Handling Optic Nerve Inflammation: Cases

David L Bejot OD
SEI Annual Disease Conference - Virtual

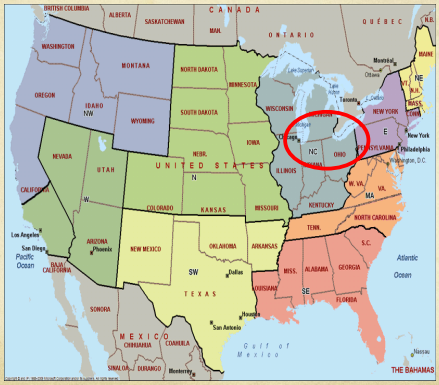
1

Dr. Alex Cherry
Glaucoma fellowship Trained Surgeon

2

Joseph Giles CEO
Jorge Lopez COO
Sean McMillen CFO
Jonathan Jean Pierre CEO of SEI

3



4

Optic disc edema

Unilateral

Systemic Disease
1. RVO
2. Uveitis

Inflammation
1. Papillitis
2. Neuro-retinitis

Vascular
1. AION

Orbital
1. Tumor
2. Thyroid
3. Cellulitis

Bilateral
1. Papilledema
   - ↑ CSF pressure
   - Brain lesion
2. Anemia
3. HTN (malignant)
4. "Pseudo papilledema
   - ON Drusen
   - Small hyperopic eyes

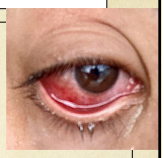
5

Has there been a Conjuctivitis that tested +C-19?

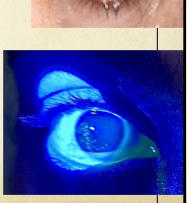
- Canadian Opth Society (April 2020)
  - Marvi Cheema MD, Helya Aghazadeh MD, Samir Nazara MD
- 3/1/20
  - 29 female x 1 day "pink eye" at family doctor's office
  - Returned to Canada on 2/29/20
  - 1 month Philippines (stayed in a hotel)
  - **+ cough, rhinorrhea & OD conjunctivitis**
    - No fever but taking Tylenol
  - Referred ophthalmology

6

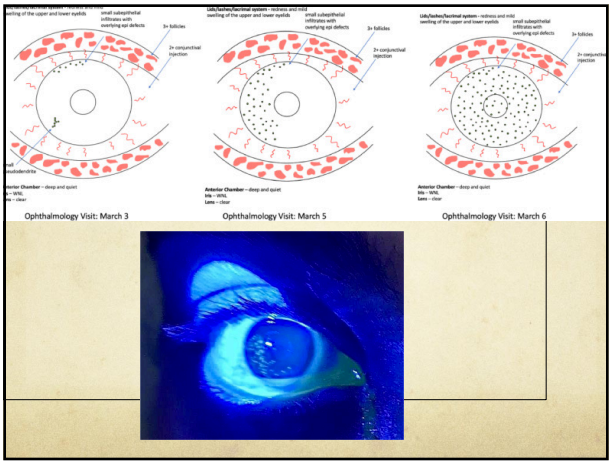
Has there been a Conjunctivitis that tested +C-19?



- **March 3rd** First Visit at Ophthalmologist
  - 20/20 ou
  - SLE + follicles, + SEI's
  - Dx: presumed HSK: Moxi / Valtrex 500mg tid
- **March 5th:** ↑ redness/pain; 20/20
  - Dx: EKC - same meds
- **March 6th**
  - ↑'SEI's(50) , epith defects (20/30 od)
  - Bact, viral, goorrhea, chlamydia swabs – NEG
  - COVID 19 Test
  - NOTE:



7



8

Take home message

1. The eye is a potential entry portal for these viruses and emphasize the importance of masking and eye protection
2. Further studies needed to determine whether the virus within the ocular surface have enough conc to transmit the infection/virus
3. Not many articles on COVID-19 / eye offer enough data on laboratory testing (guidelines) , standard operating procedure etc....
4. PPE: Masks, glasses, social distancing, shields on Slit lamps, gloves, cleaning the exam rooms betw pts, checking Temps on everyone etc.....
5. DATA CHANGES LIKE THE STOCK MARKET

