Getting It Right for Polymyalgia Rheumatica

Chetan Mukhtyar[1], Helen Twohig[2], Humphrey Hodgson[3]

Authors:

Chetan Mukhtyar, Helen Twohig, Humphrey Hodgson

Affiliations

1. Vasculitis Service, Rheumatology Department, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK
2. Primary Care Centre Versus Arthritis, School of Medicine, Keele University, Keele, UK
3. Polymyalgia Rheumatica & Giant Cell Arteritis UK, London, UK

Corresponding author

Chetan Mukhtyar

Consultant Rheumatologist and Vasculitis lead

Norfolk and Norwich University Hospital

Colney Lane

Norwich NR4 7PD, UK

Chetan.mukhtyar@nnuh.nhs.uk

07984 984039

The British and European recommendations for managing Polymyalgia Rheumatica (PMR) recommend specialist referral in the presence of atypical clinical features and failure to respond to glucocorticoids (1, 2). Getting It Right First Time (GIRFT) is an initiative to harmonise practice and learn from examples of best practice. The GIRFT report for Rheumatology (3) mirrors this ethos in recommending that PMR should in general be cared for in primary and community settings with the exception of complex cases and individuals refractory to treatment. It also states that PMR is commonly straightforward to diagnose.

Since its earliest descriptions PMR has remained a clinical diagnosis, based on satisfaction of several inclusion and exclusion criteria. The combination of common clinical manifestations, lack of a diagnostic test, and symptomatic responsiveness to glucocorticoids can lead to significant misdiagnosis as well as unnecessary glucocorticoid exposure. PMR had been diagnosed mistakenly in individuals with lung cancer, rheumatoid arthritis, giant cell arteritis, Takayasu arteritis, myeloma and axial spondyloarthritis. Many other autoimmune, infectious, endocrine, and neoplastic conditions can present with similar symptoms and careful exclusion of these is needed. Slowly evolving clinical features mean that even in the strictest 'PMR' cohorts, diagnostic revision is necessary (7% in the classification criteria validation cohort) (4). Assessing the response to glucocorticoids as a diagnostic test can be problematic. Conditions mimicking PMR will often respond to glucocorticoids, and conversely up to 30% of individuals with PMR may not (4). Therefore, there are risks of masking other emerging diagnoses and of inappropriately labelling non-responders as not having PMR.

Management of PMR in primary care is variable. A survey of twelve thousand General Practitioners reported that adequate formal exclusion of alternative diagnoses did not appear to be routine (5). Only 55% would request a CRP (a higher proportion relying on ESR), and half would consider a diagnosis of PMR and a trial of glucocorticoids in the presence of normal ESR and CRP (5). It is striking that the proportion of people with PMR who are referred to rheumatology services at some point during their disease course varies widely (16% - 44%) (6, 7). Individuals with an inadequate diagnostic work-up, who are on glucocorticoids, present a diagnostic challenge in secondary care. Glucocorticoid exposure makes subsequent investigations for inflammatory arthritis and systemic vasculitis difficult to conduct. Ultrasonography – the most effective approach to diagnosing giant cell arteritis – rapidly becomes negative after initiation of treatment. 18-fluorodeoxyglucose CT PET imaging can pick up cancer and large vessel vasculitis in this group of individuals, but there is a risk of false negative results in individuals on glucocorticoids. The only real option sometimes may be a painful wean of glucocorticoids. Glucocorticoids themselves are associated with quantifiable risks. Real-world data have recently shown that median time to cessation of continuous treatment was 1.93 years (meaning

almost 50% received treatment for >2 years) and 25% received more than 4 years of therapy (8). Prednisolone for PMR and GCA results in at least one infective episode in >50% of individuals at 5-years; >25% will have a hospital admission and >7.5% will die within 1-week of the onset of infection (9). This length of glucocorticoids is also associated with the risk of secondary adrenal failure (10). The metabolic and cardiovascular risks are also highly relevant. Given the risk of iatrogenic harm from glucocorticoids, very careful consideration is warranted before committing patients to such long durations of treatment. From a patient perspective, diagnostic uncertainties surrounding PMR result in a range of negative experiences from frustration and anxiety before the diagnosis has been mooted, to the devastation of visual loss when the diagnosis of GCA has been overlooked.

In line with previous recommendations, the British Society for Rheumatology guidance for secondary care referral is that a referral should be considered if there is diagnostic uncertainty or when there are atypical features or treatment dilemmas.(11) This caveat will encompass many people with PMR but by the time this situation arises, there will be significant diagnostic challenges in secondary care with associated patient discomfort or detriment. The premise that PMR is straightforward to diagnose needs challenging and the current recommendations should not be interpreted as justification to reconfigure rheumatology services to be less accessible for this patient group.

