber was D&Q OU
- IOP 17mmHg OD, 15mmHg OS with iCare
- Posterior segment unable to be viewed undilated OD/OS

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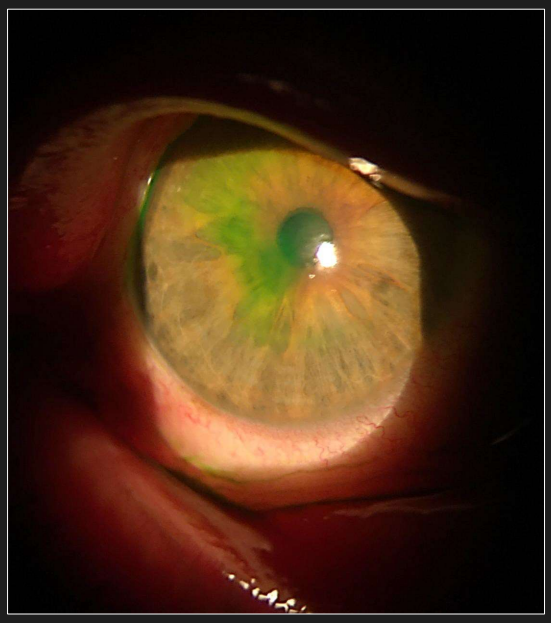

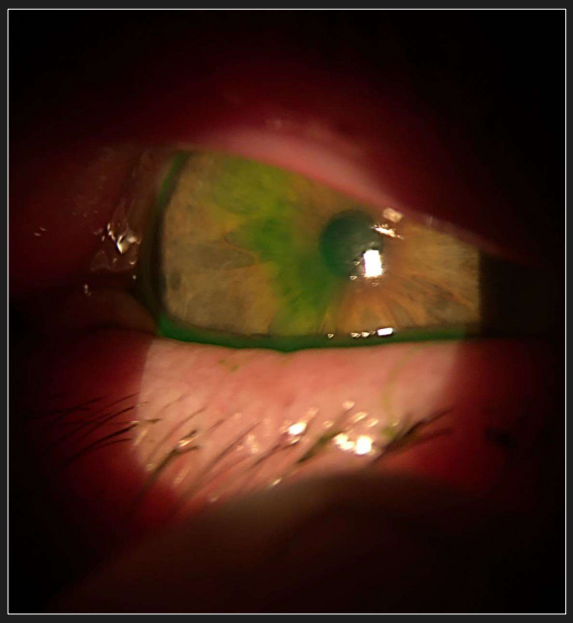

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DIFFERENTIAL DIAGNOSIS

- Corneal abrasion
- Dry eye disease
- Herpetic disease

No history of trauma
History of cold sores?
Contact lens wearer?

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REFERRAL TIMELINE

12-days prior

SPK noted with **1cm infiltrate**; **FML QID – taper,** ung at bedtime, and lid scrubs

5-day FU

Same objective findings

Ocuflox gtts QID, amniotic membrane, and BCL placed

2-day FU

No improvement

With a dry eye regimen or infectious regimen

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REFERRAL TIMELINE

1-day Follow up

3+ SPK with superior mild abrasions, palpebral conjunctiva was swabbed for FBs; FML d/c; BCL/amnion removed

4-day FU; No improvement and patient was **referred same day**

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CASE 1

- Mild steroid
- Antibiotic gtt
- Amniotic membrane
- BCL

…now what?

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CASE 1

- Started on **Valacyclovir 1g TID**
  - Continue Ofloxacin QID
  - Continue ointment at bedtime
  - Start PFAT 4-6x daily
  - Discontinue steroids
  - Stop wearing the eye patch

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Bloodwork ordered by PCP within the last month

Test	Result and Flag	Reference
Glucose	162mg/dL High	70-99
A1C	9.1% High	4.8-5.6
BUN	14md/dL	6-24
Creatinine	.75mg/dL Low	0.76-1.27
eGFR	105mL/min/1.73	>59
BUN/Creatinine Ratio	19	9-20
Sodium	139mmol/L	134-144
Potassium	4.7mmol/L	3.5-5.2
Chloride	100mmol/L	96-106
Protein, Total	7.1g/dL	6.0-8.5
Albumin	4.7g/dL	3.8-4.9
Globulin, Total	2.4g/dL	1.5-4.5
Bilirubin, Total	0.3mg/dL	0.0-1.2
AST	27 IU/L	0-40
ALT	21 IU/L	0-44