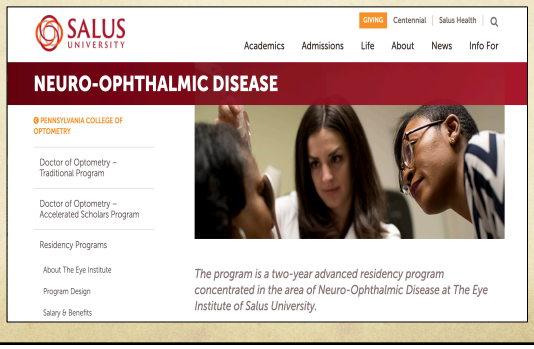
9

New specialty within Optometry
Neuro-Optometry

1. Behavioral optometry
   - Binocular Etiologies
   - TBI, "concussions" etc..
   - Vestibular therapy @ Ohio State
2. Neuro
   -) Optic nerve (disorders)
     NON-AION & AION
   -) EOM palsies
   -) Shingles – Neuro-trophic corneas
   -) Dry Eye
   -) Bell's Palsy
   -) Horner's
   -) Pupil

10

https://www.salus.edu/getattachment/Colleges/Optometry/Residency-Programs/Neuro-Ophthalmic-Disease/Neuro-Ophthalmic-Disease-Residency-Curriculum-rev-11-2019.pdf.aspx



11

Unilateral Disc Edema

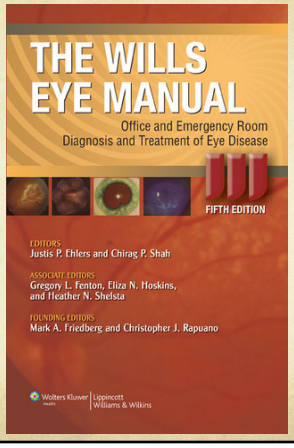
1. Demyelinating/Autoimmune
   - MS
   - thyroid eye disease
   - Lupus erythematosis
   - Neuromyelitis optica
2. Infectious
   - Herpes
   - TB
   - Lyme disease
   - Syphilis
3. Traumatic
3. Inflammatory / infiltrative
   - Drusen
   - Sarcoid
   - Orbital pseudotumor
   - PVD
   - Tumor
4. Vascular (AION)
   - Temp Arteritis
   - Non-Arteritic ischemia
     - DM
     - Noc. Hypofusion
     - HTN
     - Cholesterol
     - Medicines

Arteritic
Non-Arteritic

AION = Arteritic Optic Neuritis (+Temporal Arteritis → Giant Cell (GCA)

Non-AION = Non Arteritic Optic Neuritis (NOT Temporal Arteritis)

12

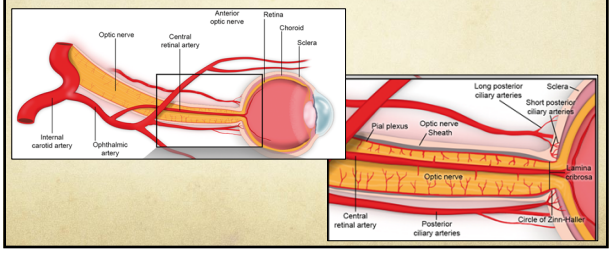


13

Dr. Sohan Singh→ 1974

Anterior ischemic optic neuropathy (AION)

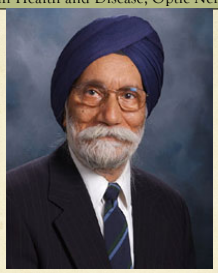
1. Non-Arteritc Optic Neuritis
2. Arteritic Optic Neuritis (Temporal arteritis / Giant Cell Arteritis)



14

Sohan Singh Hayreh MD PhD

Ocular Circulation in Health and Disease; Optic Nerve Disorders



It results from non-perfusion of the posterior ciliary blood supply to the optic nerve head. Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common type of ischemic optic neuropathy and is the most common acute optic nerve disease of adults over age 50 years.

15

Sohan Singh Hayreh MD PhD

Ocular Circulation in Health and Disease; Optic Nerve Disorders

Non -Anterior ischemic optic neuropathy (Non-AION)

1. It results from non-perfusion of the posterior ciliary blood supply to the optic nerve head.
2. Classic symptoms of anterior ischemic optic neuropathy include
   - -sudden, painless vision loss
   - - mild to severe vision loss
   - - inferior altitudinal field defect
   - -optic disc edema, which usually resolves spontaneously in Approx 2 months & → sectoral or more often generalized optic atrophy.

