Polymyalgia Rheumatica and Giant Cell Arteritis

BRIAN UNWIN, COL, MC, USA, CYNTHIA M. WILLIAMS, CAPT (R), MC, USN, and WILLIAM GILLILAND, COL, MC, USA, Uniformed Services University of the Health Sciences, Bethesda, Maryland

Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA; also known as temporal arteritis) are common, closely related vasculitic conditions that almost exclusively occur in patients older than 50 years. They may be manifestations of the same underlying disease and often coexist. Patients with polymyalgia rheumatica usually present with acute onset of stiffness and pain in the shoulder and pelvic musculature, which may be accompanied by fever, malaise, and weight loss. If untreated, polymyalgia rheumatica may result in significant disability. Giant cell arteritis may manifest as visual loss or diplopia, abnormalities of the temporal artery such as tenderness or decreased pulsation, jaw claudication, and new-onset headaches. Erythrocyte sedimentation rate and temporal artery biopsy help make the diagnosis. Giant cell arteritis requires urgent diagnosis because without treatment it may lead to irreversible blindness. Patients with either condition also may have nonspecific symptoms. Corticosteroids are the mainstay of therapy for both conditions, with higher doses required for treatment of giant cell arteritis. Duration of corticosteroid therapy can be five years or longer before complete clinical remission is achieved. Monitoring for corticosteroid-associated side effects such as osteoporosis and diabetes, as well as for relapses and flare-ups, is key to chronic management. The prognosis for either condition, if treated, is good. (Am Fam Physician 2006;74:1547-54, 1557-8. Copyright © 2006 American Academy of Family Physicians.)

Patient information: A handout on polymyalgia rheumatica and giant cell arteritis, written by Jill Giordano, MSIV, University of Medicine and Dentistry of New Jersey School of Osteopathic Medicine, is provided on page 1557.

Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA; also known as temporal arteritis) are common, interrelated inflammatory disorders that occur predominantly in persons older than 50 years. GCA most commonly involves the temporal artery, but arteries in other parts of the body also can be inflamed. It is the most common primary vasculitis among older persons and can lead to blindness if not diagnosed and treated in a timely manner.1 About 50 percent of persons with GCA also have PMR, and about 10 percent of those with PMR also have GCA.2 PMR manifests as severe stiffness and pain in the girdle muscles (i.e., neck, shoulders, buttocks, and thighs); the forearms, hands, calves, and feet usually are not affected.3 Without treatment, PMR can cause significant disability.

Pathogenesis
Although the pathogeneses of GCA and PMR are uncertain, similar cellular immune responses involving T cells, antigen-presenting cells, macrophage-derived inflammatory cytokines, genetic human leukocyte antigen molecules, and macrophages are found in both conditions.7 Because there is so much clinical and pathophysiologic overlap, the conditions are thought to be manifestations of the same disease.

In GCA, a syndrome of systemic inflammation accompanies the vascular manifestations. Arterial biopsies often reveal inflammatory changes to the tunica media vasorum and tunica adventitia, which cause narrowing or occlusion of the vessel leading to ischemia distal to the lesion. GCA most commonly affects the branches of the internal and external carotid arteries. The involvement of these branches leads to the clinical findings of headache, jaw

Epidemiology
The most important risk factor for both conditions is older age, and the number of persons at risk in developed countries is expected to double in the next 25 years as the average age of the population increases.4 PMR has a prevalence of one in 133 among persons older than 50, with women two times more likely to be affected than men.5 GCA is less common, with an annual incidence in persons older than 50 of approximately 18 per 100,000. In both conditions the incidence peaks in those between 70 and 80 years of age, and diagnosis is more common in northern latitudes.6

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Claudication, scalp tenderness, and blindness.\(^7\) However, GCA can affect vessels anywhere in the body.\(^4,8,9\)

In PMR, the systemic inflammatory response is the most prominent feature, but inflammation of the blood vessels remains clinically undetectable.

**Diagnosis**

Distinguishing between GCA and PMR is important because GCA can lead to blindness and requires higher doses of medication.

**POLYMYALGIA RHEUMATICA**

The onset of PMR usually is acute. However, symptoms generally are present for longer than one month before patients seek an evaluation. Table 1\(^4,6\) summarizes the findings associated with a diagnosis of PMR. This disease can be functionally devastating to older adults. Shoulder pain is the most common symptom,\(^6\) and the pain and stiffness experienced in the shoulders and upper arms may make hygiene and self-care tasks difficult.

