The Office of Lifelong Learning, the Division of Rheumatology & the Physician Learning Program

Rheumatology Revealed: Updates on Common Diseases and Referral Tips for Family Physicians | Pearls for practice

Navigating Polymyalgia Rheumatica: State of the art Insights and Referral Strategies for Optimal Patient Care

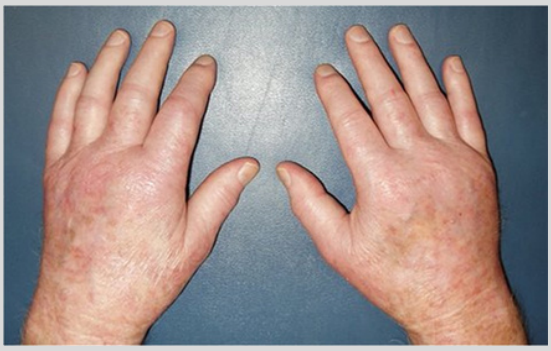
Dr. Dale Sholter

Epidemiology of Polymyalgia Rheumatica (PMR)

- Age >50 years with prevalence increasing with age
- Most common inflammatory disease other than RA at this age
- 60-75% women
- Trigger is unknown
  - Viral studies inconclusive
  - Seasonal?
  - Vaccinations?
- Associated with specific alleles of HLA DR4
- Geographical/ethnic predominance
  - Most common in Caucasians of northern European descent

RS3PE

- Remitting seronegative symmetrical synovitis with pitting edema
- May have shoulder aching
- US shows tenosynovitis, synovitis
- RF and CCP neg

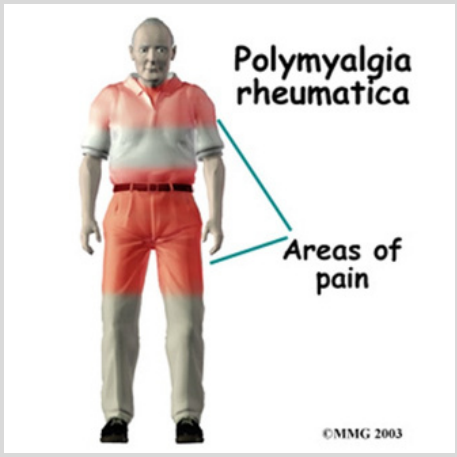


Why the Pain & Stiffness?

- Polymyalgia is not a disease of muscle
  - Muscle pathology/CK is normal
  - Interstitial fluid from involved muscles show high cytokine levels
  - High IL-6 responsible for malaise and flu-like symptoms
- Imaging (US/MR/PET) suggests articular and periarticular inflammation
  - Subacromial and subdeltoid bursitis
  - Tenosynovitis of biceps tendon
  - Interspinous bursitis in cervical spine
  - Trochanteric, iliopsoas and ischiogluteal bursitis/hamstring tendinitis
  - Synovitis in hips/shoulders

Clinical Features

- Acute/subacute onset shoulder, neck and hip girdle aching pain
- Prominent AM stiffness and often night pain
- May have distal joint symptoms <50%- hands, knees but never the ankles and feet
- Functional limitations
- Fatigue, loss of appetite, weight loss malaise, depression, and rarely fever



Investigations

- Acute phase reactants are almost always elevated
- Other non-specific lab markers suggest inflammation – anemia, leukocytosis, thrombocytosis
- Investigations to rule out other conditions may be appropriate such as RF, anti-CCP, ANA, ANCA, SPEP, TSH, CXR and cultures
- <u>Response to (low dose) prednisone is (mostly) rapid and complete</u>

Challenges in Diagnosis

- MSK symptoms are common in older individuals who may have multiple MSK diagnoses
- Most PMR symptoms are non-specific
- There are many conditions that mimic PMR
- There are no specific diagnostic tests
- Who has giant cell arteritis (GCA)?

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Differential diagnosis

-Rheumatoid arthritis -Osteoarthritis
-Regional pain syndromes
-Spondyloarthritis -Myositis
-Drug induced- statins, immune check point inhibitors
-Thyroid disease/hyperparathyroidism
-Fibromyalgia
-Malignancy (myelodysplastic syndrome), paraneoplastic syndromes
-Infection

Accessing Rheumatology

- Rheumatology is here to see inflammatory disease
- A good referral letter really helps
- Starting low dose prednisone completely reasonable if highly suspicious
- Don't hesitate to call – interim advice

Initial Management

- Prednisone typically 15 mg od (range 12.5-25 mg)
  - Occasional BID dosing
- NSAIDS are not effective or minimally effective
- Typically see a rapid response
- Gradual tapering over 1-2 year
- However, relapses are common

Prednisone

Prednisone 15 mg daily x 1 month
- 12.5 mg daily x 1 month
- 10 mg daily x 1 month
- 9 mg daily x 1 month
- then continue to reduce by 1 mg/month until off

If all goes to plan on prednisone for 12 months

Relapsing Disease

- A recent meta-analysis showed relapse and chronic course are common
- In most patients PMR has a self-limiting course
- Proportion of patients experiencing at least one relapse at 1 year from treatment initiation was 43%
- Proportion of patients still taking GCs at 1, 2, and 5 years were respectively 77% , 51% , and 25%

When to refer

- To confirm the diagnosis especially with atypical features
  - Younger patient
  - Presenting with fever
  - Prominent peripheral arthritis
  - Inadequate response to low dose prednisone
- Not comfortable managing the disease
- Relapsing disease
- If considering steroid sparing drugs
- Suspicion of giant cell arteritis

Initial Management

- Primary goal of treatment is to relieve symptoms
- Treatment has not been shown to improve prognosis or prevent GCA
- Prednisone is the first-line treatment
- Patients typically see rapid improvement within hours/days
- Prednisone is continued for 1-2 years
- Relapses are common

Co-morbidities to be assessed for and monitored

-Hypertension -Diabetes/glucose intolerance
-Cardiovascular disease -Dyslipidemia
-Peptic ulcer disease -Osteoporosis
-Cataracts/glaucoma -Chronic or recurrent infections

Floris A, et.al. Long-term glucocorticoid treatment and high relapse rate remain unresolved issues in the real-life management of polymyalgia rheumatica: a systematic literature review and meta-analysis. Clin Rheumatol. 2022 Jan;41(1):19-31. doi: 10.1007/s10067-021-05819-z.