16

Quick review of ON blood supply

Primary supply from the Posterior Ciliary Vessels

ON Head is supplied by the PC Artery circulation

Front to Back:

1. Nerve Fiber layer (NFL)
2. Prelaminar
3. Lamina Cribrosa
4. Posterior – Laminar region

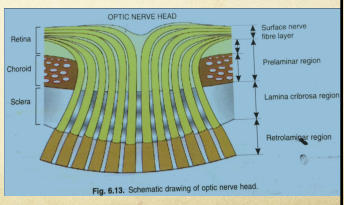
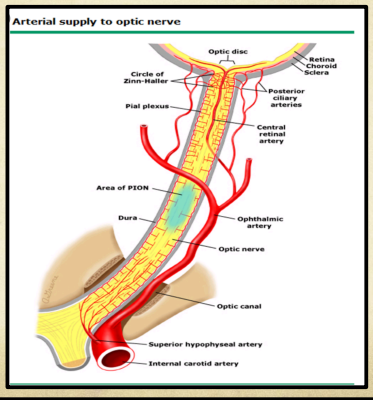


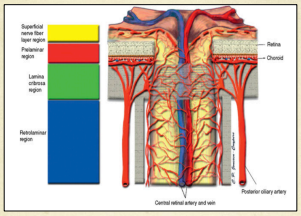
Fig. 6.13. Schematic drawing of optic nerve head.

17



18

Normal Auto-regulation ON



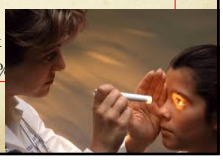
ABSENT | PRESENT | ABSENT

Perfusion Pressure

19

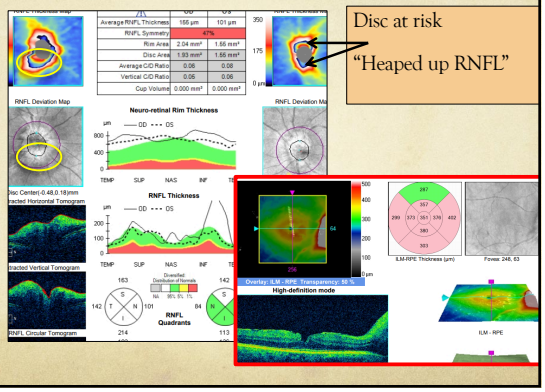
Larry (78yrs) from Defiance

- Cataract Sx (Dr Brown) OD 12/2/20 → No complications
  - MED: HTN, 2 Cholesterol Meds , MYOPE
- Dec 3rd → 1st day PCIOL OD (20/40-) " happy "
- Dec 17th → x 3days of "flashes OD superiorly
  - Va 20/50-
  - SLE clear
  - F: swollen disc inf OD, clear OS
  - c/d 0.2 but SMALL ON " disc at risk" look
  - Penlight Brightness test OD60 %/OS100 %



20

Larry



Disc at risk

"Heaped up RNFL"

21

Larry

- Dx: Optic nerve edema OD
  - Suspect Non AION
  - MUST rule out Temp Arteritis (GCA) – WHY?
    - Pt declines scalp/jaw/ temp artery area Pain
    - Strong Temporal Artery Pulse
    - No recently HA's (esp on OD area)
      - Go over how to Dx GCA
- Plan:
  - Stat Sed / CRP / CBC ?)
  - MRI with/without contrast
  - Review overall health / meds

22

More to the story...

- 1 month later (Jan) – says OS "doesn't seem right"
- Dr Tolchin in Bryan office 20/60 od 20/30 os
  - Less disc swelling OD, no swelling OS , VF OS clear
  - 1 month later (Feb)
    - Same but VF OD little more constricted, OS constricted ?
    - See Dr. Bejot 2-3 months

23

More to the story... 3 months later

- 6 months post initial NON-AION OS - last Dec 2019
- Feels NO change OU → can tell OD is not the same as OS
- VA 20/70 OD 20/30 OS
- Penlight brightness 60% OD 100 % OS NO CHANGE !
- F: No edema OU
- 24-2

24

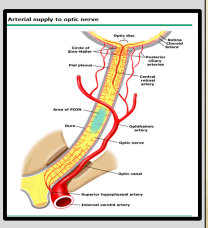
More to the story… 3 months later

- Larry notices NO problems with his vision OS and can not perceive an VF defect OS, like he can OD
- Repeat SED/CRP → normal
- Monitor → RTC 3 months repeat 24-2 OS
- Dx: Bilateral NON-AION
  - Symptomatic OD
  - NON Symptomatic OS

25

Quick review- NON- AION

- Remember ON ischemia can occur in different anatomical parts of the Optic Nerve (ON)
- Definition: AION involves the first 1mm segment of the ON and you will see ON edema
  - **AION has 2 categories**
    - 1. Non-AION (aka Larry)
    - 2. AAION (aka Temporal Arteritis /GCA)
  - Non-AION
    - Has MANY etiologies
      - → **NO Known True Mechanism of Action**
      - HTN
      - Atherosclerosis
      - Compartmental Theory (Disc-at-Risk)
      - SAS Sleep Apnea Syndrome
      - Meds → ED meds (phophodiesterase inhibitor5
        - Perfusion issues in ON
      - Diabetes
      - Nocturnal Hypofusion
      - Loss of Autoregulation



