An estimated 40 million Americans have some form of arthritis or other rheumatic condition. This number is expected to climb to 59.4 million, or 18.2% of the population, by the year 2020 largely due to the aging of the U.S. population [1]. Polymyalgia rheumatica (PMR) is a clinical condition that is becoming increasingly common with the growing population of persons older than 50 years. A decade ago, the National Institute of Arthritis and Musculoskeletal and Skin Diseases estimated that PMR was prevalent in 450,000 Americans [2]. No new epidemiologic statistics have been published since, but as this estimate preceded the wave of baby boomers reaching retirement age, it is reasonable to assume that prevalence may now be greater. PMR should be considered in any patient who presents with the clinical picture of aches and pains associated with an elevated erythrocyte sedimentation rate (ESR) and a dramatic response to low-dose corticosteroids. The pressing clinical dilemma is that there are many masqueraders of this condition. A careful history and ruling out the other possible culprits will lead to the correct diagnosis and treatment.

### CASE STUDY

**Initial Presentation**

A 72-year-old woman presents to her primary care physician with weakness in her arms, stiffness in her shoulder and hip girdles, and generalized fatigue.

**History**

During the patient’s last visit, she complained of a 2-month history of morning stiffness lasting over an hour in her shoulders and hips. She remembered the day and time that the symptoms started. She also described difficulty fastening her bra and combing her hair in the mornings. Over-the-counter acetaminophen and ibuprofen led to minimal improvement. She also reported more fatigue and muscular pains since her husband died 4 months prior. Previously active in her church and the local senior citizens group, her fatigue has limited her ability to participate as she once did. She has had no appetite and is unable to eat well. It was recommended that she seek a grievance counselor/psychologist to address her recent spousal loss.
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She presents now with a more intense feeling of weakness in her arms, stiffness in her shoulder and hip girdles, generalized fatigue, and swelling of her hands with complaints that she cannot remove her rings over the past 4 months. Her hands have become puffy and she cannot make a tight fist. She has been having great difficulty getting out of bed in the morning and on 2 occasions her daughter had to come over to help her get out of bed and stand up. On further questioning, she has been having trouble concentrating and being able to do the crossword puzzle every morning. Her lack of appetite has persisted, eating very small portions only once or twice a day. She has difficulty sleeping. She is compliant in taking medication for hypertension, type 2 diabetes, and osteoporosis. She lives alone in a senior living community.

She denies headaches, visual problems, jaw claudication, or problems swallowing. No symptoms of dry eyes or mouth, chest pain, shortness of breath, palpitations, heartburn, nausea, vomiting, diarrhea, or any new rashes are revealed by the patient.

Physical Examination

Physical examination reveals a weight of 145 lb with a height of 70 in and body mass index of 22 kg/m². She has lost 5 lb in the past 6 months. Vital signs are blood pressure, 120/90 mm Hg; heart rate, 68 bpm and regular; respirations, 18 breaths/min; and temperature, 99.1°F.

Head examination reveals mild scleral pallor and tenderness in her occipital scalp and neck. No temporal scalp tenderness is appreciated. Temporal artery pulses are 2+, and no bruits are heard. She has several tender points in her neck, trapezius area, intercostal spaces, and superior gluteal areas.

Musculoskeletal examination reveals bilateral swollen hands. There is no sign of synovitis or tenderness on palpation of any of her metacarpalphalangeal, proximal interphalangeal, or distal interphalangeal joints. She is unable to fully flex her fingers to form a fist.

Raising her arms overhead causes great discomfort, and it is difficult to maintain her arms in that position. She cannot extend her arms behind her back because of soreness. Lower extremities are mildly weak (4+) on flexion of thigh muscle groups, while all deep tendon reflexes are intact. She has no rashes on her face, eyelids, hands, or torso.

Laboratory Evaluation and Imaging

Laboratory testing reveals the following:

- White blood cell count, 7500 cells/mm³
- Hemoglobin, 10.2 g/dL
- Hematocrit, 35%
- Platelets, 225,000 cells/mm³
- Hemoglobin A₁c, 6.0%
- Blood urea nitrogen/creatinine, 25/1.2 mg/dL
- Sodium, 141 mEq/L
- Potassium, 4.4 mEq/L
- Aspartate aminotransferase, 33 U/L
- Alanine aminotransferase, 34 U/L
- Alkaline phosphatase, 102 U/L
- Total protein, 7.0 g/dL
- Albumin, 5.0 g/dL
- ESR, 74 mm/h
- C-reactive protein (CRP), 2.0
- Thyroid-stimulating hormone, 3.34 μIU/mL
- Antinuclear antibody, negative
- Anti-SSA and anti-SSB, negative
- Rheumatoid factor, negative
- Creatine kinase, 88 U/L
- Urinalysis, within normal limits

Radiographs of bilateral hips and shoulders reveal no abnormalities.

