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POLYMYALGIA RHEUMATICA – WHAT'S NEW?

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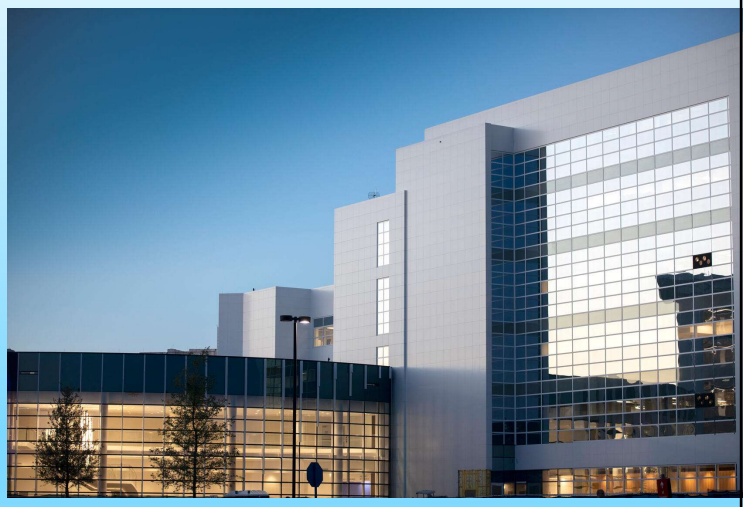


1

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

Benjamin Wang, M.D., faculty for this educational activity, has no relevant financial relationships with ineligible companies to disclose, and has indicated that the presentation or discussion will not include off-label or unapproved product usage.

2

LEARNING OBJECTIVES

- Review the clinical and laboratory features of polymyalgia rheumatica (PMR)
- Review the treatment of PMR according to current guidelines
- Recognize the features of resistant polymyalgia rheumatica and the utility of biologic therapy in PMR

3

POLYMYALGIA RHEUMATICA (PMR)

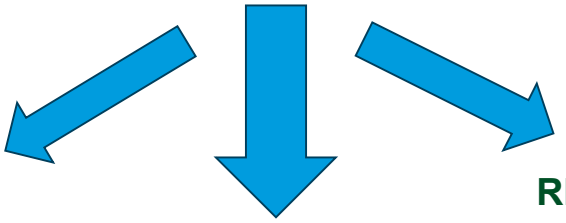
- Most common inflammatory condition in the elderly
- Age restriction (≥50 years)
  - Mean age at diagnosis 73 years
  - Peak incidence 70-79 years
- Epidemiology
  - Estimated incidence 12.7-112.6 per 100,000 people ≥50 years
- Life-time risk of developing PMR 2.43% for women and 1.6% for men
- Etiologic agent unknown

Crowson CS et al. Arthritis Rheum 2011
Gonzalez-Gay M et al. Lancet 2017

4

THREE FATES OF PMR

Polymyalgia rheumatica



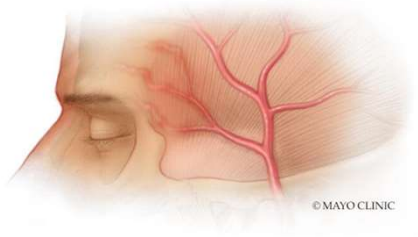
Giant cell arteritis
25%

Rheumatoid arthritis
5%

Polymyalgia rheumatica
70%

5

PMR AND GIANT CELL ARTERITIS (GCA)



- Similar demographics
- Common GCA features: unilateral scalp tenderness; jaw claudication; visual change or loss
- 50% of GCA begins as PMR
- With sensitive imaging, PMR is subclinical GCA[1] in up to 30%
- GCA requires much higher doses of corticosteroids for response

1. van der Geest KSM et al. *Eur J Nucl Med Mol Imaging*. 2021;48(12):3886-3902.

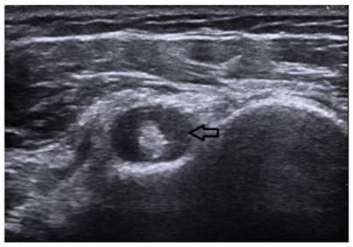
6

A WORD ABOUT THE ERYTHROCYTE SEDIMENTATION RATE

- 7-20% of patients with PMR have normal ESR at time of diagnosis
- Up to 22.5% of patients with GCA had normal ESR
- Mayo:
  - 5.4% had ESR < 40 mm/h
  - 10.8% had ESR < 50 mm/h
- A normal ESR does not rule out these conditions when other clinical findings are suggestive – don't delay treatment!

