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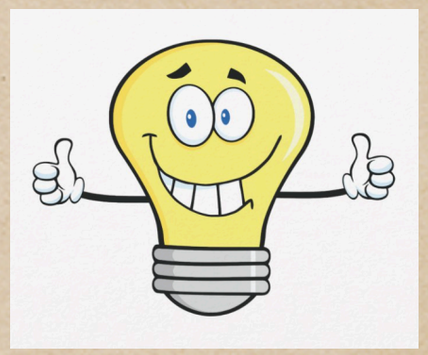
Case Report

- 68 years old white male with h/o recurrent sinusitis for many years
- h/o FESS for nasal polyps 1995 outside ENT
- Left maxillary tooth cyst removed 2001 by oral surgeon
- 2 months of right maxillary/periorbital pain/pressure, loss of smell, headache, nausea, vomiting(denies nasal obstruction, cough, vision change, diplopia, fever)

Case Report

- Underwent right concha bullosa mucocele resection/decompression and FESS without improvement in symptoms
- Neurologist treated maximally for migraine headache without success

Case Report



- Patient mentioned scalp tenderness
- ESR = 62
- CRP = 64.7
- Bilateral temporal artery biopsy positive for GCA
- Symptoms resolved on prednisone 60mg/day
- Referred to rheumatologist...

Giant Cell Arteritis (GCA)

GCA is preferred nomenclature over Temporal Arteritis

- Delay in diagnosis leading to complications

  (mean delay in diagnosis = 1.5 months)

- Diagnostic uncertainty
- Morbidity of treatment

Important to not delay diagnosis vs morbidity of steroids with empiric treatment

Giant Cell Arteritis (GCA)

- Most common form of systemic vasculitis affecting patients over 50 years and incidence increases with age (15-25 cases per 100,000)
- Characterized by granulomatous involvement of large and medium sized blood vessels of the aorta with predilection for the extracranial branches of the carotid artery
  - Inflammation of medium arteries causes occlusion
  - Wall destruction of large arteries causes aneurysm, dissection, and rupture (17x more likely to develop thoracic aortic aneurysm and 2.4x more likely to develop AAA.

Demographics of GCA

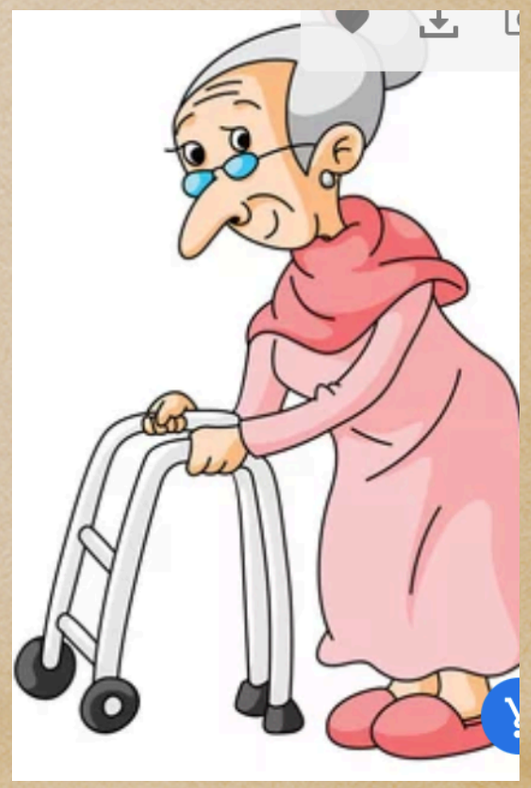
- 2:1 female to male ratio (64% F vs 36% M)
- Mean age 70 years old (incidence increases with age)
- White 74% (Scandinavian countries), Black 18%, Hispanic 6%, Asian 1.6%
- 15-30 cases per year per 100,000 > 50 yrs age
- associated with HLA-DRB1*04 possible genetic

Giant Cell Arteritis (GCA)

- Overlapping conditions of
  - Cranial GCA
  - Extra cranial GCA (large-vessel GCA)
  - Polymyalgia rheumatica (PMR)