The physical examination of a patient with PMR often is less striking than the history would suggest; however, findings may include limited range of motion in the neck, shoulders, and hips secondary to pain in the associated proximal muscles; inflammation of the bursae in the shoulder and hip regions; tenderness of the upper arms and thighs; low-grade temperature elevation; evidence of weight loss; and synovitis. Distal extremity manifestations are more prominent in PMR than in GCA. These findings may include asymmetrical peripheral wrist and knee arthritis, carpal tunnel syndrome, and swelling of the hands and feet.\(^10\)

**GIANT CELL ARTERITIS**

GCA often manifests as a new-onset headache or a headache that is different from previous headaches. The headache usually is ongoing for two to three months before patients seek medical attention. Other common

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**SORT: KEY RECOMMENDATIONS FOR PRACTICE**

<table>
<thead>
<tr>
<th>Clinical recommendation</th>
<th>Evidence rating</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>If the erythrocyte sedimentation rate is normal, then GCA is unlikely.</td>
<td>C</td>
<td>11</td>
</tr>
<tr>
<td>Patients older than 50 years with jaw claudication; diplopia; and temporal artery beading, prominence, and tenderness should have a temporal artery biopsy to diagnose GCA.</td>
<td>C</td>
<td>11, 14</td>
</tr>
<tr>
<td>Prednisone should be given as first-line therapy for treatment of PMR and GCA.</td>
<td>B</td>
<td>11, 14</td>
</tr>
<tr>
<td>Treatment of GCA should not be delayed while awaiting biopsy.</td>
<td>C</td>
<td>14</td>
</tr>
<tr>
<td>Ultrasonography and positron emission tomography are not replacements for temporal artery biopsy.</td>
<td>B</td>
<td>18-20</td>
</tr>
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</table>

GCA = giant cell arteritis; PMR = polymyalgia rheumatica.

\(^A\) = consistent, good-quality patient-oriented evidence; \(^B\) = inconsistent or limited-quality patient-oriented evidence; \(^C\) = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1463 or http://www.aafp.org/afpsort.xml.

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**TABLE 1**

<table>
<thead>
<tr>
<th>Findings Associated with Polymyalgia Rheumatica</th>
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<tr>
<td>Age 50 years or older</td>
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<tr>
<td>Erythrocyte sedimentation rate greater than 50 mm per hour</td>
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<tr>
<td>Mild, normochromic, normocytic anemia</td>
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<tr>
<td>Aching, pain, and morning stiffness in the shoulders and upper arms, hips and thighs, or neck and torso</td>
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<tr>
<td>Symptoms of systemic inflammation (e.g., anorexia, depression, fever, malaise, night sweats, weight loss)</td>
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Information from references 4 and 6.
symptoms and findings in patients with GCA are outlined in Table 2.4,6,11,12 About 40 percent of patients with GCA present with atypical symptoms. These can include dry cough, choking sensation, fever of unknown origin, and upper- and lower-extremity claudication. Neurologic manifestations may include mononeuropathies, peripheral polyneuropathies, and, rarely, transient ischemic attacks or strokes.1,6

As with PMR, physical examination in a patient with GCA may be unremarkable. Patients with gradual-onset GCA may present with a low-grade fever and abnormalities of the temporal artery (e.g., thickened, lacking pulsation, tender, erythematous, nodular). Eye examination is important to evaluate for other possible causes of vision loss. Examination should include visual acuity, assessment of pupils for an afferent pupillary defect, ocular motility, and an ophthalmoscopic examination of the retina and optic disc.13 Joint examination may reveal reduced range of motion in the shoulder and hip because of pain, or a more distal synovitis, usually of the wrists.11

Temporal artery biopsy should be performed when clinical and laboratory evidence suggests GCA.14 One meta-analysis found only a few features were predictive of a positive temporal artery biopsy.11 Findings in GCA that increase the likelihood of a positive temporal artery biopsy result are listed in Table 3.11 A normal erythrocyte sedimentation rate generally excludes the diagnoses of GCA and PMR.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for GCA and PMR includes diseases and conditions that may present with pain, fatigue, weight loss, and fever. The most common conditions that should be considered are listed in Table 4.15 In a review, about 16 percent of patients with fever of unknown origin were diagnosed with GCA.16 Infectious diseases, such as viral infections, endocarditis, hepatitis (A, B, and C), and human immunodeficiency virus or acquired immunodeficiency syndrome, also should be considered.8 Other diseases and conditions that may mimic GCA and PMR or have similar findings include cancer, systemic lupus erythematosus, and seronegative rheumatoid arthritis. GCA and PMR are rare in patients younger than 50 years and therefore should be considered only in those older than 50 years with suggestive symptoms.

