Ellerbrock Presents Grand Rounds, Part II

Moderator: Gerald Selvin, OD, FAAO

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AAO 2012 Grand Rounds Outline **Kelly A. Malloy, O.D., F.A.A.O. , Dipl**

"I Don't Understand Why I Can't See"

A 57yo presents with optic neuritis OD with no improvement after IV steroid treatment. Work-up shows no evidence of MS / other etiology. Auto-immune optic neuropathy, although poorly understood and difficult to diagnose, is considered.

CASE REPORT:

I. Case History

a. *Patient Demographics: -* 57 year-old woman

b. Chief Complaint: Sudden vision loss OD, Pain on eye movements OD

Ocular / Medical History: borderline diabetes, hypertension, status post removal of cancerous kidney cyst

Medications: - Nefidical, atenolol, furosemide, methimazole, lisinopril, and penicillin

Other Salient Information: - Patient repots paresthesias of left fingers and questionable incontinence issues.

Pertinent Findings:

c. **INITIAL VISIT**

i. *Clinical:* (photos included in presentation where appropriate)

- VA 20/100 OD and 20/20 OS.
- Ishihara color plates: 0/14 OD and 14/14 OS,
- Pupils were isocoric with a >1.8 log unit RAPD OD
- Confrontation fields: OD – dense central scotoma and superior and inferior nasal defect OS - full
- Palpebral aperture: OD – 8 mm OS – 9 mm, Exophthalmometry:OD – 23 mm OS – 22 mm
- Ocular motility normal
- Slit lamp examination unremarkable OU / IOP: normal OU / Blood pressure: normal
- Dilated fundus examination: No definite edema OU. Moderate cupping OU. No pallor OU.

ii. *Physical:* Neurologic examination: cranial nerves V, IX - XII intact

- Motor, sensory, and coordination testing:

iii. *Diagnostic laboratory Testing: (INITIAL WORK_UP)*

- CBC, ESR, C-reactive protein, platelet count, Lyme titer, ACE, ANA with reflex titer, RPR, FTA-ABS, SPEP, BUN, creatinine
- Remarkable for elevated gamma globulins and M protein on SPEP

iv. *Imaging Studies: (INITIAL WORK_UP)*

- MRI of brain and orbits with and without contrast
- Remarkable for enhancement of a long segment of the right optic nerve (confirms optic neuritis), but only a few small non-specific white matter changes of brain

d. FIRST FOLLOW-UP (5 days after initial presentation – after the MRI)

i. *Chief Complaint:* vision getting worse OD, continued pain with movements OD
ii. *Clinical:* (photos included in presentation where appropriate)
- *Visual acuity* : OD: hand motion, OS: 20/20
- *Humphrey VF*: possible early superior arcuate defect and inferior depression OS
- *SLE*: no anterior segment inflammation
- *DFE*: now papillitis is apparent OD, OS remains normal

iii. *Additional Work-Up: hospital admission, IV methylprednisolone x 5 days, oral steroid taper*

- Lumbar puncture- refused by patient
- Additional Lab Testing: unremarkable
- Additional Imaging Studies:
MRI brain / orbits with contrast – stable ON enhancement OD, no new white matter lesions
MRI of cervical spine – no abnormality associated with demyelination

e. **2nd FOLLOW-UP VISIT (14 days after initial presentation)**
i. *Chief Complaint:* vision remains poor OD, no improvement after IV steroids
ii. *Clinical:* (photos included in presentation where appropriate)
- *Visual acuity* : OD: hand motion (in temporal VF only), OS: 20/20
- *DFE*: only mild residual edema OD, no NRR pallor OU

iii. *Additional Work-Up:*
- Additional Lab Testing: IgG NMO antibody test (negative)

f. **Multiple Additional FOLLOW-UP VISITS**
i. Pt later developed pain on eye movements in OS, mild vision changes OS
ii. DFE – NRR shows 2+ pallor OD OCT- decrease in RNFL thickness OD
iii. Another dose of IV Methylprednisolone and plasmapheresis
iv. Repeat work-up – lumbar puncture, labs, Gallium scan / pulmonology consult, repeat MRI shows continued enhancement of optic nerve OD
- Remarkable for significantly elevated rheumatoid factor

v. Rheumatology Consult – no features of systemic rheumatoid arthritis, get hand x-rays
vi. Still no definitive etiology – additional lab tests (APA, ALA, ANCA), consider skin biopsy

II. **Differential Diagnoses:**
- For Optic Neuritis: multiple sclerosis, neuro-myelitis optica, idiopathic, infectious (Lyme, syphilis, TB, cat-scratch, etc), inflammatory (sarcoid, etc), auto-immune(Sjogren's syndrome, lupus, rheumatoid arthritis, etc), AON- auto-immune optic neuropathy, paaneoplastic optic neuropathy

B. Diagnosis and Discussion:

a. Atypical Optic Neuritis
i. Does not respond to steroid treatment like typical optic neuritis
ii. May be profound, or progressive vision loss
iii. Needs additional work-up to rule out more rare causes

b. Autoimmune Optic Neuropathy (is considered)
i. Proposed Diagnostic Criteria
- Multiple episodes of optic neuropathy

- Serologic evidence of autoimmune tendency OR skin biopsy consistent with vasculitis, collagen-vascular disease, or immunoreactant deposition on H&E or IF
- Absence of define collagen-vascular disease or auto-immune illness
- Absence of known systemic neurologic auto-immune disease

ii. Recommended Work-up: CXR, MRI, urinalysis, CBC, VDRL/FTA-ABS, ESR, C3, C4, CH50
Immunoglobulin levels, ANA, RF, ACE, PT, PTT, Lupus anticoagulant, ACA, LP, skin biopsy, PPD, NMO antibodies