50% of GCA patients also have PMR

20% of PMR patients also have GCA



Symptoms of GCA

- New onset headache (60%) (anywhere over the head) **PPV=46%**
- Jaw/tongue/palate claudication (23%) **pathognomonic, odds ratio=9, PPV=78%**
- Visual symptoms/ocular findings (35%)
- Temporal artery exam finding (53%) such as TA beading, prominence, or enlargement
- Polymylagia rheumatica (27%)
- Synovitis (12%), fatigue, fever, anorexia, low grade fever, weight loss, dry cough
- Scalp tenderness (allodynia) or necrosis **PPV=61%**
- Constitutional symptoms (50%) - fever, fatigue, night sweats, anorexia, weight loss
- Jaw claudication + scalp tenderness + new headache **PPV=90%**
- **Jaw claudication + vision change PPV=100%**

Myklebust G et al. (1996) A prospective study of 287 patients with polymyalgia rheumatic and temporal arteritis: clinical and laboratory manifestations at onset of disease and at the time of diagnosis. Br J Rheumatol 35: 1161-8.

Polymyalgia Rheumatica

- pain & stiffness in proximal muscles (shoulders/hips) worse in morning & after exertion abrupt onset peaks in 2 weeks
- elevated ESR
- responds rapidly to low dose prednisolone (10 mg/day)
- can occur alone or with GCA

American College of Rheumatology
1990 Criteria for Giant Cell Arteritis

A score of 3 or more has a sensitivity of 93.5% and a specificity of 91.2%.

1. age > 50 years at onset
2. new onset of localized headache
3. temporal artery tenderness or decreased pulse
4. ESR > 50
5. TA biopsy showing necrotizing arteritis

Also scalp tenderness and claudication of jaw/tongue or on deglutition

Hunder et al. (1990) Arthritis Rheum 33(8):1122-8.

Modified ACR Criteria for Giant Cell Arteritis

1. age > 50 years
2. h/o ESR>50 or CRP>24.5

Plus at least one of the following:

1. Unequivocal cranial GCA symptoms (new headache, scalp tenderness, vision loss, jaw claudication)
2. Unequivocal symptoms of PMR (shoulder/hip pain with inflammatory stiffness)

Plust at least one of the following:

1. Positive TAB
2. Large vessel vasculitis on imaging

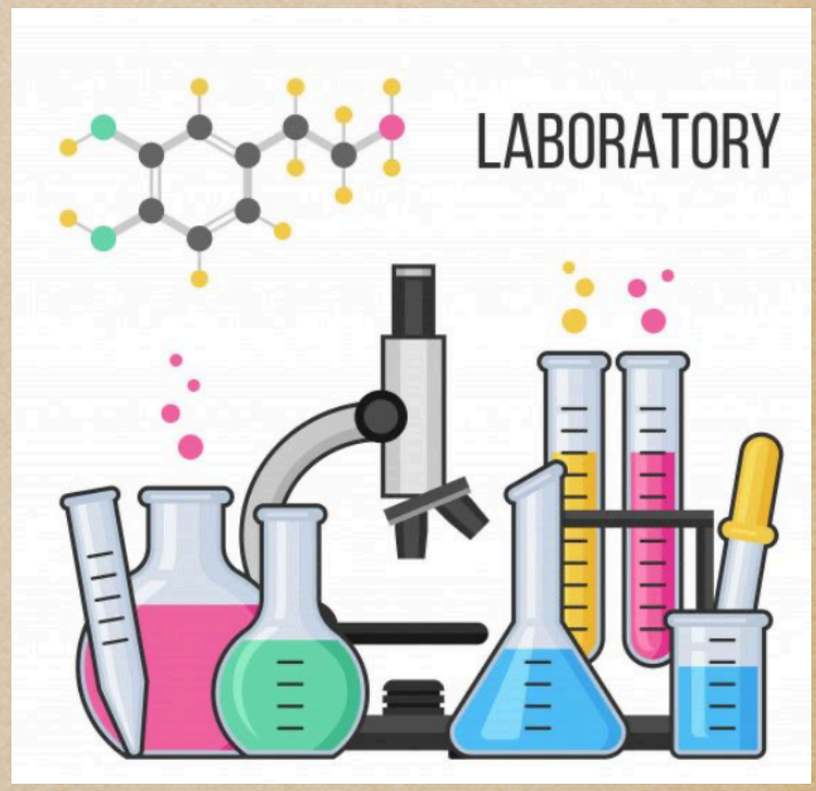
Hunder et al. (1990) Arthritis Rheum 33(8):1122-8.

