Everything you ever wanted to know about posterior segment inflammation: A clinically relevant review
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• Mohammad Rafieetary, OD, FAAO
  – Disclosures
    • Alcon/Novartis
    • Angiogenesis Foundation
    • Genentech
    • Heidelberg Engineering
    • Notal Vision
    • Optos
    • Regeneron
    • RegenXBio

Post Surgical
• Pseudophakic CME
  – Irvine-Gass
  – Incidence 4-11% as high as 41%
  – Upregulation of inflammatory mediators in aqueous and vitreous

Posterior Inflammatory Response
(Offending Agent vs Self-inflicted)

Common Optometric Referral
The Process of Assessing a Diagnosis

- 17 Y/O AfAm F referred for CSR one day after her visit with the referring doctor
- C/O Pain and sudden onset vision loss OU
- No Prior Health (medical or ocular) Conditions
- Her sister is insulin resistance no other family HX
- Vas OD: 20/50 OS: 20/70 IOP 13, 14

Typical Variations of CSR Findings

Faxed Correspondence of the 17 Y/O

Findings of The 17 Y/O

? (s) to ask yourself
Is this CSR?
If Y why?
If N
What is it?

Not Every man with a mustache is my uncle
If SRD is a CSR finding
Not every SRD is CSR

Argument: Have to call it something!

- CSR, ICSC, CSC specific entity

Posterior Uveitis Disease medical Work-up

- CBC-Diff, ESR, CRP
- Syphilis (always)
- Viral serology (herpes, CMV, HIV)
- HLA(s)
- ANA, ACE
- PPD, Quantiferon-tb
- Lyme
- Bartonella Henselae
- RA
- Chest X-ray or CT

The Dilemma of the “naming the condition” Funny Looking Retina

Posterior Inflammatory Disease

- Retina
  - Retinitis
    - Infectious
      - Toxoplasmosis (most common)
      - Cytomegalovirus
      - Acute Retinal Necrosis (ARN)
    - Inflammatory
      - Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE)
Nature vs Man

“vaccines and antibiotics have made many infectious disease the thing of the past. We’ve come to expect that public health and modern science can conquer all microbes. But nature is a formidable adversary”

– Tom Frieden an American Infectious Disease and Public Health Expert.

Long Standing Problem

Toxoplasma gondii

• Intracellular protozoan parasite
• Common infection in human (Bilions worldwide)
• Risk Factors
  – Feline definitive host
  • Un- or undercooked meat (Pork)
  • Soiled vegetables
  • Direct exposure (hand to mouth)
• Clinical Findings

Infectious Retinitis

• Toxoplasmosis a Retinochoroiditis
• Focal retinitis (retinal whitening) overlying vitritis “headlight in the fog”
  • Satellite pigmented lesions
  • Secondary nongranulomatous iridocyclitis
  • Elevated IOP
  • Retinal vasculitis and arterial occlusion
  • Papillitis, Retrobulbar ON, Neuroretinitis
53 Y/O WF is referred for ONH Swelling OD

Recurrent several years later

Neuroretinitis

- Focal inflammation of the optic nerve and peripapillary retina and/or macula (Neuronal Retina)
- Etiology
  - Infectious
  - Idiopathic
- Risk Factors
  - Exposure to offending organism
  - Immunosuppression (HIV)

Toxoplasmosis

Severe Vasculitis
Kyrieleis plaques

Diagnostic Findings

Prognosis

Congenital Toxo
Pathophysiology

- Inflammation of the optic disc vasculature with leakage of fluid into the peripapillary retina
- The exact origin of the inflammation of the optic disc vasculature is unclear
  - A flu-like prodrome in some patients supports a possible viral etiology
  - An autoimmune response or direct invasion of the nerve.

Pathophysiology

- “Aqueous phase” pass through external limiting membrane and accumulates in subretinal space (Blue Arrow)
- Exudate penetrate into the outer plexiform layer, creating the macular star pattern (Yellow Arrow)

First Case - Follow Up (1 Mo)

- Sero Negative

Neuroretinitis (Bartonella)

Case 2 - Two months and final follow-up

- Prognosis: OA
- Partial star exudates
- Resolved SRF
None of us are immune from these conditions!