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2-DAY FU

- Subjective and objective improvement
- Corneal defect measured 3mmx3mm within central vision
- Plan:
  - Continue Valacyclovir 1g TID PO
  - PFAT 4-6x daily
  - d/c Ocuflox gtts
  - Start erythromycin ung TID (with instructions)

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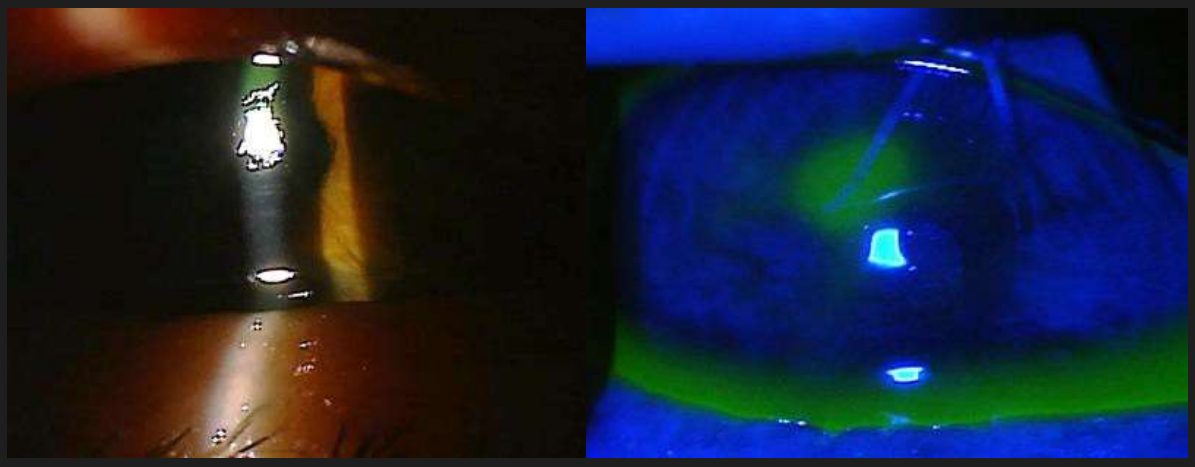

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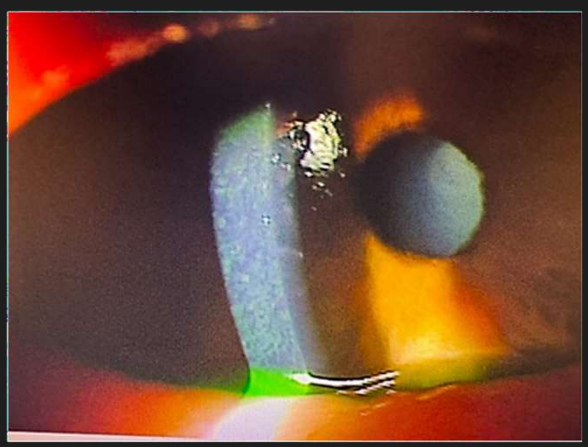

Optic section showing significant SPK, mild endothelial folds, and mild stromal haze and edema.