Complications of GCA

- Carotid stenosis
- Thoracic and abdominal aneurysm
- Stroke (2-7%) vertebrobasilar artery (75%)
- Tongue/scalp necrosis
- Diplopia, amaurosis fugax, blindness
- Vascular risk 2.75x increased risk of M.I.

Labs for GCA

- Normocytic anemia (hgb < 12) 55%
- Leukocytosis (>11,000) 28%
- Elevated alkaline phosphatase 25%
- Low albumin (<3) 28%
- *Thrombocytosis (>400k) 49%
- *Mean ESR 93 (high ESR >20)
- *Mean CRP 94 (high CRP >2.45)



Medicine September, 2005 84(5) 277-290

Odds Ratio of Positive Biopsy

- 1.5x greater with ESR 47-107
- 4.2x greater with platelets > 400,000
- 5.3x greater with CRP > 2.45

Brittain GPH et al. Br J Ophthalmol (1991) 75, 656-659.

Normal ESR & CRP in GCA

- multi-center review 119 patients TAB positive
- Sensitivity of ESR & CRP together was 99%
- Both are elevated in most patients (93.4%)
- normal ESR with elevated CRP (1.6%)
- elevated ESR with normal CRP (1.7% - 3.7%)
- 1-4% of GCA on TAB had both normal ESR & CRP

1. Parikh M et al (2006) Prevalence of a normal C reactive protein with an elevated erythrocyte sedimentation rate in biopsy-proven giant cell arteritis. Ophthalmology 113 (10): 1842-5
2. Poole TR et al (2003) Giant cell arteritis with a normal ESR and CRP. Eye 17(1): 92-3.
3. Myklebust G et al. (1996) A prospective study of 287 patients with polymyalgia rheumatic and temporal arteritis: clinical and laboratory manifestations at onset of disease and at the time of diagnosis. Br J Rheumatol 35: 1161-8.
4. Kermani TA et al (2012) Utility of ESR and CRP for the diagnosis of GCA. Semin Arthritis Rheum. 4(6):866-871.