What are characteristic findings in PMR?

PMR is an inflammatory condition of unknown etiology characterized by aching and pain in the muscles of the neck, shoulders, hips, and thighs. The onset is usually abrupt, and initial involvement of shoulder girdle muscles is common. Severe stiffness after periods of inactivity is frequently seen. Night pain is common. Patients frequently complain that they cannot get up on their own. Constitutional symptoms such as low-grade fever, weight loss, anorexia, malaise, and depression occur in more than half of patients. Fevers and chills are not considered part of the clinical spectrum.

PMR usually occurs in people older than 50 years and is rare in people younger than 50 years. Incidence of PMR increases with age, peaking in the 70- to 80-year-old age-group [3]. It is more common in women than in men in all age-groups. The geographic distribution of PMR shows higher incidences at higher latitudes such as in Norway, Denmark, and other Scandinavian countries [2,4]. In Olmsted County, Minnesota, an area with a large population of northern Scandinavian heritage, the average yearly incidence of PMR was 52.5 cases per 100,000 people aged 50 years and older [4]. Population-based studies over the past few years have shown the incidence of the condition to be stable.

PMR is a synovitis. The synovitis first described in these patients was predominantly in the shoulders and hips, producing the picture of shoulder and pelvic girdle pain and stiffness with little or nothing detected on physical examination. In some patients, the synovitis may involve distal joints as well. It has been suggested that peripheral joint
synovitis occurs in 15% to 38% of patients with PMR. These numbers may vary when imaging techniques such as ultrasonography (US) or magnetic resonance imaging (MRI) are used [1,2]. O’Duffy et al [5] found the presence of synovial inflammation, even in patients without clinically detected synovitis. This was suggested by increased articular uptake of radioisotope on bone scans in 24 of 25 PMR cases. Chou and Schumacher [6] identified microvascular changes in synovial study by electron microscopy. The joints most frequently involved are the wrists, metacarpophalangeal joints, and knees [7]. Synovitis of the sternoclavicular joints has been reported [8]. Salvarani et al [9] proposed that the presence of peripheral synovitis in PMR could constitute a more severe subset signaling a worse prognosis because it requires steroid treatment for longer periods and carries a higher number of relapses and recurrences.

• What criteria are used to diagnose PMR?

An accurate diagnosis of PMR relies on a detailed patient history, the presence of elevated acute phase reactants, exclusion of differential diagnoses, and the hallmark response to low-dose corticosteroids. Different diagnostic criteria sets have been proposed (Table 1). More recently, an American College of Rheumatology work group reported on a 3-stage consensus-based approach to developing potential classification criteria for PMR [13,14]. In stage 1, a group of experts rated 68 criteria. They were then provided with the results and asked to rerate them. Stage 2 identified 50 criteria, of which 43 received at least 50% support. In stage 3, over 70% of survey respondents agreed on the importance of 7 core criteria: age 50 years or older, duration of 2 weeks or more, bilateral shoulder and/or pelvic girdle aching, duration of morning stiffness greater than 45 min, elevated ESR, elevated CRP, and rapid steroid response (> 75% global response within 1 wk to prednisolone/prednisone 15–20 mg daily). A prospective study is planned to validate these criteria.