1-week FU
Punctate staining
No excavation of the cornea

Reduced Valacyclovir 500mg BID PO + dry eye regimen

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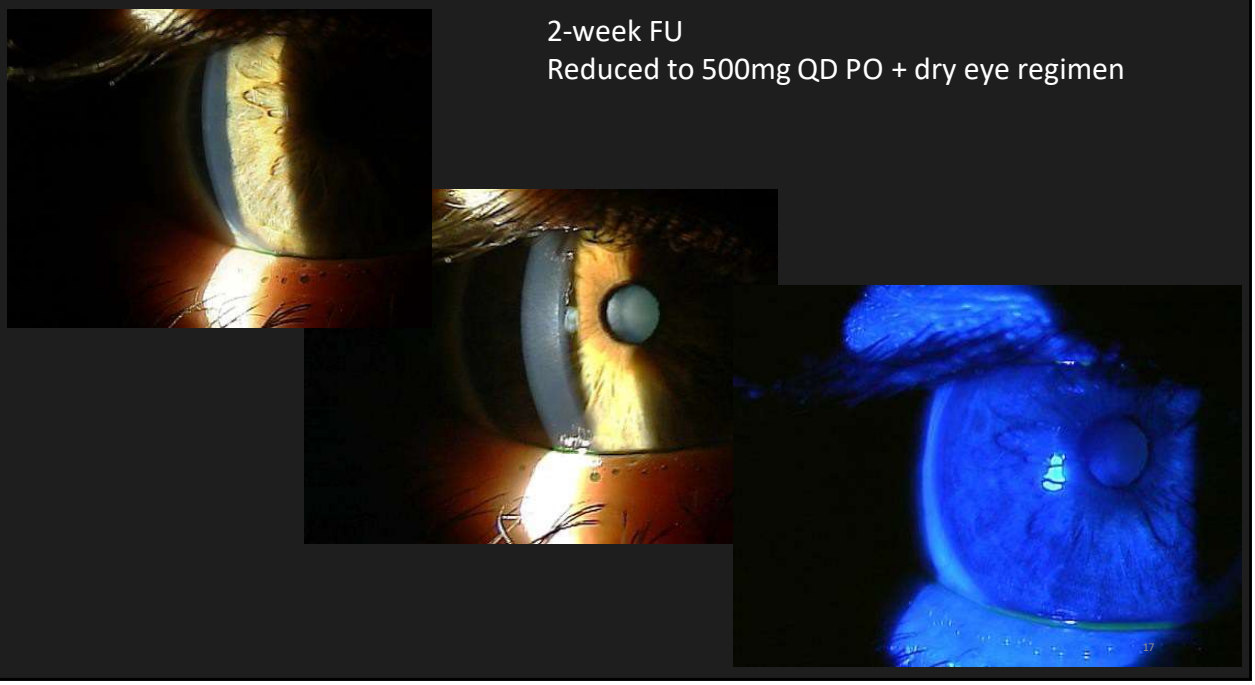

2-week FU
Reduced to 500mg QD PO + dry eye regimen

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Herpes Review

- Blinding condition, especially in recurrent cases
- Rarely present classically and considered a “masquerader”
- HSV-1 almost universal and contracted in early childhood

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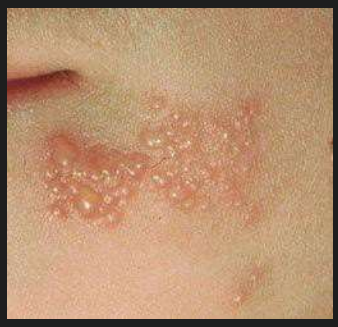
HSV Primary Ocular Infection

- Initial presentation of HSV
  - Unilateral
  - Often blepharoconjunctivitis or simply a vesicular skin rash - often near the eyes
  - CHAT w/ my follicles
    - Follicular conjunctivitis can be observed in the primary form
  - Subclinical systemic findings
    - Fever, malaise, etc.



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Pathogenesis

Rate of ocular recurrence – 10% at 1 year and 50% at 10 years

After primary infection, virus is carried to the trigeminal ganglion where latent infection is established

Stressors can reactivate the virus including illness, menstruation, sunlight exposure, trauma (esp. to CN5), uncontrolled diabetes…

When the virus replicates, it is transported in the sensory neurons to the periphery

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Herpes Review

- Initial infection, HSV remains dormant in nerve cells
- Reactivates leading to recurrent outbreaks
- Latency of disease can make disease etiology difficult

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Recurrence

- Patient was pain free for over a month
- Ocular condition recurred with seasonal illness
- Patient upped Valacylovir dosage on his own and improved within 1-2 days
- Seen in clinic within the week, no corneal defect
  - Valacyclovir 1g BID

