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Polymyalgia rheumatica: clinical update

Background

Polymyalgia rheumatica is a relatively common inflammatory rheumatic disease. There are no validated international guidelines available for the diagnosis and treatment of PMR; however, diagnostic and classification criteria are currently being developed.

Objective

The aim of this article is to summarise the main management options suggested by American College of Rheumatology and discusses the role of the general practitioner in the diagnosis and early management of PMR.

Discussion

Diagnosis is made on the basis of a combination of clinical and laboratory findings. Patients typically present with shoulder and hip girdle pain with pronounced stiffness. Inflammatory markers are usually elevated and an ultrasound and MRI of the shoulder and hip can be done to localise inflamed tissues. Response to steroids should not be used as a defining feature of PMR but treatment with low dose prednisone should be considered. PMR has an excellent prognosis if diagnosis is prompt and therapy adequate.

Keywords

polymyalgia rheumatica, rheumatology

giant cell arteritis (GCA) and 40–50% of patients with GCA have associated PMR. Despite the similarities in age of onset and some of the clinical manifestations, the relationship between GCA and PMR is not yet clearly established.⁴ PMR is seen mainly in people of North European ancestry, although it can occur in any ethnic group. It is almost never seen in people under the age of 50 years and its prevalence increases with increasing age. The average age of onset is 70 years and 75% of patients are women. The cause of PMR is unknown, although genetic and environmental factors contribute to disease susceptibility and severity. PMR has a modest familial aggregation and is linked to the HLA DR4 allele in Caucasian populations. Epigenetic changes and differential expression of genes that regulate the expression of inflammatory cytokines probably account for the variability in disease phenotypes.⁵

Clinical features

The hallmarks of PMR are shoulder and hip girdle pain with pronounced stiffness. The stiffness may be so profound that patients have great difficulty turning over in bed, rising from a bed or a chair, or raising their arms above shoulder height, for example, to comb their hair.⁶ Despite being so common, there is surprisingly little sound evidence from randomised controlled trials for diagnosis and management. Most of the evidence for the diagnosis and treatment of PMR comes from case series, expert opinion and individual clinical experience rather than randomised controlled trials. Guidelines developed in 2009 by the British Society for Rheumatology (BSR) and the British Health Professionals in Rheumatology (BHPR) (*Table 1*) attempted to standardise the

Polymyalgia rheumatica (PMR) is a relatively common inflammatory rheumatic disease in elderly people and a common indication for long-term corticosteroid therapy.¹ PMR has many non-specific features and a wide differential diagnosis. No 'gold standard' diagnostic test is available, so the diagnosis is made primarily on clinical grounds, which can lead to diagnostic error.² PMR is managed mainly in primary care but also in secondary care by rheumatologists and other specialists.³ In the UK, it is one of the most common indications for long-term steroid use in the community, accounting for 22% of prescriptions.² About 15% of patients with PMR develop

diagnosis and treatment of PMR.⁷ The lack of standardised classification criteria has been a major factor hampering the evaluation of patients and development of rational therapeutic approaches.⁸

New diagnostic criteria for PMR

In 2012 the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) established a working party to seek expert opinion and analyse all previously

published criteria to produce a list of potential discriminating variables. They conducted a 6-month prospective cohort study that included a cohort of patients with new-onset PMR and a comparison cohort of non-PMR patients with various conditions that mimic PMR. Patients with and without PMR underwent ultrasound evaluation of shoulders and hips.

Key differences between the existing BSR criteria and the new EULAR/ACR criteria include the absence of response to steroid treatment (this was not found to have sufficient discriminating

value to be included) and the addition of shoulder and hip abnormalities on ultrasound (*Table 1*).⁸ The EULAR/ACR criteria are classification criteria primarily intended to select patients with definite disease for inclusion in clinical trials and thus sacrifice sensitivity for specificity. Nevertheless, they still have valuable diagnostic utility. In addition, these criteria may be applied only to those patients in whom the symptoms are not better explained by an alternative diagnosis.

