Update On
Giant Cell Arteritis and Polymyalgia Rheumatica

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CME Disclosure Statements

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Unlabeled use of commercial products

To date, there are no therapeutic agents FDA approved for the treatment of giant cell arteritis or polymyalgia rheumatica

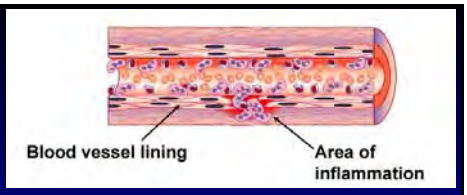
All references to use of a commercial product discussed in this presentation constitute an unlabeled use of the product

Speaker relationship to products discussed in this presentation

Bristol-Myers Squibb
Genentech
GlaxoSmithKline

} provide funding for clinical trials on which the speaker is an investigator

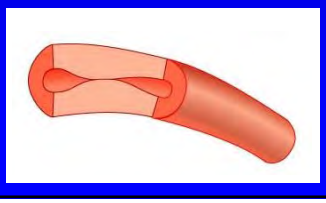
Vasculitis = Inflammation of the Blood Vessel



blood vessel damage

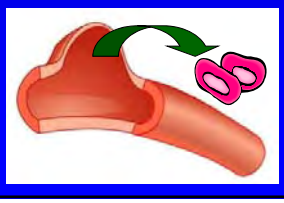
compromise of vessel lumen

organ ischemia

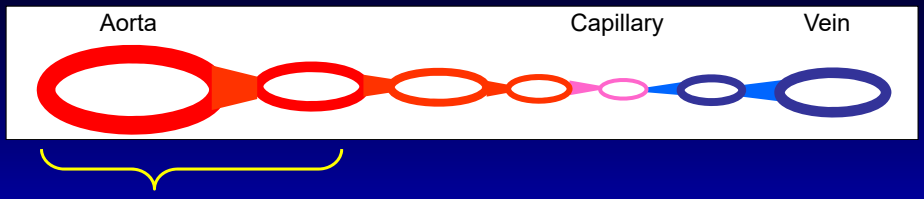


attenuation of vessel wall

aneurysm formation
hemorrhage



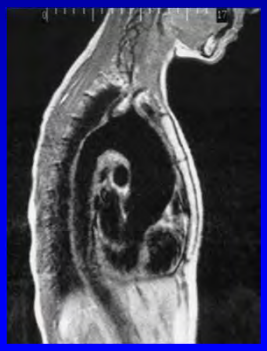
Vasculitis Can Affect Any Vessel



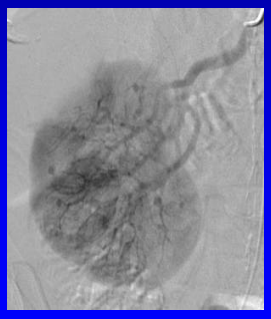
Large Vessel

Medium Vessel

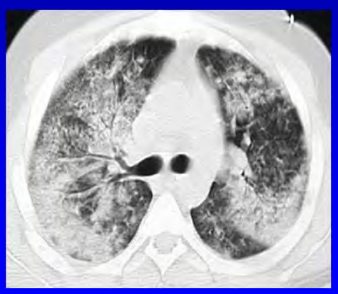
Small Vessel



Takayasu Arteritis



Polyarteritis nodosa



Microscopic polyangiitis

Large Vessel Vasculitis: Not Just One Disease

Primary Vasculitis

Unique disease entities in which vasculitis is occurring due to an as yet unknown cause

- Giant cell arteritis
- Takayasu arteritis
- Cogan syndrome
- Behçet's disease
- Kawasaki disease
- GPA (Wegener's)
- Microscopic polyangiitis
- EGPA (Churg-Strauss)
- Polyarteritis nodosa
- Isolated (focal) aortitis

Secondary Vasculitis

Vasculitis is occurring in the setting of an underlying disease or exposure

- Infection
  - Syphilis
  - Staphylococcus
  - Salmonella
  - Tuberculosis
  - Fungus
- Spondyloarthropathies
- Sarcoidosis
- Systemic lupus erythematosus
- Relapsing polychondritis
- Trauma
- Previous surgery
- Atherosclerosis

Giant Cell Arteritis
Epidemiology

- Has also historically been called temporal arteritis
- The most common form of systemic vasculitis - 26 per 100,000
- Occurs in people over the age of 50 (average age in 70's)
- 2:1 Female:Male
- Granulomatous vasculitis

Weyand, et al. NEJM 2014;371:50
Buttgereit et al. JAMA 2016;351:2442

GIANT CELL ARTERITIS

Giant Cell Arteritis
Polymyalgia Rheumatica

Clinically characterized by:

- Age ≥ 50 years
- Bilateral shoulder aching
- Increased ESR and/or CRP

required

* • Hip girdle pain/aching
* • Morning stiffness > 45 minutes
* • Typical absence of other joint involvement
* • Absence of RF and anti-CCP
- Prompt response to prednisone 10-20 mg daily

* = 2 points
* = 1 point

PMR = all required + either
- 4 points without ultrasound
- 5 points with ultrasound

Diagnosis:

- No definitive lab or imaging findings
- Diagnosis based upon compatible features and ruling out other processes

2012 Classification criteria for PMR *(Dasgupta et al. A&R 2012)*

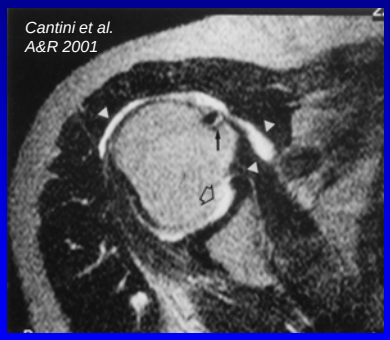
- Not intended for diagnosis of the individual patient
- Based on clinical features ± ultrasound findings