26

Quick review- NON- AION

- Risk Factors
  - 2-10 per100,000
    - THE MOST common cause acute NON-AION > 50 yrs old
    - > 90% caucasion
- Mechanism of Action
  - Makes is so difficult → No one mechanism demonstrated
  - Do know → circ insufficiency / infract → short Post Ciliary Arteries
  - 97% c/d < 0.3 " Disc-at-Risk" aka Crowding phenomenon
  - Small optic nerve diameter (1.0-1.2 mm)

27

Quick review- NON- AION

- Mechanism of Action
- Then there is:
  1. **Vasculo-pathic" Risk Factors**
  2. Autoregulation of ON
  3. Disc at Risk
  4. "It can BE Devastating to vision"
  5. Don't forget to think about Sleep Apnea

28

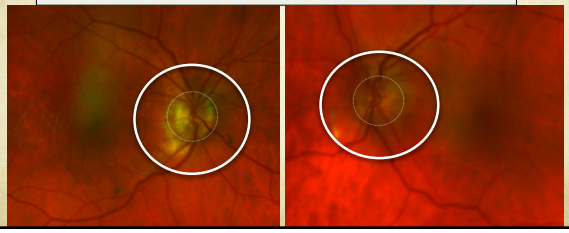
Back to Larry

1. Wife said he is " world's worst snorer"
   a) PCP will arrange Sleep Apnea Evaluation
2. On 2 cholesterol meds – not done >1yr
   a) Serum Lipids eval
3. Discuss overall health → regular check ups with PCP
4. Ask him if he was taking ED meds?

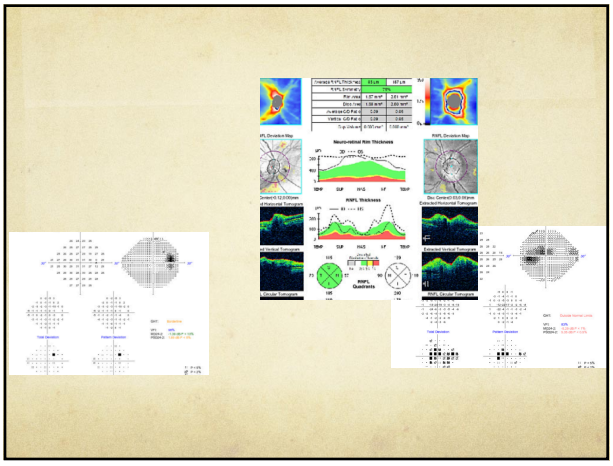
29

NON-AION
Devastating to your life

- Bob → Retired firefighter
  - Hasn't seen doctor for awhile x3 yrs
  - NO Meds
  - Disk-at-Risk look
- **April 2019**
  - Ref for loss vision OS 20/25od 20/50- os



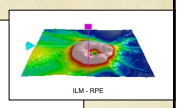
30

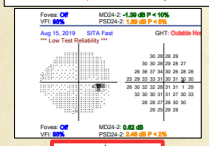


31

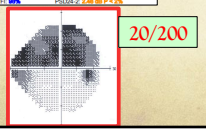
NON-AION
Devastating to your life

- April 2020
- Same thing is happening to my OD eye
  - "my only eye left"
  - 20/50- od 20/800 os

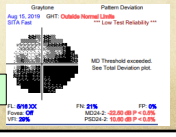




1 year prior
20/25 OD / OS



20/200

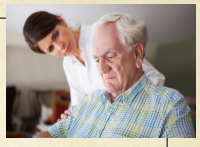


20/800

32

NON-AION
Devastating to your life

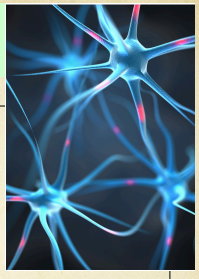
- For me… No known Treatments
  1. Rule out Temp Arteritis
  2. MRI
     1. Could be demyelinating disease
     2. Tumor / other
  3. Overall health
     1. HTN
     2. Cholesterol
  4. Sleep Apnea
  5. Medicines



% of occurrence in the contralateral eye → 15%/5 years

33

Future ???