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Relapse or Flare?

- Very common for patients to have arthralgia/myalgia with steroid tapering
- Reasons for this are variable
  - Was prednisone masking other unrelated MSK symptoms such as OA or bursitis?
  - Is there an alternative diagnosis such as RA?
  - Some patients develop fibromyalgia like symptoms with steroid withdrawal that are not accompanied by increased in CRP
  - Adrenal insufficiency

How to manage Flares (Dr Sholter's experience)

- With relapse of symptoms suggest going to previously effective prednisone dose for 1-2 months and then continue to taper if all is well
- If there continues to be a "sticking point" prednisone dosage, consider staying at the lowest effective dosage for 3 months and then restart tapering perhaps in longer intervals
- If cannot get below about 7 mg I will consider a steroid sparing drug
- If flares occur at a very low dose of prednisone, I will sometimes just leave them on the low dose i.e.) 2-3 mg as morbidity is low

Steroid Sparing Therapies

- The role of steroid sparing therapies is not defined
  - Most patients will not require such treatments
  - Most do well with low dose prednisone
  - Low dose prednisone generally has low morbidity
  - PMR itself has a low rate of morbidity
- Consider if preexisting comorbidities (osteoporosis, decompensated diabetes mellitus)
  - development of glucocorticoid-related side effects
  - multiple relapses of symptoms (unable to taper prednisone to acceptable levels)

Biologic Drugs

- Anti TNF agents (infliximab/etanercept)
  - Small negative studies- 62 patients received infliximab and 28 patients etanercept
- Rituximab (B cell inhibitor)
  - A single dose of 1000 mg IV, greater proportion of patients were in glucocorticoid free remission at 21 weeks and 1 year
- Tocilizumab (IL-6 inhibitor)
  - 2 positive studies (36 patients and 100 patients)

Methotrexate

- Most common agent but there is a paucity of evidence on its effectiveness
- ACR/EULAR Guidelines suggest considering MTX in those with relapse/high risk of relapse or steroid morbidity

Sarilumab

- IL-6 inhibitor
- Positive RCT of 118 patients with relapsing PMR
- Approved by FDA for PMR patients who cannot tolerate prednisone taper
- Role of this drug has not been fully defined
- Not yet approved in Canada

Spiera R, et.al Sarilumab for Relapse of Polymyalgia Rheumatica during Glucocorticoid Taper. N Engl J Med 2023;389:1263-1272
DOI: 10.1056/NEJMoa2303452

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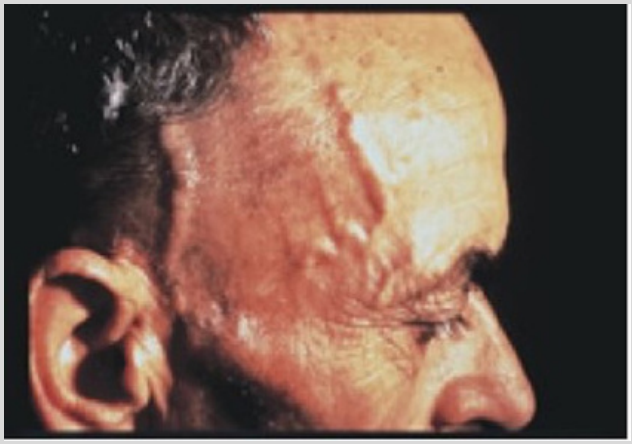
Giant Cell Arteritis (GCA)

- GCA may precede, coexist or follow PMR
- 10% of PMR (50% of GCA has PMR)
- GCA may occur in patients on treatment for PMR
- Always look for the classic GCA symptoms – new onset headache, visual change, scalp tenderness, jaw claudication
- Patients should be educated about GCA so they are aware of this complication
- There are probably a significant number of PMR patients with subclinical GCA
- A 2022 meta-analysis showed more than 25% of PMR patients had subclinical GCA based on TA biopsy, ultrasound or PET scan (27%)
- How these patients should be treated remains unresolved

Hemmig, A. K., et.al (2022). Subclinical giant cell arteritis in new onset polymyalgia rheumatica: A systematic review and metaanalysis of individual patient data. SEMINARS IN ARTHRITIS AND RHEUMATISM, 55, Article 152017.

Diagnosis of GCA

- Temporal artery biopsy (gold standard)
  - Quicker the better but never too late
  - Ophtalmology will do biopsy if there are visual symptoms
  - General Surgery
- Imaging
  - Ultrasound
  - PET/C



Pearls for Practice FMR

- Most patients can be successfully treated with low dose steroids and will have a self-limiting course after 2 years
- While flares are common, mostly they can be managed by very modest increases in steroid dose
- Steroid sparing drugs are indicated in some patients with co-morbidities, serious glucocorticoid side-effects and frequent relapses or chronic disease
- There is lack of good quality studies of steroid sparing drugs
- Data for IL-6 inhibition (and rituximab) show promise but more experience is needed to determine who best would benefit from these expensive treatments

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