C. Treatment / Management:

a. *Treatment / Response:*

i. IV Methylprednisolone – no improvement of vision OD (not typical of MS associated ON)
ii. Plasmapheresis – no improvement of vision OD
iii. ? Should immunosuppressiontreatment be considered

b. Bibliography / Literature Review:

i. Goodwin J. Autoimmune optic neuropathy. Clin Neurol Neurosci Rep 2006 Sep;6(5):396-402.
ii. Kupersmith MJ, Burde RM , Warren FA, et al, Autoimmune optic neuropathy: evaluation and treatment. JNNP 1988;51:1381-1386.
iii. Frohman L, DelaTorre K, Turbin R, Bieory L. Clinical characteristics, diagnostic criteria and therapeutic outcomes in autoimmune optic neuropathy. Br J Ophthalmol 2009;**93**:1660-1666
iv. Chen YH, Wang AG, Lin YC, Yen MY Optic Neuritis as the First Manifestation of Rheumatoid Arthritis. Journal of Neuro-Ophthalmology 28(3):237-238. September 2008.
v. Frohman L. Autoimmune Optic Neuropathy – lecture delivered at NANOS meeting 2007

***III.* Conclusion:**

c. Optic neuritis with a poor visual acuity or lack of improvement after IV steroids is inconsistent with MS
d. Optic neuritis can have many etiologies, some of which can be very uncommon and difficult to diagnose.
e. Auto-immune related optic neuropathy can be the initial presentation of an auto-immune disease.
f. Auto immune optic neuropathy is reserved to identify optic neuropathy in the setting of no defined auto-immune or collagen-vascular disease.
g. The treatment for auto-immune optic neuropathy may consist of steroids and immunosuppressant drugs in attempt to restore vision and protect the fellow eye.

Flecked Retina Syndromes; Similar in Appearance Greatly Different in Prognosis

Sara Shkalm OD, FAAO

Flecked Retina Syndromes; similar in appearance, greatly different in prognosis

Abstract

Flecked retina syndromes have commonalities in terms of ocular history and findings; however, they also have distinct prognoses that require different management strategies. Early ocular and genetic testing is imperative in order to provide the patient with proper diagnosis and visual rehabilitation.

I. Case History
   a. A thirteen year old Hispanic patient first presents to the Feinbloom Rehabilitation Center with a chief complaint of moderate vision loss at distance and near, and nyctalopia. Previous ocular history was remarkable positive for amblyopia; systemic history was unremarkable.

II. Pertinent Findings
   a. Best corrected acuity was 20/40 OD and 20/30 OS with a refractive error of +3.75-2.50x045 OD and +3.00-2.50x145 OS. Cover test revealed one diopter of esophoria at distance and near. Pupils were equal, round, and reactive to light, with no afferent defect. Confrontation fields were full to finger count OD and OS. Extraocular muscles were full and smooth OU. Color vision testing with Ishihara plates revealed no color defects OD, OS. Slit lamp examination revealed healthy, unremarkable findings OU. Intraocular pressures were 10 mm Hg OD, 12 mm Hg OS using Goldmann Applanation Tonometry, The patient was cyclopleged with no significant change of refractive error. Dilated fundus examination reveals optic disc hyperplasia OU, macular edema OU, and multiple white flecks located through the posterior pole and mid-periphery OU. Cirrus-OCT reveals macula edema OS greater than OD. The patient was referred for a retinal consultation, an ERG, and genetic testing to rule out several white dot syndromes. The ERG revealed decreased rod, and cone function in both eyes; mixed ERG amplitudes were within normal range in both eyes. Our patient is still undergoing genetic testing.

III. Differential Diagnoses
   a. Based on the ocular history and findings, our differentials included:
      i. Retinitis punctata albescens (RPA)
      ii. Fundus albipunctatus (FA)
      iii. Fundus flavimaculatus
      iv. Familial dominant drusen
      v. Fleck retina of Kandori
      vi. Bietti's crystalline retinal dystrophy
   b. Because of the various prognoses these conditions have, proper testing is essential for correct patient education to ensue.

IV. Based on the ocular history and findings, the most likely diagnosis is either Fundus Albipunctatus or Retinitis Punctata Albscens.

a. Fundus albipunctatus (FA) is an autosomal recessive condition. The inheritance pattern is autosomal recessive, and it has been reported that most FA is caused by mutations in the *RDH5* gene, which encodes 11-*cis* retinol dehydrogenase (11-*cis*-RDH). Studies have shown that patients with FA with the *RDH5* mutation had extensive cone dysfunction, typically found to be more severe in older patients. This condition is characterized by congenital stationary night blindness and delayed dark adaptation after exposure to bright light, which typically presents during early childhood. The fundi of affected individuals contain multiple small, white or pale yellow dots in the retinal pigment epithelium, which may or may not involve the macula. These dots can remain unchanged, become more prominent, or can fade during aging; new dots may also appear. The dark-adaptation curve of affected individuals features prolonged recovery of cone and rod sensitivity and ERG cone and rod amplitudes are markedly reduced after 30-40 minutes of dark adaptation; however, they may come to normal or near-normal levels after many hours of adaptation. A patient diagnosed with FA would not be expected to produce progressive visual loss. However, new research has indicated that there are variants of FA that are associated with cone dystrophy, and may worsen over time.
b. Retinitis punctata albescens (RPA) is a progressive degenerative condition consisting of numerous white dots at the level of the retinal pigment epithelium. RPA is a retinal dystrophy featuring early-onset severe night blindness and tiny, white deposits in the fundus. RPA is associated mostly with mutations in *RLBP1* and occasionally in *RHO*, *RDS*, and *RDH5*. The dots are found throughout the fundus. Despite affecting the same parts of the retina as retinitis pigmentosa, the pigmentary changes are absent. RPA acts like retinitis pigmentosa and results in progressive visual field loss, night-blindness, and retinal vascular attenuation.
c. While there are several other flecked syndromes, they were ruled out due to ocular history and complaints. Fundus flavimaculatus is a progressive form of juvenile macular degeneration and may be considered a syndromal cone-rod dystrophy because of overlapping clinical features such as loss of color vision and photophobia in some patients. The onset of vision loss is in the first/second decade of life usually with rapid progression. Dark adaptation is prolonged but night blindness does not usually occur (thus being ruled out) and peripheral visual fields are normal. Familial Dominant Drusen is a commonly diagnosed fleck syndrome, yet is not accompanied by the ocular complaints our patient expressed. Fleck retina of Kandori is associated within the Japanese population base making this a less likely diagnosis.