7

PMR: IMAGING MSK FINDINGS



- MRI and US
  - Inflammation periarticular structures (tendons, bursae)
  - Tenosynovitis of the long head of the biceps more prevalent in PMR
  - *Presence of subacromial/subdeltoid bursitis most helpful*
  - Can distinguish from non-inflammatory causes but not RA, SpA
- PET
  - FDG uptake at interspinous bursae, hips, ischial tuberosities, shoulders and sternoclavicular joints

Dasgupta B et al. Ann Rheum Dis 2012
Mackie SL et al. Ann Rheum Dis 2015
Camellino D et al. Clin Exp Rheumatol 2022

8

TREATMENT OF PMR (2015 EULAR/ACR GUIDELINE)

Prednisone 10-25 mg/d for 2-4 weeks

↓ Reduce by 2.5 mg weekly

Prednisone 10 mg/d Within 4-8 weeks

↓

Taper by 1 mg monthly until discontinued

- Use single daily dose (not divided)
- Not recommended: NSAIDs alone
- Consider methotrexate (data inconsistent):
  - GC toxicity
  - Relapses – inability to taper
- Lowest rate of relapse

Dejaco C, Singh YP, Perel P, et al. *Ann Rheum Dis*. 2015;74(10):1799-1807.

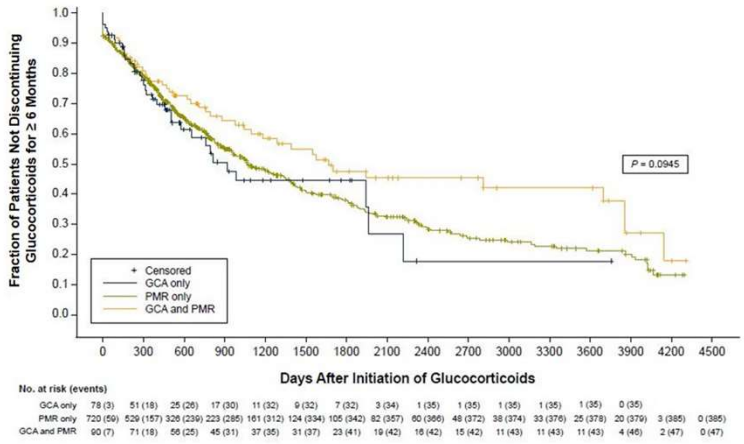
9

TREATMENT OF GCA AND PMR

GCA	PMR
• Prednisone 40-60 mg/d	• Prednisone 10-25 mg/d
• Gradual response	• Rapid response
• IV pulsed steroids if vision threatened (up to 1 g/d)	• Poor response – wrong diagnosis, or refractory?
• Usually 1-2 years	• Usually 1-2 years
• MTX: conflicting data	• MTX: incomplete data
• Relapses common	• Relapses common

10

TREATMENT-RESISTANT PMR



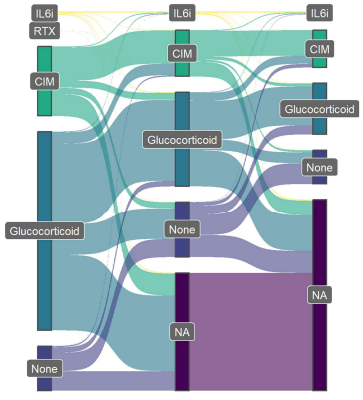
Time to discontinuation of glucocorticoids for ≥ 6 months. *GCA* giant cell arteritis, *PMR* polymyalgia rheumatica

- 779 patients with PMR
- 32% had discontinued GC by 12 months
- 23% remained off GC at 2 year
- At 5 years, mean dose of prednisone was 8.8 mg/d, median 5 mg/d

Craig G, Knapp K, Salim B, et al. *Rheumatol Ther*. 2021;8(1):529-539.

11

TREATMENT-RESISTANT PMR



Sankey plot for therapies used over time in patients with polymyalgia rheumatica new to rheumatology practice. Conventional immunomodulatory drugs (CIMs) included hydroxychloroquine, methotrexate, leflunomide, and sulfasalazine. Interleukin 6 inhibitors (IL-6i) included tocilizumab and sarilumab. NA = not available; RTX = rituximab.

- ACR registry with 26,102 patients with PMR (64% new)
- At registry baseline, 92% on GC, 23% on GC-sparing therapy
- At 12-24 months, 64% still on GC, and 39% on GC-sparing therapy

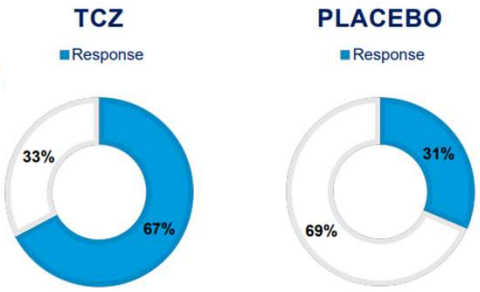
Sattui SE et al. *Arthritis Care Res (Hoboken)*. 2024;76(2):259-264.

