# Rheumatology Revealed 2.0: Advanced Insights and Evolving Best Practices for Family Physicians | Pearls for practice

Recognizing and Managing Giant Cell Arteritis: An Update for Primary Care Dr. Alison Clifford

#### Introduction

- What is Giant Cell Arteritis (GCA)?
  - Granulomatous vasculitis of large arteries
  - Loss of immunotolerance against vessel wall
    - Inflammatory cells enter via vasa vasorum
    - Recruit cells, produce cytokines & growth factors
  - Leading to: Inflammatory cells within the arterial wall and Vessel wall damage (necrosis, destruction of media, fragmentation of internal elastic lamina)
- Who is affected by GCA?
  - 3 x women > men
  - Affects people >=age 50 years
  - Incidence increases with increasing age
    - peak incidence in 8<sup>th</sup> decade of life
    - mean age at diagnosis is 76.7 years
    - the older the patient is the more seriously GCA should be considered

Hunder et al. Arthritis Rheum, 1990; Gonzalez Gay et al, Arthrits Rheum, 2009, Kermani et el, Ann Rheum Dis, 2010

## Who gets GCA? Patients with Polymyalgia Rheumatica (PMR)







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### At Macroscopic level

- Stenosis= Ischemia
- Occlusion = Infarct
- Aneurysm:
  - Asymptomatic, until dissection or rupture

- In GCA:
  - Large & medium vessel involvement
    - Aorta
    - Temporal arteries
    - Subclavian arteries
    - Vertebral arteries

### **GCA Clinical Presentation**

- Constitutional symptoms
- Cranial Symptoms
  - New headache (unlike other headaches)
  - Scalp tenderness
  - Jaw claudication
- Visual symptoms: partial or total
  - Early
  - sudden onset
  - painless
  - permanent
  - 50% risk vision loss to 2<sup>nd</sup> eye in next 1 week
  - Some may have amaurosis first: WARNING Sign
  - Diplopia
- MSK Symptoms
- Large Artery Symptoms

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### GCA Clinical Presentation cont.

#### Large Vessel Involvement

- Most (70%) GCA patients have LVV
- Common targets:
  - Thoracic aorta (aneurysm)
    - Often silent>>may progress
    - Risk of dissection
  - Vertebral artery (stenoses)
    - Posterior stroke
  - Subclavians>Femorals (stenoses):
    - limb claudication, loss of pulses (+LR 6.01)
    - Asymmetrical blood pressures

### **GCA** Investigations

- Send urgent labs same day:
  - CBC/diff, ESR, CRP, creatinine, glucose
  - Expect:
    - Normal to elevated WBC's (neutrophilia)
    - Normocytic anemia
    - Thrombocytosis
    - Elevated ESR & CRP
- Caution: 5% biopsy-proven GCA have normal ESR & CRP

# Once there is intermediate-high suspicion

- Cover empirically with prednisone and pursue confirmation:
- Tissue: Temporal artery biopsy (if not sure if GCA: do one!)
  - Under local anesthesia
  - Very few adverse events
  - Histologically confirms arteritis
  - Sensitivity 61%, Specificity 98%1
  - Still useful in patients on prednisone!
    - Best yield is within 2 weeks of prednisone
      - 40 TAB+ pts repeat biopsies on treatment: 75% + at 6 mos, 40% +at 12 mos2



# GCA Physical Exam

- Cranial exam: Temporal artery abnormalities
  - Swollen (+LR 4.7)
  - Absent (+LR 3.25)
  - Tender (+LR 3.14)
- Visual field, EOM +/- Ophthalmology
- Cardiac & Vascular exam:
  - Blood pressure asymmetry >10 mm Hg
  - Absent radial and/or brachial pulses
  - Cardiac auscultation
- MSK Exam: shoulders/hips
- Neuro/ENT exam: other headache ddx

### Provincial GCA Care Pathway



Physician Learning Program



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### **Options for GCA Confirmation: Imaging**

- Cranial and/or Extra-cranial vessels
- What's available:
  - CT angiogram chest/abdo/pelvis
    - Benefits: vascular anatomy/damage, Limits: cost/access, no info on activity, no TA's
    - Limits: timing
  - PET/CT +/- angiogram
    - Benefits: whole body (cranial & extracranial), info about disease activity, finds other diagnoses
    - Limitations: cost/access, yield lowered by prednisone > 3 days

### Once there is intermediate-high suspicion

- Temporal artery U/S
  - Benefits: point of care tool, assess all branches of TA
  - "Halo sign"
  - Pooled sensitivity 93%, specificity 94% (clinical dx)
  - Limitations: access, user-dependent, yield lowered by prednisone > 4 days

https://www-clinicalkeycom.login.ezproxy.library.ualberta.ca/#I/search/%20temporal%2520artery%2520ultrasound/%7B %22facetouery%22%5B%22\*contenttype:IM%22%5D%7D?page=2