We would argue that PMR is a condition that is relatively straight-forward to manage, providing the diagnosis is correct. It is imperative to the get the diagnosis right first time, not after a trial of glucocorticoids. Both British and European recommendations suggest that alternative differential diagnoses be actively excluded. Rapid access diagnostic pathways for PMR have shown that making the resources of secondary care available to primary care in a timely and easily accessible manner ensures improved diagnosis and patient journeys (12). We suggest it is time for a paradigm shift in the way that PMR is managed. Service configurations should consider the evolution of diagnostics, the recognition of mimics, the healthcare costs of misdiagnosis and the burden of glucocorticoids. The labels of ‘Primary care’ and ‘Secondary care’ encourage working in silos. This model of care does not work for patients with proximal limb girdle stiffness and pain. Clinicians working in the community should be able to access hospital services for these patients. Clinicians that meet the patient along new and hybrid pathways could further triage patients toward the relevant service – early arthritis, vasculitis, orthopaedics, oncology etc. Once the mimics have been identified in a timely manner, a person with securely diagnosed PMR could be appropriately managed in the community.

In summary, PMR is a chronic autoinflammatory condition for which there is no diagnostic test, yet it is one of the few conditions where long-term, potentially harmful, glucocorticoids are initiated and maintained in primary care. To reduce the pitfalls of empirical diagnosis after trials of glucocorticoids,

there is an urgent need to develop integrative pathways to assist people with suspected PMR, balanced between the Scylla of debilitating musculoskeletal symptoms and the Charybdis of glucocorticoid toxicity.

Acknowledgements

We are grateful to Dr Peter Lanyon for his help and advice during the preparation of this manuscript.

Conflicts of Interest

The authors have declared no conflicts of interest.

Funding

No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

References

1. Dasgupta B, Borg FA, Hassan N, Barraclough K, Bourke B, Fulcher J, et al. BSR and BHPR guidelines for the management of polymyalgia rheumatica. Rheumatology (Oxford). 2010;49(1):186-90.

2. Dejaco C, Singh YP, Perel P, Hutchings A, Camellino D, Mackie S, et al. 2015 Recommendations for the management of polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Ann Rheum Dis. 2015;74(10):1799-807.

3. Kay L, Lanyon P, Macgregor A. Rheumatology: GIRFT Programme National Specialty Report. 2021.

4. Dasgupta B, Cimmino MA, Maradit-Kremers H, Schmidt WA, Schirmer M, Salvarani C, et al. 2012 provisional classification criteria for polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Ann Rheum Dis. 2012;71(4):484-92.

5. Helliwell T, Muller S, Hider SL, Zwierska I, Lawton S, Richardson J, et al. Challenges of diagnosing and managing polymyalgia rheumatica: a multi-methods study in UK general practice. Br J Gen Pract. 2018;68(676):e783-e93.

6. Helliwell T, Hider SL, Mallen CD. Polymyalgia rheumatica: diagnosis, prescribing, and monitoring in general practice. Br J Gen Pract. 2013;63(610):e361-6.

7. Barraclough K, Liddell WG, du Toit J, Foy C, Dasgupta B, Thomas M, et al. Polymyalgia rheumatica in primary care: a cohort study of the diagnostic criteria and outcome. Fam Pract. 2008;25(5):328-33.

8. Partington RJ, Muller S, Helliwell T, Mallen CD, Abdul Sultan A. Incidence, prevalence and treatment burden of polymyalgia rheumatica in the UK over two decades: a population-based study. Ann Rheum Dis. 2018;77(12):1750-6.

9. Wu J, Keeley A, Mallen C, Morgan AW, Pujades-Rodriguez M. Incidence of infections associated with oral glucocorticoid dose in people diagnosed with polymyalgia rheumatica or giant cell arteritis: a cohort study in England. CMAJ. 2019;191(25):E680-E8.

10. Borresen SW, Thorgrimsen TB, Jensen B, Hilsted L, Bartels EM, Feldt-Rasmussen U, et al. Adrenal insufficiency in prednisolone-treated patients with polymyalgia rheumatica or giant cell arteritis-prevalence and clinical approach. Rheumatology (Oxford). 2020;59(10):2764-73.

11. British Society for Rheumatology Clinical Affairs Committee. Adult Rheumatology Referral Guidance. London: British Society for Rheumatology; 2021 06/10/2021.

12. Frolund LL, Vaben C, Dam M, Kjaer SG, Nielsen BD, Ostgard RD, et al. Fast track clinic for early diagnosis of polymyalgia rheumatica: Impact on symptom duration and prednisolone initiation. Joint Bone Spine. 2021;88(5):105185.