Managing Uveitis: Tips for Success

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Bio

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Disclosures: None

Tips to successful uveitis management:

1) Get a thorough review of systems

Review of Systems

Constitution: fever, malaise, weight loss/gain

Dermatological: rashes, sores, dry skin, vitiligo

Rheumatological: personal or family hx of autoimmune disease

Respiratory: shortness of breath, cough, wheezing

GI: stomach upset, irritable bowel, abdominal pain, diarrhea

GU: ulcers/sores, painful urination, discharge, hx of STD

Muscuoloskelatal: joint pain/arthritis, muscle aches

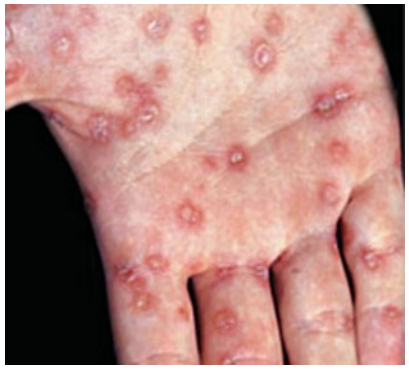
Social Hx: drug abuse?, STDs?, animal exposure? (puppies, cats/kittens)

Condition		Signs/Sxs
Ankylosing spondylitis	Male predominance, presents in early adulthood,	low back/hip pain, chest pain
Reiter's syndrome/ Reactive Arthritis	Young male	triad = arthritis, urethritis, conjunctivitis
Juvenile idiopathic arthritis	Slight male predilection	sacroiliitis common
IBD (ulcerative colitis and Crohn's)	Generally diagnosed early adulthood	Diarrhea, abdominal cramps, blood in stool
Sarcoidosis	AA predominance, F>M Can include posterior segment inflammation (ie vasculitis, vitritis)	Causes hilar adenopathy Cough, SOB, weight loss, night sweats, fatigue, rash on shins/ankles. May be asymptomatic.
Tuberculosis	Latent or active Lung granulomas on X-ray, CT	cough, fever, chills, night sweats, weight loss
Syphilis	Acquired by sexual contact	Rash (palms of hands and soles of feet), chancre sores, fever, malaise, joint pain
Toxoplasmosis	Caused be exposure to cats or from eating undercooked meat; consider in pt with immunocompromised state	retinal lesions with adjacent vitreous haze or "headlight in the fog" sign
Rheumatoid arthritis	Attacks the synovium (membrane surrounding joints)	Tender, swollen joints (smaller first)

Behcet's disease	M=F, diagnosed in 20s-30s, middle eastern and far east decent	Painful oral and genital ulcers, arthritis
Systemic lupus erythematosus (SLE)	F>M	butterfly rash, malaise, fatigue, fever
Lyme disease	Carried by ticks	Early: bulls-eye rash, fever, chills, fatigue, joint aches
Granulomatosis w/ polyangiitis (formerly Wegener's)	Vasculitits; causes sinus, pulmonary, kidney disease	scleritis>uveitis Weight loss, fatigue, fever, nose bleeds, congestion, SOB, bloody cough

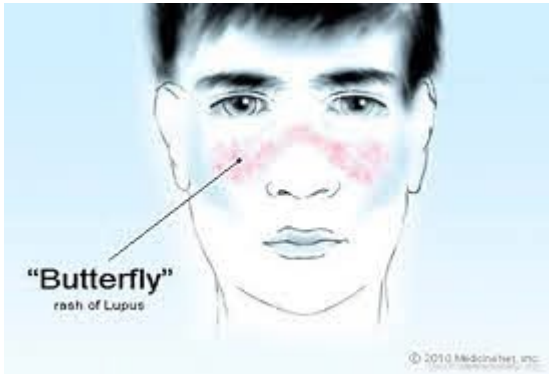
Rashes

Syphilis
- Copper penny rash
  - typically found palms of the hands and soles of the feet.
  - found in secondary stage - 6 weeks to 6 months after exposure



Copper penny in syphilis
WebMD

Lupus
- Butterfly rash “malar”
  - Covers cheeks and bridge of nose; flat or raised
  - Rosacea is most common cause of malar rash



Lyme
- Erythema migrans
  - Circular rash that expands associated with early Lyme
  - Classic pattern is bullseye

Joint Pain

Rheumatoid arthritis (RA)

- Affects multiple joints in a bilateral and symmetric pattern
- Worse in morning
- Small and large joints
- systemic lupus erythematosus (SLE) and polymyalgia rheumatica can have similar complaints

Spondyloarthropathies (HLA-B27 +)

- Joint paint is asymmetric
- Targets the sacroiliac joints and lower spine

Lyme

- Early disease has migratory symptoms: joint sxs resolve and then reappear in different joints

Tips to successful uveitis management:

1) Get a thorough review of systems
2) **Know when and what labs to order**

Categorizing Uveitis

Location: anterior, posterior, intermediate, pan

Duration: acute, chronic, recurrent

Laterality: OD, OS or OU

Type of inflammation: granulomatous or non-granulomatous

Workup

When is it necessary?

- Recurrent
- Bilateral
- Granulomatous

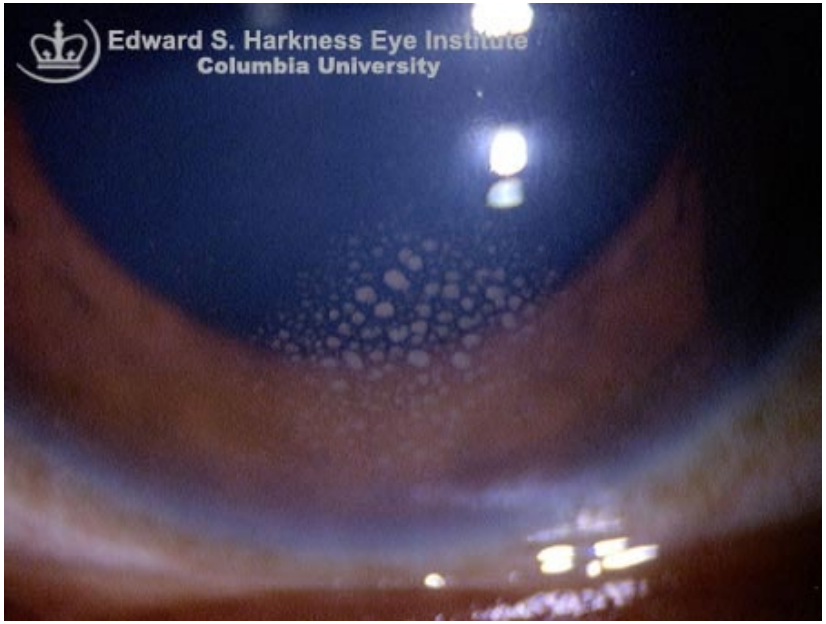
Granulomatous Uveitis

Characteristics:

- Cornea: large, greasy “mutton fat” KPs
- Iris: Koeppe nodules (pupillary margin), Busacca nodules
  ↑ risk of synechiae

Etiology:

- Sarcoid
- TB
- Syphilis
- Lyme disease



Nongranulomatous Uveitis

Characteristics:

- Cornea: smaller KPs
- Iris: less risk of synechiae

Etiology (acute presentation):

- Non-specific to particular autoimmune disease
- heavy flare and fibrin -> think HLA B27

Other:

- JRA (chronic)
- Fuch's heterochromic (chronic)
- Trauma/postoperative
- Herpetic/viral

Lab Work

Complete blood count w/ differential (CBC)

- Useful to determine pts general health status

C-reactive protein (CRP)

- Nonspecific marker for inflammation

Erythrocyte sedimentation rate (ESR)

- Nonspecific marker for inflammation

Lab work

Test:	Conditions:
Angiotensin-converting enzyme (ACE)	Sarcoid
Human leukocyte antigen B27 (HLA-B27)	Spondyloarthopathies: Ankylosing spondylitis, reactive arthritis/Reiter's syndrome, Crohn's disease, psoriatic arthritis
Purified protein derivative (PPD)	TB
QuantiFERON-TB gold	TB
Antinuclear antibody (ANA)	SLE, scleroderma, juvenile arthritis, polymyosistis, IBD, psoriasis, Sjögren's syndrome
Rheumatoid factor (RF)	Rheumatoid arthritis, Sjögren's syndrome
RPR, VDRL, FTA-ABS	Syphilis
ELISA or Western blot for Lyme	Lyme disease
SS-A, SS-B	Sjögren's syndrome
ANCA	Vasculitis (ie GPA/Wegner's), ulcerative colitis
HLA-B5	Behcet's
Toxoplasma IgG/IgM	Toxoplasmosis

HLA B27

- Human leukocyte antigens (HLAs) are proteins on WBCs
- 6% of the population is HLA-B27 positive
  - +HLA B27 persons have much higher risk of developing spondyloarthropathy

HLA-B*27 Disease Association

Disease	% HLA-B*27 Positive
Ankylosing spondylitis	88%–96%[8,9]
Acute anterior uveitis	40%–70%[6,9]
Reactive arthritis (Reiter's syndrome)	40%–80%[10]
Aortic regurgitation (with cardiac conduction abnormality)	67%–88%[7,9]
Inflammatory bowel disease (with sacroiliitis)	33%–75%[9]
Psoriatic arthritis (with sacroiliitis)	40%–50%[7,9]
Undifferentiated sponyloarthropathies	70%[7]

https://www.labcorp.com/tests/related-documents/L1187

Lab testing for syphilis

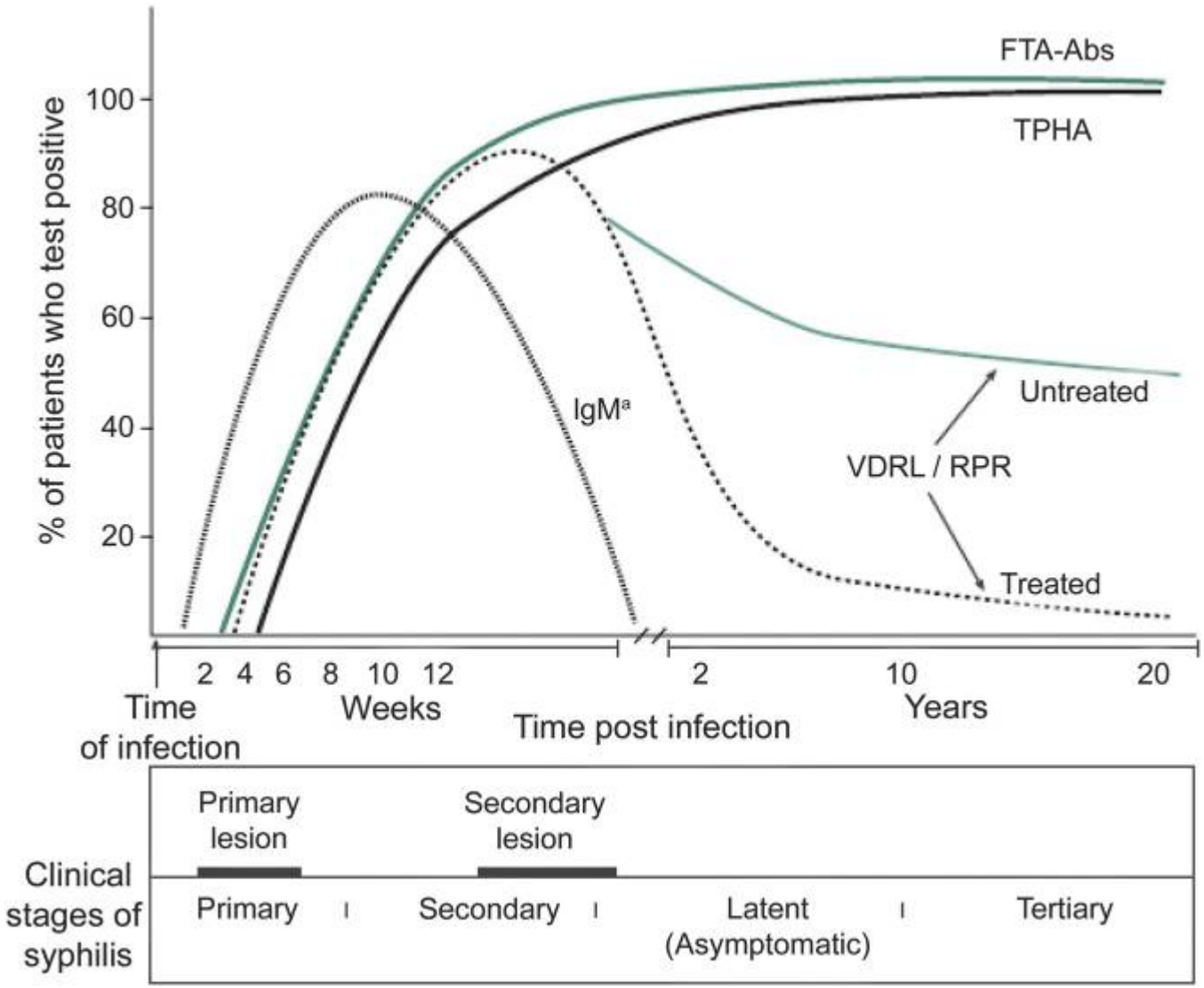
Non-treponemal tests:

- Rapid plasma regain (RPR)
- Venereal disease research lab (VDRL)
  - Tests for antibodies to *Treponema pallidum*
  - Reflection of disease activity and response to therapy
  - (+) in primary and secondary; (-) in tertiary or latent and after treatment
  - RPR easier to run and cheaper
  - False positives can be seen in viral infections, lymphoma, TB, CT disease, pregnancy, autoimmune diseases

Lab testing for syphilis

Treponemal tests:

- Fluorescent treponemal antibody absorption test (FTA-ABS)
  - Detects presence of the bacteria; regardless of stage (unless very early, first few weeks) or if pt has been successfully treated
  - Less sensitive in HIV+ patients
- Other treponemal tests:
  - Microhemagglutination-Treponema pallidum (MHA-TP)
  - Treponema pallidum particle agglutination assay (TP-PA)
  - Treponema pallidum hemaglutination assay (TPHA)



Henao-Martínez AF. Neurol Clin Pract. 2014

Imaging

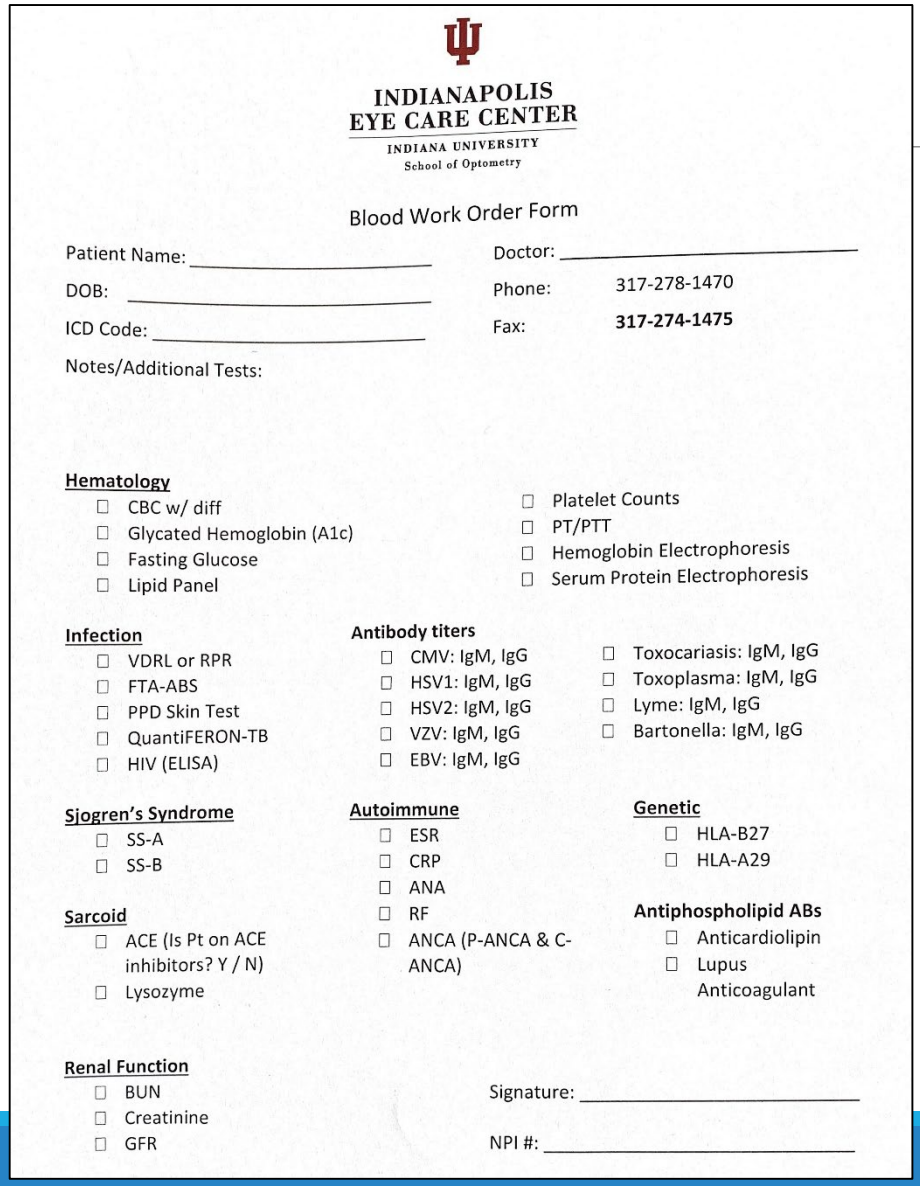
Granulomatous

- Chest X-ray -> rule out sarcoid, TB
- May need chest CT

Non-Granulomatous, +HLA-B27

- X-ray of the sacroiliac (SI) joints is useful for ankylosing spondylitis
  - Causes chronic inflammation of the spine and SI joints
- MRI can pick up earlier involvement if high suspicion with clear X-ray

Design your own lab orders. It makes life easier.



