

## Fibromyalgia and Polymyalgia Rheumatica: Sound Alike, but Worlds Apart

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### ABSTRACT

*This case is one of a male patient in his mid-60s with a prior diagnosis of polymyalgia rheumatica and suspected seronegative rheumatoid-type polyarthritis who presented with 15 months of progressive generalized musculoskeletal pain, morning stiffness, fatigue, cognitive dysfunction, and non-restorative sleep. Repeated laboratory investigations, including inflammatory markers and an extensive rheumatologic work-up, were normal. Physical examination demonstrated no synovitis or objective inflammatory findings. Administration of the 2016 American College of Rheumatology (ACR) fibromyalgia criteria yielded a score of 22, meeting the diagnostic threshold.*

### Keywords

Polymyalgia rheumatica, Fibromyalgia, Nociceptive pain, Chronic widespread pain, Rheumatology, American College of Rheumatology criteria.

### Introduction

Chronic musculoskeletal pain often presents a diagnostic challenge, particularly when inflammatory and non-inflammatory syndromes share overlapping clinical features. Polymyalgia rheumatica (PMR) is among the most common inflammatory rheumatic diseases in individuals over 50 years of age [1,2]. Fibromyalgia, by contrast, is a chronic primary pain disorder characterized by widespread pain and multisystem symptom burden in the absence of objective inflammation [3,4]. Failure to distinguish these conditions may lead to prolonged exposure to immunomodulatory therapies without benefit and leading to potential harm, while delaying implementation of appropriate multidisciplinary pain strategies.

### Case Report

A gentleman in his mid-60s with a carried-forward diagnosis of PMR and tendency toward overlap between PMR and seronegative polyarthritis of rheumatoid variety presented for routine rheumatology follow-up. For approximately 15 months he

was experiencing the following symptoms:

- Diffuse generalized musculoskeletal pain
- Morning stiffness lasting approximately 20 minutes
- Shoulder pain exacerbated by overhead movements
- Severe fatigue
- Cognitive impairment (“brain fog”)
- Non-restorative sleep
- Allodynia and hyperalgesia

He endorsed that his symptom burden had been a significant hindrance, greatly reducing his quality of life. His ability to engage in enjoyable activities and his workplace performance had been negatively impacted. Physical examination demonstrated no synovitis, no peripheral edema, and no focal tenderness to palpation. Serial laboratory evaluations, including inflammatory markers and extensive rheumatologic work-up (including various autoantibodies specific for various systemic inflammatory immune-mediated rheumatic diseases, were/are consistently within normal limits. When on prednisone 20 mg per day, he endorsed an improvement in symptoms of less than 50%. He had previously received sarilumab therapy for one year without meaningful improvement and had not yet initiated tocilizumab biosimilar therapy.

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Given the discordance between symptom-burden and the absence of objective inflammation, the 2016 ACR fibromyalgia diagnostic assessment was administered. The assessment concluded with a score of 22, surpassing the necessary score to assign the diagnosis of fibromyalgia.

## Discussion

PMR is a systemic inflammatory condition primarily affecting individuals older than 50 years, predominantly women, with the prevalence of disease being highest among those aged 70-80 years [1]. It is characterized by pain and stiffness in the neck, shoulders, and pelvic girdle along with systemic symptoms and elevations in acute phase reactants such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) [2]. PMR has a reported incidence of 63.9 cases per 100,000 patients and prevalence of 701 cases per 100,000 in those older than 50 years [1]. PMR has a close association with giant cell arteritis (GCA); approximately 40-60% of patients with biopsy or imaging proven giant cell arteritis have polymyalgia rheumatica [1].

Diagnosis of PMR is clinical and supported by laboratory and musculoskeletal ultrasonographic findings. The 2012 European Alliance of Associations for Rheumatology (EULAR)/American College of Rheumatology (ACR) classification criteria include age  $\geq 50$  years, bilateral shoulder aching, abnormal CRP and/or ESR as the entry criterion for PMR [5]. Further criteria that must be assessed in those satisfying entry criteria are morning stiffness duration greater than 45 minutes, hip pain or limited range of motion, absence of rheumatoid factor (RF) or anticitrullinated protein antibody (ACPA), absence of other joint involvement, and supportive musculoskeletal findings on ultrasound [5]. A rapid response to low-dose glucocorticoids, no more than 20mg/day of prednisone or its equivalent, further supports the diagnosis [1]. Importantly, persistent musculoskeletal symptoms in the setting of repeatedly normal inflammatory markers should prompt reconsideration of alternative diagnoses.

In contrast, fibromyalgia reflects altered central pain processing and does not produce inflammatory biomarker elevation [3,4]. This case underscores the importance of re-evaluating persistent symptoms in patients with presumed inflammatory rheumatic disease when objective findings are minimal to absent. Fibromyalgia is classified as a nociplastic pain condition, reflecting altered central pain processing rather than peripheral inflammatory pathology [6]. Fibromyalgia can typically present with a constellation of symptoms characterized by central nervous system pain amplification with concomitant fatigue, memory problems, poor quality sleep, and mood disturbances. The best-established pathophysiological features of fibromyalgia are those of central sensitization (i.e., augmented pain and sensory processing in the brain), with increased functional connectivity to pro-nociceptive brain regions and decreased connectivity to anti-nociceptive regions, and accompanying changes in central nervous system (CNS) neurotransmitters, as well as in the size and shape of brain regions [4]. This leads to the stereotypic features of allodynia

and hyperalgesia. The disease has a female: male ratio of 2:1 [3]. Fibromyalgia can develop at any age, even including childhood [3]. The 2016 ACR criteria require assessment of the Widespread Pain Index (WPI) and Symptom Severity Scale (SSS). WPI assesses symptoms present for at least 3 months and generalized pain in at least four of five body regions. SSS assesses the severity of fatigue, waking unrefreshed, and cognitive symptoms over the past week. The assessment always evaluates for the presence of headache, pain/cramps in lower abdomen, and depression during the previous 6 months [7]. Notably, these criteria permit diagnosis in the presence of other medical conditions provided the generalized pain is not otherwise explained. Laboratory studies in fibromyalgia are typically normal, and inflammatory biomarkers are not elevated [3].

