Polymyalgia rheumatica (PMR) is commonly found in Northern Europe and in persons of Scandinavian extraction in the US, with an annual incidence of around 50 per 100,000 population over 50 years of age, in whom it should be considered in the differential diagnosis of musculoskeletal disorders. The disorder is twice more common in women than in men. PMR is closely related to giant cell arteritis and both disorders are considered to have a common pathogenesis, associated with genetic and environmental factors (viral and bacterial infections). There is no gold diagnostic standard for PMR and the diagnosis rests on a high index of suspicion in persons older than 50 years with musculoskeletal symptoms. As an aid in diagnosis, several sets of diagnostic criteria have been used, usually related to age at onset, duration, symptoms, inflammatory markers, and response to corticosteroids. Patients with PMR 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. The symptoms of PMR seem to be related to synovitis of proximal joints and extra-articular synovial structures. PMR may occur as an isolated syndrome or accompany other diseases, mainly giant cell arteritis. It usually responds quickly to once-daily, low-dose prednisone, but some patients require treatment for several years. Monitoring for corticosteroid-associated side effects such as osteoporosis and diabetes, as well as for relapses and flare-ups, is key to chronic management.

Keywords: Pain, stiffness, polymyalgia rheumatica, corticosteroids

INTRODUCTION

Polymyalgia rheumatica (PMR) is a vascular inflammatory disorder with musculoskeletal manifestations and is closely related to giant cell arteritis (GCA), as both disorders may coexist in the same individual. Of the two conditions, PMR is more common and is characterized by bilateral pain and stiffness, typically affecting the shoulders, arms, neck, and hips. PMR affects Caucasian women and men over age 50 in a 2:1 ratio.\(^1\)\(^-\)\(^3\) PMR and GCA are most frequent at northern latitudes, the incidence being highest in Scandinavian countries and in parts of the US with large population of Scandinavian extraction. In general, the prevalence of PMR in individuals older than 50 years is 0.5-0.7%
and the estimated annual incidence in the US is 12-50 per 100,000. In Northern Europe the reported incidence is between 20.4 and 68.3 per 100,000 population older than 50 years, while in the United Kingdom (UK) between 1990 and 2001 the incidence of PMR has increased by 35%. A retrospective cohort study on PMR in primary health care patients in the UK found an overall annual incidence of 11.3 per 10,000 patients aged 50 or over. GCA is less common, with an average annual incidence in the US of 18 per 100,000 population among persons over 50 years of age. The lowest prevalence of GCA of 1.47 per 100,000 population older than 50 years was reported from Japan. GCA is found in 10-15% of PMR patients and approximately 50% of persons with GCA also have PMR. The incidence of PMR and GCA increases after the age of 50 years and peaks between 70 and 80 years of age. There is no specific test for PMR, thus the diagnosis should be considered in a patient older than 50 years with the characteristic symptoms and history.

Pathogenesis

The exact cause of PMR is unknown, but the disorder is believed to be influenced by infectious and genetic factors. The condition is associated with HLA-DR antigens, which seem to induce immunological responses to certain proteins. Some theories have postulated viral infection of the immune system in genetically susceptible persons, such as the respiratory syncytial virus (RSV), which may induce the production of anti-RSV antibodies. Other viral etiologies may be associated with an increased incidence of PMR and epidemics of *Mycoplasma pneumoniae*, parvovirus B19, and *Chlamydia pneumoniae*. Patients with PMR frequently have increased levels of interleukin-2 (IL-2) and interleukin-6 (IL-6). Pain and stiffness is due to the activity of inflammatory cells and proteins that normally are part of the immune system for combating disease. In PMR, it appears that inflammatory activity is concentrated in the tissues with effects on joints. The associated muscle pain is due to referred pain.