INDIANAPOLIS EYE CARE CENTER
INDIANA UNIVERSITY
School of Optometry

Blood Work Order Form

Patient Name: _____ Doctor: _____

DOB: _____ Phone: 317-278-1470

ICD Code: _____ Fax: **317-274-1475**

Notes/Additional Tests:

Hematology
- ☐ CBC w/ diff
- ☐ Glycated Hemoglobin (A1c)
- ☐ Fasting Glucose
- ☐ Lipid Panel
- ☐ Platelet Counts
- ☐ PT/PTT
- ☐ Hemoglobin Electrophoresis
- ☐ Serum Protein Electrophoresis

Infection
- ☐ VDRL or RPR
- ☐ FTA-ABS
- ☐ PPD Skin Test
- ☐ QuantiFERON-TB
- ☐ HIV (ELISA)

Antibody titers
- ☐ CMV: IgM, IgG
- ☐ HSV1: IgM, IgG
- ☐ HSV2: IgM, IgG
- ☐ VZV: IgM, IgG
- ☐ EBV: IgM, IgG
- ☐ Toxocariasis: IgM, IgG
- ☐ Toxoplasma: IgM, IgG
- ☐ Lyme: IgM, IgG
- ☐ Bartonella: IgM, IgG

Sjogren's Syndrome
- ☐ SS-A
- ☐ SS-B

Autoimmune
- ☐ ESR
- ☐ CRP
- ☐ ANA
- ☐ RF
- ☐ ANCA (P-ANCA & C-ANCA)

Genetic
- ☐ HLA-B27
- ☐ HLA-A29

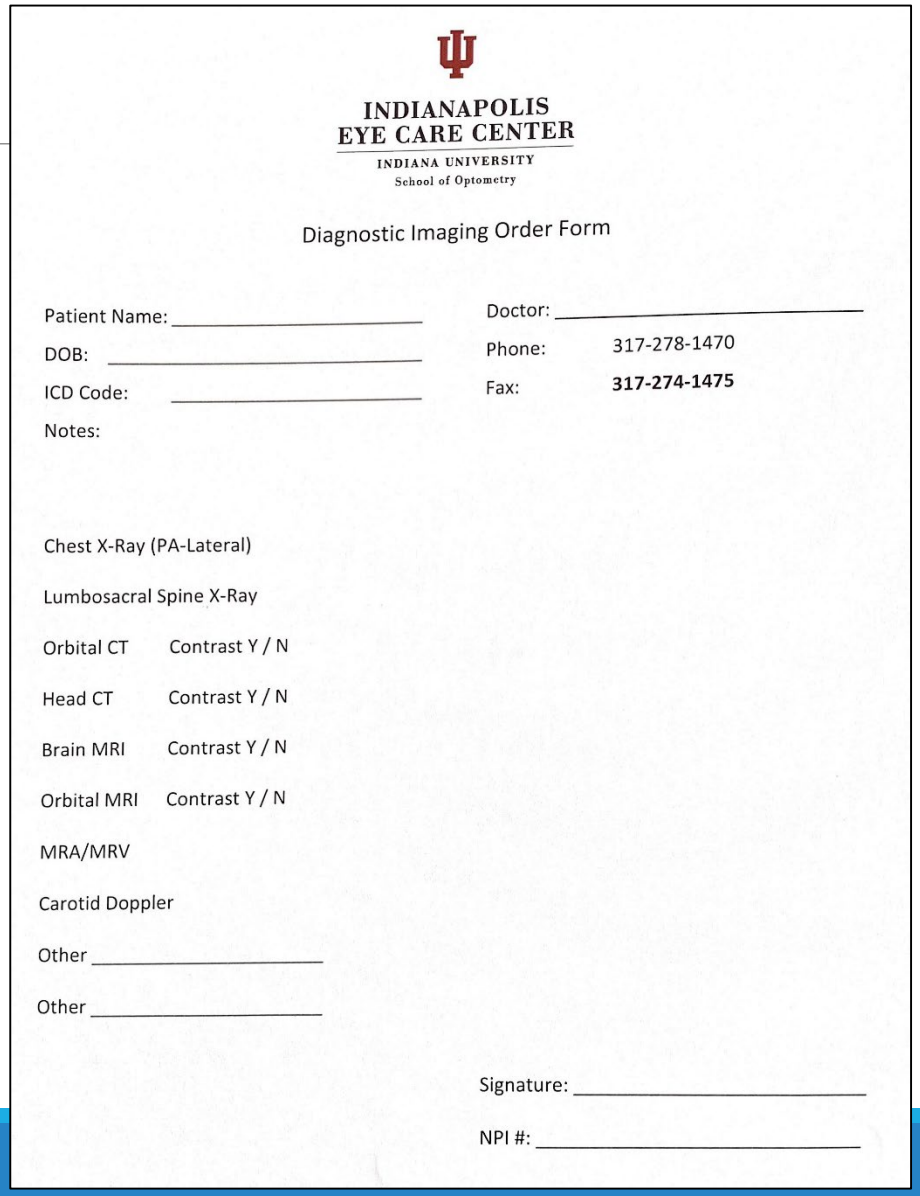
Sarcoid
- ☐ ACE (Is Pt on ACE inhibitors? Y / N)
- ☐ Lysozyme

Antiphospholipid ABs
- ☐ Anticardiolipin
- ☐ Lupus Anticoagulant

Renal Function
- ☐ BUN
- ☐ Creatinine
- ☐ GFR

Signature: _____

NPI #: _____



INDIANAPOLIS EYE CARE CENTER
INDIANA UNIVERSITY
School of Optometry

Diagnostic Imaging Order Form

Patient Name: _____ Doctor: _____

DOB: _____ Phone: 317-278-1470

ICD Code: _____ Fax: **317-274-1475**

Notes:

Chest X-Ray (PA-Lateral)

Lumbosacral Spine X-Ray

Orbital CT Contrast Y / N

Head CT Contrast Y / N

Brain MRI Contrast Y / N

Orbital MRI Contrast Y / N

MRA/MRV

Carotid Doppler

Other _____

Other _____

Signature: _____

NPI #: _____

Case example

48 year old AA female

CC: presents for urgent care with blurred vision R eye x 2 weeks, mild redness, mild discomfort, seen at immediate care 3 days ago given moxifloxacin drops with no improvement

Medical Hx: seizure disorder (controlled on keppra)

Ocular Hx: none

ROS: **+cough x 2 months**

Exam Findings

BCVA: **20/30- NIPH OD**, 20/20 OS

Pupils: irregular, fixed OD; reactive OS

Slit lamp:

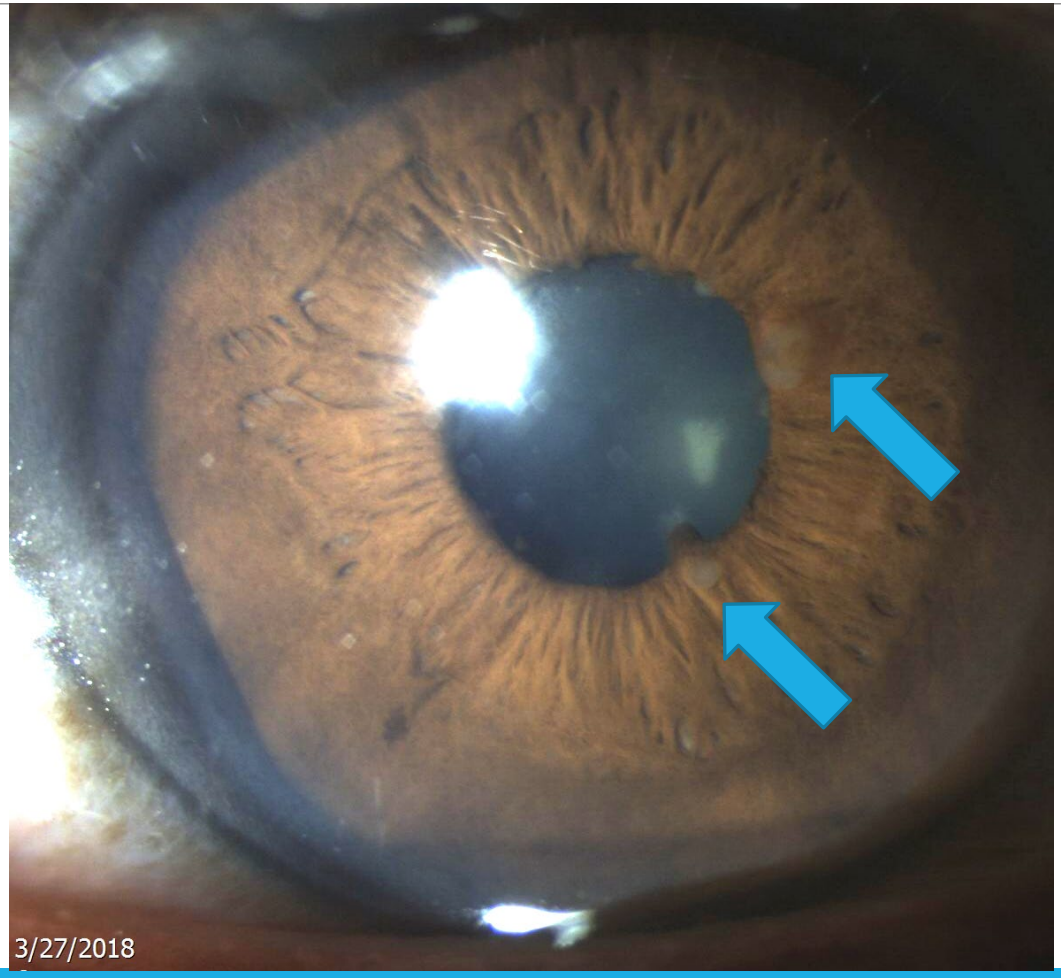
- Lids/lashes: clear OU
- Conj: **2+ diffuse injection OD,** clear OS
- Cornea: **fine, diffuse KPs**, clear OS
- Iris: **synechiae, nodules OD**, clear and flat OS
- A/C: **deep with 2+ cell, 2+ flare OD,** clear OS

Goldmann IOP: 20/19

Dilation (1% tropicamide, 5% homatropine):

- Vitreous: **1+ cell OD**, Cl OS
- Retina: normal, (-)snowbanking

Koeppe nodules



A/P

Assessment: acute mostly anterior, **granulomatous** uveitis OS
ROS: +cough

Plan: start pred forte 1% q1h OS, cyclopentolate 1% BID OS
D/C moxifloxacin
Order labs: CBC, ESR, ACE, PPD, ANA, FTA-ABS, HLA-B27,
chest X-ray

Follow up course

Lab results: elevated ACE, ESR

Chest X-ray: suspicion for **sarcoid**, confirmed on chest CT

Started on oral steroids for sarcoid

OD uveitis responded well to topical steroids, synechiae broke with cycloplegic

Tips to successful uveitis management:

1) Get a thorough review of systems
2) Know when and what labs to order
3) **Dilate!**

Why Dilate?

Dilation is essential to diagnose posterior uveitis and CME

Opportunity to instill cycloplegic -> make the patient feel a little better

Posterior Uveitis

INFECTIOUS

Toxoplasmosis

Toxocariasis

Tuberculosis

Syphilis

Bartonella

Viral (HSV, VZV, CMV)

NON-INFECTIOUS

Sarcoid

White dot syndromes (APMPPE, MEWDS, MFC etc)

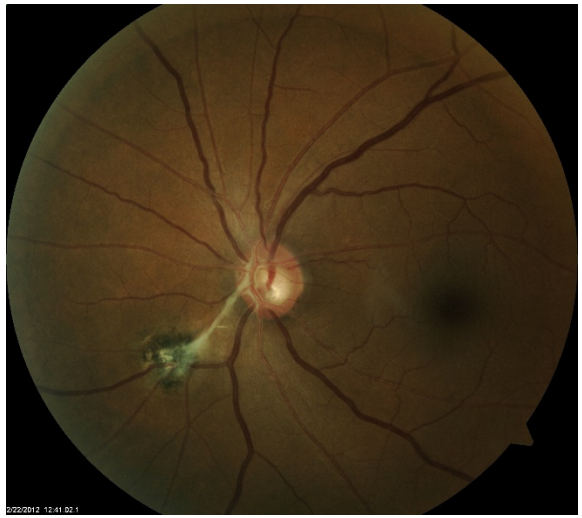
Diffuse unilateral subacute neuroretinitis (DUSN)

Retinal pigment epithelitis (Krill's disease)

Infectious Posterior Uveitis

Parasitic

- Toxoplasmosis
  - Most common cause of posterior uveitis
  - Usually diagnosed by clinical picture (“headlight in fog”) rather than lab testing
  - Tx: Bactrim + oral steroids
- Toxocariasis
  - Parasitic disease from dog/cat roundworm
  - Central or peripheral granuloma with overlying vitritis
  - Cause of leukocoria in children
- DUSN (diffuse unilateral subacute neuroretinitis)
  - nematode infiltrates subretinal space