Polymyalgia Rheumatica
Utility of Ultrasound for Diagnosis

Ultrasound has long been known to demonstrate findings in PMR

Subacromial / Subdeltoid bursitis *(Salvarani et al. Ann Int Med 1997)*

- Although ultrasound was used in the 2012 Classification criteria for PMR it includes options without ultrasound *(Dasgupta et al. A&R 2012)*
- Ultrasound does not distinguish between PMR and other causes of bursitis



Role of ultrasound in PMR continues to evolve
Ultrasound by itself is not diagnostic for PMR
Ultrasound does not need to be routinely performed for possible PMR

Giant Cell Arteritis
Polymyalgia Rheumatica

PMR can occur as an isolated entity or as part of GCA

Hernández-Rodriguez et al. Medicine 2007;86:233

– 73 patients where PMR preceded GCA
– 20% developed ischemic complications (16 visual, 3 stroke, 1 large vessel)

Aortitis and cranial arteritis can occur later in patients with PMR

Giant Cell Arteritis
Systemic / Inflammatory Disease

Symptoms and Signs

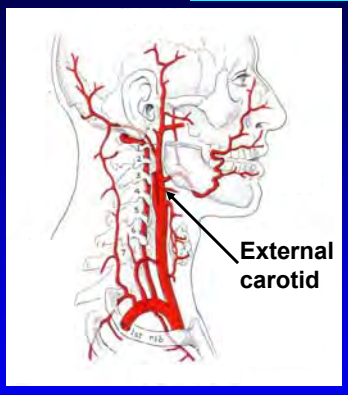
- Fever
- Night sweats
- Fatigue, malaise
- Anorexia, weight loss

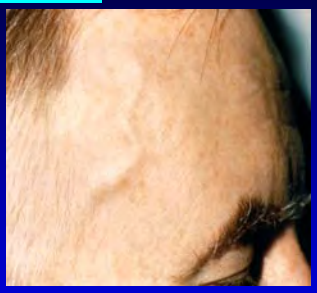
Laboratories

- CBC: anemia, leukocytosis, thrombocytosis
- Increased CRP
- Increased ESR

Can accompany PMR, cranial, or large vessel presentations
but
Can also occur in isolation as a presenting phenotype of GCA

Giant Cell Arteritis
Cranial Disease



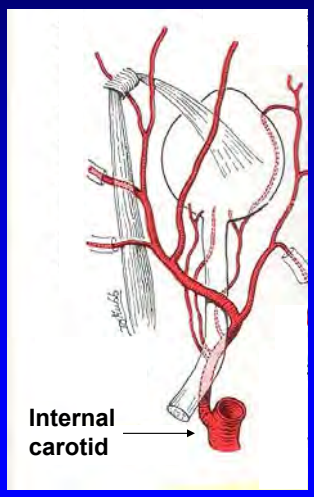


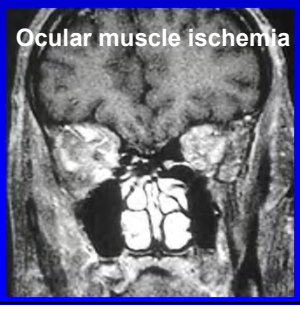
Symptoms and signs

- headache
- temporal artery abnormalities
- jaw and/or tongue claudication
- scalp tenderness and/or ischemia

Giant Cell Arteritis
Cranial Disease

Visual Features





Giant Cell Arteritis
Cranial Disease

- Most dreaded clinical manifestations of cranial disease:

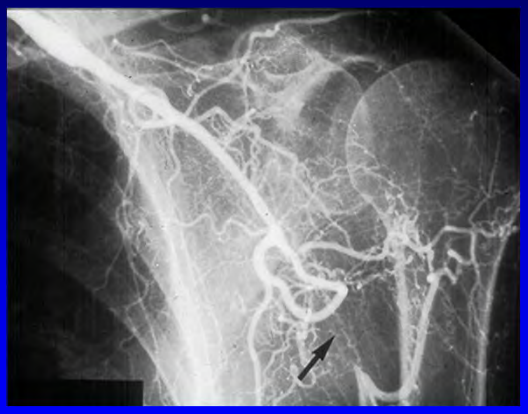
  Cranial ischemic complications (CIC)

  Ischemia of tissue due to vessel occlusion
  - visual loss - 14% (6-42%)
  - stroke - 3-8%
  - tongue ischemia
  - scalp ischemia

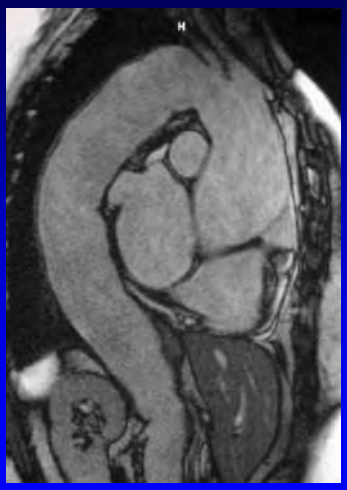
- Risk factors for permanent CIC
  - transient CIC (amaurosis fugax, diplopia, TIA)
  - prior CIC

Cid et al. Arth Rheum 1998;41:26
Gonzales-Gay et al. Arth Rheum 1998;41:1497
Nesher et al. Medicine 2004;83:114

Giant Cell Arteritis
Large Vessel Involvement



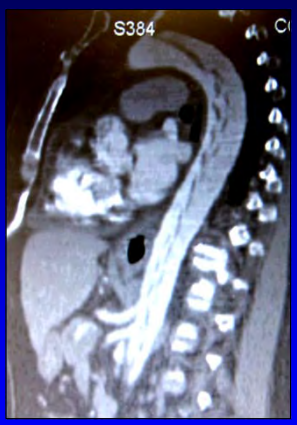
Subclavian Artery Stenosis



Thoracic Aortic Aneurysm

Giant Cell Arteritis
Large Vessel Involvement

Evans et al. Arthritis Rheum 1994; 37:1539
Evans et al. Ann Intern Med 1995; 122:502