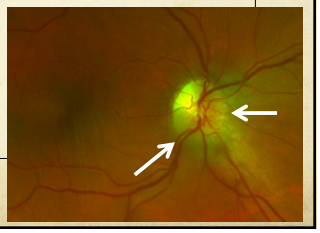


- Quark Study → Phase 2/3
  - Quark Pharmaceuticals
  - July 2018 -2019
  - ClinicalTrials.gov # NCT023342560
  - Molecule QPI-1007
- The Effect of QPI-1007
  1. Visual fxn with recent Non-AION
  2. Safety of med
     1. IntraVitreal Injection
  3. Sham study 1.5mg QPI-1007, 3.0mg, & Sham (N=732)
     1. All randomized in 1:1:1 study

34

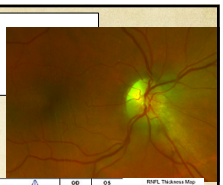
Robert from Bryan
65 yrs old

- Referred in OD nerve swelling → APRIL 2020 + COVID 19
  - " looks like I'm looking through a dirty screen"
  - Med: None
  - Va 20/30—od/ 20/20 os
  - Ta 15 ou
  - F: inf edema OD
    - Few small hems inf
    - OS clear
    - Disc Edema OD



35

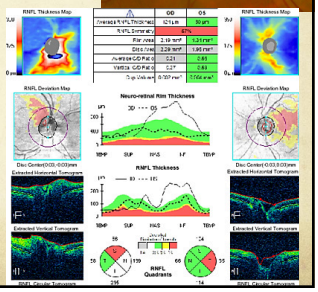
Robert from Bryan
60 yrs old



Dx: Disc Edema OD

1. Prob NON Aion
2. Rule out GCA
   1. Denies any sym
   2. Ask about health hx as he is 65 and no meds

BP 183/121



36

Robert from Bryan
65 yrs old

- Dx: Disc Edema OD
  - Secondary to undiagnosed HTN !
  - Therefore " Most likely" NON-AION
- Plan: called PCP → Dr Rowan
  - Send to urgent due to C-19
  - Stat sed/Crp/cbc
  - MRI
  - Sleep Apnea eval
  - Gave his wife my cell# ☺

37

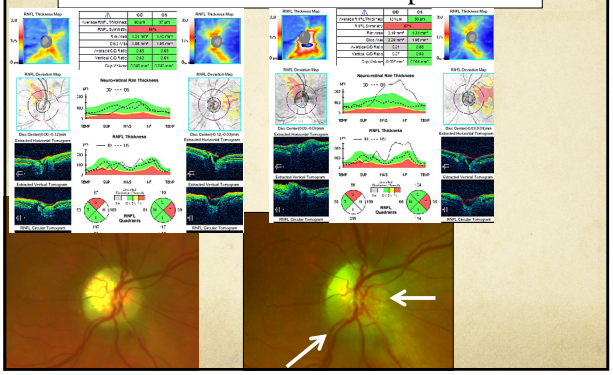
Robert from Bryan

- Follow up call
  - MRI clear
  - Sed 10
  - CRP 0.1
  - LDL 138 (high!)
  - HDL 40 (barely normal)
  - Tot Chole 275 (high)
  - Pt saw dr at Urgent care (Lisinopril- ACE inh)
    - Wife commented:

Bob feels a lot better now – he did not realize his problems.

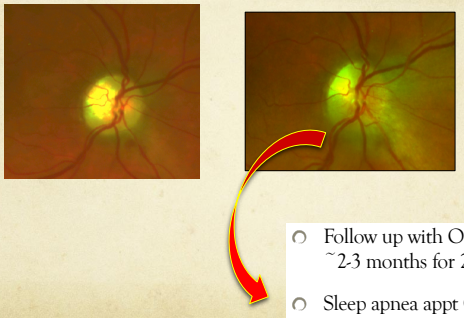
38

Robert from Bryan
1 month follow up



39

Robert from Bryan
1 month follow up (July)



- Follow up with OD in Bryan ~2-3 months for 24-2
- Sleep apnea appt Oct (C-19)

40

Sleep Apnea

Optic Nerve Dysfunction in Obstructive Sleep Apnea: An Electrophysiological Study

Claudio Liguori, MD,1 Maria Giuseppina Palmieri,

- N-27 for each group
  - OSA, without medical comorbidities, present VEP alteration as documented by lower amplitude and longer latency of the P100 component than healthy controls. These altered electrophysiological findings may be the expression of optic nerve dysfunction provoked by hypoxia, acidosis, hypercarbia and airway obstruction, frequently observed in patients with OSA. Hence, we hypothesize that OSA *per se* may impair optic nerve function.

41

Polysomnography

- sleep apnea is based on the Respiratory Distress Index (RDI) –
  - the number of respiratory disturbances per hour of sleep (apnea plus hypopnea (low blood oxygen).
- American Academy of Sleep Medicine (AASM), an RDI
  1. 0 to 5 in normal
  2. 5 to 20 is mild
  3. 20 to 40 is moderate
  4. > 40 is considered severe.