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Herpes Review

- Early disease often presents as punctate staining and often undertreated or mistreated
  - Ulcerations can enlarge and become “geographic”
- Classic dendritic lesion
  - Dichotomous branching with terminal bulbs
  - Stains with fluorescein dye and borders stain with rose Bengal
- Diagnostic testing rarely needed (PCR, serology, culture)
- **Most useful:** history, external and ocular examination with dyes, and hypoesthesia testing

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HZO Versus HSV

- Denied any rashes
- Denied history of chicken-pox
- Denied HZV vaccination

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Herpes Zoster Ophthalmicus (HZO) Pathogenesis

- 1-million Americans yearly
- HZO is shingles involving the ophthalmic division of the trigeminal nerve
- Primary infection is Varicella virus
  - Virus remains dormant in the trigeminal and dorsal root ganglia and cranial nerve sensory ganglia
- Reactivation is thought to occur after VZV-specific cell mediated immunity has faded
  - Usually age-related

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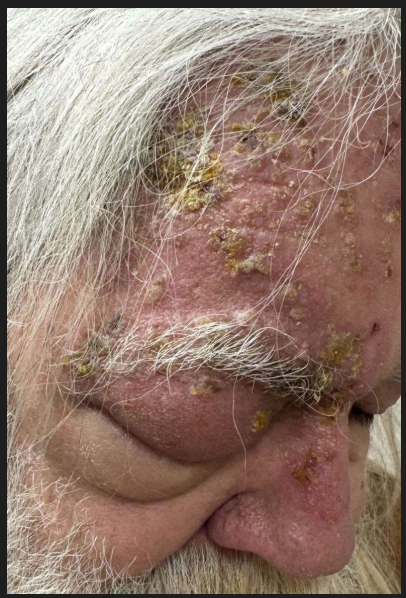
Hutchinson's Sign:

- Lesion on the tip of the nose
- Nasociliary branch of ophthalmic division of trigeminal nerve (V)
- Indicated possible ciliary (ocular) involvement



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Herpes Simplex Epitheliopathy

SYMPTOMS

- Mild-moderate discomfort (sometimes severe but rare)
- Redness
- Photophobia
- Watering
- Blurred vision

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Herpes Simplex Epitheliopathy

SIGNS

- Reduced corneal sensitivity
- Mild sub-epithelial haze
- Vesicular lesions
- Mild A/C reaction
- Follicular conjunctivitis
- Elevated IOP
- Conjunctivitis
- Epithelial Erosions

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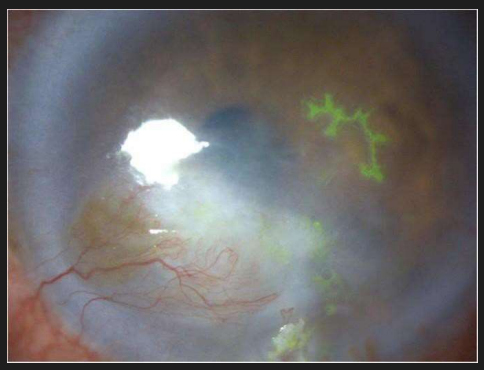
Epithelial Keratitis: Classic Dendritic Ulcer

Slit lamp and ocular signs:

- Branching linear ulceration (dendrites)
- Swollen epithelial borders (terminal end bulbs)
- Contain active virus



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Work-up

- Herpes zoster and herpes simplex often clinically evident until it isn't
- Slit lamp examination with and without vital dyes
- Corneal sensitivity testing
  - Cochet-Bonnet
  - Cotton tip
- Clinical manifestations vary:
  - Blepharoconjunctivitis (HBC)
  - Epithelial keratitis
  - Immune stromal keratitis (ISK)
  - Endotheliitis
  - Iridocyclitis

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Epithelial Keratitis: Management

- Generally unnecessary due to clinical diagnosis
  - PCR (polymerase chain reaction)
  - Viral scrapings sent for culture
  - Giemsa stain shows multinucleate giant cells
  - Blood titers confirming primary exposure can be tested

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Epithelial Keratitis: Standard Management