Thoracic aortic aneurysms (TAA)
Abdominal aortic aneurysms (AAA)

- AAA 2.4 x more likely than the general population
- TAA 17.3 x more likely than the general population
- TAA can occur late and have serious outcomes that may be fatal
- In those who had surgery only 50% had active inflammation

Giant Cell Arteritis
Large Vessel Involvement

Nuenninghoff et al. Arthritis Rheum 2003; 48:3522 and 3532

168 GCA patients - 27% had large vessel complications

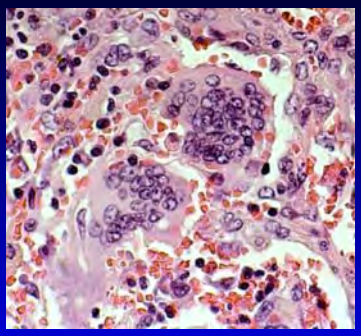
18% aortic aneurysm (1 out of every 5)

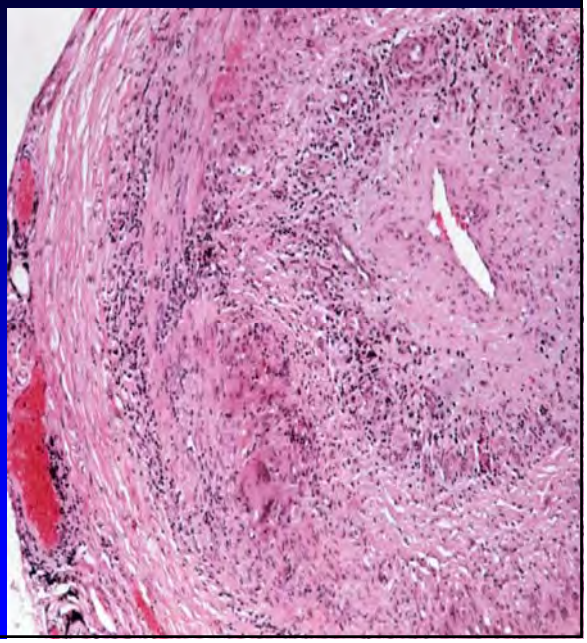
13% large-artery stenosis (1 out of every 8) { subclavian, carotid/vertebral, iliac

No difference in overall mortality rate in those with large-artery involvement
Thoracic aortic dissection in GCA is associated with increased mortality

Large vessel disease is not uncommon in GCA
Awareness of thoracic aortic aneurysm risk is important

Giant Cell Arteritis – Temporal Artery Biopsy





Positive in only 30-70%

(In large vessel disease positive in < 30%)

Giant Cell Arteritis
What Factors Are Associated with a Positive Biopsy ?

Smetana and Shmerling. JAMA 2002;287:92

Meta-analysis of 21 studies from 1966-2000
2680 patients who had a temporal artery biopsy – 39.2% positive

Not discriminatory:
- Headache
- PMR
- Visual symptoms (except diplopia)

Most powerful predictors of (+) biopsy:
- Jaw claudication
- Diplopia
- Abnormal temporal artery by physical exam

Giant Cell Arteritis
Does Treatment Influence Biopsy Results ?

Achkar et al. Ann Internal Med 1994;120:992.

535 patients with temporal artery biopsies 1988-1991

- (+) biopsies were found in:
  - 31% who did receive prednisone before biopsy
  - 35% who did not receive prednisone before biopsy

- Arteritis could still be detected after 14 or more days of treatment

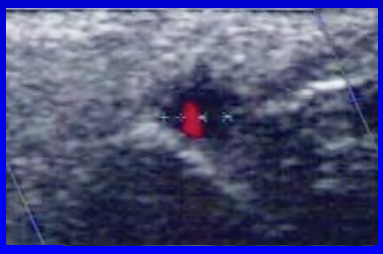
Provide support that glucocorticoid treatment should not be delayed in patients where there is a high degree of suspicion for GCA

Giant Cell Arteritis
Utility of Ultrasound

Color Duplex Ultrasonography

Hypoechoic Echo

Corresponds to a dark area
around the lumen of an inflamed artery



Transverse section

Longitudinal section

Karahaliou et al. Arth Care and Res 2006

Giant Cell Arteritis
Utility of Ultrasound

Schmitt et al. NEJM 1997;337:1336
- 73% of GCA and 0% controls had a halo around the lumen of the temporal artery
- In patients with typical features and halo, biopsy may not be necessary

Salvarani et al. Ann Internal Med 2002;137:232
- 86 patients with suspected GCA who had ultrasound and biopsy
- Halo did not improve diagnostic accuracy beyond physical exam

Karassa et al. Ann Internal Med 2005;142:359
- Meta-analysis of 23 studies examining ultrasound in GCA
- Cautious interpretation based on clinical features, pretest probability is imperative

Ultrasound is a very user dependent technique

This together with the available data raises concern about the ability of ultrasound to diagnose GCA in most clinical practices

Giant Cell Arteritis
General Approach to Disease Monitoring

History
- Cranial, PMR, large vessel, constitutional symptoms

Physical Examination
- Temporal arteries
- 4 extremity BP
- Peripheral pulse inequality
- Auscultation – cardiac for insufficiency murmurs, vascular for bruits

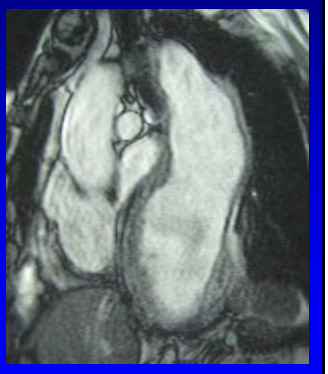
Laboratories
- On medications: chemistries, CBC, ESR, CRP every month
- On no medications: CBC, ESR, CRP every 1-3 mo