CMV

Acute Retinal Necrosis

ARN
Vasculitis
16 Y/O
Blurred Vision
Systemic work-up
no associated etiology.

Five years later, Still no etiology for this vasculitis.

Seeing Black Spots

Pigmenteed paravenous retinochoroidal atrophy (PPRCA)

Infectious Etiology

• Ocular Histoplasmosis
  – A chorioretinitis

Uvea-Uveitis

– Infectious or Inflammatory Disease

Infectious or Inflammatory Disease

OHS
OHS (Late)

Post Uveitis (Syphilis)

Ophthalmomyiasis (Similar Findings as DUSN)

Reactive RPR and FTA-ABS

Toxocara Canis

48 YO professional recent migrant from India referred for RD

Loss of central vision for 1 week
Only known medical history high cholesterol. No constitutional symptoms
Has not seen any healthcare providers since his move to the US
OD 20/20 OS 20/100 IOP 16/14
What are these skin lesions?

TB

- BCG (Bacille Calmeete-Gurein)
- CXR and PPD
- QuantiFERON-TB (QTF)
  - An interferon-gamma release assay
  - More sensitive than TST
  - Unaffected by BCG
- This patient was positive QTF DX Choroidal Tuberculoma
- Treatment for TB (best by ID, and Health Dep)
  - Isoniazad, Rifampin, Pyrazinimide, Ethambutol (long course)

Inflammatory and Autoimmune Etiology

Faces of Inflammatory Auto-Immune Disease

61 Y/O WF, +SLE on 400 mg hydroxychloroquine
Plaquenil Toxicity

Joseph P. Shovlin, OD, FAAO

Hydroxychloroquine

Sarcoidosis
1. prodromal: fever, meningismus, tinnitus, dysacusis
2. uveitic: bilateral granulomatous uveitis with vitritis, serous RD (2-6 weeks)
3. T-cell mediated AI reaction against antigens against melanocytes
4. chronic recurrent: glaucoma, CNV, recurrent inflammation

Harada disease: isolated posterior segment findings
3/3/2019

Neoplastic and Paraneoplastic Masquerades

- Cancer Associated Retinopathy
- Case here Primary Intraocular Lymphoma

White Dot Syndromes

Bilateral Diffuse Uveal Melanocytic Proliferation (BDUMP)

Lesions of (FAP) Gardner’s
White Dot Syndromes

- Group of Conditions
  - Noninfectious-Inflammatory Chorioretinopathies
  - Not Common
    - Cases reported here mostly OD referrals
    - Different references list different conditions in this group

White Dot Syndromes (WDS)

- Common Features
  - Affect Younger Patients
  - Extensively Studied for Etiology = Unknown
  - Most have no standard treatment
  - Most have good or reasonable prognosis

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Duration</th>
<th>Etiology</th>
<th>Treatment</th>
<th>Recurrence</th>
<th>CNV</th>
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<tbody>
<tr>
<td>AMPPE</td>
<td>2-6 wks</td>
<td>Unknown</td>
<td>None</td>
<td>Good (&gt;20/40)</td>
<td>Very Rare</td>
</tr>
<tr>
<td>MEWDS</td>
<td>2-6 wks</td>
<td>Unknown</td>
<td>None</td>
<td>Good (20/40)</td>
<td>Rare</td>
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<tr>
<td>Birdshot</td>
<td>Chronic</td>
<td>Unknown</td>
<td>Steroid</td>
<td>Poor</td>
<td>Common</td>
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<tr>
<td>SFU</td>
<td>Chronic</td>
<td>Unknown</td>
<td>Steroid</td>
<td>Poor</td>
<td>Common</td>
</tr>
<tr>
<td>PIC</td>
<td>Chronic</td>
<td>Unknown</td>
<td>Steroid</td>
<td>Poor</td>
<td>Common</td>
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<tr>
<td>SFU              &amp; Panuveitis</td>
<td>Chronic</td>
<td>Unknown</td>
<td>Guarded-Poor</td>
<td>Chronic</td>
<td>Possible</td>
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<tr>
<td>AMN</td>
<td>&gt;6 wks</td>
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<td>None, +</td>
<td>Good, +</td>
<td>+ Scotoma</td>
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<tr>
<td>UAIM</td>
<td>4-6 wks</td>
<td>Unknown</td>
<td>None</td>
<td>Good</td>
<td>Not Reported</td>
</tr>
<tr>
<td>AZOOR</td>
<td>Chronic</td>
<td>Unknown</td>
<td>Steroid</td>
<td>Poor</td>
<td>Not Reported</td>
</tr>
</tbody>
</table>