V. Discussion/Take away
a. In young patients, RPA can be clinically indistinguishable from FA, posing a considerable differential diagnostic challenge. The first distinction between FA and RPA was made by Lauber in 1910. Recent evidence for compromised cone function and macular dystrophy in FA, as early as in childhood, has also challenged the classical notion that FA itself is a benign, fully stationary disease. Our patient had a fundus presentation that could be classified as either an early stage of RPA or an atypical form of FA. The presence of hypopigmented lesions anterior to the arcades and within the posterior pole could have been consistent

with a possible diagnosis of RPA; however, no vessel attenuation or pigment clumping was noted. Thus, there are serious implications and visual rehabilitation strategies that will greatly differ depending on whether or not our patient's acuity and field will worsen over time, or stay consistent. Further testing is crucial in helping to determine the correct diagnosis. Electrodiagnostic testing, fundus autofluorescence, and genetic testing have all been used to better differentiate between the two conditions and provide insight to the progressive nature and expectations of the disease process. Upon further research, FA with cone dystrophy appears to be the likely diagnosis as studies have shown macular swelling as a possible ocular finding.

VI. Additional Pearls

a. Preparing a family and patient who may continue to lose vision over time requires proper guidance and support. Providing this information equips individuals and empowers them with the knowledge necessary to make decisions that are appropriate for their personal and family circumstances. Additionally, early genetic testing information and proper diagnosis can qualify the patient for benefits that can provide educational, medical, and vocational assistance.

b. Our patient was previously diagnosed with amblyopia, which was explained to the family as the cause of vision changes. It is an important take away to recognize that patients are capable of having more than one underlying cause of visual complaints and recognizing that night vision complaints deserve proper work-up and diagnostic testing to determine the cause.

References

1. Yamamoto H, Simon A, Eriksson U et al (1999) Mutations in the gene encoding 11-cis-retinol dehydrogenase cause delayed dark adaptation and fundus albipunctatus. Nat Genet 22(2):188–191. doi:10.1038/9707

2. Gonzalez-Fernandez F, Kurz D, Bao Y et al (1999) 11-cis Retinol dehydrogenase mutations as a major cause of the congenital night-blindness disorder known as fundus albipunctatus. Mol Vis 5:41–45

3. Okada T, Ernst OP, Palczewski K, Hofmann KP (2001) Activation of rhodopsin: new insights from structural and biochemical studies. Trends Biochem Sci 26(5):318–324. doi:10.1016/S0968-0004(01)01799-6

4. McBee JK, Palczewski K, Baehr W, Pepperberg DR (2001) Confronting complexity: the interlink of phototransduction and retinoid metabolism in the vertebrate retina. Prog Retin Eye Res 20(4):469–529. doi:10.1016/ S1350-9462(01)00002-7
5. Carr RE (1974) Congenital stationary night blindness. Trans Am Ophthalmol Soc 72:448–487
6. Niwa Y, Kondo M, Ueno S et al (2005) Cone and rod dysfunction in fundus albipunctatus with RDH5 mutation: an electrophysiological study. Invest Ophthalmol Vis Sci 46(4):1480–1485. doi:10.1167/iovs.04-0638
7. Nakamura M, Skalet J, Miyake Y (2003) RDH5 gene mutations and electroretinogram in fundus albipunctatus with or without macular dystrophy: RDH5 mutations and ERG in fundus albipunctatus. Doc Ophthalmol 107(1): 3–11. doi:10.1023/A:1024498826904
8. Ellis DS, Heckenlively JR (1983) Retinitis punctata albescens: fundus appearance and functional abnormalities. Retina 3:27–31. doi:10.1097/00006982-198300310-00007
9. Humbert G, Delettre C, Se´ne´chal A (2006) Homozygous deletion related to Alu repeats in RLBP1 causes retinitis punctata albescens. Invest Ophthalmol Vis Sci 47(11): 4719–4724. doi:10.1167/iovs.05-1488
10. Demirci FY, Rigatti BW, Mah TS, Gorin MB (2004) A novel compound heterozygous mutation in the cellular retinaldehyde-binding protein gene (RLBP1) in a patient with retinitis punctata albescens. Am J Ophthalmol 138(1):171–173. doi:10.1016/j.ajo.2004.02.060
11. Fishman GA, Roberts MF, Derlacki DJ et al (2004) Novel mutations in the cellular retinaldehyde-binding protein gene (RLBP1) associated with retinitis punctata albescens: evidence of inter-familial genetic heterogeneity and fundus changes in heterozygotes. Arch Ophthalmol 122(1):70–75. doi:10.1001/archopht.122.1.70

The Great Masquerader Strikes Again
Stephanie Klemencic OD, FAAO

ABSTRACT : This case represents a rare maculopathy, presumed Syphilitic Posterior Placoid Chorioretinits, resulting in blindness due to delayed antibiotic therapy. Prompt intervention with appropriate dose of penicillin therapy is imperative to protect vision and save lives.