Imaging
- CXR annually
- CTA or MRA for any features of large vessel disease
- CTA or MRA for known large vessel disease every year

There remains no definitive means of accurately determining active disease

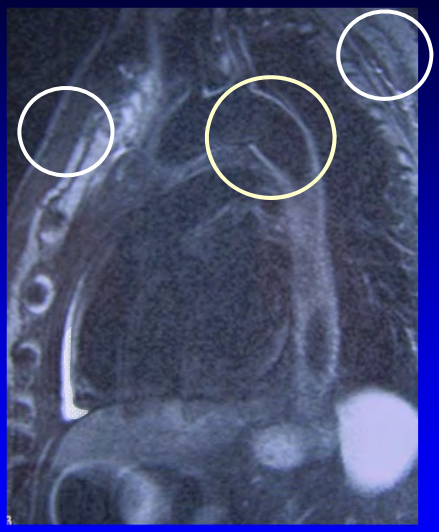
Giant Cell Arteritis
Large Vessel Imaging - Arteriography

Catheter–directed dye arteriogram
- Central pressure measurements
- Intervention
- Precise definition of anatomy (distal lesions)

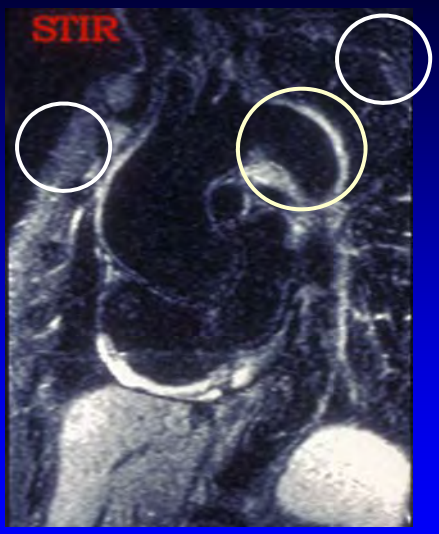


CTA or MRA
- Non-invasive
- Visualization of whole large vessel tree
- Allows imaging of the vessel wall

MR to Assess the Vessel Wall



Isointense compared to muscle
No Edema



Hyperintense compared to muscle
Edema – (? Inflammation ?)

Giant Cell Arteritis
Large Vessel Imaging - MRI

Are vessel wall changes (signal intensity)
useful to serially assess disease activity in large vessel vasculitis ?

Tso et al: Arthritis Rheum 2002;46:1634

Study of large vessel changes by MRI in Takayasu arteritis

Vessel wall edema seen in:

- 94% active disease
- 81% uncertain disease activity
- 56% apparent clinical remission

55% had vessel wall edema by serial MR without new vascular lesions

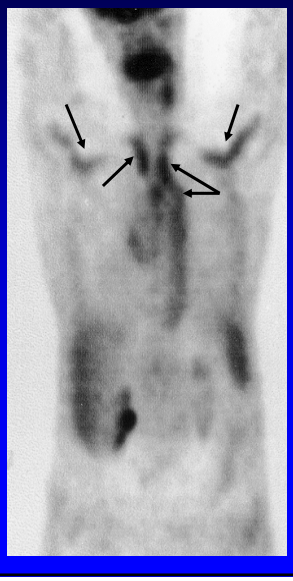
Absence of edema was also seen in patients who had active disease

Raises doubts about utility of edema on MRI to assess disease activity

Giant Cell Arteritis
Large Vessel Imaging - PET

Positron Emission Tomography (PET)

Utilizes radiolabeled fluorodeoxyglucose (FDG) to visualize metabolically active tissue.



Utility of PET for Diagnosis of GCA

Blockmans et al. Rheumatol 1999;38:444

- Pre-treatment GCA (n=6), PMR (n=5) and 23 controls
- Thoracic aorta uptake: 4/6 GCA, 4/5 PMR, 1/23 control

Prieto-Gonzáles et al. ARD 2014

- 32 patients GCA, prednisone < 3 days, 20 controls
- Sensitivity 80%, specificity 79% for GCA

Could PET be useful for monitoring in GCA ?
Is PET useful in long-term disease ?

Giant Cell Arteritis
Large Vessel Imaging – MRI and PET

Both et al. Ann Rheum Dis 2008;67:1030

- Evaluated MRI/PET for measurement of disease activity in 25 patients with complicated GCA who had received immunosuppressive therapy
- MRI was only valuable for stenoses or aneurysms (lumenography)
- MRI/PET showed no statistical correlation with ESR/CRP or BVAS

Questions the reliability and utility of MRI/PET as a measure of disease activity in patients who have had long term disease

Giant Cell Arteritis
Relationship with Takayasu Arteritis

Are Takayasu arteritis and Giant cell arteritis related diseases ?

Unknown

Similarities:

- Involvement of large vessels
- Histologic evidence of granulomatous inflammation

Differences:

- Age of involvement
- Distribution of vessel involvement
- ? Treatment response

Maksimowicz-McKinnon K et al. Medicine 2009;88:221

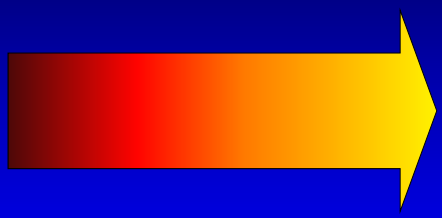
Giant Cell Arteritis
Treatment Goals

1. Prevent serious morbidity and/or mortality
2. Reduce symptoms that affect quality of life
3. Stop disease relapse
4. Avoid treatment-induced toxicity

Giant Cell Arteritis
Treatment

1950

Prednisone
+
Aspirin



2016

Prednisone
+
Aspirin

What is the data for their use ?