White Dot Syndrome

- Multiple evanescent white dot syndrome (MEWDS)
- Punctate inner chorioiditis (PIC)
- Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)
- Birdshot chorioretinopathy
- Acute zonal occult outer retinopathy (AZOOR)
- Serpiginous choriditis
- Multifocal choriditis and panuveitis (MCP)

WDS

- Subretinal Fibrosis and Uveitis (SFU)
- Acute Macular Neuroretinopathy (AMN)
- Unilateral Acute Idiopathic Maculopathy (UAIM)
Acute Macular Neuroretinopathy

- Rare Unknown Etiology (first reports in 1970s)
  - Vascular, Hormonal (BCP), excessive caffeine
- Most common young to middle-age F
- Acute onset one or more paracentral scotomas one or both eyes
- No treatment

Multiple evanescent white dot syndrome (MEWDS)

- **Demographic** (first report 1984, Jampol)
  - Healthy age 15-50
  - Women 4X more than Men
  - Viral Prodrome
- **Symptoms**
  - Acute Unilateral Painless Vision Loss (rare bilateral)
  - Photopsias
  - Dyschromatopsia
  - Temporal or Paracentral scotoma

**Fundus**

- Flat, Multifocal, grey-white lesions (100-200 µm)

23 Y/O WF- Recent history of sinus infection otherwise healthy. C/O Flashes on temporal side X1 week Blind Spot on temporal side X 2days VA OD: 20/20 (+0.25+ 0.25X20) OS: 20/25 (+0.75+0.25X5) IOP OD: 12, OS: 8

MEWDS

- Lesions at the level of RPE
- Mild Posterior vitritis
C/O "seeing a flash of light temporal quadrant last week, then seeing multiple floaters, now seeing a stream of floaters and slow flashes in the shape of a "C". Noted vision is becoming more blurred."

42 Y/O WF

20/20 OD/OS (SC)

FA

MEWDS

- Treatment
  - Self Limiting (2-10 weeks)
  - Flashes may last several months
  - 10% Recurrence
  - Prognosis usually good

Since last visit, severe headache lasting two days. No longer sees floaters 1 week, flashes continues.
23 Y/O WF (Dad had bilateral RD)
Recent onset flashes (temporarily) OD
Referred for a "macular cyst"
20/20 OD/OS, IOP 11 and 13

Started prednisone PO 10 mg (4 daily) with OTC ranitidine (H2 antagonist)
RTC 10 days
Taper off pred

37 Y/O WF
Not as extensive clinically vs ICG
Macula Involved TX!
6 months
Punctate inner choroiditis (PIC)

[Recognized as a distinct entity by Watzke in 1984]

- **Demographics**
  - 90% Female (Myopic) Usually Healthy
  - Ages 16-40 (mean 27)
  - Bilateral
    - No AC or Vitreous Cells (difficult DDX w POHS)

- **Symptoms**
  - Blurred vision, Photopsia
  - Partial scotomas. Typically central (at times peripheral). Temporary or Permanent

**Management**
- Observation if Lesions Non-Vision Threatening
- Systemic Steroids
- Regional Steroid Therapy
- Treatment of CNV
  - OD: Dexamethasone intravitreal implant (OZURDEX®)
  - Medical Work-Up