## GCA Treatment: Immunosuppression

- High dose prednisone 1st line
  - Ex: 1 mg/kg/day x 1month (~60 mg/day)
  - IV pulse if sight-threatening disease (500 mg to 1 g IV daily x 3)
  - Start if intermediate-high likelihood of GCA
    - In monotherapy: taper by 10 mg every week till 30 mg, then by 5 mg/wk till 20 mg, then 2.5 mg/q 2 wks till 10 mg, then by 1 mg increments
  - Usual course if monotherapy is ~ 18-24 mos
  - ~ 50% relapse
  - Associated with LOTs of side effects





Pooled sensitivity 76%, specificity 95% (clinical dx)



Information and resources for Physicians and Patients (links)

- <u>RheumInfo</u>
- Alberta Rheumatology
- Vasculitis Foundation Canada

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COVID-19 Information	Giant Cen Arteritis	Rheumatoid Arthritis	
Inflammatory Arthritis	What is Giant Cell Arteritis?	Fibromyalgia	
Ankylosing Spondylitis	Giant Cell Arteritis (GCA), also known as Terre	Gout	condition that causes inflammation in both large a
Descriptic Arthritis	medium sized blood vessels, a process called vi	Lopus	flow and can cause pain, inflammation, tenderness
	around the temples. In some people, it can cau	Myositis	sion so it is important to start treatment quickly. So
Kheumatoid Arthritis	blood vessels are more likely to be affected that	Osteoporosis	on the sides of the head) and the aorta (in the chest)
Fibromyalgia	must commonly ametico aloop vesses in GCA	Osteoarthritis	
Gout	What causes GCA?	Polymyalgia Rheumatica	
Lupus	Of A is caused by an over-active immune posts	Regional MSK Disorders	al acilly and causes them to seeill and become
Long & Deserves	narrower. Less blood can flow through these in	Scleroderma	do not know what triggers GCA. Some factors that
copus o reegoancy	thought to contribute to its development are y	Sjogren's	e.
Sjogren's	Who is affected by GCA?	Vasculitis	
Myositis			
Osteoarthritis	GCA affects adults over the age of 50 years with	most patients being betwe	En the age of 70 to 80. Females are more often affects
Osteoarthritis FAQ	than males (JCL) People with Polymyaga Knea	natica (Print) nave a righer i	isk of having u.c.A.
	What symptoms should you look out for?		





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### Steroid-sparing Drugs: Tocilizumab (TCZ)

- Tocilizumab is a monoclonal ab against IL-6 receptor
  - Approved for new or relapsing patients with GCA
    1 year course
  - Significantly reduces risk of relapse & steroid-sparing
- Some patients need longer-term treatment
  - After 1 yr tx, 42% stay in long-term remission, 58% relapse & need re-treatment
  - Can reapply for Tocilizumab

Stone et al, NEJM, 2017; Stone et al, Lancet Rheumatol, 2021

#### Important Issues with TCZ

- Small increased risk of serious infection
  - If patient is sick/febrile---hold the medication until resolved, antibiotics are completed
- TCZ blocks hepatic synthesis of CRP:
  - If patient is taking it, they will NOT mount a CRP
  - It also significantly inhibits ESR
  - Once a patient is on TCZ, their CRP is NOT a reliable indicator
- Other AE's:
  - Neutropenia, thrombocytopenia, transaminitis
  - Can increase lipid profile
  - V. rare reports gut perforation (pts hx of diverticulitis--contraindication)

### **Prognosis of GCA**

- Overall, no increased mortality in patients with GCA
- There is higher mortality in some subgroups
  - 1st 2 yrs from diagnosis
  - Stroke
  - Patients with aortic damage (aneurysm or dissection)
- Causes of mortality:
  - Cardiovascular disease (39%)
  - Cerebrovascular disease (14%)
  - Infection (13%)



# Select GCA- Upadacitinib (Upa)

- Upadacitinib: oral, selective JAK-1 inhibitor
- Used already in RA, PsA, IBD
- Largest RCA in GCA to date: 428 GCA pts, 100 sites, 24 countries
- Found: significantly higher sustained remission & steroid-sparing
  - 46.4% with Upa vs 29% pred monotherapy, p=0.002;
  - Prednisone exposure 1.6 g vs 2.9 g, p<0.001
  - Less overall infection than placebo (ns), exception: zoster
     Blockmans at el, NEJM, 2025

### Adjunctive Agents

- Aspirin?
  - Not needed for everyone
  - Retrospective data for reduced risk of ischemic events (vision loss, stroke)
  - No prospective data
  - ACR/EULAR recommendations: use if otherwise indicated for cardio/cerebrovascular disease, or if flow-limiting disease in vertebrals or carotids
- Bone protection: for all (calcium, vitamin D, and bisphosphonate or other agent)
- GI protection: high dose prednisone + risk factor

### End Organ Damage/Long term monitoring

- Vision loss:
  - Affects ~ 6-15% patients
  - Risk factors: early, transient visual symptoms, low ESR/CRP, high plts
- Stroke:
  - Affects ~3-7.4% patients with GCA
  - Risk factors: vision loss, 1st few months of diagnosis
- Aortic aneurysm
  - Affects ~15% at baseline
  - Risk factors: increased time since diagnosis (>5 yrs), hx of aortitis
- Patients are followed lifelong





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