Why have alternatives not yet been identified ?

Giant Cell Arteritis
Treatment with Glucocorticoids

Shick et al. 1950

- Mayo Clinic – first report of use and benefit

Birkhead et al. 1957

- B/L blindness went from 17% to 9% after glucocorticoid introduction

Ross Russell 1959

- Visual failure 38% salicylates versus 0% glucocorticoids

Aiello et al. 1993

- 1% probability of visual loss after initiating glucocorticoids

Compelling evidence that glucocorticoids protect vision

Giant Cell Arteritis
Data for Initial Glucocorticoid Dose

Retrospective Series from the 1970-1980's

1st Author	Prednisone (PD) or Prednisolone (PN) dose (in mg)
Fauchald	PD 40-60
Sorensen	PD 30-60
von Knorring	PN 30-40
Fernandez-Herlihy	PD 40-80
Graham	PD 80
Bengtsson	PN < 20-60

Formed the basis for initial use of prednisone 40-60 mg daily

Prospective trials since have largely used prednisone 40-60 mg daily

Giant Cell Arteritis
Data for Initial Glucocorticoid Dose

Use of Low Dose Prednisone (20 mg daily)

- Effective dose for PMR
- Data for use in GCA in retrospective series
  ? Influence of clinical picture on dosage chosen
- There have been no prospective trials of safety and efficacy

Current data favor initial use of prednisone 40-60 mg daily
to prevent visual and vascular complications

Giant Cell Arteritis
Relapse and Duration of Glucocorticoid Treatment

Relapse rate:

Estimation of relapse rate has been variable based upon how it is defined

From retrospective series	Relapse rate 26-90%
Recent prospective trials	Relapse rate 75-90%

Treatment Duration:

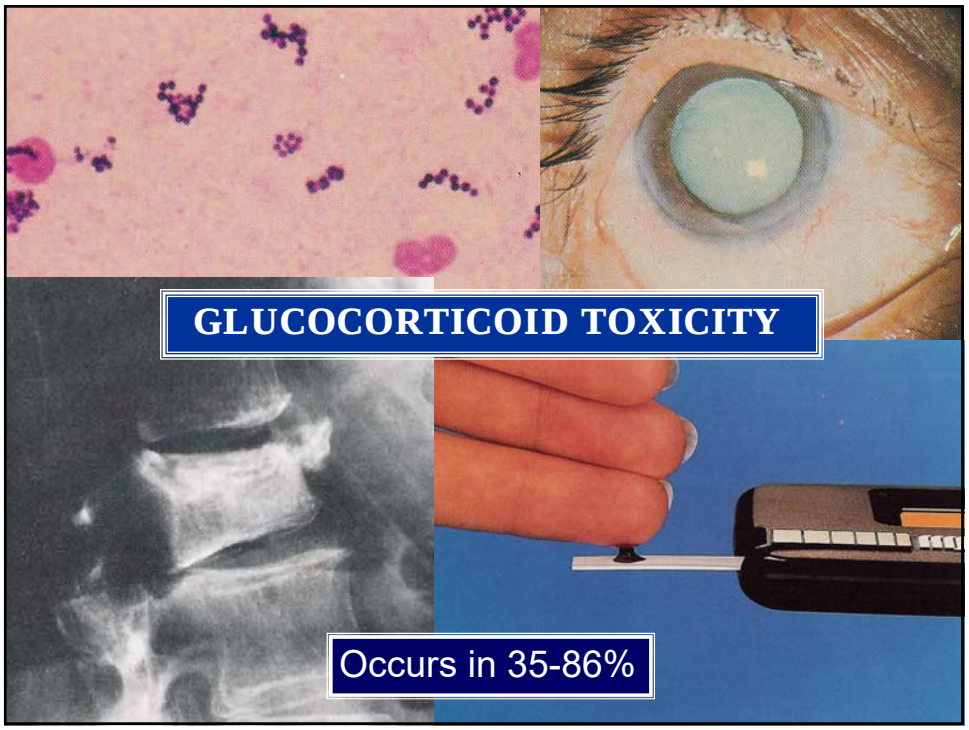
From historical series: Duration is typically over 2 years, for many is over 4

Proven et al. Arthritis Rheum 2003;49:703

125 patients, 87 followed to discontinuation of prednisone

- Time to discontinuation: median 22 months (range 2.3-122 months)

Glucocorticoids do not prevent disease recurrence and
an extended treatment duration is required in most patients



Giant Cell Arteritis
Role of Pulse Methylprednisolone (IV MP)

Are there toxicity/relapse benefits to starting all patients on IV MP ?

Mazlumzadeh et al. Arthritis Rheum 2006;54:3310

- 27 patients randomized to IV MP or placebo then prednisone 40 mg/d
- Higher number taking ≤ 5 mg prednisone at 36 weeks in the IV group (p=0.003)
- Higher number of sustained remissions in the IV group
- Only 6 of 14 in IV MP group were able to sustain remission without prednisone
- IV MP did not reduce frequency of prednisone side effects
- Insufficient evidence for IV MP to become standard treatment in all patients

When is IV MP (1 g/day x 3 days) commonly used in practice ?

- Vision loss in one eye (to protect vision in the other eye)
- Transient vision loss or diplopia
- TIA or other fixed or transient cranial ischemic events

Is IV MP more effective than prednisone 40-60 mg/d ?