Table 1. Proposed Diagnostic Criteria for Polymyalgia Rheumatica

<table>
<thead>
<tr>
<th>Bird criteria [10]</th>
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<tbody>
<tr>
<td>Bilateral shoulder pain and/or stiffness</td>
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<td>Onset of illness within 2 wk</td>
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<td>Initial ESR &gt; 40 mm/hr</td>
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<tr>
<td>Morning stiffness &gt; 1 hr</td>
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<tr>
<td>Age &gt; 65 yr</td>
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<tr>
<td>Depression and/or weight loss</td>
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<tr>
<td>Bilateral upper arm tenderness</td>
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<tr>
<td>A diagnosis of probable PMR is made if 3 or more criteria are met (sensitivity, 92%; specificity, 80%)</td>
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<thead>
<tr>
<th>Hunder criteria [11]</th>
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<tbody>
<tr>
<td>Age &gt; 50 yr</td>
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<tr>
<td>Bilateral aching and tenderness for &gt; 1 mo of Neck or torso</td>
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<tr>
<td>Shoulders or upper arms</td>
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<tr>
<td>Hips or thighs</td>
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<td>ESR &gt; 40 mm/hr</td>
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<tr>
<td>Exclusion of other diagnoses</td>
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<td>Definite PMR = patient meets all criteria</td>
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<tr>
<th>Healey criteria [12]</th>
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<tr>
<td>Persistent pain (≥ 1 mo) involving 2 of the following areas: Neck</td>
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<td>Shoulders</td>
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<tr>
<td>Pelvic girdle</td>
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<tr>
<td>Morning stiffness lasting &gt; 1 hr</td>
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<tr>
<td>Rapid response to prednisone (&lt; 20 mg/day)</td>
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<tr>
<td>Absence of other diseases capable of causing musculoskeletal symptoms</td>
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<tr>
<td>Age &gt; 50 yr</td>
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<tr>
<td>ESR &gt; 40 mm/hr</td>
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<tr>
<td>The diagnosis of PMR is made if all the above criteria are met</td>
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ESR = erythrocyte sedimentation rate; PMR = polymyalgia rheumatica.

• What conditions can mimic PMR?

Differential Diagnosis

Many conditions can mimic PMR and the differential diagnosis is broad (Table 2).

Hypothyroidism

Characteristics signs for hypothyroidism (ie, slow relaxation of deep tendon reflexes, a low serum thyroxine concentration, and an elevated thyroid-stimulating hormone concentration) are not seen in PMR. Our patient had normal thyroid function.
Table 2. Differential Diagnosis of Polymyalgia Rheumatica

<table>
<thead>
<tr>
<th>Rheumatologic diseases</th>
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<tr>
<td>Early-onset rheumatoid arthritis</td>
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<td>Osteoarthritis</td>
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<td>Collagen vascular diseases</td>
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<tr>
<td>Vasculitis (eg, giant cell arteritis)</td>
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<tr>
<td>Remitting seronegative symmetrical synovitis with pitting edema</td>
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<tr>
<td>Fibromyalgia</td>
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<tr>
<td>Late-onset spondyloarthritis</td>
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<tr>
<td>Polymyositis and dermatomyositis</td>
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<tr>
<td>Hypothyroidism</td>
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<tr>
<td>Depression</td>
<td></td>
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<tr>
<td>Malignancy</td>
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<tr>
<td>Carcinoma (lung, colon, kidney)</td>
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<tr>
<td>Multiple myeloma</td>
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<tr>
<td>Lymphomas (non-Hodgkins and Hodgkins)</td>
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<tr>
<td>Infective endocarditis</td>
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<tr>
<td>Parkinson’s disease</td>
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<tr>
<td>Bursitis and tendonitis</td>
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</table>

Depression

Patients who are depressed usually improve with counseling and pharmacologic intervention, such as a selective serotonin reuptake inhibitor, but will not respond to corticosteroids. A careful history and attention to life events in the elderly are critical to decipher this common mimic. Although our patient was depressed and grieving her husband’s death, she had symptoms beyond what one would expect of a person with depression.

Rheumatoid Arthritis

Our patient did not have peripheral synovitis to suggest that she has active rheumatoid arthritis (RA). Differentiating between PMR and early-onset RA can be difficult because these conditions may have a similar clinical presentation. Important features characterizing both diseases are acute involvement of the girdles, severe morning stiffness, raised ESR, and good response to low doses of prednisone. Elderly-onset RA is characterized by peripheral arthritis, but patients with PMR may also show distal musculoskeletal manifestations. Some authors have suggested that RA with PMR-like onset and PMR may be the same entity [15]. Others have studied how to differentiate these conditions by means of clinical data, human leukocyte antigen (HLA) typing, lymphocyte subsetting, additional laboratory tests, imaging, or invasive methods. Patients with early-onset RA may show progressive joint erosions over time, whereas PMR patients do not [16,17]. Ceccato et al [18] studied the clinical utility of anti-cyclic citrullinated peptide (CCP) antibodies to help with the differential diagnosis. In comparing patients with an early-onset RA diagnosis and patients with a PMR diagnosis, he found that a statistically significant number of patients with early-onset RA tested positive for anti-CCP antibodies at the beginning of the disease. One third of seronegative patients with early-onset RA tested positive for anti-CCP antibodies at onset [5]. All PMR patients tested negative for anti-CCP antibodies.