42

Polysomnography

https://www.aastweb.org/blog/what-is-polysomnography

- Blood Oxygen Levels
- Brain Waves (EEG)
- Breathing Rates and Patterns
- Body Positioning
- Eye Movements
- Heart Rates and Rhythms
- Leg Movements
- Sleep Stages
- Snoring and Noises Made While Sleeping
- Unusual Movements or Behaviors
- Bruxism (teeth grinding)
- Central Sleep Apnea
- Circadian Rhythm Sleep-Wake Disorders
- Complex (or Mixed) Sleep Apnea
- Idiopathic Hypersomnia
- Narcolepsy
- Chronic Sleep Apnea
- Periodic Limb Movement Disorder (PLMD)
- REM Behavior Disorger (RBD)
- Parasomnias
  - Unusual behavior of nervous sys during sleep

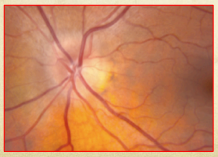
43

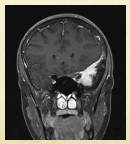
Save a life.....

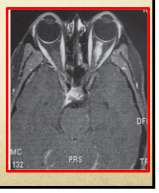
44

Why MRI?

- No Need if GCA is the Dx
- NON-AION
  - MS in pts < 50
  - Many etiologies
  - 2 cases of a meningioma that present as " swollen optic nerve "





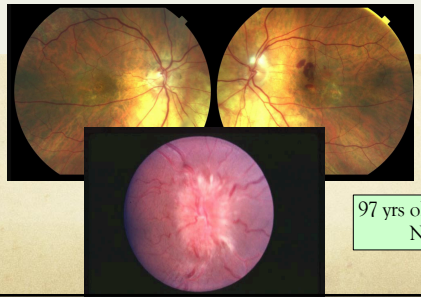


https://eyerounds.org/index.htm

45

A quick review of Temp Arteritis

- I have had ~ 9 in the 1 ½ yrs



97 yrs old lady is now NLP OU

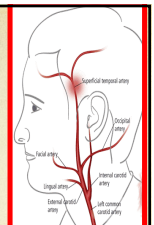
46

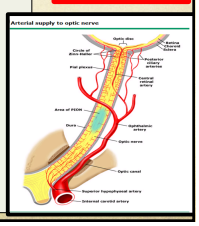
Temporal Arteritis GCA / Cranial Arteritis

Def'n: **Autoimmune / Systemic disease where Inflammation occurs in the large arteries in → head & neck region**

- Greater 50 yrs of age (70-79 peak)
- Incidence: 10-15 per 100,000 a year in United States
- Most common in European decent, rarely in African Americans
- Women 3 : 1
- Polymyalgia rheumatica PMR 15 %
- Classic signs
  1. Jaw/scalp pain
  2. Temporal artery tenderness or inflamed
  3. New Ha's / localized

How to Diagnosis ????





47

GCA : Signs & Symptoms

- It's the great debate → How to be more accurate
- Its VERY variable in clinical presentations
  - HA / Jaw / Scalp / Fatigue / Weight loss / "visual Δ's"
- Visual : amaurosis fugax, loss of Va , non descriptive "eye pain", Diplopia
- "No two patients are really the same "
- American College of Rheumatology 1990

48

American College of Rheumatology

- In 1990 criteria for classification of temporal arteritis

at least **3** of the following **5** items must be present

- **(sensitivity 93.5%, specificity 91.2%)**

1. Age of onset older than 50 years
2. New-onset headache or localized head pain
3. derness to palpation or reduced
4. tation rate (ESR) greater than
5. psy (TAB +)

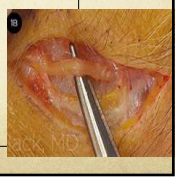
49

American College of Rheumatology (ACR)

Criteria for Dx Giant Cell Arteritis

Positive TAB (Gold Standard)

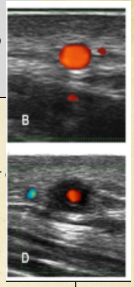
1. Multi cases where TAB + biopsy but do not meet the other criteria
2. High False Positive with TAB - biopsy (10-25%)
   1. ACR study ~ 8 % with GCA were TAB neg
3. 10-20% are TAB + on one side only
4. Length of TA biopsy
5. Skip areas
6. THEREFORE
   1. Always Tx since potential cause of Blindness



50

What about the Lab Tests?

- ESR ≥ 50
  - Highly variable in norms, ↑ Age,
  - Documented cases where very low
  - However, a very high ERS > 90-100 extremely sensitive for
  - **HOWEVER →** Normal ESR does NOT rule out GCA
- CPR ≥ 2.5 mg/dl
  - NOT age dependent, protein from liver, raises in acute inflammation (IN-6)
  - Norm ~ 0.5 mg/dl
  - CRP elevated (4x) very sens for GCA
  - OVERALL 87% sensitivity / 84% specificity with both ESR/CPR
- Thrombocytosis
  - Platelets ≥ 400 x 10(3)/microliter - um) is a useful marker of a positive temporal artery biopsy.