- Unclear – no comparative studies
- Risk versus benefit must be weighed in the individual patient

Giant Cell Arteritis
Role of Acetylsalicylic Acid (ASA)

Nesher et al. Arthritis Rheum 2004;50:1332

175 patients retrospectively reviewed for cranial ischemic complications (CIC)

- ASA treated patients were 5x less likely to have CIC prior or after diagnosis
- CIC developed in 3% of ASA-treated patients vs 13% (P=0.02)

Only 10 patients would need to be treated with ASA to prevent one CIC

Lee et al. Arthritis Rheum 2006;54:3306

143 patients retrospectively reviewed for ischemic complications

- 16% on therapy had an ischemic event compared to 40% not on therapy
- No increase in risk of bleeding complications

In patients without contraindications, ASA 81 mg/day appears to provide adjunctive benefit in the treatment of GCA

Giant Cell Arteritis
Methotrexate

Jover et al. Ann Int Med 2001		*Hoffman, INSSYS. A & R 2002*
48	Patients	98
Single center, RDBPC	Design	Multi-center, RDBPC
MTX = placebo	Disease related serious morbidity	MTX = placebo
MTX < placebo (P=0.018)	Relapse	MTX = placebo (P=0.26)
MTX < placebo (P=0.01)	Cumulative GC dose	MTX = placebo
MTX = placebo	GC toxicity	MTX = placebo

Evidence does not suggest that MTX reduces the risk of GC toxicity

Methotrexate (MTX) in Giant Cell Arteritis

Mahr et al. Arthritis Rheum 2007; 56:2789

Methods:

Meta-analysis of:
- Jover et al. Ann Internal Med 2001;134:106
- Hoffman et al. Arthritis Rheum 2002;46:1309
- Spiera et al. Clin Exp Rheumatol 2001;19:495

Results:

- Have to treat 4 patients with MTX to prevent first relapse
- Have to treat 11 patients with MTX to prevent a cranial relapse
- MTX was associated with a reduction in cumulative steroid dose
- MTX did not reduce frequency of prednisone side effects

Absolute reduction in relapse by MTX is at best very modest

Decision to use MTX must weigh risk against small margin of benefit

Potential Disease Mechanisms in Giant Cell Arteritis

NEJM 2003

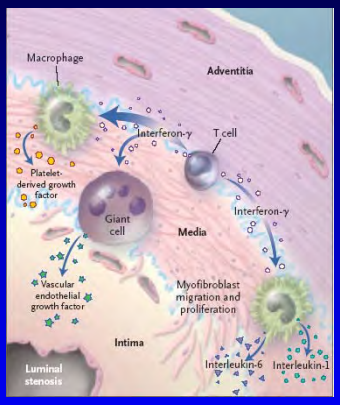
Evidence of GCA as an antigen driven disease

Macrophages

Dendritic cells

T lymphocytes

- *Brack et al. Mol Med 1997;3:530*
- *Weyand, Goronzy. NEJM 2003;349:160*
- *Ma-Krupa et al. J Exp Med 2004;199:173*

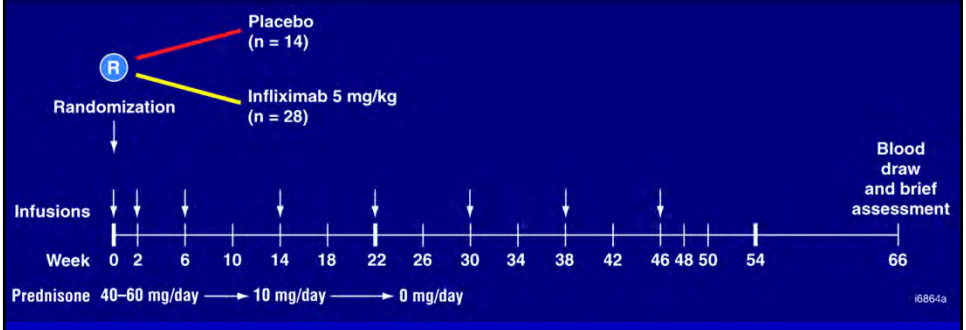


When TNF inhibitors became available in the late 1990's
There was interest in whether these would be effective in GCA

Infliximab in Giant Cell Arteritis

Hoffman et al. Ann Intern Med 2007; 146:621

Enrolled 44 patients with newly diagnosed GCA



- Primary Endpoint: proportion of relapse-free subjects through week 22
- Safety Endpoint: incidence of adverse events

Infliximab in Giant Cell Arteritis

Hoffman et al. Ann Intern Med 2007; 146:621

Efficacy:

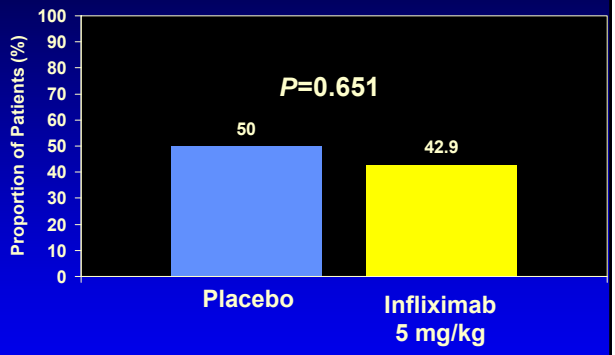
Proportion of Relapse-Free Subjects through Week 22

No difference in cumulative prednisone dose

Safety:

Infection:

- 71% infliximab
- 56% placebo



Infliximab does not provide benefit in the treatment of GCA

Also negative GCA trials with other TNF inhibitors:

- Etanercept *(Martinez-Taboada et al. ARD 2008;67:6254)*
- Adalimumab *(Seror et al. ARD 2013,July)*

Infliximab in Polymyalgia Rheumatica (PMR)

Salvarani et al. Ann Intern Med 2007; 146:631

Methods:

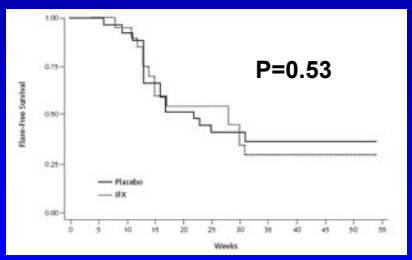
- 51 patients with newly diagnosed PMR
- All received prednisone 15 mg/d tapered to 0 mg/day over 16 weeks
- Randomized to receive: infliximab 3mg/kg at weeks 0, 2, 6, 14 and 22 vs placebo

