Polymyalgia Rheumatica and Giant Cell Arteritis
A Review and Updates

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COMP
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OBJECTIVES

• Be able to identify the demographic groups most at risk for polymyalgia rheumatica (PMR) and giant cell arteritis (GCA).
• Be able to identify the clinical features of PMR and GCA.
• Work-up a patient suspected of having PMR or GCA.
• Communicate the complications /clinical course of GCA and PMR to patients.
• Explain various management strategies for PMR and GCA.
Giant Cell Arteritis and Polymyalgia Rheumatica

- Giant Cell Arteritis is an inflammatory vasculitis that occurs in medium and large arteritis with well-developed wall layers and an adventitial vasa vasorum.
  - The vascular beds that are affected include the external carotid branches (temporal and occipital arteries, ophthalmic) vertebral, distal subclavian, and axillary and thoracic.
  - Vasculitis leads to luminal occlusion and therefore ischemic optic neuropathy
- Polymyalgia rheumatica is an inflammatory condition of the bursas and periarticular structures
The Importance of these Two Inflammatory Cousins

- Often identified and treated by primary care physicians
- The most common diagnosis that necessitates the use of long-term steroids.
- Significant overlap between the two diseases
  - Up to 26% of PMR cases involves GCA
  - Up to 53% of GCA cases involve PMR
Demographics

- Women are 2-3 times more likely than men to have PMR or GCA
- PMR prevalence is 20-50 cases per 100,000 for those older than 50 in North America.
- Prevalence and incidence of GCA is about a third of PMR
- In areas with high concentrations of Northern European descent, the prevalence is 1 in 143 for PMR and 1 in 500 for GCA
- Peak incidence is between 70 and 80 for both PMR and GCA.

PMR & GCA Signs and Symptoms
PMR Signs and Symptoms

- Shoulder (70-95%) and Hip girdle pain (50-70%) and stiffness for at least 30 minutes.
  - Pain can radiate to the elbows or knees.
- Constitutional signs can be seen up to a third of patients
- Myalgia and arthralgia develop over weeks to months
- Worse at night and with movement
- Arthritis can be seen
- Sometimes tenosynovitis, carpal tunnel syndrome and pitting edema

GCA Signs and Symptoms

• Headache affects up to 85% of patients. They are sensitive to combing or touching
• Jaw or tongue claudication
• Jaw claudication and visual symptoms are particular warning signs for blindness or stroke
• Blurred vision, diplopia, amaurosis fugax in 44% of patients often precedes vision loss by hours to days
• The contralateral eye can be effected within days to weeks
GCA Signs and Symptoms

• Atypical Presentations
  • Upper extremity claudication or Raynaud phenomenon
    • 10-15% of patients have involvement of the aortic arch, particularly the subclavian and the axillary arteries
  • Thoracic aortic aneurysm or dissection is typically a late complication
    • Thoracic aneurysm is 17 times as likely in GCA patients than in those without disease. Often taking place years after the disease subsides.
  • Aortic involvement occurs in 15% of cases.
  • Mesenteric ischemia
  • Sudden neurosensory hearing loss
GCA- Exam

- Temporal artery; nodular, tender thick or normal
Labs
Labs

- **ESR**
  - Nonspecific and used to determine the level of *suspicition* for PMR. Usually at least 40.
- **Normal**
  - Men: age divided by 2
  - Women: \((\text{Age} + 10)/2\)
- The mean ESR for PMR is 65 mm/hour and 83 mm/hr in GCA
- ESR greater than 100 raises concerns for GCA or malignancy
- A normal ESR is found in 6-20% of PMR patients although CRP will be elevated


Labs

• 10% of GCA patients have a rate of less than 50 mm per hour
• The highest visual loss occurs in patients who have a ESR of 70-100.
• ESR with an elevated CPR reaches a sensitivity of 99%

Labs for both GCA & PMR

• Mild normocytic anemia may be seen
• Rarely elevated liver enzymes
• Normal CK
Pathology for GCA

• A panarteritis that is most pronounced in the media composed of lymphocytes and macrophages
• Giant cells are common but not required for the pathological diagnosis
• There should not be fibrinoid necrosis
• Disruption of the internal elastic lamina
Criteria for PMR

TABLE 1. TWO SETS OF DIAGNOSTIC CRITERIA FOR POLYMYALGIA RHEUMATICA.*

<table>
<thead>
<tr>
<th>Criteria of Chuang et al.,17 1982</th>
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<tbody>
<tr>
<td>Age of 50 years or older</td>
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<td>Bilateral aching and stiffness for one month or more and involving two of the following areas: neck or torso, shoulders or proximal regions of the arms, and hips or proximal aspects of the thighs</td>
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<tr>
<td>Erythrocyte sedimentation rate greater than 40 mm/hour</td>
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<td>Exclusion of all other diagnoses except giant-cell arteritis</td>
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<table>
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<th>Criteria of Healey,18 1984</th>
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<tr>
<td>Pain persisting for at least one month and involving two of the following areas: neck, shoulders, and pelvic girdle</td>
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<tr>
<td>Morning stiffness lasting more than one hour</td>
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<tr>
<td>Rapid response to prednisone (≥20 mg/day)</td>
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<tr>
<td>Absence of other diseases capable of causing the musculoskeletal symptoms</td>
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<tr>
<td>Age of more than 50 years</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate greater than 40 mm/hour</td>
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*For each set of criteria, all the findings must be present for polymyalgia rheumatica to be diagnosed.
### Table 1. Classification Criteria for Giant-Cell Arteritis and Polymyalgia Rheumatica.\(^\ast\)