It is interesting to note that there has been a genetic link with HLA-DR4, HLA-DRB1*04 relating to a greater susceptibility to PMR [19]. In southern France, the HLA-DRB1 genes associated with susceptibility for developing RA and PMR are different. Both diseases are associated with HLA-DRB1*01, but only RA is significantly associated with HLA-DRB1*04 [20]. Further study is needed before the genetic links can help differentiate between RA and PMR.

Late-Onset Spondyloarthritis

There is no evidence to suggest that the case patient has a spondyloarthropathy. These include ankylosing spondylitis, reactive arthritis, psoriatic arthritis, and arthritis associated with inflammatory bowel disease. In older patients with these conditions, the presentation may be quite different than it would be in a younger patient. For example, the radiologic aspects of ankylosing spondylitis may be difficult to interpret because of the radiologic changes seen in the elderly. Late-onset peripheral spondylarthropathies are characterized by severe disease, marked elevation of acute phase reactants, oligo- and polyarthritis of the extremities and even edema of the extremities. These ailments rarely respond to low-dose corticosteroids as treatment [3,21].

Polymyositis

The case patient had complaints of stiffness, but this was not associated with pain. Her mild shoulder tenderness was secondary to stiffness. She was found to have a normal creatine kinase level. Patients with idiopathic inflammatory myopathies such as polymyositis or inclusion body myositis present with muscle weakness. In these conditions, the patient presents with symmetrical proximal muscle weakness but not shoulder or hip pain. Muscle enzymes are usually dramatically elevated, and an abnormal electromyography with the pathological correlation of a positive biopsy solidifies the diagnosis of polymyositis.

Remitting Seronegative Symmetrical Synovitis with Pitting Edema

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is similar to PMR in that it presents as arthralgia attributable to tenosynovitis and muscle pain, occurring most commonly in the elderly, and responds well
to corticosteroid treatment [22,23]. Patients with RS3PE have sudden onset of polyarthritis, negative rheumatoid and anti-CCP factor, and are older than age 50 years. Many of these patients follow 1 of 2 paths: complete remission with low-dose corticosteroids or a progression to an RA-type picture needing more aggressive treatments. The case patient had some hand swelling of unclear etiology but no peripheral synovitis to suggest RS3PE.

Malignancy
A PMR-like syndrome may be the initial manifestation of an underlying malignancy [24]. PMR may be associated with malignancies, mostly those arising from hematopoietic and lymphatic tissues [25,26]. Patients with malignancy may have a paraneoplastic syndrome mimicking PMR [27,28]. Some of these cases respond to removal of the malignant tumor [28]. The nature of the association of PMR and malignancy is unclear. It may be due to chance coexistence of 2 separate diseases that appear mainly in older age-groups [29]. If the case patient’s appetite and weight loss had not resolved or if she had new complaints, a malignancy workup would have been necessary.

Infective Endocarditis
Patients with infective endocarditis have persistent fevers that suggest an infection. Signs of infective endocarditis are high spiking fevers, positive blood cultures, dermatologic findings such as Janeway lesions, and splinter hemorrhages. The presence of valvular vegetations on cardiac echocardiography is diagnostic of infective endocarditis. There was no evidence to suggest this diagnosis in the case patient.

Vasculitis
Other than the common association with giant cell arteritis (GCA), the other vasculitides can present in a manner similar to PMR. Some patients will have elevated acute phase reactants and arthralgia. A careful history and physical examination will reveal pulmonary, renal, even peripheral nervous manifestations that would not typically be seen in PMR. Many of the other vasculitides may present with dermatologic findings and have a positive antineutrophil cytoplasmic antibodies (ANCA). There was no evidence to suggest this diagnosis in the case patient.

Bursitis and Tendinitis
It is very common to have shoulder and hip pathology as patients progress through their 60s, 70s, and even 80s. Common entities that mimic PMR shoulder pain are subdeltoid and subacromial bursitis, rotator cuff tendinitis, and even shoulder synovitis [30]. The tenderness is minimal in most cases of PMR, while patients with bursitis or tendinitis are devoid of constitutional symptoms, have low ESR (as was the case in our patient), are not anemic, and have unilateral joint involvement.