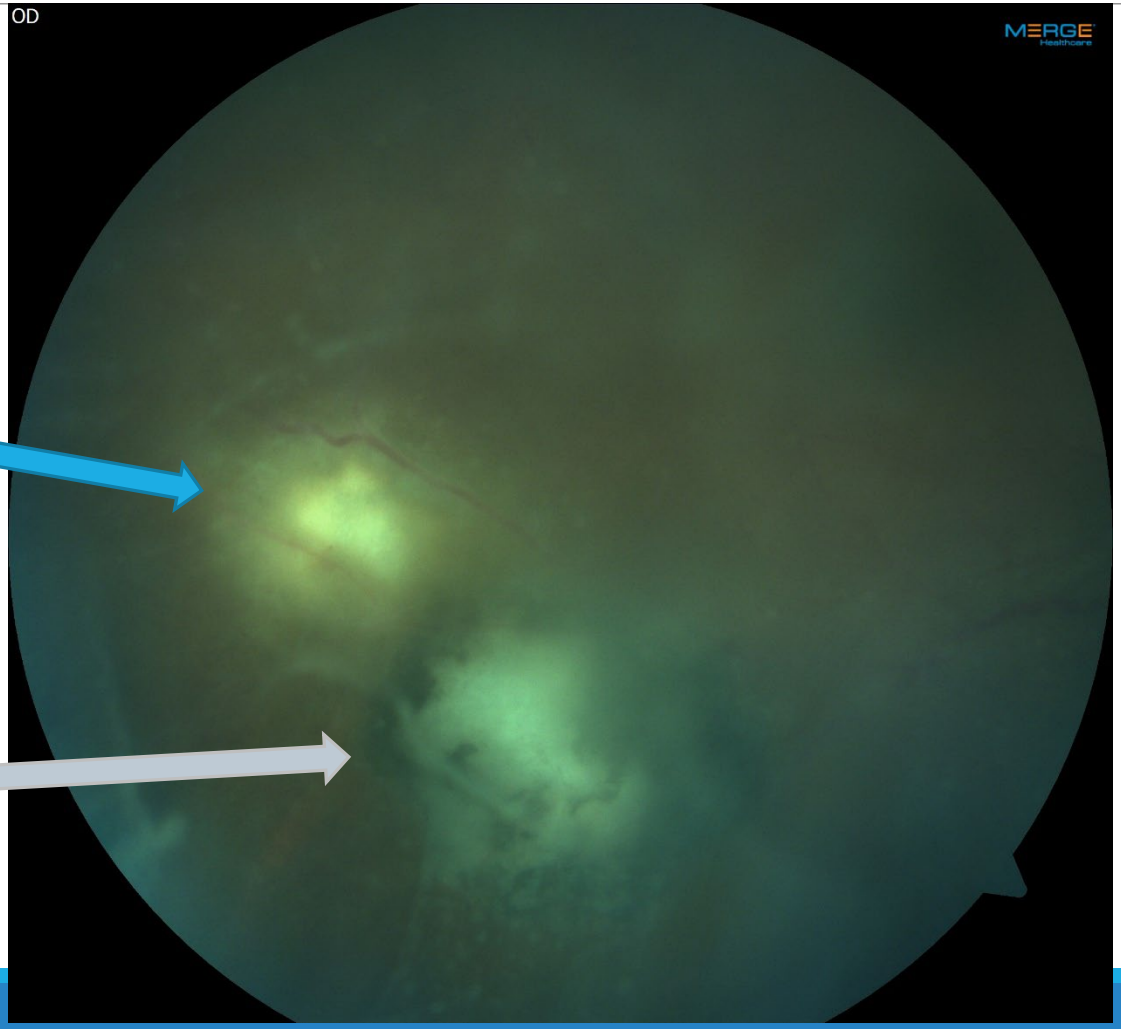


Inactive toxocariasis

Active Toxoplasmosis

Chorioretinitis with overlying vitritis "headlight in fog"

Often located near inactive scar



Infectious Uveitis

Bacterial

- Cat scratch disease
  - *Bartonella henselae*
  - Transmitted by scratch, lick or bite from infected cat (usually kitten)
  - **Neuroretinitis** (optic nerve edema + macular star) +/- ant chamber rxn, vitritis
- Syphilis
  - *Treponema pallidum,* spirochete
  - anterior or posterior uveitis, optic nerve involvement highly suggestive for neurosyphilis
- Tuberculosis
  - *Mycobacterium tuberculosis*
  - Characterized by caseating granulomas
  - Optic nerve can be involved in ocular TB
- Lyme disease
  - *Borrelia burgdorferi*, spirochete
  - Optic neuritis, neuroretinitis can occur in the early and disseminated stages
    - Regarded as CNS involvement; IV antibiotic therapy

Infectious Uveitis

Viral

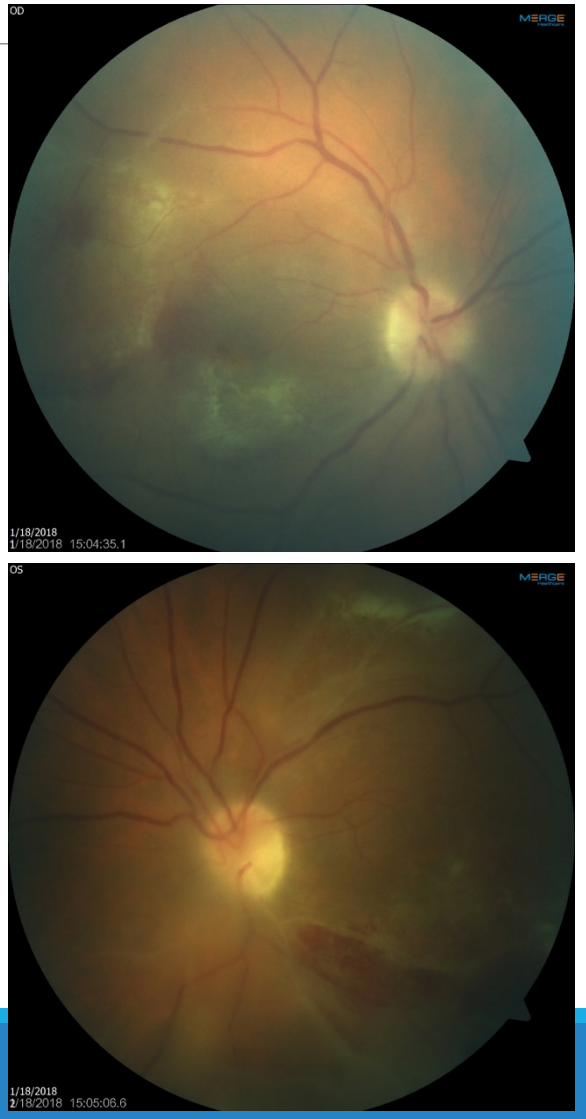
- Herpes family (HSV, VZV, CMV)
- Anterior uveitis:
  - Viral associated with elevated IOP (from trabeculitis) and iris atrophy; +/- corneal findings
  - KPs can have non-granulomatous or granulomatous appearance
  - Recurs in same eye

Clinical Pearl: Viral uveitis can be tricky to recognize. Clinical suspicion should be high for viral if elevated IOP at onset of sxs and/or presence of iris atrophy (sectoral or diffuse).