I. Case History

a. 40 y/o African American Male
b. Painless, progressive decreased vision, with associated flashes and floaters OU x 2 years
c. Last eye exam: 5 years prior – reading only Rx and reports "had good perfect vision."
d. No known systemic medications (last physical – 5 years prior, unremarkable)
e. Submandibular mass on right side – x 3 years
    1. Stable
    2. Per patient, evaluated 1 year prior at county hospital told "not cancer" and may be related to "wisdom tooth problem"
f. Denies previous red eye episodes
g. Denied smoking, drinking or drug use
h. Occupation – accountant – out of work over 1 year due to vision deficit
i. (Further history after DFE: lost 50 lbs over 2 years without effort – thought due to "stress" taking care of terminally ill grandmother; denied risk for sexually transmitted diseases, tick exposure, breathing problems, headaches, vertigo, nausea or paresthesias)

II. Pertinent Findings

a. Clinical
    1. Entering VA 20/200 NIPH OD, 20/200 OS NIPH
    2. Pupils, EOM's, Confrontation VF's - WNL OD, OS
    3. Slit lamp OU – normal findings; no cells/flare
    4. Goldmann IOP: 12mm Hg OD, 10 mmHg OS
    5. Blood pressure: 115/70 mmHg
    6. External exam: Large, right side submandibular mass (photo)
    7. DFE (photos):
        1. Bilateral, large, placoid, peri-macular RPE hyperplasia and disruption
        2. Bilateral vitritis with diffuse chorioretinitis
        3. Significant artery and venous attenuation with peri-phlebitis OU
        4. 2+ optic nerve pallor OU
b. Spectral Domain OCT (have images)
    1. Full thickness macular atrophy OU
c. Patient referred same day to Uveitis Specialist
d. Initial Laboratory work-up ordered (by uveitis specialist)

1. RPR, FTA-ABS, HIV antibody, ACE, PPD, Chest X-ray, Toxoplasmosis IgG and IgM titers, mass biopsy
2. Results (to be presented after DDX)
    1. RPR (1:128), FTA-ABS reactive
    2. HIV antibody +
    3. Mass biopsy: Parotid gland cyst
    4. ACE, PPD, Chest X-Ray, Toxoplasmosis titers all negative

e. Further lab tests (ordered by infectious disease specialist)
    1. HIV confirmed with Western Blot analysis
    2. CD4 count: 117 cells/mm3
    3. Viral load: 250,215 copies/ml
    4. Lumbar puncture – CSF analysis – negative
    5. Pneumocystis carinii - negative

III. Differential Diagnosis

a. Syphilitic Chorioretinitis
b. Metastatic non-Hodgkin's lymphoma
c. Sarcoidosis
d. Tuberculosis
e. Toxoplasmosis
f. White dot syndrome

IV. Diagnosis and Discussion:

a. Diagnosis:
    1. Diffuse, punctate syphilitic chorioretinitis OU in the presence of AIDS
    2. Macular scarring secondary to presumed syphilitic posterior placoid chorioretinitis.
    3. Large parotid cyst right side (secondary to AIDS)

b. Syphilis is a systemic disease caused by Treponema pallidum.
c. Brief Stages Review – based on clinical findings, divided into a series of over-lapping clinical stages used to help guide treatment and follow-up.
    1. Primary
        1. Ulcer, chancre at infection site
    2. Secondary
        1. skin rash, mucocutaneous lesions, and lymphadenopathy
    3. Neurologic
        1. cranial nerve dysfunction, meningitis, stroke, acute or chronic altered mental status, loss of vibration sense, and auditory or ocular abnormalities

4. Tertiary
    1. i.e., cardiac or gummatous lesions
5. Latent – lacking any clinical manifestations

d. Brief Epidemiology of Syphilis – from CDC
    1. Rate of reported cases decreased 1990's
    2. Increased annually from 2000-2009
    3. 1.6% decrease in 2010
    4. Remains major health problem in South and Urban areas of U.S.

e. Syphilitic Uveitis
    1. Known as the "Great Imposter," syphilitic ocular manifestations present a diagnostic dilemma by mimicking any type of inflammatory process.
    2. May be anterior (granulomatous or non-granulomatous), posterior or both
    3. Posterior segment may present with vitritis, retinal vasculitis, retinitis, chorioretinitis or papillitis.
    4. In immunocompromised patients, the infection may have an atypical appearance.
    5. Recent studies suggest that posterior uveitis is the predominant clinical manifestation
    6. Co-infection with HIV can accelerate the natural course of syphilis causing a greater frequency of ocular involvement, neuro-syphilis, treatment failure and recurrence.

f. Syphilitic Chorioretinitis
    1. Several forms of syphilitic chorioretinitis have been reported: confluent, placoid and punctate.
        1. Confluent form presents with large confluent areas of chorio-retinal whitening.
        2. In 1990, Gass described Acute Syphilitic Posterior Placoid Chorioretinitis (ASPPC) as large, placoid, yellowish lesions with faded centers at the level of the retinal pigment epithelium (RPE) in the macula and/or juxtapapillary areas, with an associated vitritis.
            a. Typical FA appearance: early hypofluorescence with leopard spot pattern in faded part of lesions and late staining.
            b. Natural course is unclear, as most reported cases in literature treated with antibiotics early in the disease

process, resulting in improved visual acuity to normal or near normal levels.

c. Few cases that did not improve acuity received intraocular steroid injections before syphilis diagnosis was determined.
d. The case presented here resulted in severe macular retinal pigment epithelial hyperplasia and blindness, likely due to delayed antibiotic therapy.

3. Punctate areas of chorio-retinal whitening

V. Treatment/Management

a. 2010 CDC Guidelines for treatment of syphilitic eye disease
    1. Ocular disease considered Neuro-syphilis
    2. Aqueous penicillin G 18-24 million units per day intravenous for 10-14 days.
    3. Alternative: Procaine penicillin 2.4 million units intra-muscular once daily for 10-14 days PLUS Probenecid 500mg orally four times daily for 10-14 days
    4. Syphilitic uveitis or other ocular manifestations should be treated with either of the above recommendations, which are the same for patients with neurosyphilis.
    5. A cerebrospinal fluid evaluation is also recommended for all patients with syphilitic have syphilis and symptoms or signs suggesting neurologic disease (e.g., meningitis and hearing loss) or ocular disease (e.g., uveitis, iritis, neuroretinitis, and optic neuritis).
    6. All HIV+ patients should be monitored for treatment failure at 6,12,18 and 24 months.
        1. No alternatives for IV penicillin have been adequately examined for penicillin allergic HIV + patients – CDC recommends desensitized and receive PCN.
        2. Some small studies suggest ceftriaxone 1–2 g IV daily for 10-14 days might be effective in neurosyphilis.
b. This patient was hospitalized and received 24 million units per day IV aqueous PCN G x 10 days. Highly active antiretroviral therapy (HAART) was also initiated.
c. Vitritis and chorioretinitis were resolved six weeks post treatment. Macular scarring and optic pallor remain. Visual acuity (20/200), scarring and pallor have remained stable over four years. (photos)
d. The patient's parotid cyst was drained, and has not returned.
    1. Parotid swellings described in 5-20% of HIV+ patients
    2. May be presenting clinical sign