LABORATORY EVALUATION

The most useful laboratory test for diagnosing polymyalgia rheumatica and giant cell arteritis is the erythrocyte sedimentation rate.

The erythrocyte sedimentation rate is the most useful laboratory test for diagnosing polymyalgia rheumatica and giant cell arteritis.
sedimentation rate is estimated using the following formulas:

for men: \(\text{age} \div 2\)

for women: \((\text{age} + 10) \div 2\)

One meta-analysis showed the mean erythrocyte sedimentation rate for patients with GCA to be 88 mm per hour.\(^{11}\)

Most patients with PMR or GCA have an elevated C-reactive protein level.\(^{11}\) Normochromic, normocytic anemia; reactive thrombocytopenia; microscopic hematuria; and mild elevation of liver-associated enzymes also may be found.

Biopsy of the temporal artery has a pivotal role in the diagnosis and subsequent management of GCA. Because treatment involves prolonged courses of corticosteroid therapy, it is important to confirm the diagnosis with a biopsy even when the clinical probability is high. Long biopsy specimens (i.e., greater than 2 cm) of the temporal artery, serial sectioning, and experienced pathologic assessment improve diagnostic yield. Frozen sections demonstrate higher rates of false-negative biopsies. Empiric bilateral temporal artery biopsies offer no significant benefit in diagnostic yield for temporal arteritis. A contralateral biopsy could be considered if clinical suspicion is high and an initial temporal artery biopsy result is negative.\(^{13,17}\)

A negative temporal artery biopsy result does not rule out GCA because other arteries can be involved, or the artery with inflammation may not be biopsied. However, it should prompt reassessment of the differential diagnosis.

### Table 3

<table>
<thead>
<tr>
<th>Finding</th>
<th>Positive LR* (95% CI)</th>
<th>Negative LR† (95% CI)</th>
<th>Sensitivity‡ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beaded temporal artery</td>
<td>4.6 (1.1 to 18.4)</td>
<td>0.93 (0.88 to 0.99)</td>
<td>0.16 (0.07 to 0.28)</td>
</tr>
<tr>
<td>Prominent or enlarged temporal artery</td>
<td>4.3 (2.1 to 8.9)</td>
<td>0.67 (0.50 to 0.89)</td>
<td>0.47 (0.40 to 0.54)</td>
</tr>
<tr>
<td>Jaw claudication</td>
<td>4.2 (2.8 to 6.2)</td>
<td>0.72 (0.65 to 0.81)</td>
<td>0.34 (0.29 to 0.41)</td>
</tr>
<tr>
<td>Diplopia</td>
<td>3.4 (1.3 to 8.6)</td>
<td>0.95 (0.91 to 0.99)</td>
<td>0.09 (0.07 to 0.13)</td>
</tr>
<tr>
<td>Absent temporal artery pulse</td>
<td>2.7 (0.55 to 13.4)</td>
<td>0.71 (0.38 to 1.3)</td>
<td>0.45 (0.26 to 0.66)</td>
</tr>
<tr>
<td>Tender temporal artery</td>
<td>2.6 (1.9 to 3.7)</td>
<td>0.82 (0.74 to 0.92)</td>
<td>0.41 (0.30 to 0.52)</td>
</tr>
<tr>
<td>Any temporal artery abnormality</td>
<td>2.0 (1.4 to 3.0)</td>
<td>0.53 (0.38 to 0.75)</td>
<td>0.65 (0.54 to 0.74)</td>
</tr>
<tr>
<td>ESR &gt; 50 mm per hour</td>
<td>1.2 (1.0 to 1.4)</td>
<td>0.35 (0.18 to 0.67)</td>
<td>0.83 (0.75 to 0.90)</td>
</tr>
<tr>
<td>ESR abnormal</td>
<td>1.1 (1.0 to 1.2)</td>
<td>0.2 (0.08 to 0.51)</td>
<td>0.96 (0.93 to 0.97)</td>
</tr>
<tr>
<td>White race</td>
<td>1.1 (0.99 to 1.2)</td>
<td>0.86 (0.62 to 0.97)</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>0.83 (0.72 to 0.96)</td>
<td>0.32 (0.29 to 0.35)</td>
<td></td>
</tr>
</tbody>
</table>

* Likelihood ratio; CI = confidence interval; ESR = erythrocyte sedimentation rate.
† Decreased likelihood of giant cell arteritis if the finding is absent.
‡ Proportion of patients with biopsy-confirmed giant cell arteritis in whom the finding is present.