Infectious Uveitis

Viral

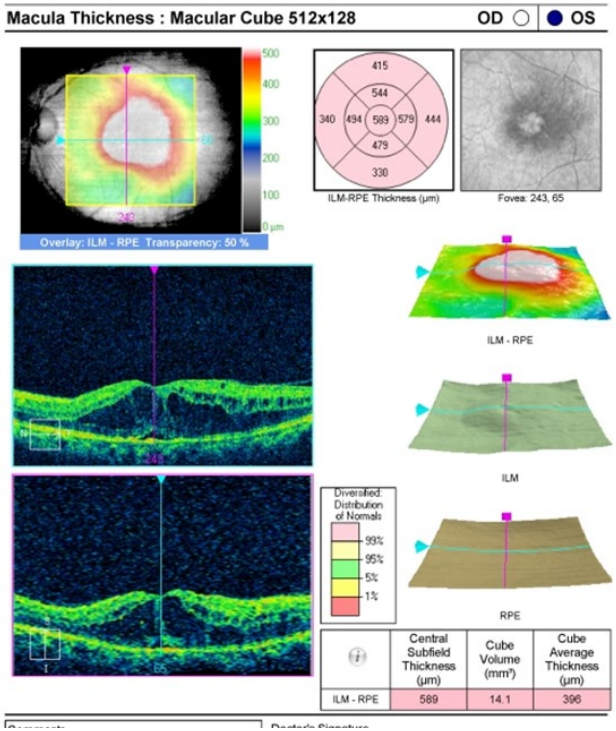
- Posterior - rare
  - Immunocompromised patients
    - CMV retinitis – less common now with modern HIV treatment
    - Progressive outer retinal necrosis (PORN)
      - VZV > HSV
  - Immunocompetent
    - Acute retinal necrosis (ARN)



PORN: AC tap positive for VZV

CME

- Common cause of decreased vision and vision loss in uveitis
- More likely to occur with intermediate or posterior inflammation
- Assoc with formation of ERM
- Can be difficult to tx as it may persist even though inflammation is controlled
- Tx options:
  - Corticosteroids
    - Topical, oral, injection, implants
  - NSAIDs
  - Oral CAI
  - Anti-VEGF (if inflammation is otherwise controlled)
  - ERM peel (if contributing factor)



Benefit of cycloplegia

- Break/prevent synechiae
- Reduce patient discomfort
- Stabilize blood-aqueous barrier
  - Reduces cell and flare

Options:

Atropine (most potent): 0.5, 1, 2%

Scopolamine : 0.25% ⟵

Homatropine: 2, 5% ⟵

Often limited supply in pharmacy

Cyclopentolate: 0.5, 1, 2%

Tips to successful uveitis management:

1) Get a thorough review of systems
2) Know when and what labs to order
3) Dilate!
4) **Don’t fear the steroids**

Steroids in Anterior Uveitis

Hit hard with steroids from the start.

Minimum initial dosage: q2h while awake (pred acetate)

Don’t taper until AC clear or significantly improved!! Then taper slow, some over weeks-months.

Failure to respond to topical therapy alone may indicate need for oral steroids or immunosupressants

Steroids in Uveitis

PredForte (prednisolone acetate) 1%

- Suspension
- Generic often works just as well as brand

Durezol (difluprednate) 0.05%

- Emulsion – does not need to be shaken
- Stronger than PF – can be dosed half as often as PF
- Cons: causes steroid response (more often than pred), cost

Overnight coverage if needed:

- FML ung
- Lotemax ung

Injectables

Triamcinolone acetonide injectable suspensions:

- Kenalog - periocular
- Triesence

Sustained drug delivery options:

intravitreal implants approved to treat chronic non-infectious post uveitis, dissolve over months

- Ozurdex – 0.7 mg dexamethasone
- Retisert - 0.59 mg fluocinolone acetonide
- Yutiq - 0.18 mg fluocinolone acetonide - effect lasts 30-36 months

Risks: glaucoma (many requiring glaucoma surgery); inevitable cataract development

Tips to successful uveitis management:

1) Get a thorough review of systems
2) Know when and what labs to order
3) Dilate!
4) Don’t fear the steroids
5) **But watch the IOP**

IOP in Uveitis

Mechanisms for glaucoma development:

- Acute blockage of the TM with cellular uveitic debris
- Steroid response
  - Causes outflow resistance in the TM
  - Usually occurs 2-4 weeks into tx
- Chronic damage to the TM from uveitis
  - Peripheral anterior synechiae formation -> secondary angle closure
  - Posterior synechiae -> iris bombe -> secondary angle closure

Can be multifactorial.

Uveitic Glaucoma

Treatment for elevated IOP:

- Treat the inflammation
- First choice to lower IOP: β-blocker, CAI, α-agonist (or combo)
- Avoid prostaglandins if possible
- Start steroid taper if uveitis controlled
- Some may go on to need glaucoma surgery, particularly in chronic cases

*10-20% of uveitis develops glaucoma

Tips to successful uveitis management:

1) Get a thorough review of systems
2) Know when and what labs to order
3) Dilate!
4) Don’t fear the steroids
5) But watch the IOP
6) **Consider atypical causes**

Other uveitis…

Posner-Schlossman Syndrome (PSS) – mild uveitis with elevated IOP

- IOP is often > 40 mmHg and out of proportion to the degree of ocular inflammation, does not cause synechiae
- Presumably trabeculitis with spillover to ant chamber
- Evidence now supports links to CMV>HSV, VZV
  - Tx: oral antiviral + topical steroid