3. Response to virus invading parotid gland
4. Some resolve with HAART therapy, some may be drained but may recur, others require parotid gland removal.

VI. Conclusion

a. Syphilitic ocular manifestations present a diagnostic dilemma by mimicking any type of inflammatory disease process.
b. Syphilis remains major health problem in U.S.
c. Optometrists can play a key role in protecting visual function and saving lives by prompt work up and referral for appropriate antibiotic therapy.

Bibliography

1. Browning DJ. Posteror segment manifestations of active ocular syphilis, their response to a neurosyphilis regimen of penicillin therapy, and the influence of human immunodefi ciency virus status on response. Ophthalmology. 2000;107:2015-2023.
2. Gaudio PA. Update on ocular syphilis. Curr Opin Ophthal. 2006; 17:562-566.
3. Chao JR, Khurana RN, Fawzi AA, Reddy HS, Narsing AR. Syphilis: reemergence of an old adversary. Ophthalmology. 2006;113:2074-2079.
4. Anshu A, Cheng CL, Chee S-P. Syphilitic uveitis: an Asianperspective. Br J Ophthalmol. 2008;92:594-597.
5. Hughes EH, Gusowski M, Simunovic MP, Hunyor AP, McCluskey P.Syphilitic retinitis and uveitis in HIV positive adults. Clin Exp Ophthalmol 2010;38:851-6.
6. Wickremasinghe S, Ling C, Stawell R, Yeoh J, Hall A, Zamir E. Syphilitic punctate inner retinitis in immunocompetent gay men. Ophthalmology. 2009;116:1195-1200.
7. Gass JDM, Braunstein RA, Chenoweth RG. Acute syphilitic posterior placoid chorioretinits. Ophthalmology. 1990;97: 1288-1297.
8. Harris T, Marshall EC. Ocular syphilis associated with syphilitic resurgence in a human immunodeficiency virus-infected man. Optometry. 2008;79:687-691.
9. Baglivo E, Kapetanios A, Safran AB. Fluorescein and indocyanine green angiographic features in acute syphilitic macular placoidchorioretinitis. Can J Ophthalmol. 2003;38:401-405.
10. Reddy SR, Cunningham ET, Spaide RF. Syphilitic retinitis with focal infl ammatory accumulations. Ophthalmic Surgery, Lasers & Imaging. 2006;37:429-431.
11. Song HS, Hong YT, Kwon OW. Acute syphilitic posterior placoid chorioretinitis following intravitreal triamcinolone acetonide injection. Graefes Arch Clin Exp Ophthalmol. 2008;246: 1775-1778.
12. Joseph A, Rogers S, Browning A, Hall N, Barber C, Lotery A, et al. Syphilitic acute posterior placoid chorioretinitis in nonimmuno-compromised patients. Eye. 2007;21:1114.
13. Meira-Freitas D, Farah ME, Hofling-Lima AL, Aggio FB. Optical coherence tomography and indocyanine green angiography findings in acute syphilitic posterior placoid choroidopathy: case report. Arq Bras Ofalmol. 2009;72:832-835.
14. Center for Disease Control: Sexually Transmitted Diseases Treatment Guidelines 2010: Syphilis. http://www.cdc.gov/std/treatment/2010/genital-ulcers.htm#syphilis. Last accessed January 21, 2012.
15. Amaratunge BC, Camuglia JE, Hall AJ. Syphilitic uveitis: a review of clinical manifestations and treatment outcomes of syphilitic uveitis in human immunodeficiency virus-positive and negative patients. Clin and Exp Ophthlamol 2010;38(1):68-74.

16. Owotade FJ, Fatusi OA, Adebiyi KE, Ajike SO, Folayan MO. Clinical experience with parotid gland enlargement in HIV infection: a report of five cases in Nigeria. J Contemp Dent Pract. 2005 Feb 15;6(1):136-45.
17.

Submacular Choroidal Neovascular Membrane in a 7 Year Old Female
Kenneth Sorkin OD, FAAO

Sub-macular Choroidal Neovascular Membrane in a 7 Year Old Female

I. Case Report

A. Patient demographics - C.D. is a 7 year, 4 month old Caucasian female who presented to our office with her mother.

B. Chief complaint - C.D. failed a pediatric vision screening the previous week. She denied any visual disturbance or other ophthalmic complaint.

C. Ocular history - When C.D. presented, it was her first visit to our office. Aside from mild seasonal allergies, there were no preexisting ocular conditions. C.D. is a healthy 7 year old with no medical problems. She had a normal developmental history.

D. She was on no medications.

E. No exposure dogs or cats. No travel outside the U.S. and no camping history.

II. Pertinent findings

A. Clinical

1. DVA sc OD: 20/25, OS: 20/250 $^{+2}$ PH:NI NVA sc OD: J1, OS J8 $^{-2}$

2. Low angle exophoria, full smooth EOM function OU, normal convergence, reduced (200 arc sec) stereo

3. Pupils: normal reactions, no APD

4. Biomicroscopy: Small notch in the pupil border at 3 o'clock position OS. All other tissues were normal and clear of inflammatory signs. Palpation IOP: Globes were soft and equal bilaterally.