Systemic Lupus Erythematosus
Systemic lupus erythematosus (SLE) occurs predominantly in women of childbearing age and more commonly in African-American and Hispanic populations. Its presentation can vary and it has a variable course characterized by exacerbations and remissions. Serologically, the antinuclear antibody is a very sensitive test, and the anti–double-stranded DNA antibody test is highly specific for renal involvement in the active lupus patient. New-onset depression in an older patient raises the possibility of connective tissue diseases such as SLE or Sjögren’s syndrome. This patient’s depression has stemmed from the recent loss of her spouse. Her negative antinuclear antibody and negative anti-SSA and anti-SSB antibody tests give no further support for either diagnosis.

Fibromyalgia
Most patients with fibromyalgia are younger than age 50, have widespread musculoskeletal pain but no constitutional symptoms, have no obvious abnormalities on physical examination, and have normal ESR and CRP. This patient had features that were suggestive of fibromyalgia such as a sleep disturbance, depression, and tender points on examination; however, her constitutional symptoms and abnormal ESR were suggestive of PMR.

• What is the relation between GCA and PMR?

GCA is a chronic panarteritis that targets medium- and large-sized arteries. Patients have involvement of the second-to fifth-order branches of the proximal aorta, which possess well-defined internal and external elastic laminae. The inflammatory infiltrate is frequently granulomatous in nature and presents multinucleated giant cells. GCA presents most commonly in patients aged older than 50 years. Common symptoms include headaches, scalp tenderness, jaw claudication, fatigue, low-grade fever, depression, and weight loss. The most serious symptom is visual disturbances such as amaurosis fugax, scotoma, blurry vision, and visual loss. These changes, if not identified early in the disease process, can lead to irreversible blindness. These patients often present with very elevated acute phase reactants and prompt initiation of high-dose corticosteroids can salvage their vision [2]. A missed diagnosis of GCA in a patient with PMR symptoms is associated with potential vision loss.

PMR is 2 to 3 times more common than GCA, but there are many similar findings in both conditions that have led experts in the field to believe that they are a single disease
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process manifesting in different presentations [4,31–34]. Similarities include similar age at onset with greater frequency as patient age increases, presence of increased acute phase reactants, and similar affected populations, with females affected 2 to 3 times more often than males. Both disorders tend to respond dramatically to corticosteroids, with PMR responding to lower doses [2]. Population-based studies have shown that 16% to 21% of patients with PMR have GCA, and PMR is present in 40% to 60% of patients with GCA [4,33,35]. It has been observed that PMR can begin before, during, or after signs of GCA emerge. A few patients with PMR without findings of GCA at diagnosis have a positive temporal artery biopsy or develop GCA during follow-up [36,37]. It is thought that patients with PMR do not have a evidence of vasculitis, but 1 study using positron emission tomography showed increased uptake of vascular fluorodeoxyglucose at the subclavian artery in 30% of PMR patients at the time of diagnosis even though they had negative temporal artery biopsy [36]. This suggests that even with negative temporal artery biopsy findings, there may be large-vessel vasculitis in PMR.

- What laboratory findings and imaging studies can be helpful in PMR?

There are no pathognomonic laboratory or imaging findings for PMR. Inclusion of clinical history and presentation combined with serologic values can assist in ruling in PMR and ruling out the mimics. ESR and CRP are measures commonly used to help with diagnosis due to their relative low cost and quick results. Sedimentation rates can vary greatly (from 30 to 100 mm/hr). It is important to note that approximately 10% to 20% of patients with PMR present with a normal ESR [38], so the adjuvant use of other acute phase reactants interleukin-6 (IL-6), fibrinogen, serum amyloid A (SAA) protein [39], and von Willebrand factor (VWF) [40] may assist in making the diagnosis. IL-6 has recently been thought to be the most sensitive marker of this disease by some investigators [38,41]. This is of great interest because of the recent evolution of biologic therapeutics that may block IL-6. They have not been formally tested in clinical practice and are probably still considered investigational in routine practice.