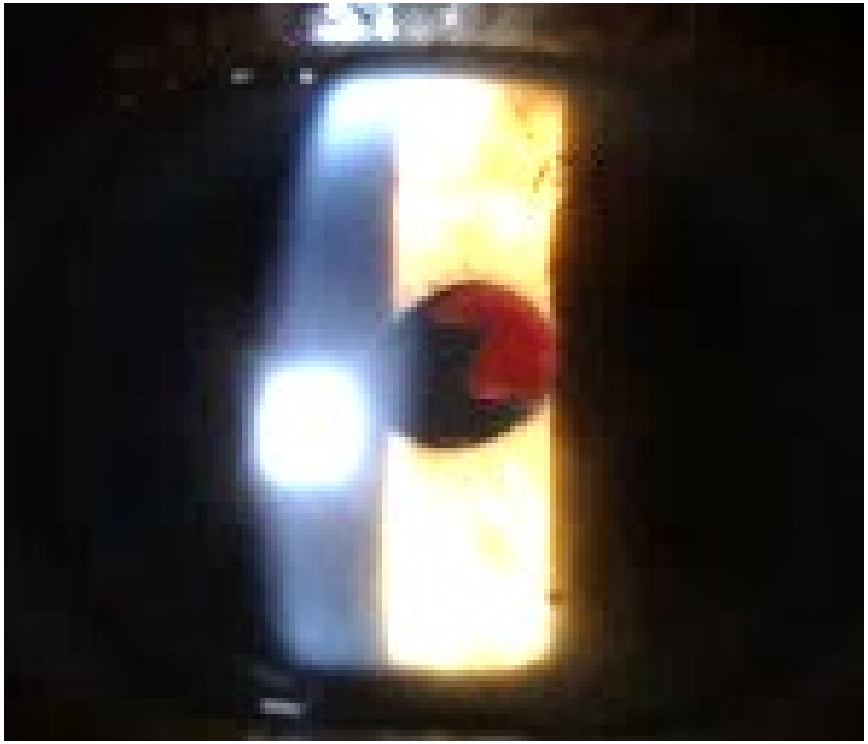
Fuch's heterochromic uveitis – chronic, mild uveitis in minimally symptomatic or asymptomatic pts

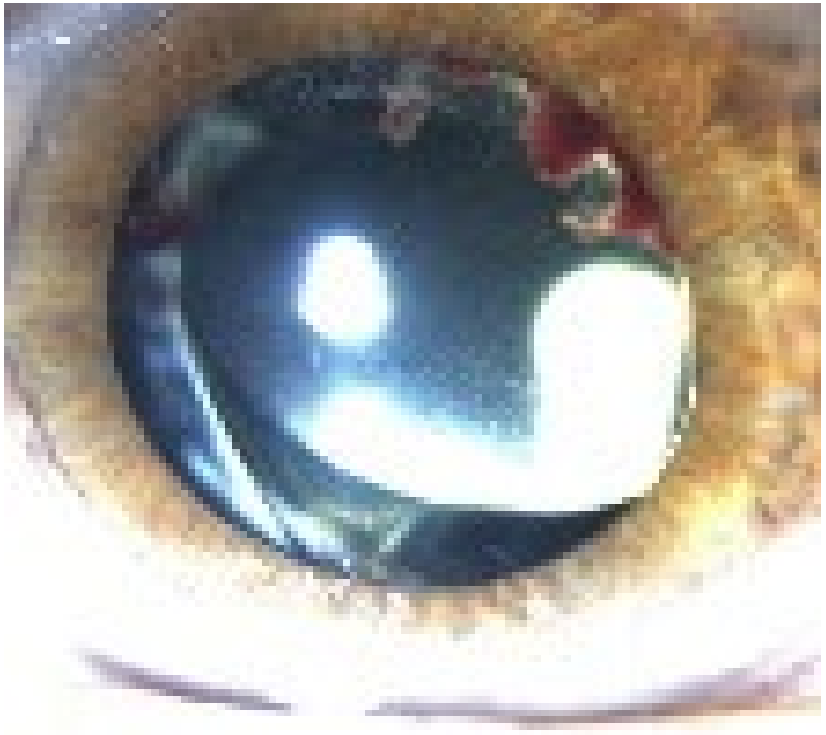
- Diffuse stellate KPs
- May result in heterochromia (lighter iris in the involved eye)
- Linked to rubella

UGH syndrome (triad of uveitis, glaucoma and hyphema)

- Caused by a malpositioned PC IOL
- Can occurs months – years after surgery

UGH Syndrome





Images courtesy of Dr. Larissa Krenk

Case example

82 year old AA female

CC: +intermittent pain and redness OD

Medical Hx: DM, HTN, depression, low thyroid

Ocular Hx: poor vision from a CRVO about 8 years ago OD, POAG OU, cataract surgery OS

Meds: Clonazepam, Sertaline, Levothyroxine, Clopidogrel, Amlodipine, Crestor, Novolin

Ocular Meds: Travatan Z OS, Combigan OD

Exam findings

BCVA: LP OD, 20/20 OS

Pupils: Fixed-non reactive pupil OD, reactive OS

Slit lamp:

- Lids/lashes: clear OU
- Conj: **2+ diffuse injection OD,** clear OS
- Cornea: **diffuse pigmented KPs OD**, clear OS
- Iris: **synechiae OD,** clear OS
- A/C: Deep chamber with **3+ cell, 2+ flare OD**, clear OS

Goldmann IOP: 14/14

Gonio: open to SS 360 OU

Exam findings

Dilation:

- Lens**: 4+ NS/3+ PSC/2+ cortical OD**, PC IOL OS
- No view beyond lens OD; fundus normal OS

B-scan: retina intact OD

Assessment

82 year old female with chronic, anterior uveitis with posterior synechiae OD

ROS: (-) ulcers, cough, joint pain, rashes

Age atypical for onset of autoimmune related uveitis ⇦

Autoimmune disease is typically diagnosed in young-middle age

Diagnosis: phacolytic uveitis due to hypermature cataract

Treatment: patient was managed short-term with topical steroids and cycloplegic until cataract surgery was arranged

Other Uveitis…. Phacolytic

Phacolytic Cataract – hypermature cataract that is leaking protein material

Phacolytic or Lens Induced Uveitis - an immunologic response to the leaking protein

- Pathogenesis is still poorly understood
  - A clear lens leaks small amounts of protein

Phacolytic Glaucoma - proteins and inflammatory mediators can also clog up the trabecular meshwork, causing elevated IOP and glaucoma

Treatment – decrease inflammation and IOP if needed and then proceed to cataract surgery

The End

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