51

Treatment Protocols

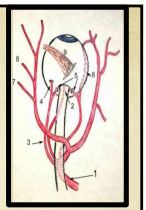
- IV Steroids in Ocular Involvment
- Oral steroids
  - 60-80mg / day (Wide variety)
    - Q 2 weeks decrease 10 mg until 20 mg
    - Then decrease 2.5 mg every 2 weeks until down to 10 mg / day
    - Then decrease 1 mg every 1-2 weeks
  - Constant monitoring of CRP and ESR
  - Maybe on steroids for 1-2 yrs +
    - Can reoccur (64%) experienced at least 1 relapse, and 38 (36%) experienced 2 or more
  - Worry about
    - DM / Osteoporosis (Vit D/ Fosamax) / GI issues (Prilosec)
  - Biologs : Acterma (Genetech) ; 1st FDA approved Biolog for GCA
    - Inter-Leukin Inhibitors (IL-6)

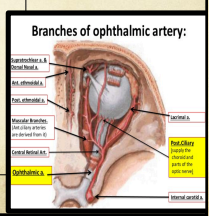
52

Temporal Arteritis GCA / Cranial Arteritis

Studies: will eventually cause blindness if untreated

- **Up to 70% have Ocular manifestations**
  1. **AION**
  2. **OIS**
  3. **CRAO / BRAO**
  4. **Posterior ischemic optic neuropathy**
  5. **Cranial Nerve Palsies ; Esp CN 3 and 6**
     a) ischemia arises due to vasculitis affecting branches of the posterior ciliary artery





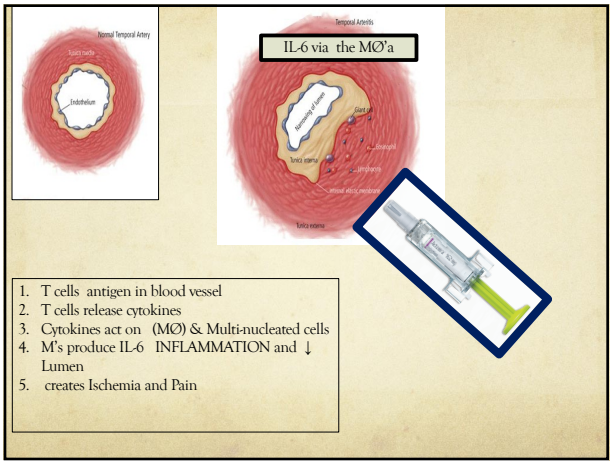
53

Risk factor for early visual deterioration in Temporal Arteritis

J Neurol Neruosurg Psychiatry Nov 2007

- N= 341 patients underwent TAB suspected GCA over 15 years
- Steroids may not stop the progression of visual loss
- 91 out of 341 tested positive for TAB
  - → those TAB+ were in the study
  - 91% of biopsies done with 5 days of dx
  - 23% showed progressive visual symptoms DESPITE steroid treatment
    - Of which 17% had permanent vision loss
- Mean age 74.6; age range = 59-93 yrs of age
- **WORST % for vision loss : ON swelling / HTN / age/ CRP**

54



1. T cells antigen in blood vessel
2. T cells release cytokines
3. Cytokines act on (MØ) & Multi-nucleated cells
4. M's produce IL-6 INFLAMMATION and ↓ Lumen
5. creates Ischemia and Pain

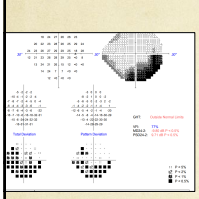
55

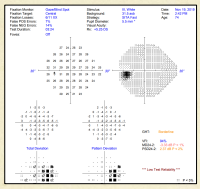
56

Patricia L
Tuesday morning

- 74 female
- Feels good → + floaters and Hazy vision OU
- Va(cc) 20/60 OD 20/40 OS
- Ta 13 OU
- SLE: 2+ NS OU / 2+ Fuch's OU
- F:

57





- **OD: Inf temp loss**
  - PSD 9.71
    P=0.5%
- **OS: Prob Incr Blind spot**
  - PSD 2.37

58

Patricia L
Tuesday morning
Dec 2019

- Papilledema / bilateral edema Optic Nerve
  - Tumor / Aneurysm
  - CSF issues
  - Blood dyscrasias
- CRAO's (bilateral?)
- Meningioma
- GCA
- NON-ANION (bilateral ?)