Results:

No difference in placebo and infliximab:

- Relapse/recurrence at 52 weeks

- Relapse/recurrence at 22 weeks
- Proportion off steroids at week 22
- Total number relapse/recurrence
- Duration of prednisone
- Dose of prednisone
- Adverse events – 8 in each group



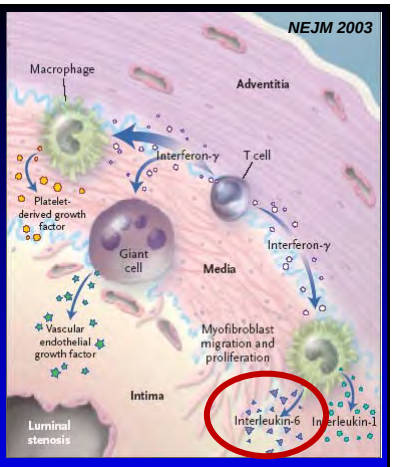
Infliximab does not provide benefit in the treatment of PMR

IL-6 in GCA

IL-6 has been of longstanding Interest in GCA

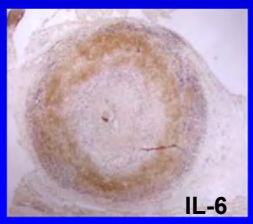
Utility as a acute phase reactant – variable

- *Dasgupta et al. Br J Rheum 1990;29:456*
- *Roche et al. A&R 1993;36:1286*
- *Weyand et al. A&R 2000;43:1041*
- *García-Martínez et al. AC&R 2010;62:835*



Expression and production in GCA tissue

- *Weyand et al. Ann Int Med 1994;121:484*
- *Hernández-Rodríguez et al. Rheum 2004;43:294*



Tocilizumab in GCA

Question: Could tocilizumab provide benefit in GCA ?

	GCA
Christidis et al. 2011	1
Seitz et al. 2011	5
Beyer et al. 2011	2
Sciascia et al. 2011	2
Salvarani et al. 2012	2
Vinit et al. 2012	1

	GCA
Besada et al. 2012	1
Unizony et al. 2012	7
Lurati et al. 2012	1
Işik et al. 2012	1
Ashraf et al. 2013	1
Loricera et al 2014	22

- Overall a beneficial response was observed
- 1 report of active vascular inflammation seen on histology despite treatment with tocilizumab *(Unizony et al. AC&R 2012;64:1720)*
- Supported the need for further study

Tocilizumab (Anti-IL6 Receptor)

Villiger PM et al. Lancet 2016; 387:1921-7

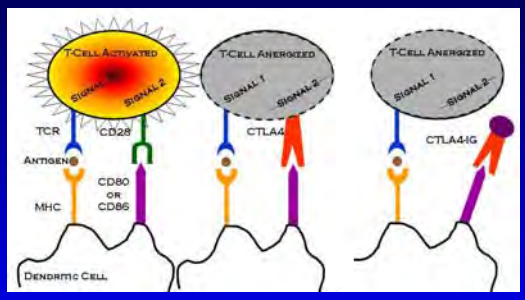
- Design
  - Phase 2 double-blind, newly diagnosed or relapsing GCA
  - Randomized 2:1 - 20 Tocilizumab/prednisone vs 10 placebo/prednisone
  - Standardized prednisolone taper – 1mg/kg/day to ~ 7 mg/day week 12
- Results
  - Week 12 remission: 85% Toc/pred vs 40% placebo/pred (p=0.05)
  - Week 52 remission: 85% toc/pred vs 20% placebo/pred (p=0.001)
  - Serious adverse events: 35% toc/pred vs 50% placebo/pred (p=0.46)
    - GI adverse events: 4 toc/pred (3 serious) vs 1 placebo/pred
- Challenges with tocilizumab in GCA:
  - Acute phase reactants (ESR and CRP) are suppressed by this agent
  - Potential for side effects (cytopenias, AST/ALT, lipids, GI perforation)
  - Not a replacement for prednisone – used together

Efficacy of anti-IL-6 is encouraging

Results from a large phase 3 study pending (GiACTA)

Abatacept in Giant Cell Arteritis

T cell activation has been felt to play an important role GCA



Abatacept (CTLA4-Ig)

Intervention with T cell activation

Studies of Abatacept in GCA and TAK (AGATA)

- Multicenter, randomized withdrawal design trial
- Presented at 2016 ACR late-breaking abstracts (*Langford et al. A & R 2016*)
- Further results to be provided in publication

Th17 Pathways in Giant Cell Arteritis

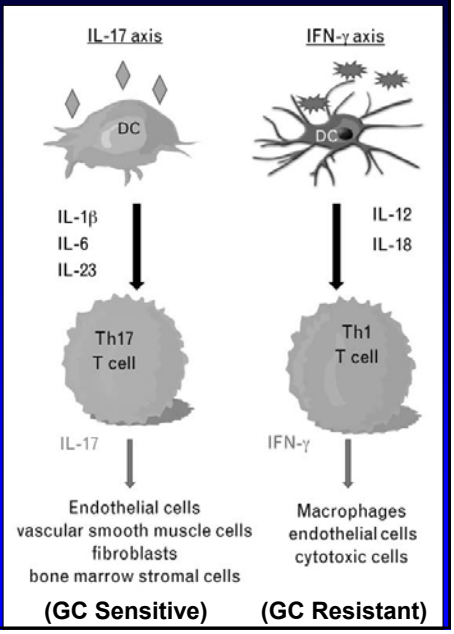
Deng et al. Circulation 2010;121:906

Examined Th17 pathways in peripheral blood and temporal artery biopsies

- Circulating Th1 and Th17 cells expanded
- Glucocorticoids (GC) suppressed IL-17 producing cells, spared cells secreting IFN-γ
- GC inhibited Th17 promoting cytokines and recruitment and survival of Th17 cells

Suggests that 2 distinct T cell subsets promote vascular inflammation in GCA

Future avenue for therapeutic investigation ?