12

PMR TREATMENT: IL-6 INHIBITION

SEMAPHORE TRIAL

- Double-blind, placebo-controlled, RCT
- PMR with **persistent disease** activity
- TCZ 8 mg/kg IV Q4 weeks x 24 weeks (N=51) vs placebo (N=50)
- Predefined GC taper
- Primary endpoint week 24
  - Low PMR disease activity
  - And GC ≤5 mg or decrease in GC ≥ 10mg

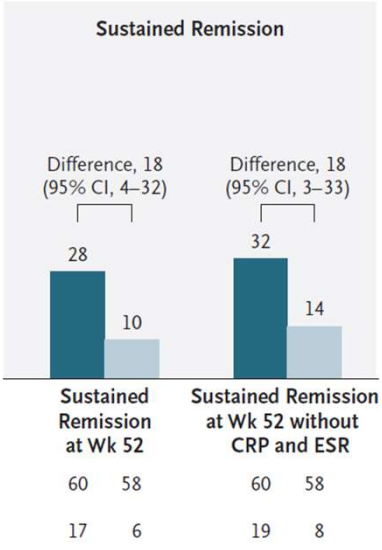


Devauchelle-Pensec V et al. *JAMA*. 2022;328(11):1053-1062.

13

SAPHYR TRIAL: SARILUMAB FOR RELAPSE OF POLYMYALGIA RHEUMATICA DURING GLUCOCORTICOID TAPER

- Humanized monoclonal antibody to IL-6
- Double-blind, placebo controlled RCT – PMR with 1 or more relapses
- **Sarilumab (SAR) 200 mg Q2Wk x 52 weeks + GC taper over 14 weeks (N=60) VS. Placebo + GC x 52 weeks (N=58)**
- Primary endpoint: sustained remission at week 52
  - resolution of signs and symptoms of PMR and CRP normalization (<10 mg per liter) by week 12
  - absence of disease flare from weeks 12 to 52
  - sustained CRP normalization from weeks 12 to 52
  - adherence to the assigned prednisone taper from weeks 12 to 52
- SAR 28% vs Placebo 10%
- Adverse effects: SAR 95% vs Placebo 85%
- Serious adverse events: SAR 14% vs Placebo 21%
- FDA approved October 2023 for inadequate response or unable to taper GC



14

PMR TREATMENT: OTHER BIOLOGICS

- Rituximab (anti-B cell): effect demonstrated in 2 phase II trials (Marsman DE, et al. Lancet Rheumatol 2021 Bolhuis TE, et al. Lancet Rheumatol 2023)
  - Delayed onset of action up to 24 weeks
  - Larger trials ongoing
- Abatacept (anti-T cell): 12 week dbRCT of Abatacept vs Placebo (Saraux A et al., Lancet Rheumatol 2023 Allard B et al, Eur J Nucl Med Mol Imaging 2023)
  - 50% low disease activity in ABA vs 22% Placebo (p=0.07)
  - SAE6% ABA vs 17% Placebo
  - PET scan – no difference at week 12
- IL-17 vs IL-1 vs GC, response at 2 weeks (Matteson EL, et al. Arthritis Rheum 2014 [abstract])
  - No short term complete response in biologics patients
  - Partial response in 2 biologics and 3 GC patients

15

TAKE HOME MESSAGES

1. Polymyalgia rheumatica (PMR) is the most common inflammatory disorder of older adults presenting with inflammatory pain and stiffness of the shoulder and pelvic girdle
2. PMR may be a prelude to giant cell arteritis or rheumatoid arthritis – clinician beware!
3. PMR is highly responsive to low-dose glucocorticoids (GCs) and can be managed with slow GC tapering
4. Half of patients with PMR are still on steroids at two years and are resistant to GC tapering
5. Immunosuppressants such as methotrexate may be tried in GC-resistant PMR but are often ineffective
6. Biologics, especially IL-6 antagonists such as sarilumab are effective in GC-resistant PMR

16

REFERENCES

1. Espígol-Frigolé G, Dejaco C, Mackie SL, et al. Polymyalgia rheumatica. *Lancet*. 2023;402(10411):1459-1472. doi:10.1016/S0140-6736(23)01310-7
2. Spiera RF, Unizony S, Warrington KJ, et al. Sarilumab for Relapse of Polymyalgia Rheumatica during Glucocorticoid Taper. *N Engl J Med*. 2023;389(14):1263-1272. doi:10.1056/NEJMoa2303452
3. Nepal D, Putman M, Unizony S. Giant Cell Arteritis and Polymyalgia Rheumatica: Treatment Approaches and New Targets. *Rheum Dis Clin North Am*. 2023;49(3):505-521. doi:10.1016/j.rdc.2023.03.005

17

QUESTIONS & DISCUSSION

18