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Risks

- Not Same Patient

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**PIC**

32 Y/O WF. C/O Photopsia OU X4 days. “Dark spotty cloud @ 2:00 OD” changes in intensity.

OD: 20/20 (-7.75) OS: 20/20 (-6.25). IOP 13/12

FA

ICG
44 Y/O WF
Multiple dark spots OD x 1 week
20/80 and 20/20

FA
Ozurdex OD

She was stable for 10 months
To avoid IOP
IVA RTC 1 month

10 months from initial episode VA 20/70 OD

37 Y/O WF Blurred vision OS X2days. 20/20, 20/30 IOP 13 OU

8 months from initial visit VA OS 20/30

No further episodes

PIC-CNVM
Chronic PIC

Recurrent symptoms 3 yrs later no symptoms, txed

PIC-DDX and MisDX

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)

- Demography
  - Patient age 15-40 usually female
  - Usually Bilateral
  - Visual symptoms usually preceded by flu-like symptoms (fever, cough, soar throat, headache)
  - Skin lesions (erythema nodosum, livedo reticularis)

- Symptoms
  - Sudden Onset Vision Loss
  - Photopsia, Scotomas

- New cases need systemic work up to R/O CNS vasculitis
APMPPE (OS)

APMPPE (OD)

APMPPE

Management:
Self-limiting
Cases with lesions
near ONH and/or
Foveal area systemic
steroids
This case: Prednisone
60mg qd

16 Y/O WF C/O "curtain effect nasal field of each eye" X10 days
HX of Migraine HAs
OD: 20/20, OS: 20/20 (SC) (wt: 150 lbs)
APMPPE

• Prognosis
  – Vision: Most cases good
  – Occasional Co-existing Vasculitis with Neurologic Complications
    • Headache
  • Rare Recurrence
  • Rare CNV

Overlapping WDS

34 Y/O WF Good Health, Daily Smoker C/O Sudden onset flashes, X1 week, OS Dark spots in vision and decreased vision.
VA OD 20/20 OS 20/50
Placoid
Punctate

Challenges
OHS?
PIC?
MEWDS?
APMPPE?

51 Y/O AfAM F Dxed with OHS in the past. Sudden Onset Vision loss OS OD 20/20 OS 20/25
IVA
Uveitis Work-up

Patient returns 5 years later
OS 20/400

Due to previous reoccurrence IVA- FLU 2 MO later (7th MO from first visit) 20/50 IVA

Birdshot Chorioretinopathy

• Birdshot Uveitis or HLA-29 Uveitis
• Demography
  – Caucasian 4th to 6th decade
  – Bilateral progressive posterior uveitis
  – Rare (2% of all uveitis cases)
  – Strong HLA-A29 association (HLA-A29 also present in 7% of normal population)
• Symptoms
  – Blurred vision
  – Floaters
  – Photopsia
  – Nyctalopia

Birdshot

48 Y/O WM Peripheral visual disturbance (spots) 2-3 weeks. Central floaters few days.
VA 20/25 OD/OS. IOP 13/12
Buspirone 10 mg (anxiety), citalopram 20 mg (depression). Ventolin Valcyclovir (preventive infected partner)
Birdshot
- He has had visual symptoms for few years have been dismissed by eyedocs, PVD, getting older etc!

- Dx made based on this and clinical finding
- Pt Received second opinion from uveitis specialist.
  - Cellcept and cyclosporine

One year later
VA 20/20
Mild
Posterior Uveitis and Vasculitis

Birdshot-Poorly TX
Acute zonal occult outer retinopathy (AZOOR)

- Demography
  - Idiopathic
  - Usually Young Otherwise Healthy Female
  - One or Both Eye

- Symptoms
  - Photopisa
  - Acute Progressive Field Defect
    - Typically begins as enlargement of blind spot

Misleading Nomenclature “Occult”

- Early Phase Maybe Difficult to See Clinically

28 Y/O WF Healthy “Blind Spot” X 1week temporal field OS. VA: D 20/20 and S 20/30 IOP 15/16
3 months later

Patient gives history of rapid “side vision” loss 1.5 years ago feels like getting worse
VA OD 20/20 OS 20/25, IOP 19/18