5. Refractive data (cycloplegic)

OD: +1.25 -0.25 x 170 20/20 OS: +1.50 -0.50 x 170 20/150 $^{-2}$

6. C.D. was unable to reliably perform Amsler grid test

7. Fundus - OD: C/D ratio 0.35 with pink, healthy nerve tissue with clear distinct borders. Mild peripapillary atrophy. Normal macula and retinal periphery. OS: C/D ratio 0.30 with peripapillary choroidal prominence. Posterior pole showed a 2/3 disc diameter round, elevated, yellow macular lesion involving the fovea. Mild RPE clumping noted at the nasal side of the lesion. The well defined, 2.5 disc diameter peri-macular region showed diffuse fluid in the sub-retinal space. The nerve fiber layer appeared undisturbed. Small exudative deposits were seen at the edge of the raised retinal tissue. Deep retinal structures appeared clear. No surrounding retinal inflammation or hemorrhage was seen. The rest of the peripheral retinal exam was normal as was the overlying vitreal cavity OS.

B. Laboratory Studies

1. CBC with differential: WNL Eosinophil count: WNL Toxoplasmosis: neg IgG and IgM: neg, Toxocara: neg, ELISA: neg

C. Imaging studies

1. OCT study - OD: normal, OS: sub-retinal fluid with adjacent cystic changes. Possible signs of contracture of sub-retinal neovascular membrane.

2. Fluorescein angiography (FA) was normal OD. OS: leakage consistent with sub-retinal neovascular membrane.

III. Differential diagnosis

A. Primary: Choroidal neovascular membrane with early disciform scar OS

B. Others: Sub-retinal cyst of parasitic etiology, Best's vitelliform dystrophy

IV. Diagnosis and discussion

A. C.D.'s parents sought the opinion of the retinologist that I recommended and a second one suggested by a family friend. Both ran similar tests but the second one was convinced of an infectious etiology despite the negative results of the blood panel. His recommendation was to seek the opinion of a CDC affiliated infectious disease (ID) specialist to look further. Ultimately, after discussing the options with myself and the two retina specialists, the parents decided to establish care, treatment and follow-up with the initial practitioner whose diagnosis was <u>idiopathic sub-retinal central fibrosis with an active choroidal neovascular membrane</u>.

B. I believe the rarity of this diagnosis in a patient of this age is what led to the initial disbelief by the other retinologist that this was not a parasitic macular lesion. Despite the negative blood test results, central sub-retinal nets "just don't happen to 7 year olds". Mine and the first specialist's opinion was "yet, there it is". Seeking out a CDC ID specialist, running more blood tests and waiting for the likely negative results didn't seem prudent. Rather than delay, giving the leakage more time to cause more extensive scarring, a treatment plan was laid out (see below).

C. In addition to the negative blood panel, the patient's lifestyle led to no known exposure to the likely vectors of infectious transmission, namely cats and dogs. The clinical picture also didn't support an infectious or inflammatory etiology. C.D. felt well and did not display signs or symptoms sickness. Her left eye was comfortable, white and quiet. The overlying vitreous and surrounding retina were also clear.

D. Macular dystrophy was quickly ruled out once fluorescein results came in. Although her macular did have a vitelliform lesion by definition, these disorders generally don't reduce vision to 20/200 and cause sub-retinal fluid leakage. Electro-oculogram (EOG), the definitive test to confirm it, was deferred.

V. Treatment, management

A.A. The decision was made to treat the lesion with an intraocular injection of 0.3mg ranibizumab (Lucentis) which took place 44 days after the initial presentation to my office. Her vision had dropped to counting fingers @ 2' at that point. There were no unexpected side-effects to treatment. At the 11 day follow-up, vision had improved to 20/70. C.D. saw the retinologist again 6 weeks later and the vision was 20/60. The central fibrosis and a small amount of sub-retinal fluid were still present; confirmed with OCT. FA was repeated and showed leakage from the active net. The current plan is re-treatment with 0.3mg Lucentis within the next 2 weeks. C.D.'s case is on going.

A.B. Other treatment options in the pediatric population are limited to photodynamic therapy with verteporfin, sub-macular microsurgical membrane removal, laser photocoagulation.

A.C. Bibliography

1. Mehmet, C, Osman, C, Yilmaz OF. Intravitreal bevacizumab for idiopathic choroidal neovascularization. J AAPOS. 2009;13: 296-8

2. Rhee DY, Reichel E, Rogers A, Strominger M. Subfoveal choroidal neovascularization in a 3-year-old child with North Carolina macular dystrophy. J AAPOS. 2007;11: 614-5

3. Yıldırım C, Çetin EN, Yayla K, Avunduk AM, Yaylalı V. Photodynamic therapy for unilateral idiopathic peripapillary choroidal neovascularization in a child. Int Ophthalmol. 2011 Aug;31(4):333-5.

4. Daniels AB, Jakobiec FA, Westerfeld CB, Hagiwara A, Michaud N, Mukai S. Idiopathic subfoveal choroidal neovascular membrane in a 21-month-old child: ultrastructural features and implication for membranogenesis. J AAPOS. 2010 Jun;14(3):244-50.

5. Giansanti F, Virgili G, Varano M, Tedeschi M, Rapizzi E, Giacomelli G, Menchini U. Photodynamic therapy for choroidal neovascularization in pediatric patients. Retina. 2005 Jul-Aug;25(5):590-6.

Polypoidal Choroidal Vasculopathy: A ""Favorable"" Form of Choroidal Neovascularization?