- Topical antivirals - gancyclovir 0.15% (Zirgan) 5 x per day until dendrite clears then TID for 1 week (and if not available, trifluoridine 9x per day)
- Cyclopegia for pain/AC reaction
- Preservative free artificial tears
- Debridement in persistent cases
- Oral anti-virals for 5-10 days
  - 500 mg valacyclovir 3x/day
  - 400 mg acyclovir 5x/day
  - 250 mg famvir 2x/day

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Treatment and Management

Drug	HSV Dosing (Epithelial)	HZV Dosing
Acyclovir	400 mg PO 3-5 times daily for 7-10 days	800 mg five times daily for 7-10 days
Valacyclovir	500 mg PO twice daily for 7-10 days	1 g three times daily for 7 days
Famciclovir	250 mg PO twice daily for 7-10 days	500 mg three times daily for 7 days
Trifluridine ophthalmic solution 1% (Viroptic)	Instillation of 1 drop into affected eye(s) 9 times daily for 7 days, taper	Topicals are not used in the treatment of HZV
Ganciclovir ophthalmic gel 0.15% (Zirgan)	Instillation of 1 drop into affected eye(s) 5 times daily while awake until healing of corneal ulcer, taper	Topical are not used in the treatment of HZV

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CASE 2

- Patient referred for persistent corneal ulcer
- Reports symptoms beginning 6 weeks ago
- Current meds: alternating ciprofloxacin and gentamicin Q1H
- Cultured, no results yet
- (+) CL overwear

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CASE 2

- VAcc OD: 20/20, VAsc: 20/200 OS
- Prelims within normal limits
- 1.4mm vertical by 1mm horizontal corneal ulcer with neovascularization encroaching on the visual axis
- Cochet-Bonnet: 1
- Cold sore noted on upper lip

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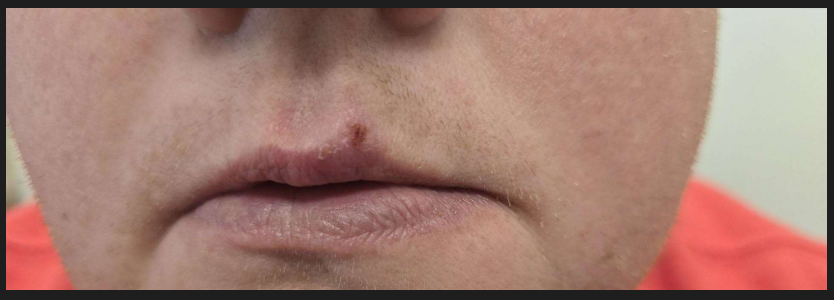

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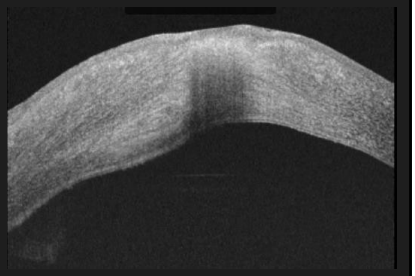

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CASE 2

- Neurotropic and suspect herpetic etiology
- D/c gentamicin gtts
- Continue ciprofloxacin q1H while awake
- PFAT QID
- Erythromycin ung QHS
- Valacyclovir 1g TID
- Doxycycline 50mg PO BID
- Vitamin C PO QD

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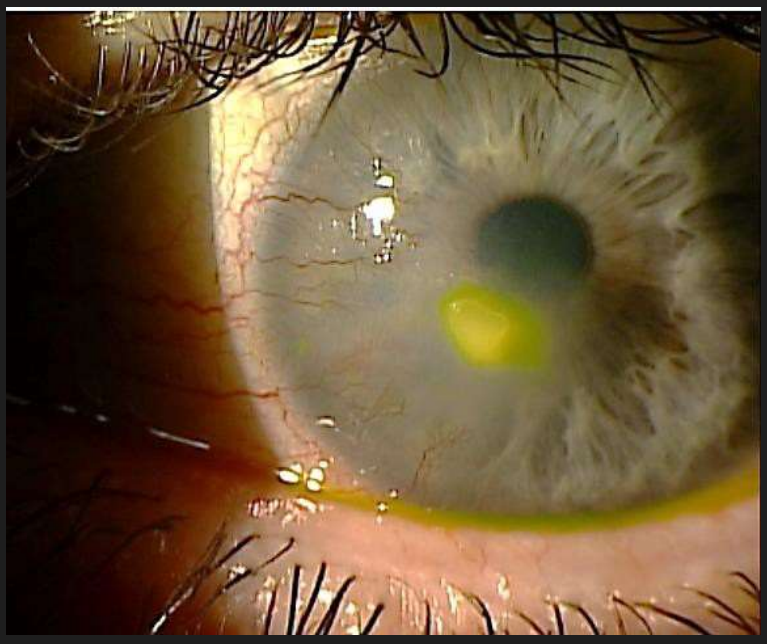
CASE 2