A moderate normochromic normocytic anemia is commonly seen with elevation of platelets. Liver enzymes can be elevated as well, especially alkaline phosphatase as part of this inflammatory condition. Muscle enzymes, creatinine, urinalysis are all normal in PMR, even in the picture of extreme muscle aches and pains. It is unusual to find anti-nuclear antibodies, ANCA, elevated serum immunoglobulin levels (IgG, IgA, IgM), and low or elevated complement (C3, C4, CH50). If values are abnormal, further investigation is needed as the initial diagnosis of PMR may be incorrect.

For decades, the only imaging studies that were employed were conventional radiographs, which were used to look at the patient’s hands, shoulders, and hips with minimal clinical input. Newer imaging modalities have begun to be used, including US and MRI. Some studies using MRI and US have shown proximal synovitis in PMR patients [5,30,42]. Subacromial and subdeltoid bursitis are the most common lesions found when using MRI and US in these patients. A recent case-control study showed that US and MRI were equally effective in confirming bilateral subacromial and subdeltoid bursitis in PMR patients [42]. The evidence of bilateral bursitis on US had a sensitivity of 92.9% and a specificity of 99.1% for the diagnosis of PMR. In 1 study with patients that had PMR but normal ESR, US demonstrated bilateral subacromial bursitis [43].

- What are treatment options for PMR?

The mainstay of treatment for PMR is corticosteroids. There is often a dramatic response to low-dose prednisone. An initial dose of 10 to 20 mg of prednisone controls severe myalgias and causes a dramatic and rapid improvement in clinical symptoms and laboratory parameters. Rarely, higher doses are needed to reach clinical improvement. Usually, patients experience almost complete resolution of symptoms within 2 to 4 days, but clinical responses to lower prednisone doses can be delayed. Incomplete responses or recurrence of symptoms after treatment has been initiated may indicate need to reevaluate the diagnosis or increase steroid dose.

Initial doses are maintained for 2 to 4 weeks, followed by careful tapering. Usually, the steroid dose can be reduced by 10% every 2 to 4 weeks to 10 mg per day [44]. Daily doses are then reduced by 1 to 2 mg every month until treatment is stopped. About 50% of patients experience disease flares as the corticosteroids are being tapered. Increased initial doses of corticosteroids and rapid tapering were accurate predictors of relapse. Hence, great emphasis should be placed on starting and maintaining patients on the lowest possible tolerable dose of glucocorticosteroids and to taper them very slowly to avoid relapses [41,45].

The acute phase reactants ESR and CPR are usually measured to monitor disease status. ESR and CPR trend downward to normal levels, but CRP very infrequently reaches a normal level. CRP and especially IL-6 has become very suggestive marker of an inflammatory disease state [41,46].
The levels of IL-6 have shown to decline with corticosteroid treatment. Patients with nonresponsive IL-6 elevations during the first 4 weeks of therapy appear to have more severe disease [47].

It is important to note that acute phase reactants combined with improvement in morning stiffness and shoulder range of motion are principal indicators of treatment need and guide therapy. Since very low doses of corticosteroids are sufficient to control symptoms, only small incremental increases of corticosteroids are needed to control recurrent myalgias or increase in acute phase reactants [38].

• How long should patients receive treatment?

Commonly, a treatment course lasting 1 to 2 years is needed to maintain patients symptom-free, while other patients with frequent disease relapse will need to be maintained with low-dose corticosteroids for many years. Each of these cases needs to be closely monitored by the physician and health care team.

• What are the alternative treatment options for patients on long-term corticosteroids?

The use of chronic corticosteroids in the elderly population has been problematic. The development of steroid-induced diabetes, hypertension, cataracts, advanced atherosclerosis, and osteoporosis with various fractures are all well documented when using corticosteroids chronically.

Other medications that have been tried in the treatment of PMR as steroid-sparing drugs are methotrexate and anti-tumor necrosis factor (TNF) inhibitors. Methotrexate is a purine synthesis inhibitor that works by inhibiting dihydrofolate reductase (resulting in a decrease in metabolically active folates). However, methotrexate also inhibits AICAR transformylase, which leads to increased levels of AICAR and in turn stimulates the release of adenosine. Adenosine is a potent inhibitor of neutrophil function and acts as a very strong anti-inflammatory agent. Methotrexate has been tried and studied as a corticosteroid-sparing drug in PMR. Research on the potential efficacy of the steroid-sparing effects of methotrexate in PMR has been inconclusive. Some studies have hinted at efficacy in PMR, yet a randomized controlled trial was negative [48]. A recent study suggested that combination therapy with prednisone and methotrexate can be effective in PMR when methotrexate is administered for at least 1 year from disease onset at a dose of at least 10 mg per week. This schedule was found to reduce the incidence of flare-ups and the amount of prednisone required to maintain remission [49].