What About B Cell Depletion in GCA ?

Interest in B cell based therapies was initially limited due to the paucity of evidence supporting their participation in pathogenesis

Hoyer et al. Ann Rheum Dis 2012; 71:75
- 17 TAK patients - observed disturbances of B cell homeostasis in which increased numbers of plasmablasts correlated with disease activity
- 3 patients with refractory TAK treated with rituximab achieved remission

Three other case reports of rituximab use in TAK and GCA
- *Bhatia et al. Ann Rheum Dis 2005; 64:1099*
- *Galarza et al. Clin Rev All Immunol 2008; 34:124*
- *Ernst et al. Case Rep Rheum 2012: Epub*

Unclear if rituximab warrants further study in GCA

No current clinical role for B cell depleting therapies in GCA

Is Treatment of GCA Large Vessel Disease Different ?

- Unknown
- Trials in GCA have almost exclusively involved cranial disease
- Might other agents play a greater role in GCA large vessel disease ?

ie: Methotrexate is used in Takayasu arteritis

- However -

Even in Takayasu, methotrexate use is based only on open-label trials

Currently, GCA large vessel and cranial disease is treated similarly
Potential exists for there to be differences in treatment responsiveness

Giant Cell Arteritis
Non-Medical Management of Large Vessel Disease

Surgical treatment for sequelae of aneurysmal disease

- Aortic root / valve replacement
- Aortic aneurysm thoracic / abdominal

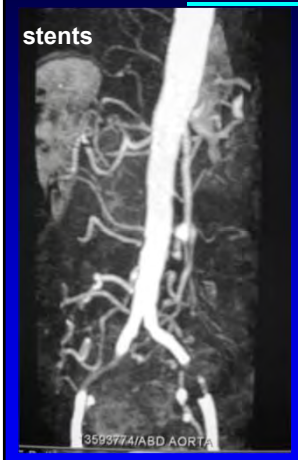
Non-medical management of fixed stenotic lesions causing ischemia

- Severe limb claudication affecting quality of life
- CNS: TIA / cerebral ischemia / stroke
- Renal artery stenosis (hypertension, renal insufficiency)
- Angina
- Bowel ischemia / infarction

Interventional recommendations:

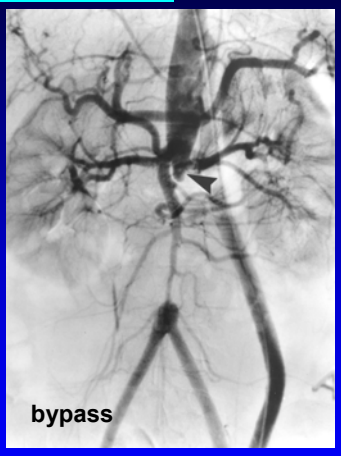
- If possible, avoid intervention during active disease
- Base stenosis intervention on symptoms – not just presence of lesion
- Avoid arm intervention unless symptoms are severe – collateral potential

Giant Cell Arteritis
Non-Medical Management of Large Vessel Disease



Modalities:

- PCTA
- Stent
- Open surgical bypass



Limitation of revascularization – occlusion

Patency rate has varied between series
Long-term series are important to assess efficacy

Giant Cell Arteritis
Non-Medical Management of Large Vessel Disease

Liang et al. J Rheumatol 2004; 31:102

Data on 52 revascularization procedures in Takayasu arteritis

Procedure	# performed	Occlusion # (%)	Time to occlusion
PCTA	7	3 (43%)	1-72 months
Stent	7	5 (71%)	2-45 months
Bypass	31	11 (35%)	1 day -168 months

Endovascular revascularization procedures (PCTA, stent) are associated with:

- Good short-term outcome
- Favorable safety with low morbidity/mortality
- High long-term failure rate in TAK

Surgical bypass grafts have the best long-term outcome TAK
Although non specifically studied in GCA – would view this similarly

Giant Cell Arteritis
Outcome

Mortality

- GCA does not influence overall patient survival (Matteson et al. A&R 1996)
- Large vessel disease does not lower survival *(Nuenninghoff et al. A&R 2003)*
- Increased in 1st 2 years in ≥ 70 years *(Mohammad et al. ARD 2014; Jan)*
- Thoracic aortic dissection in GCA is associated with increased mortality

Morbidity

- Substantial !
- Much is a result of glucocorticoids
- Disease related morbidity:
  - Cranial ischemic events: blindness
  - Large vessel events: Stroke, extremity claudication
- Appears to be an increased risk of cardiovascular events (MI/CVA/PVD) particularly within 1st month *(Tomasson et al. Ann Int Med 2014; 160:73)*

Giant Cell Arteritis
Summary

- GCA is an important disease of older individuals
- GCA - cranial and large vessel disease, PMR, systemic inflammation
- Large vessel thoracic aorta aneurysms can occur late and cause mortality
- Morbidity occurs as a result of both disease and treatment

- Glucocorticoids prevent blindness and are the foundation of GCA treatment
- Patients may require prednisone for over 4 years
- Aspirin 81 mg/d should be given with prednisone when possible
- To date, there remain no efficacious treatments beyond prednisone+aspirin

Future questions:

- how do we better assess disease activity in GCA ?
- if GCA is an antigen driven disease - what is the antigen ?
- why are certain vessels preferentially affected in GCA ?
- are GCA and TAK part of the same spectrum or are they unique diseases ?
- how can understanding these lead us to novel treatments ?