Treatment of fibromyalgia is a multimodal and multidisciplinary approach. It primarily consists of patient education, exercise, and other pillars of Lifestyle Medicine including nutrition, physical activity, mindfulness, social connectedness and sleep hygiene have demonstrated improvement in endorsed symptoms [8]. Pharmacologic options are available for fibromyalgia. Antidepressants are effective in treating comorbid depression and sleep disturbance. Systematic reviews suggest that amitriptyline, duloxetine, and pregabalin demonstrate effectiveness in addressing the pain associated with fibromyalgia [9]. Gabapentin is shown to modulate pain perception in fibromyalgia patients [10]. New revelations are coming in the treatment of fibromyalgia, offering patients new options with promising results. The U.S. Food and Drug Administration (FDA) has recently approved a new pharmacological treatment for fibromyalgia for the first time in over 15 years. The new medication is Tonmya, sublingual cyclobenzaprine [11]. A phase 3 randomized controlled trial of patients with fibromyalgia, the RELIEF Trial was conducted to test this new concept of an older medication. The trial concluded with the determination that patients who received treatment with sublingual cyclobenzaprine reported both significant improvements in daily pain and descriptive improvements in sleep quality and fatigue, demonstrating that the sublingual formulation of cyclobenzaprine and dosing regimen studied can meaningfully improve core fibromyalgia symptoms [12]. One very interesting treatment modality under current investigation is fecal microbiota transplantation (FMT). Recent studies have shown that the gut microbiota of women with fibromyalgia is different from that of healthy individuals. Research has demonstrated that FMT from women with fibromyalgia induced the development of a host of fibromyalgia-symptoms in mice, just four weeks post transplantation. The symptoms included mechanical hypersensitivity, thermal hypersensitivity, cold hypersensitivity, spontaneous pain and muscle pain hypersensitivity. These mice were given FMT from healthy individuals, which reversed mechanical hypersensitivity and alleviated cold and heat hypersensitivity as well as spontaneous pain. This prompted a small human study, consisting of fourteen women with fibromyalgia. After the participants were subject to antibiotics and bowel cleansing, they received FMTs. Twelve of the fourteen patients reported a decrease

in pain. Symptomatic burden was reported to decrease. Participants appreciated improvement in scores regarding anxiety, depression, sleep quality, and physical quality of life [13]. Much more research is necessary, but the therapeutic future for fibromyalgia is most certainly brighter than it has ever been.

This case highlights the importance of differentiating inflammatory rheumatic disease from nociplastic pain syndromes like fibromyalgia. PMR is a systemic inflammatory rheumatic disease that typically affects individuals over 50 years of age and has a classical presentation of bilateral shoulder and hip girdle pain, pronounced morning stiffness, elevated acute phase reactants, and a rapid response to low to moderate dose glucocorticoid administration [1,2]. Fibromyalgia is a complex centralized biopsychosocial pain disorder characterized by widespread musculoskeletal pain, fatigue, sleep disturbance, and cognitive symptoms [3,14]. The potential for overlapping clinical features may lead to diagnostic uncertainty, particularly early in the disease course/process. Treatment with prolonged glucocorticoid therapy, common in PMR, places the patient at risk for infection, diabetes, and osteoporosis, etc. Fibromyalgia treatment focuses primarily on non-pharmacologic modalities such as exercise therapy, patient education, and lifestyle modification, although, pharmacologic intervention is a topic of focus [15]. The history and physical examination, as well as limited laboratory testing, are usually sufficient to differentiate polymyalgia rheumatica from fibromyalgia [16].

Key distinctions between PMR and fibromyalgia include (please note that specific biomarkers for both are not available yet):

Feature	PMR	Fibromyalgia
Age of onset	>50	Any age
Inflammatory markers (ESR/CRP)	Elevated	Normal
Pain distribution	Proximal girdle (pectoral and pelvic), nape of the neck	Widespread
A whole inventory of pan-positive review of systems with little signs of systemic involvement	Absent	Present
Pathophysiology	Cytokine-mediated inflammation	Central sensitization
Steroid-response	Rapid miraculous improvement	No sustained benefit
Use of IL-6 inhibition	Helpful	No response
Association with GCA	Yes	No
Specific Biomarkers	Not available	Not available

## Conclusion

PMR is a systemic inflammatory disorder seen in older adults characterized by proximal girdle pain and cytokine-mediated systemic inflammation. However, persistent widespread pain with normal laboratory findings should prompt reassessment. Systematic application of validated diagnostic criteria is critical in distinguishing inflammatory rheumatic disease from nociplastic pain syndromes. Recognition of fibromyalgia in patients previously diagnosed with PMR can significantly alter therapeutic

direction, prompting reorientation of management away from immunomodulatory escalation and toward multidisciplinary pain-directed therapy, improving patient-centered outcomes. The patient's lack of elevated inflammatory markers, absence of synovitis/bursitis/tenosynovitis, prolonged symptom duration, prominent fatigue, cognitive dysfunction, and sensory amplification and suboptimal responsiveness to a low to a trial of moderate dose of corticosteroids strongly supported fibromyalgia rather than active PMR.

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