Adapted with permission from Smetana GW, Shmerling RH. Does this patient have temporal arteritis? JAMA 2002;287:97-8.

### Table 4

<table>
<thead>
<tr>
<th>Differential Diagnosis of PMR and GCA</th>
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<tbody>
<tr>
<td>Fibromyalgia</td>
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<tr>
<td>Multiple myeloma</td>
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<tr>
<td>Myalgias from statin therapy</td>
</tr>
<tr>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Polymyositis</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
</tr>
</tbody>
</table>

PMR = polymyalgia rheumatica; GCA = giant cell arteritis.

diagnosis. Of 68 patients who had suspected temporal arteritis with negative biopsies, 21 percent had PMR, 22 percent had a neurologic disorder, and 15 percent had another connective tissue disorder.11 Malignancy, arteriosclerotic peripheral vascular disease of the carotids, diabetes, ischemic optic atrophy, sinusitis, endocarditis, and amyloidosis also were found in this group of patients.11

**IMAGING**

The use of ultrasonography and positron emission tomography in the diagnosis and management of GCA and PMR still is experimental. Color-coded duplex ultrasonography sometimes is performed by trained technicians to assess GCA using specific protocols. Sensitivity and specificity for histologically confirmed GCA have been reported as 95 percent and 76 percent, respectively, when hypoechoic halo, stenosis, or occlusion were evident on examination.16 One third of patients with acute GCA in one study had sonographically detectable occlusions.16 However, other studies indicate that color-coded duplex ultrasonography cannot distinguish precisely between inflammatory and degenerative arterial disease.18,19 Ultrasonography may be helpful in selecting ideal temporal artery segments for biopsy.18,19 A negative result on ultrasonography of the temporal arteries should not be used to exclude GCA.20

Positron emission tomography has been studied in several small trials involving patients with GCA and PMR, and its use with radioactively labeled fludeoxyglucose F 18 has demonstrated large-vessel inflammation in these patients.21 Positron emission tomography is not suitable for use in evaluation of the temporal arteries because of their small size, but it may be useful in patients with unexplained inflammation or fever of unknown origin with unexplained somatic symptoms.21

**Treatment**

Low-dosage prednisone (10 to 20 mg per day) usually improves symptoms of PMR within days. Optimal response to corticosteroid therapy usually develops over two weeks. Tapering of the corticosteroid dosage should be individualized and should begin after the patient has been stabilized for two to four weeks. A general suggestion is to decrease the prednisone dosage by 1 mg per day each week until most symptoms have resolved. Duration of therapy commonly is two to three years.14,22 Patients with a clinical diagnosis of PMR whose symptoms do not respond to low-dosage corticosteroid therapy should be evaluated for an alternative diagnosis such as GCA.

A disease activity score for PMR, termed the Polymyalgia Rheumatica Activity Scale (PMR-AS), has been developed (Table 5).23 This score is derived from five variables: a visual analog scale for pain from the patient, a visual analog scale for the physician’s assessment, C-reactive protein level, morning stiffness time (measured in minutes), and assessment of the ability to elevate the upper limbs. PMR-AS scores less than 7 suggest low disease activity, scores of 7 through 17 suggest medium disease activity, and scores greater than 17 suggest high disease activity. This scale is used to help monitor and adjust therapy based on the patient’s response.

Prednisone also is first-line therapy for GCA, but much higher dosages (usually 40 to 60 mg per day) typically are required for suppression of disease activity. In patients

**TABLE 5**  
**Polymyalgia Rheumatica Activity Scale**

| Total disease activity score = CRP (mg per dL) + VASp + VASph + (MST x 0.1) + EUL |
|---------------------------------|---------------------------------|
| Score less than 7 suggests low activity |
| Score of 7 through 17 suggests medium disease activity |
| Score greater than 17 suggests high disease activity |

CRP = C-reactive protein; VASp = visual analog scale–patient derived (0-10); VASph = visual analog scale–physician derived (0-10); MST = morning stiffness time (measured in minutes); EUL = elevation of upper limbs (3 = none, 2 = below shoulder girdle, 1 = up to shoulder girdle, 0 = above shoulder girdle).