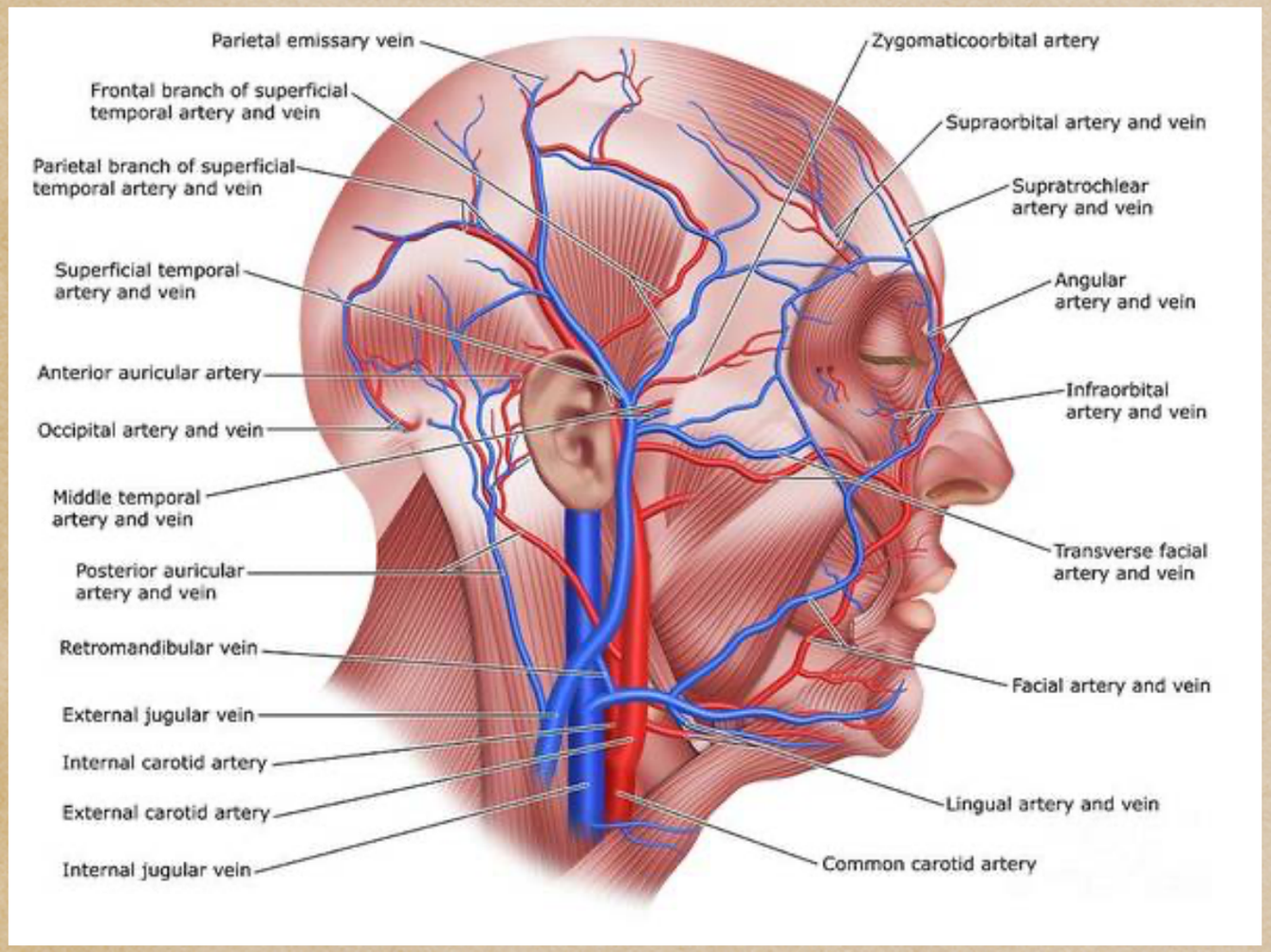
Biopsy of Temporal Artery

- TAB is gold standard for diagnosis of GCA
- Sensitivity of TAB = 87%
- 15% of GCA will be biopsy negative
- TAB removes later doubt about diagnosis
  - If treatment causes complications
  - If patient fails to respond to therapy

Niederkohr RD et al. Invest Ophthalmol Vis Sci. 2007; 48(2):675-80.

Biopsy of Temporal Artery

Risks of surgery include facial nerve injury & scalp necrosis.



Unilateral vs. Bilateral Biopsy?

- Unilateral *if the specimen length and processing are adequate 3 studies:
  - 1. concordance rate of two sides = 99%