Todd Peabody OD, FAAO

II. Case History

o Patient demographics: 60 year old Filipino female

o Chief complaint: Presented for completion of exam including dilation

- No complaints

o Ocular, medical history

- History of macular scar OD with a "possible" retinal surgery three years ago OD, unsure of details
- History of hysterectomy and appendectomy
- History of hypertension and asthma x "many years"
  - "Stable"

o Medications:

- Singular (asthma)
- Hydrochlorothiazide (hypertension)
- Aspirin 81mg
- Naproxen

III. Pertinent findings

o Clinical

- BCVAs 20/30 OD, 20/25 OS
  - NIPH
- Pupils: PERRLA (-)APD
- EOMS: Smooth, Full OU
- Slit lamp:
  - Anterior Segment: Normal OD,OS
  - IOPs: OD 11mmHg, OS 10mmHg (Goldmann)
  - Lenses: Gr 2+ Nuclear Sclerosis OD,OS
  - Anterior Vitreous: Clear OD,OS
  - Optic Nerves: healthy OD, OS
  - Retinal Vessels: normal and healthy OD, OS
  - Peripheral Retina: flat and intact OD,OS

- Maculae:
  - OD:
    - Previously noted macular scar superior to macula
    - Choroidal lesion located 0.5 DD inferior temporal to optic disc
      - Elevated
      - Fluid-filled
      - ¾ disc diameter in size

- Others

    - Fluorescein Angiography findings
    - Pictures
    - ICG findings
    - OCT

IV. Differential diagnosis

- Primary/leading: Pigment epithelial detachment

- Others:

    - Exudative Age Related Macular Degeneration
        - Usually bilateral
        - Characterized by drusen and pigmentary changes
        - Can have choroidal neovascular membranes
        - Typically affects lightly pigmented people

    - Choroidal Neovascular Membrane due to disease process that has breaks in Bruch's membrane
        - Toxoplasmosis
        - Presumed Ocular Histoplasmosis Syndrome
        - Angioid Streaks
        - Pathologic Myopia

    - Primary choroidal tumor
        - Usually appear outside of posterior pole and generally not seen hemorrhaging
    - Toxoplasmosis
        - Caused by a parasite, either acquired after contact with cats or eating poorly handled meat or congenital
        - Leaves chorioretinal scars similar to the one in the patient's right eye
        - May be the site of CNVs
        - Serosanguineous PEDs are not generally seen with Toxoplasmosis lesions
        - Also seen bilaterally

    - Polypoidal choroidal vasculopathy
        - Usually appears as a serosanguineous RPE detachment in the macular or peripapillary area of darkly pigmented people

V. Diagnosis and discussion

o Diagnosed with pigment epithelial detachment for following reasons:

- Darkly pigmented skin
- No drusen or pigmentary changes
- Not bilateral
- Not macular

o Retinal specialist confirmed PED with underlying hemorrhage

- Indocyanine Green Angiography confirmed suspected diagnosis of Polypoidal Choroidal Vasculopathy

- Polypoidal Choroidal Vasculopathy
  - Considered to be variant of CNV
    - Abnormal inner choroidal vasculature
    - Resultant polypoidal lesions responsible for episodic leakage and hemorrhages that cause serosanguineous RPE detachments
  - Typically macular or peripapillary
  - Course is characterized by persistent, recurrent serous and hemorrhagic RPE and neurosensory retinal detachments
  - Typically good visual outcomes
  - Seen at much higher frequency in darkly pigmented people including blacks, Asians, and Hispanics
  - Classic clinical appearance is serosanguineous PED
  - ICG critical in diagnosis
    - Highly specific and sensitive
      - Due to wavelength of light
  - OCT very useful in diagnosis as well
    - Polypoidal lesions appear as sharp dome-like elevations of the RPE with moderate inner reflectivity
  - Often misdiagnosed as classic CNV as part of AMD
    - Different racial demographics
    - Much less likely to cause severe vision loss
      - PCV less commonly results in fibrotic scarring of the central macula

VI. Treatment, management

- Treatment of our patient

  - Observation

  - Lesion resolved and has not recurred

- Conservative course typical

  - Close observation

- Unless lesion is sight threatening
    - Then ICG-guided laser is considered
    - Photodynamic therapy (PDT) also safe and effective

o Bibliography

- Conclusion
    - Important to consider patient demographics in addition to lesion characteristics to diagnose
    - ICG and OCT aid in diagnosis
    - Most often, close observation is best management

Atypical Presentation of Toxoplasmosis Retinochoroiditis
Anjali Desai OD

Abstract:

IV. An atypical presentation of toxoplasmosis retinochoroiditis in a 67 year old white male without a history of toxoplasmosis.

I. Case History

-Patient demographics: 67 year old white male

-Chief complaint: Foreign body OS, constant black spot in vision that started 4 days ago after moving the lawn.

-Ocular history: Presurgical cataracts, Presbyopia

-Medical history:

- Diabetes – HgA1c 6.6% 10/11
- Hypertension
- Gout
- Chronic kidney disease – with acute renal failure due to diabetic and hypertensive meds
- Hypothyroidism
- Coronary artery disease status post CABG

- Medications: Amlodapine 5mg, Gabapentine 1800mg, Glipizide 15mg, Hydrocodone 10/Acetoaminophrn 500mg 1500mg, Levothyroxine 0.025mg, Rosuvastatin 20mg

-Other salient information

- Patient denies eating raw/uncooked meats; or drinking goat milk
- Exposure to cats/cat litter
- Denies immunosuppression
- No known history or family history of toxoplasmosis from birth to present

II. Pertinent findings

-Clinical:
Visual Acuity: without correction
OD: 20/50 Pinhole: 20/40 Potential pinhole acuity: 20/20
OS: 20/40 Pinhole: 20/NI Potential pinhole acuity: 20/40-

Pupils: (+) Direct and consensual response without APD
Extraocular muscles: Full Range of Motion, OU
Confrontation fields: Full to Finger Counting, OU
Slit lamp exam:
Lids and lashes: OD: Normal
OS: Normal
Conjunctiva: OD: Normal
OS: Normal
Cornea: OD: 2+ guttata
OS: Linear area of negative staining sup nasal to visual axis, Keratic precipitates inferior 1/3, 1-2+ guttata
Anterior Chamber: OD: no cells/flare
OS: 1-2+ mixed white blood and pigment cells, no flare