It is crucial to exclude active infection, cancer and other inflammatory conditions. Clinicians

Table 1. Classification criteria for PMR

BSR and BHPR guidelines (2009) ⁷	New EULAR/ACR classification (2012) ⁸
Age >50 years, duration >2 weeks	Age ≥50 years with new bilateral shoulder pain
Bilateral shoulder or pelvic girdle aching, or both	New hip involvement (pain, tenderness, limited movement)
Morning stiffness for >45 min	Morning stiffness for >45 min
Evidence of an acute-phase response	Elevated C-reactive protein and/or ESR
Normal inflammatory markers if there is a classical clinical picture and response to steroids	In the absence of peripheral synovitis or of positive RA serology
	Ultrasound findings of bilateral shoulder abnormalities (subacromial bursitis, bicipital tenosynovitis, glenohumeral effusion) or abnormalities in one shoulder and hip (hip effusion, trochanteric bursitis)

Table 2. Conditions that can mimic PMR⁶

Inflammatory disorders	Clinical features
Rheumatoid arthritis	Mainly distal joint symptoms; may be positive for RF and anti-CCP; erosive joint disease on radiography
Late-onset spondyloarthropathy, including ankylosing spondylitis, psoriatic arthritis	Predominantly low back stiffness and pain; may have large and distal joint symptoms; spinal ankylosis on radiography; psoriasis
Remitting seronegative symmetric synovitis with pitting oedema (RS3PE) syndrome	Peripheral hand or foot oedema
Systemic lupus erythematosus, scleroderma, Sjögren's syndrome, vasculitis	Fatigue, stiffness, multisystem disease, presence of antinuclear antibodies and anti-neutrophil cytoplasmic antibodies
Dermatomyositis, polymyositis	Proximal muscle weakness, rash; creatine kinase raised
Non-inflammatory disorders	
Osteoarthritis, spinal spondylosis	Articular pain of shoulder, neck and hip joints; gelling; degenerative changes on radiography
Rotator cuff disease, adhesive capsulitis (frozen shoulder)	Periarticular pain, restricted range of motion; ultrasound and magnetic resonance imaging may show characteristic bursa and synovial inflammation
Infections, including viral syndromes, osteomyelitis, bacterial endocarditis, tuberculosis	Fever, weight loss, heart murmur, deep soft tissue and bone pain, microscopic haematuria
Chronic pain syndromes, fibromyalgia, depression	Fatigue, longstanding pain, tender points, sadness, loss of usual interests
Endocrine and metabolic diseases, such as thyroid and parathyroid disorders and osteomalacia	Bone pain, fatigue; abnormalities of thyroid and parathyroid hormone, calcium, phosphorus, vitamin D concentrations
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must be aware of conditions that mimic PMR. Such conditions include the inflammatory and non-inflammatory (eg. mechanical) disorders (Table 2). Polymyalgic-onset rheumatoid arthritis (RA) is an important condition that can mimic PMR. Antibodies against cyclic citrullinated peptide (anti-CCP) are the earliest serological markers for RA.⁹ The updated EULAR/ACR criteria have incorporated anti-CCP to help discriminate between RA and PMR. The importance of this distinction is made more urgent because of the appreciation of the need to treat RA early and of the provision of more effective agents such as the biological disease modifying antirheumatic drugs (DMARDs).

Referral to a rheumatologist should be considered if atypical features such as age <60 years, chronic onset, lack of shoulder involvement or inflammatory stiffness, lack of response to steroids or red flags such as prominent systemic symptoms, weight loss or night pain.⁷

GCA should always be considered in the differential diagnosis because it occurs in 16–21% of patients with PMR. Whenever GCA is suspected, a thorough clinical evaluation¹⁰ should be performed and should be supported by the measurement of inflammatory markers and temporal artery biopsy (TAB). Clinical diagnostic criteria for GCA as per ACR specify that the diagnosis may be made when patients meet three of the five criteria listed in Table 3. TAB should not delay the prompt institution of high-dose corticosteroid therapy if GCA is suspected.¹¹ TAB should be performed preferably within 1 week of starting corticosteroids.¹² Some reports suggest that TAB may remain positive for 2–6 weeks after initiation of corticosteroids;^{12,13} however, we would not recommend delaying TAB for more than 2 weeks. There is considerable overlap in the diagnoses of PMR and GCA. Patients with

Table 3. ACR diagnostic criteria for GCA¹⁰
Age >50 years
New onset of localised headache
Temporal artery tenderness or decreased temporal artery pulse
ESR ≥50 mm/hr
Positive temporal artery biopsy

‘pure’ PMR lack the classical findings of GCA, such as temporal artery tenderness, headache, jaw and tongue claudication and visual loss. In the absence of such signs or symptoms, a TAB is not indicated, as a positive result is rare in this setting.¹⁴ Ongoing monitoring for symptoms or physical findings suggestive of GCA in those diagnosed with PMR is required.