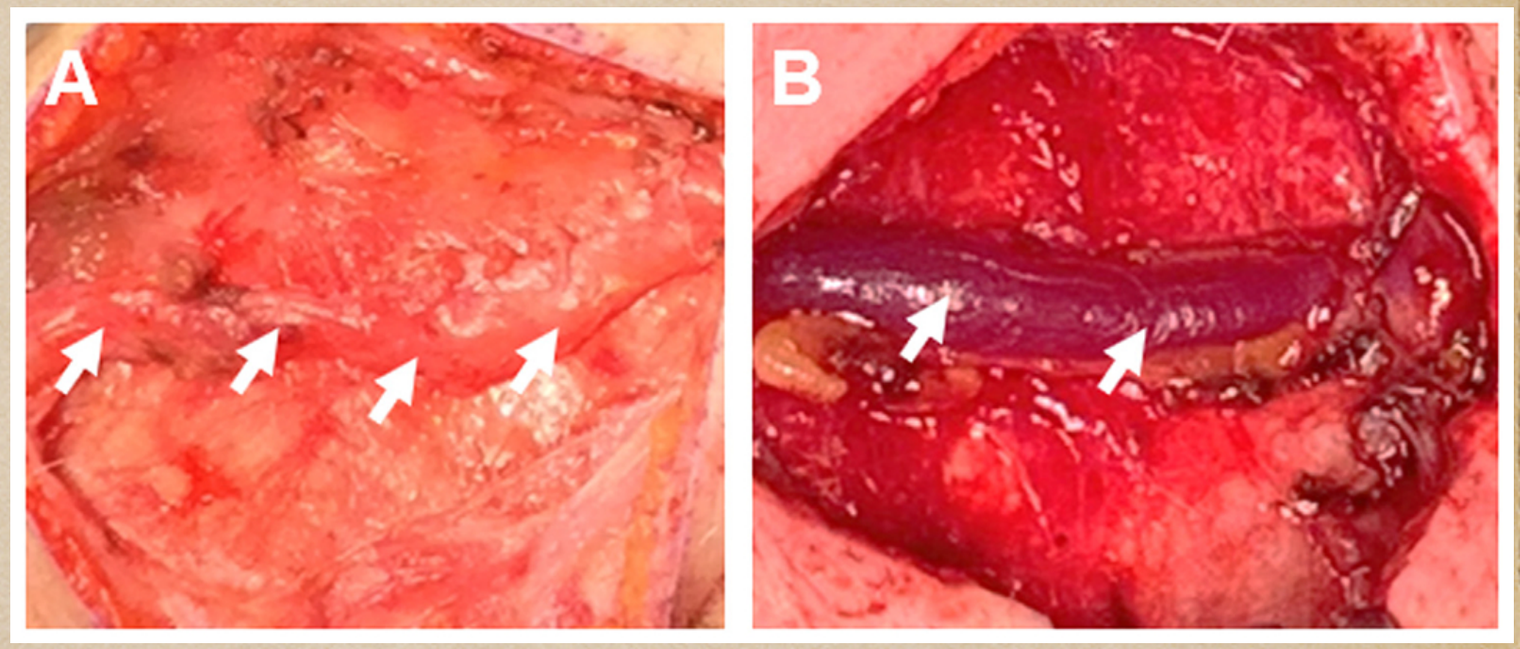
    Danesh-Meyer H et al. Low diagnostic yield with second biopsies in suspected giant cell arteritis. J Neuroophthalmol (2000), 20(3):213-5.
  - 2. concordance rate of two sides = 97%

    Boyev LR et al. Efficacy of Unilateral Versus Bilateral Temporal Artery Biopsies for the Diagnosis of Giant Cell Arteritis. Am J Ophthalmol (1999), 128(2):211-215.
  - 3. concordance rate = 94.1%, 439 patients in 4 studies,

    Hayreh et al. Management of GCA: our 27-year clinical study: new light on old controversies. Ophthalmologica 2003; 217: 239-59.

    TAB should be done on symptomatic side

Surgeon's Intraop Findings



- Thick artery
- Pale artery
- Occluded lumen
- Nodular & tortuous artery
- Minimal bleeding/back flow
- 4-5 considered grossly positive, 2-3 indeterminate, <2 negative.
- Specificity 97.9%; accuracy 98.2%. (retrospective study of 108 patients)

Ophthal Plast Reconstr Surg Vol.24 (5) 2008, 372-377.

Shrinkage

(of temporal artery biopsy specimen)

- Mean shrinkage of specimen 15%
- Biopsy should be at least 2.5 cm length (segmental involvement/skip lesions)
- Proper meticulous sectioning of specimen by pathologist is required

Ophthal Plast Reconstr Surg Vol. 28 (4) 2012, 261-263

Pathologic Findings of Temporal Artery Biopsy

- Typical temporal arteritis (49%)
  - transmural inflammation with T lymphocytes and macrophages
  - at least one giant cell with mixed mononuclear cells (lymphocytes, histiocytes, and plasma cells)
- Atypical temporal arteritis (51%)
  - inflammation without giant cells or
  - inflammation mainly in the adventitia (rather than media)