59

Worst case scenario

Plan: Ordered Blood work: Sed Rate and CRP today STAT

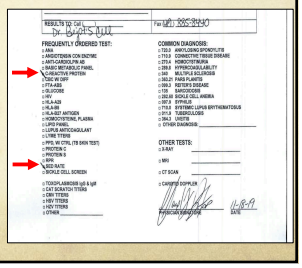
**pt states that she is going to St. Anne's Hospital

Gave patient Dr. Bejot's cell # (call if any problems)

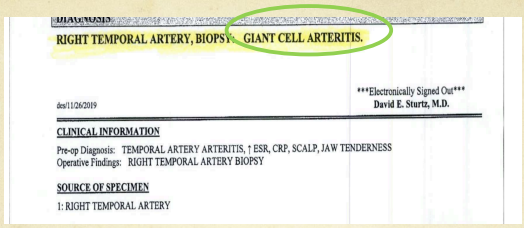
-) pt's cell Phone number 419-xxx-xxxx

60

- Imp: Disc edema OD > OS
  - Asymptomatic : No scalp /jaw/ temp artery pain.
  - NEED SED AND ESR STAT



61

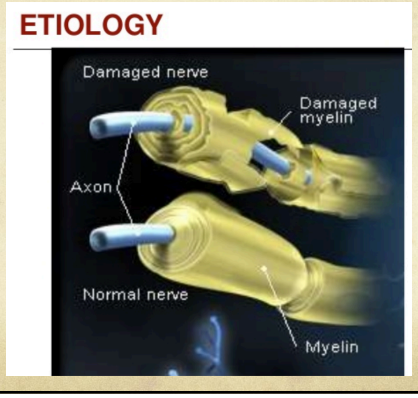


62

Optic Neuritis Demyelination Etiology

- Can create both
  1. Inflammation of the Optic Nerve (looks like NON-AION)
  2. Retrobulbar Inflammation of Optic Nerve
- Mechanism of Action
  - Immune reaction of the myelin sheath in the ON
- Pts under the age of 50
  - MRI to look for demyelination plaques
  - See Neurologist
  - Steroids

63



64

General Info on MS & ON Inflammation

- ✓ 15 yr risk for dev MS following actue Optic neuritis = 50%
- ✓ Only 25% if MRI shows " Negative Lesions"
  - ✓ 70% with multiple ones
- ✓ Most show as retrobulbar ON inflammation
- ✓ 20-50 yrs of age (mean =30 yrs of age)
- ✓ 80-90 % have pain on " eye movement"
- ✓ Temporal ON atrophy is a "hallmark " sign

65

Treatment

- IV steroids + Oral steroids
  1. Gilenya
  2. Tecfidera
  3. Vumerity
  4. Aubagio
  5. Mayzent
  6. Mavenclad
- Infusions
  1. Ocrevus (Ocrelizumab)
  2. Tysabri (Natalizumab)
  3. Campath (Alemtuzumab)

www.mayoclinic.org/diseases-conditions/multiple-sclerosis/diagnosis-treatment/drc-20350274

66

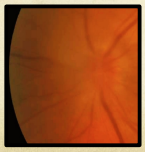
Patricia L
Tuesday morning

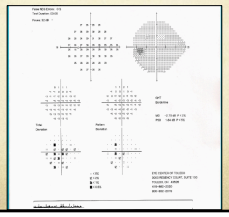
- What did I do?
  - phoned (900pm) St Anne's ER physician
  - Called Patricia
  - Told her she needs to go the ER ASAP
  - Did not want to wait until 900 am the next morning → PCP opens
  - Called her friend to drive her
  - Called NP the next morning (just out of college)
- Call pt on Sunday afternoon→ " how are how doing"

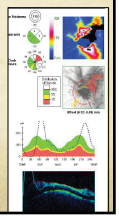
67

Sudden Flashes and Floaters OD

+ flashes / floaters x 2 days
56 yrs old
Healthy → + statin
Va 20/20 od 20/30- os
NO APD
Penlight brightness / Red cap normal
F: Large Weiss Ring → Acute PVD





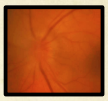


68

Sudden Flashes and Floaters OD
Dr. Tia Tucker
OSU Disease Resident (2009-10)

F: + PVD
1. secondary ON edema (trauma)
a) Etiology → very strong vitreo-retinal tractionprior to his PVD, esp at the ON head

RTC 4 weeks
a) 20/20 OU , NO Optic nerve edema OS



69

The End !

- Thank you !!!!!!!!!!!!!!
- David L Bejot OD
- Cell 419-343-6750
- Email dllbtecot@yahoo.com
- dbejot@specialtyeyeinstitute.com

70