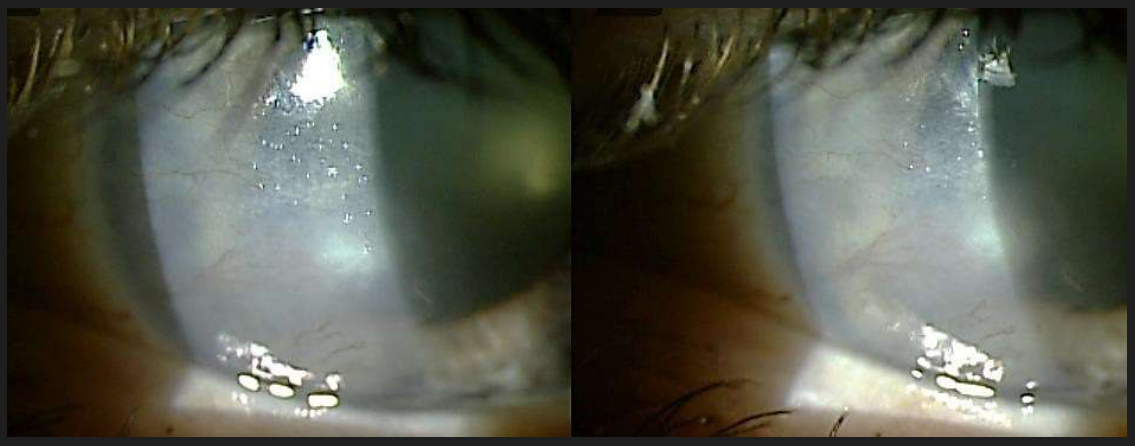
- 3- day follow up
  - "Best days I've had in 6 weeks"
  - Ulcer decreased in size, neo started to regress

2-DAY FU



FOLLOW UP #3

VA 20/100 PH 20/40



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FOLLOW UP #3

- Increased doxycycline to 100mg
- PFAT Q1H
- Continue Valacyclovir 1g TID
- Erythromycin ung BID

- Trifluridine QID and Pred acetate QID were started (instructed to alternate drops and to prevent washout)

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FOLLOW UP #4

20/100
PH 20/40

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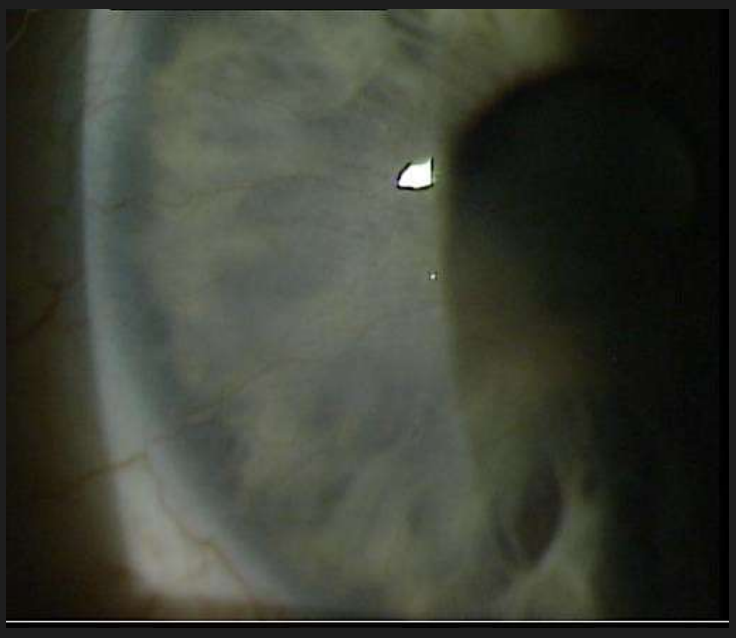
FOLLOW UP #5