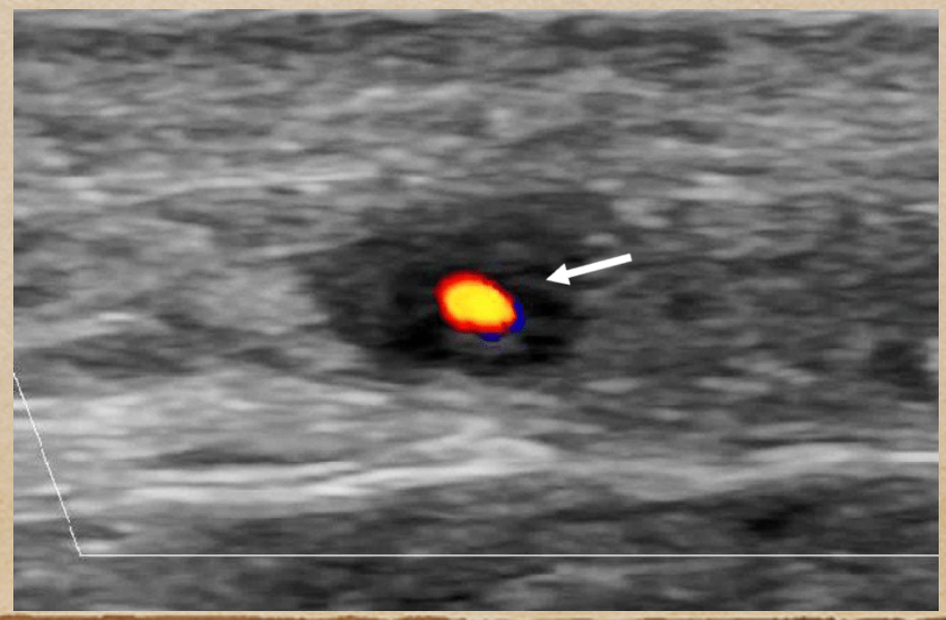
Does Previous Steroid Treatment Affect Biopsy Findings?

- Mayo study 535 patients
- Biopsy shows arteritis even after more than 14 days of steroids!
- Untreated group had biopsy positive rate of 31%
- Treated group had biopsy positive rate of 35%
- Trend towards atypical path with higher dose/longer duration of steroid therapy but arteritis was still detectable.

Achkar AA et al. How Does Previous Corticosteroid Treatment Affect the Biopsy Findings in Giant Cell (Temporal) Arteritis? Ann Intern Med 1994; 120: 987-992
Narvaez J et al (2007) Influence of previous corticosteroid therapy on temporal artery biopsy yield in giant cell arteritis. Semin Arthritis Rheum 37(1): 13-19.

Imaging Options for GCA

- Ultrasound - halo sign - sensitivity 68%, specificity 91% (bilateral halo 100% specificity)
  - Requires expertise in US for GCA; recommended over TAB if available
- Must be done before starting treatment (unlike TAB)



Vision loss in GCA

- Risk factors for visual loss in giant cell (temporal) arteritis: a prospective study of 174 biopsy proven patients.
- Transient ischemic visual symptoms 28% with permanent vision loss in 13%.
- Risk factors for permanent visual loss
  - 1. Prior transient visual ischemic symptoms (odds ratio 6.3)
  - 2. Thrombocytosis - platelet count > 400k (OR=3.7)
  - 3. Age
  - 4. Jaw claudication
- Lower CRP & ESR - more common with vision loss

Liozon E., et al Am J Med. 2001 Aug 15;111(3):211-7.

Vision loss in GCA

- Visual recovery is uncommon
- Visual deterioration can occur despite high dose (250mg solumedrol q 6 h) IV steroids (3%) greatest risk is in the first 6 days
- Pale swollen optic disc with flame-shaped hemorrhages, cupping of optic disc
- Loss of vision, visual field defects, complex visual hallucinations, loss of color vision, ptosis, diplopia, tonic pupils.

Ophthalmic manifestations of giant cell arteritis. Br J Hospital Medicine, January 2011, Vol 72, No. 1, 26-30.