TNF is a potent cytokine stimulant in inflammatory responses. Blocking the stimulatory pathway and cytokine cascade of TNF has reduced the disease process and resulted in clinical improvement of rheumatologic diseases such as RA and the seronegative spondyloarthropathies. TNF inhibitors have become a primary and powerful agent in the armamentarium of battling chronic disabling rheumatic diseases. Several trials have reported using TNF-blocking drugs in the initial treatment of PMR and in glucocorticosteroid-resistant PMR [50–52]. Further study is needed to determine the benefits versus harms of biologic agents in PMR.

• What is the prognosis for PMR?

The prognosis is modestly good with proper treatment and good clinical observation for the development of GCA. PMR patients are usually treated for approximately 1 to 2 years and can eventually have their corticosteroids tapered. There has been no evidence of increased mortality with PMR alone [30]. A great emphasis must be placed on the very stringent use and tapering of corticosteroids because of the secondary effects of bone turnover, hypertension, cataracts, and increased blood glucose in these already frail elderly patients. Management of comorbidities (blood pressure, lipids, and glucose) and prophylaxis for osteoporosis should be emphasized. Patients should have a baseline dual energy x-ray absorptiometry scan and be evaluated for bisphosphonate/antireabsorptive agents as well as for proper bone health with calcium and vitamin D supplementation.

• When should a patient be referred to a specialist?

Patients suspected of having PMR or GCA should be referred to a rheumatologist to determine the need for bilateral temporal artery biopsies and initiation of corticosteroid therapy. Primary disease management by a rheumatologist is indicated in patients who relapse during reductions of...
corticosteroid doses or who develop new signs or symptoms of vasculitic involvement.

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References

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CME EVALUATION: Polymyalgia Rheumatica: To Unmask the Real Culprit

**DIRECTIONS:** Each of the questions below is followed by several possible answers. Select the ONE lettered answer that is BEST in each case and circle the corresponding letter on the answer sheet.

1. A patient diagnosed recently with polymyalgia rheumatica (PMR) is started on 20 mg prednisone daily. She has been taking this dose for the past 2 weeks with no improvement in her symptoms. The next best step would be to
   A. Increase the dose of prednisone to 60 mg/day
   B. Add ibuprofen 400 mg 3 times daily to the current dose of prednisone
   C. Begin methotrexate 20 mg once weekly with the current dose of prednisone
   D. Reconsider the initial diagnosis and evaluate for other possible causes

2. The diagnosis of PMR is a clinical one; however, the initial workup of a patient with a possible diagnosis of PMR would include
   A. Antinuclear antibody, antineutrophil cytoplasmic antibodies, rheumatoid factor, and anti-cyclic citrullinated peptide antibody
   B. Erythrocyte sedimentation rate (ESR) and C-reactive protein
   C. Radiographs of bilateral hands and sacroiliac joints
   D. Magnetic resonance imaging of lumbar sacral spine area

3. A patient with aches, pains, and morning stiffness for over 1 hour in her shoulders, hands, hips, and thighs and a normal ESR does NOT have PMR
   A. True
   B. False

4. The most common clinical mimics of PMR are
   A. Hypothyroidism, depression, and polymyositis
   B. Remitting seronegative symmetrical synovitis with pitting edema, rheumatoid arthritis, and bursitis
   C. Fibromyalgia, systemic lupus erythematosus, and malignancy
   D. All of the above

5. Once a patient has been diagnosed with PMR and started on low-dose corticosteroids, the most proper treatment regimen to follow is
   A. Wean patient off the corticosteroids rapidly to avoid corticosteroid-induced side effects such as hypertension, steroid-induced diabetes, cataracts, osteoporosis, and cushingoid features
   B. Keep the patient on the same dose of corticosteroid and add a disease-modifying antirheumatic drug such as methotrexate while monitoring ESR
   C. Titrate the corticosteroid to the lowest possible tolerable dose in which the patient does not experience resurgence of symptoms
   D. Stop corticosteroid treatment and substitute with a tumor necrosis factor inhibitor
EVALUATION FORM: Polymyalgia Rheumatica: To Unmask the Real Culprit

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