Investigations

Inflammatory markers (ESR or C reactive protein) are elevated or normal. Muscle enzymes, thyroid function tests and serum calcium levels are normal.¹⁵ Rheumatoid factor, anti-CCP, antinuclear antibodies and complement levels are usually normal. Although PMR causes severe pain and stiffness in the proximal muscle groups, no evidence of disease is present on muscle biopsy. Muscle strength and electromyography findings are normal. Ultrasonography and MRI can be used in PMR to localise inflamed tissues, showing bursitis and joint synovitis associated with tenosynovitis in both shoulder and pelvic girdle.¹⁶

Pharmacotherapy

Pharmacotherapy is based on empirical experiences because few randomised clinical trials are available to guide treatment decisions. The therapeutic goals are to control painful myalgia, improve muscle stiffness and resolve constitutional features of the disease. Corticosteroids (prednisone or prednisolone) are considered the treatment of choice because they often cause complete or near-complete symptom resolution and reduction of the ESR to normal. Prednisone or prednisolone are considered to be equally potent at equivalent doses. A systematic review by Hernandez et al,¹⁷ which included 30

studies, found that remission of PMR seemed to be achieved for most patients with a starting dose of prednisone at 15 mg/day. A slow tapering of the prednisone, less than 1 mg/month, was associated with fewer relapses. There is no consistent evidence for an ideal steroid regimen suitable for all patients. Therefore, the approach to treatment must be flexible and tailored to the individual as there is heterogeneity in the course of the disease. BSR and BHPR have suggested a prednisolone-tapering regimen for PMR⁷ and GCA¹⁸ (Table 4). Dose adjustment may be required for disease severity, comorbidity, side effects and patient wishes. The core clinical response criteria include improvement in morning stiffness, ability to raise the arms above shoulder height consistent with the patient’s baseline mobility before onset of polymyalgic symptoms, improvement in the patient and doctor’s global assessment (preferably performed on a visual analogue scale) and a reduction in the C-reactive protein or ESR (or both).⁶ Usually 1–2 years of treatment is needed. In patients with relapses, a rapid improvement of symptoms is generally observed following the resumption or an increase in the dose of prednisolone.

It is recommended that clinicians assess bone mineral density (BMD) before initiating corticosteroid treatment, which is likely to last longer than 3 months. The following steps should be taken at the commencement of steroid therapy:

- start adequate supplementation of calcium (1200 mg/day) and vitamin D3 (cholecalciferol, 800 IU/day)
- assess lumbar and hip spine BMD
- If BMD T-score is –1.5 or less consider an oral bisphosphonate such as alendronate (70 mg/week) or risedronate sodium (35 mg/week).

Table 4. BSR/BHPR prednisolone-tapering regimen for GCA and PMR^{7,18}

GCA	PMR
Prednisolone 40–60mg (not <0.75 mg/kg) continued for 4 weeks (until resolution of symptoms and laboratory abnormalities)	Prednisolone 15 mg for 3 weeks
Reduction by 10 mg every 2 weeks to 20 mg	12.5 mg for 3 weeks
Reduction by 2.5 mg every 2–4 weeks to 10 mg	10 mg for 4–6 weeks
Reduction by 1 mg every 1–2 months provided there is no relapse	Reduction by 1 mg every 4–8 weeks or alternate day reductions (eg. 10/7.5 mg alternate days)

The Pharmaceutical Benefits Scheme (PBS) usually subsidises treatment for steroid-induced osteopenia if a patient is on long-term (at least 3 months) high-dose (at least 7.5 mg per day prednisone or equivalent) corticosteroid therapy, a BMD T-score is -1.5 or less and patient is not receiving concomitant treatment with any other PBS-subsidised anti-resorptive agent for this condition.¹⁹ Corticosteroid-sparing agents (such as methotrexate and azathioprine) are sometimes considered in patients with PMR to reduce corticosteroid-related adverse effects; however, no long-term beneficial outcome has been reported in randomised clinical trials.^{20,21}

Conclusion

PMR is usually self-limiting and patients who are not treated often feel unwell and have an impaired quality of life. PMR has an excellent prognosis with prompt diagnosis and adequate therapy. A trial of corticosteroids is not an alternative diagnostic test as it may be misleading because of a non-specific response.

Key points

- A diagnosis of PMR should be considered in patients aged >50 years who have sub-acute to acute onset of bilateral shoulder pain and stiffness.
- Any patient with PMR should be considered at risk of GCA and referred for temporal artery biopsy if suggestive features are present.
- Treatment with corticosteroids should be commenced urgently and in higher doses if GCA is suspected.
- Most patients require 1–2 years of therapy and slow tapering of the dose reduces relapses.
- Prevention and treatment of corticosteroid-induced complications should be considered early in course of the disease.
- Referral to a rheumatologist should be considered if atypical features are present.

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Competing interests: None.

Provenance and peer review: Not commissioned; externally peer reviewed.

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