Vision loss in GCA

- 185 patient retrospective study
- 41 (22%) with vision loss
  - 46% unilateral, 37% sequential, 17% simultaneous
- Sequential eye involvement was only seen with oral steroid treatment (not IV)
- In patients with vision loss (treated with IV)
  - **34% improved**, 49% unchanged, 17% worsened
  - acuity (15%) may improve without better visual fields (5%)

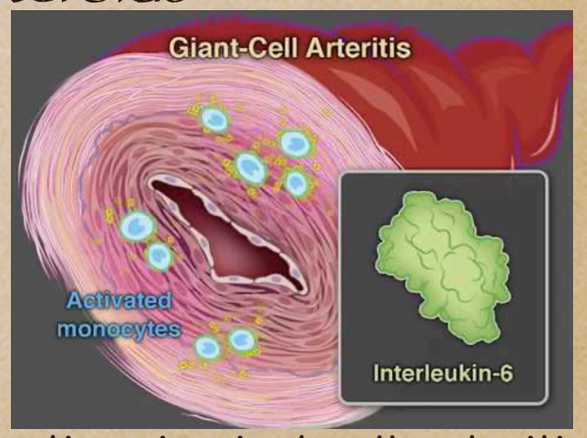
Visual Morbidity in Giant Cell Arteritis. Ophthalmology, November 1994, Vol 101(11), 1779-1785.
Poor Prognosis of Visual Outcome after Visual Loss from Giant Cell Arteritis. Ophthalmology, June 2005, Vol 112(6), 1098-1103.

Vision loss in GCA

- 80% of vision loss is due to Anterior Ischemic Optic Neuropathy (AION) - occlusion of posterior ciliary artery -> optic nerve head
- 10% Posterior Ischemic Optic Neuropathy (PION) - occlusion of collaterals off the ophthalmic artery -> optic nerve away from retina so not fundoscopically visible
- 10% Central Retinal Artery Occlusion (CRAO)

Treatment of GCA

- Oral prednisone 1 mg/kg/day, up to max 60mg/day until symptoms and labs resolve, then very slow taper over 2 years due to high relapse rate. (Up to 80% relapse if steroids are stopped in one year.)
- Response to steroid is rapid (2-3 days)
- Low dose ASA with steroids can reduce incidence of CVA & vision loss
- Tocilizumab (IL-6 inhibitor)
  - 162mg weekly with slow steroid taper is superior to steroids alone.
  - only FDA approved drug for GCA
  - Reduces steroid exposure, reduces relapse,



Nesher G et al. (2004) Low-dose aspirin and prevention of cranial ischemic complications in giant cell arteritis. Arthritis Rheum 50(4): 1332-7.

Possible Future GCA Treatment Options

- Ustekinumab - binds IL-12/23 p40 Chron's & ulcerative colitis, case report in GCA
- Guselkumab IL-23 psoriatic arthritis, case report in GCA
- Secukinumab IL-17A, effective in GCA study of 52 patients
- ** Mavrilimumab immunoglobulin G4 blocks GM-CSF, effective in GCA study of 70 patients
- Ixekizumab IL-17A skin psoriasis and psoriatic arthritis, case report in GCA
- * Baracitinib (pill) Janus kinase inhibitor rheumatoid arthritis, effective in GCA study of 14 patients
- * Upadacitinib (pill) second generation Janus kinase inhibitor, case report in GCA
- Anakinra IL-1 blocker, 3 case reports in GCA
- Abatacept biologic, recombinant fusion protein - modulates activation of T cells, mildly effective in prospective study of 49 patients.

Costanzo, G et al. Giant cell arteritis and innovative treatments. Pharmacotherapy and evidence-based medicine. August 2023, Vol 23(4)

Top 10 Take Home Points for GCA

- 10. Check ESR, CRP, CBC, CMP
- 9. Normal ESR & CRP almost rules out GCA, but not completely (1-4%)
- 8. TAB has specificity and PPV of 100%, but sensitivity of 85%
- 7. Biopsy is ok within 2 weeks of starting steroids
- 6. Unilateral biopsy of 2.5cm length is sufficient, but proper processing of biopsy specimen is important

Top 10 Take Home Points for GCA

- 5. GCA patients will have negative biopsy 15% of time
- 4. 20% of GCA cases have loss of vision and may present without other symptoms of arteritis
- 3. Outpatient treatment is prednisone 1mg/kg/day and daily 81mg aspirin with weekly tocilizumab
- 2. Need inpatient high dose IV steroids for <u>any</u> transient visual symptom or platelets > 400k
- 1. No increase in mortality rate in steroid treated GCA patients (except aortic aneurysm/dissection patients)

Thank you!

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