Additionally
Normal ERG
VF
OD Normal
OS Scotoma Corresponding to the CRS

6 months later no change

Hyper-reflectivity caused by DR atrophy
Idiopathic Multifocal Choroiditis with Outer Retinal and Choroidal Atrophy

Serpiginous choroiditis

- Demography
  - AKA Geographic or Helicoid Choroidopathy
  - Chronic Progressive Inflammatory Disease
    - Rare
    - Men=Women
    - 20-70
    - R/O TB
- Symptoms
  - Painless vision loss, metamorphopsia or central scotoma
Topical Pred
Uveitis Work-up Return in One Week

Serpiginous Choroiditis

• Treatment
  — Aimed to stop chorioretinal inflammation especially with progressive lesions threaten the fovea
  — Systemic or periocular corticosteroids
  — Systemic steroid-sparing Immunomodulators
  — Long term management is challenging
  — 25% of the eyes have a final visual acuity less than 20/200
  — CNV up to 35%

Serpiginous Choroiditis

• Complications
  — CNV 35%
    • Anti-VEGF
  — Subretinal fibrosis
  — cystoid macular edema
  — branch vein occlusion
  — serous retinal detachment
  — NVD
  — Anterior uveitis.
Serpiginous choroiditis

Two Year Progression

Five Years

Challenges
50 Y/O WF Myopia
2008 to 2013 (OS Remained stable)
Progressive Degenerative Myopia
Lacquer cracks, Fuchs’ spots, DR Atrophy, CNV

Spectrum of the disease
Multifocal Choroiditis and Panuveitis (MCP)

- Characteristics
  - Intraocular inflammation
  - Multifocal choroidal lesions
  - Absence of any known ocular or systemic disease
  - Typically bilateral
  - Predilection for females 2nd-6th decades (median age of 28 to 33)
  - Blurred vision, floaters, photopsias, and scotomata including an enlarged blind spot

MCP

- FA
  - Active lesions may show early hypofluorescence with late hyperfluorescence
  - CME 14% to 41% cases
- ICG angiography
  - More hypofluorescent lesions than observed by ophthalmoscopy.
- VF
  - Enlarged blind spot and defects corresponding with the extent of multifocal lesions.
- ERG
  - May show progressive deterioration.

MCP

- Medical Evaluation
  - No specific diagnostic laboratory test and diagnosis is one of exclusion
  - Rule out other causes of uveitis and systemic diseases in the differential diagnosis, such as birdshot retinochoroidopathy (HLA-A29), sarcoidosis (chest x-ray, ACE), Vogt-Koyanagi-Harada syndrome (VKH, consider lumbar puncture and audiometry), syphilis (RPR or VDRL and MHA-TP or FTA-ABS), and tuberculosis (tuberculin skin test, chest x-ray), Diagnostic Vitrectomy

MCP

- Examination
  - Active stage anterior chamber and vitreous cells
    - These are absent in OHS or POHS
  - Choroidal lesions range 50-350 μm located in the posterior or peripheral fundus
    - Concentrated in the macula or forming peripheral linear streaks.
    - Active lesions appear as yellowish-white choroidal infiltrates and may be associated with neurosensory retinal detachments, vascular sheathing, disc edema, and cystoid macular edema.
    - Inactive lesions appear as variably pigmented, punched-out areas of chorioretinal atrophy.
    - Late stage findings Peripapillary scarring and extensive subretinal fibrosis.

MCP

- Management
  - Prognosis Guarded
  - Same as Serpiginous
Subretinal Fibrosis and Uveitis Syndrome

- A rare posterior uveitis characterized in the early stages by a multifocal choroiditis, followed by progressive subretinal fibrosis. It usually is seen in otherwise healthy, young myopic women with no systemic disease.
- Poor Prognosis
- Treatment

Conclusion

- Rare isn't rare if it is in your chair
- Recognize the S&S for proper management
- Challenges
  - Patient Experiencing Vision Loss
  - No Cure
  - Wax and Wane