**ACR classification criteria for giant-cell arteritis, 1990\(^\dagger\)**

At least three criteria must be met:
- Age at disease onset ≥50 yr
- New headache, either new onset or new type of localized pain in the head
- Abnormal temporal artery, with tenderness to palpation or decreased pulsation
- Elevated ESR, >50 mm/hr during first hr of testing (Westergren method)
- Biopsy evidence of vasculitis with predominance of mononuclear-cell infiltration or granulomatous inflammation, usually with multinucleated giant cells

**Provisional ACR–EULAR classification criteria for polymyalgia rheumatica, 2012\(^\dagger\)**

**Mandatory criteria:**
- Age ≥50 yr
- Aching in both shoulders
- Abnormal C-reactive protein level, ESR, or both

**Additional criteria\(^\dagger\):**
- Morning stiffness lasting >45 min (2 points)
- Hip pain or reduced range of motion (1 point)
- Negative rheumatoid factor or antibodies to cyclic citrullinated peptides (2 points)
- Absence of peripheral synovitis (1 point)
- Ultrasonographic findings
  - At least one shoulder with subdeltoid bursitis, biceps tenosynovitis, or glenohumeral synovitis
  - At least one hip with synovitis or trochanteric bursitis (1 point)
  - Subdeltoid bursitis, biceps tenosynovitis, or glenohumeral synovitis in both shoulders (1 point)
Differential Diagnosis

GCA
• Neoplasms
• Systemic infections
• Intracranial pathology
• Herpes zoster
• Cervical spondylosis
• Temporomandibular disorder
• Atherosclerosis
• Other vasculitides

PMR
• Myositis
• Parkinsons
• Thyroid Disorder
• Adhesive Capsulitis
• Pseudogout
• Paraneoplastic Syndrome
• Systemic Infections
• Fibromyalgia – must have normal ESR
Management
Management

• Inflammatory markers when suspicious for GCA
• Biopsy for the diagnosis of GCA
• Patient who are older than 50 and have a new headache or other symptom suggestive of a neuro ophthalmological complication and have an elevated ESR.
• Suspected GCA should be considered an emergency
  
  Administration of corticosteroids should not be delayed 1mg/kg of prednisone

• Labs should be performed immediately
• Biopsy should be performed within one week.
Labs and Other Studies to Order

- Complete blood count
- Measurement of inflammatory markers
- Blood chemistries
- Urinalysis
- Chest radiography annually
Work-Up

• The temporal artery should be biopsied on the patient’s most symptomatic side
  • 2-3 cm on length should be obtained
• In the light of clinical suspicion, a negative biopsy does not preclude the diagnosis
  • 8-20% of biopsies are negative with most false negative results being from skip lesions or inadequate samples.
  • Biopsy of the contralateral side is often recommended and increases the yield by 9-12%.
• The risks of temporal biopsy include hemorrhage, scalp necrosis, and infection, but are rare.
Management of PMR

- Prednisone 12.5 to 25 mg a day tapered over a minimum of a year.
  - Taper to 10 mg a day over 4-8 weeks, then by 1 mg a month
- Do not use less than 7.5 mg/d and not more than 30 mg/d as an initial dose.
- Some evidence for methotrexate as a steroid sparing agent, but may be considered for “at risk patients,” relapse patients or those with arthritis.

Management of GCA

- Prednisone 60 mg a day or equivalent doe of methylprednisolone. No less than 0.75 mg/kg for four weeks (until resolution of symptoms and normalization of ESR/CRP)
  - Taper by 10% every 2 weeks once stable
- If acute visual loss, the 1,000 mg of methylprednisolone q day for three days.
- PJP (*Pneumocystis jirovecii*) Prophylaxis with trimethoprim-sulfamethoxazole three time a week.
- Steroid Sparing: Methotrexate – shown to reduce flares. IL-6 Inhibitor
- Aspirin 75-150 mg/d – reduces ischemia
- Proton Pump inhibitor
- Bone protection Calcium Vitamin D and Bisphosphonate

Weyand, C et al., N.Engl J Med 371;1 2014
Management of GCA

• Relapses can occur
• If relapse, increase prednisone to the last effective dose
• Steroid Sparing: Methotrexate – shown to reduce flares, but historically debated.
  
  Tocilizumab. IL-6 Inhibitor

• Surveillance in the absence of concern for large vessel involvement by getting a chest –x-ray every two years
• If the results are abnormal, then order a echo, PET scan MRI or CT
• Pts with large vessel involvement require an annual CT angiogram

Weyand, C et al., N.Engl J Med 371;1 2014
Complications of Therapy

• In a 10 year follow-up of GCA patients, 80% had at least one of the following complications:
  • Hypertension
  • Hyperglycemia
  • Bone Loss

New and Investigational Treatments

- Tocilizumab: (8mg/kg IV monthly)
- Ustekinumab: anti-Interleukin-12 and 23 antibody
- Abatacept: anti-CTLA -4 (10mg /kg IV every 12 weeks after loading)
- Anakinra: IL-1 Inhibitor
- Baricitinib: oral Jak-1/Jak-2 Inhibitor
- Sirukumab: IL-6

Roberts, J, Clifford,A. Ther Adv Chronic Dis 2017, Vol. 8(4-5) 69–79
Thank You