1- week FU
BCVA 20/20
Large change in RX

D/c Viroptic
Continue doxy 100mg, vitamin C, and valacyclovir 1g BID PO



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FOLLOW UP #5

- D/c Viroptic
- Start Durezol QID OS
- Continue doxy 100mg and vitamin C
- Continue Valacyclovir 1g BID

Treatment and Management

- Topical agents
  - Ganciclovir (Zirgan), trifluridine (Viroptic) and topical acyclovir (outside US)
  - Challenging to find, $$$, toxic to anterior segment
- Oral agents
  - Valacyclovir, Acyclovir, Famciclovir
  - High bioavailability and do not compromise corneal epithelium further
  - GI upset and headaches
  - Valacyclovir > acyclovir due to renal impairment
  - Famcyclovir preferred in >65YO increased risk of crossing BBB

Herpes Stromal Keratitis

- Causes of stromal haze, scarring and neovascularization are primarily related to inflammation

- **SIGNS**
  - Reduced corneal sensitivity
  - Stromal haze/ring infiltrate
  - Corneal neovascularization
  - Mild A/C reaction is possible
  - Elevated IOP
  - Red eye

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Treatment and Management:

- HEDS I
  - Conclusion: topical steroids reduced stromal inflammation and prophylactic oral acyclovir reduced the recurrence of HSV

- HEDS II
  - Adding oral anti-virals did not reduce the recurrence of epithelial HSV
  - Adding oral anti-virals significantly reduced recurrence and severity of stromal HSV (41% and 50% in severe presentations within a year)

Pitch deck 48

Hsv Stromal Keratitis Treatment

- Topical corticosteroids:
  - Difluprednate QID
  - Prednisolone acetate Q2H
- Prophylaxis with PO Acyclovir (400 mg bid) or Valtrex (1000mg QD) or topical anti-virals for 5-10 days
- Prophylaxis may also include topical anti-virals
- Cycloplegia if needed

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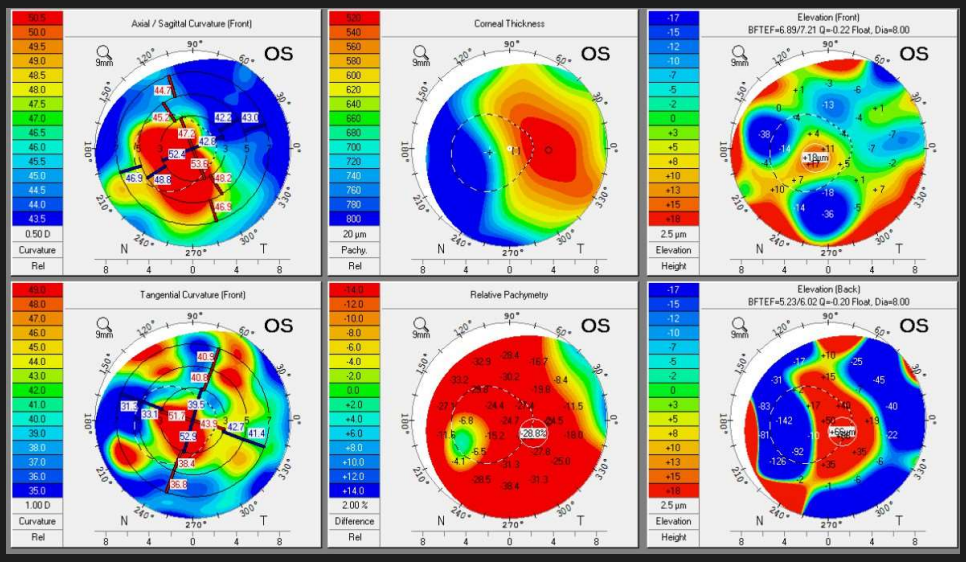
THE OUTCOME



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QUESTIONS?

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