Iris: OD: Normal, no TIDs
OS: Normal
Intraocular pressure: OD: 16 OS: 20 mmHg at 2:47pm by Tonopen
Lens: OD: Trace NS
OS: Trace NS, no break in lens capsule

DILATED FUNDUS EXAMINATION:
Vitreous: OD: Clear
OS: 2+ WBCs with dense large white debris, Trace pigment cells, PVD
Cup/Disc ratio: OD: 0.20/0.20 pink and healthy
OS: 0.20/0.20 no gross edema/pallor
Macula: OD: Normal
OS: grossly normal
Vessels: OD: 2/3 a/v
OS: grossly normal
Periphery: OD: Normal, without holes/tears
OS: white superficial lesion 7:00, ~1DD in size without heme/retinal break noted on scleral depression

-Physical – Patient denies any skin rashes, tick bites, breathing/coughing problems, not on immunosuppressive therapy.

-Laboratory studies: - CBC, ANA, ACE, RPR, FTA-ABS, Lyme titer, toxoplasmosis ELISA, HLA-B27, HIV screening

-Radiology studies: B-scan of orbits done to rule out retinal breaks

III. Differential diagnosis

- Primary: Acute toxoplasmosis retinochoroiditis OS
- Underlying etiology/Differential diagnosis: Intraocular foreign body, acute focal retinochoroiditis, tuberculosis, sarcoidosis, syphilis, Vogt-Kayanagi-Harada syndrome, viral retinitis, lymphoma.

IV. Diagnosis and discussion

- Test Results:
  - Labs –

- CBC, ACE, ANA – normal
- RPR – non-reactive; FTA-ABS – negative
- HLA-B27 – negative
- Toxo Ig G and Ig M – Positive
- HIV screen – negative

- B-scan –
  - Hyperintense debris in vitreous, partial PVD, no gross retinal breaks

- Final Diagnosis: Toxoplasmosis retinochoroiditis OS

-Elaborate on the condition:

Toxoplasmosis retinochoroiditis is caused by an intracellular protozoan parasite which is neurotrophic and affects the central nervous system tissue. The host of the parasite is cat. It is also transmitted by uncooked meats and drinking goat milk. A majority of the cases of ocular toxoplasmosis are recurrences of congenitally acquired toxoplasmosis. Pregnant women who acquire this parasite may transmit it to the fetus as a tachyzoite which can potentially cause severe ocular, central nervous system and systemic complications.

Active toxoplasmosis presents as new onset of floaters, and blurred vision due to the cells exuding from an active focus of retinitis. A granulomatous inflammation with increased IOP can occur with recurrent disease. The retinitis presents as a unilateral yellow-white retinal lesion in the posterior pole with overlying vitreal haze often adjacent to an old chorioretinal scar.

Toxoplasma retinitis can also present as punctate peripheral retinal lesions known as punctate outer retinal toxoplasmosis (PORT). It may also cause disc edema, vitreous precipitate, granulomatous iritis, localized vasculitis, retinal artery or vein occlusion, localized lymphadenopathy, polymyositis, encephalitis, pneumonitis, exanthemas or psychiatric disturbances.

-Expound on unique features:

- No previous chorioretinal scars adjacent to active lesion

- Toxoplasmosis chorioretinitis lesion was found in the periphery

- Patient not immunosuppressive therapy

V. Treatment, management

-Treatment and response to treatment:

- Patient started on Pred forte q1h OS and Homatropine bid OS to treat anterior uveitis pending labs
    - 2 day follow-up – subjective reduction in floaters by 50%, slight improvement in vision, and stable clinical presentation. Retina consult.
    - 5 day retina consult – slight worsening in vision, no change in clinical presentation. Consult infectious, disease pending labs.
    - ID consult 1 week – Diagnosis of acute left chorioretinitis suspected toxoplasmosis, pending toxo studies. Started on Leucovorin 20mg PO qday, Pyrimethamine 200mg PO once then 75mg qday, Sulfadiazine 1500mg PO q6h all for 1 month.
    - 9 day retina follow-up – slight worsening in vision, improved anterior chamber reaction, stable posterior segment findings. Follow-up scheduled 1 week. Toxo labs pending.
    - Positive toxoplasmosis Ig G and Ig M.

-Refer to research where appropriate

Patients in their second through fourth decades of life account for most observed episodes.

Congenital *T. gondii* infection at an early stage of retinal development could favor macular involvement (before vascularization of the peripheral retina is complete. Macrophages, which participate in host defenses against *T. gondii* infection, were significantly less common in the macula than in the peripheral retina.

Older patients may have not only a higher prevalence of ocular involvement, but ocular disease of greater severity as well.

Long-term, intermittent antimicrobial treatment has been shown to reduce the incidence of recurrences in high-risk populations. Toxoplasmic retinochoroiditis is usually treated with a finite course of one or more antimicrobial drugs, to hasten the resolution disease activity, and concurrent oral corticosteroids, to reduce the risk of tissue damage by the associated inflammatory response

-Bibliography, literature review encouraged

Ehlers, Justis P., Shah, Chirag P., ed. *The Wills Eye Manual: Office and Emergency Room Diagnosis and Treatment of Eye Disease*. 5th ed. Philadelphia: Wolters Kluwer, 2008.

v. Hollar, Gary. Ocular toxoplasmosis: the influence of patient age. Mem. Inst. Oswaldo
vi. Cruz vol.104 no.2 Rio de Janeiro Mar. 2009.
vii. http://dx.doi.org/10.1590/S0074-02762009000200031

Onofrey, Bruce E., Skorin, Leonid., Holdeman, Nicky R. Ocular Theraputics Handbook: A Clinical Manual. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2005.

VI. Conclusion

-Clinical pearls, take away points if indicated:

- Important to confirm diagnosis with labs even though results might not be back before systemic treatment initiated.
- Watch out for atypical presentations of conditions