Information from reference 23.
PMR and GCA

with visual symptoms, treatment often is initiated with intravenous formulations, such as methylprednisolone (Medrol). Treatment should not be delayed while awaiting temporal artery biopsy. Corticosteroid therapy has no effect on biopsy results for up to four weeks after initiation.

Symptoms should resolve within days, and high-dosage therapy should be continued for two to four weeks before a slow taper is initiated. Alternate-day therapy has not been shown to be effective and may increase symptoms. Corticosteroid doses should be maintained at a sufficient level to reduce visual complaints, fever, headache, and myalgia complaints. High-dosage corticosteroid therapy to normalize sedimentation rates is unnecessary. Typically, corticosteroids can be tapered to a low dosage (7.5 to 10 mg per day) after six months, with complete tapering to discontinuation within two to three years. Flare-ups and relapses usually respond to corticosteroid increases to the level at which symptoms previously were controlled. Protracted courses of therapy often are necessary.

Use of adjuvant methotrexate to treat GCA is not routinely recommended. Studies using methotrexate as an adjunct to therapy in GCA are inconclusive. In one study, methotrexate therapy combined with daily prednisone therapy was more effective than prednisone alone in preserving remission and reducing overall corticosteroid exposure. However, another study using alternate-day prednisone with methotrexate showed no benefit. Use of methotrexate for PMR demonstrated little additional benefit over prednisone alone. Subspecialty consultation may be considered for patients who want methotrexate therapy, those who are intolerant of glucocorticoid therapy, and those with significant comorbidities that may complicate therapy.

Monitoring Complications

Complications related to GCA and PMR and to therapy for these conditions include osteoporosis, corticosteroid myopathy, bruising, emotional symptoms (e.g., insomnia, restlessness, hypomania, depression), hypertension, diabetes, elevated cholesterol, and fluid retention.

Baseline ophthalmologic evaluation is essential to assess any development of ischemic optic atrophy from GCA. Most visual loss occurs early in the disease. Late visual loss while receiving therapy is uncommon.

Bisphosphonates, vitamin D, and calcium have been found to be effective for preventing bone loss in patients treated with corticosteroids. The American College of Rheumatology recommends calcium supplementation (1,200 mg per day), vitamin D supplementation (800 U per day), lifestyle modification, regular weight-bearing exercise, and bisphosphonate therapy for prevention of glucocorticoid-induced osteoporosis, and suggests bone-density assessment for patients receiving long-term glucocorticoid therapy. Hormone replacement and calcitonin should be considered as second-line therapies when there are contraindications to or intolerance of bisphosphonates.

Hypertension can precede or develop from corticosteroid therapy. Assessment of bilateral upper- and lower-extremity blood pressures is particularly relevant in patients with subclinical vasculitis. Hypertension, diabetes, and edema should be treated as usual to prevent complications.

Corticosteroid myopathy can cause falls or weakness associated with rising from a chair. It is improved only on reduction in corticosteroid dose. Interventions include fall precautions, home safety assessment, physical therapy, and assistive devices. These interventions also are helpful in managing the bruising and tissue-healing difficulties encountered with long-term corticosteroid use.

Depression, sleep disturbance, and emotional lability typically respond to appropriate reductions in corticosteroid dosing. However, treatment with antidepressants may be required to reduce symptoms. Sedative hypnotics and benzodiazepines should be avoided because they increase the risk for falls and confusional states.

Any limitation of strength, range of motion, cognition, or vision should prompt consideration of assessment for driving fitness.
Prognosis

The prognosis for patients with GCA or PMR is dependent on the underlying condition and control of corticosteroid-associated complications. GCA and PMR are not associated with increased mortality. When treated, patients with PMR experience relief of pain and other symptoms and a return to previous function. Patients with GCA also experience relief with treatment, but spontaneous relapses are common and unpredictable within the first years of the disease. Partial or complete loss of vision occurs in about 15 to 20 percent of patients. Blindness in both eyes is rare.11

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army and Navy Medical Departments or the U.S. Department of Defense.

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