Signs and symptoms

PMR is a disorder of rapid onset, initiated by severe, deep-seated rheumatic pains in the shoulders (most frequent), neck, lower back, buttock, hip, and thigh. The pain usually has a symmetrical pattern and may be aggravated by movement of the adjacent joints. The pain may also appear at rest, and frequently the patient wakes up at night on account of the pain. The patient has difficulty buttoning his/her clothes, putting on a jacket, or standing up from a sitting position. The joint pain is felt upon active as well as passive movement (shoulder pain in 70-94% of cases, hip and neck pain in 50-70%). The presence of bilateral upper arm muscle weakness is not a feature of the disorder, but may be due to disuse atrophy. All above symptoms constitute the most evident features of PMR. The patient also suffers from stiffness (of more than 1 hour duration) in the involved parts, particularly in the morning or after a long period of inactivity, such as after long-distance car driving. Some patients have joint swelling, usually in the knee, wrist, and sternoclavicular joints. In addition, there may be systemic symptoms, such as lethargy, mild fever, malaise, fatigue, lack of appetite, loss of weight, and occasionally depression.

Diagnostic criteria

In the absence of a gold standard diagnostic test, the diagnosis of PMR is based on some recommended criteria, such advanced by Bird, Hunder, Chuang, Healy, Hazelman and others. Most criteria include age over 50 years, although Bird differed in using age over 65 years. Minimum duration of illness is usually taken as one month, but here Bird again used a different period, namely two weeks. The various sets of diagnostic criteria usually have the following four in common: age over 50, bilateral shoulder or hip pain, morning stiffness, and erythrocyte sedimentation rate (ESR) >40 mm/
In addition, the response to a standard dose of corticosteroids may also be used to aid in establishing the diagnosis.\(^{(2)}\)

Evaluation of the validity of PMR specificity and sensitivity data is hampered by the fact that there is no gold standard diagnostic investigation for PMR.\(^{(5)}\)

**Physical examination**

On physical examination the patient is commonly found to be fatigued, subfebrile, with swelling of distal extremities and pitting edema. On musculoskeletal evaluation, the muscles are of normal strength, and there is shoulder pain and hip pain on movement, without clinically significant swelling. In addition, the patient has synovitis of the knee, wrist and sternoclavicular joints. The muscles are flaccid, with impaired movement of the hips and legs, and/or shoulders and arms. In advanced stages there is disuse atrophy of muscles and weakness of proximal muscles and even contracture of the shoulder capsule, limiting active and passive movements.\(^{(17)}\) PMR accompanies GCA in approximately 50\% of cases, therefore the diagnosis of GCA may be made if the prominent musculoskeletal discomfort is presumably due to PMR.\(^{(18)}\) Musculoskeletal pain of abrupt onset occurring in the early morning hours, and responding dramatically to glucocorticoids, is suggestive of PMR.\(^{(19)}\)

**Laboratory evaluation**

The following investigations are required for establishing the diagnosis of PMR:\(^{(20)}\) (i) tests for inflammatory markers (ESR, plasma viscosity, and/or CRP); (ii) routine blood tests; (iii) ultrasonography of hips and shoulders; and (iv) other diagnostic tests, such as magnetic resonance imaging (MRI), bone scan, and radionuclide scan. ESR values of >40 mm/hr are characteristic of PMR, even though in normal persons the ESR may be raised by more than 20\%. In this connection, CRP level is more sensitive than ESR.

MRI, bone and radionuclide scans are of lesser importance in establishing the diagnosis of PMR. Ultrasonography shows the characteristic pathological findings at the shoulder and hip joints that may differentiate PMR from other disorders. The pathological findings consist of subdeltoid bursitis, tenosynovitis of the long head of the biceps, and synovitis of the glenohumeral joint. At the hips synovitis and trochanteric bursitis are frequently found. Although knee joint synovitis with effusion is common in patients with PMR, there is rarely a need for arthrocentesis.\(^{(21)}\)

The diagnosis of PMR is based on the typical history of persistent muscle and joint pain and stiffness, accompanied by increased levels of inflammatory markers, such as ESR. Slight increases in liver function tests are also not uncommon.\(^{(13)}\)

High ESR values are a sensitive but non-specific indicator of PMR. The ESR is on average over 40 mm/hr, but may be up to 100 mm/hr. In 20\% of cases, the ESR is not unduly raised and may even be normal. In these cases the diagnosis is established by a rapid response on administration of oral prednisone 10-15 mg/day.\(^{(22)}\) The differential count shows mild normocytic normochromic anemia. The white blood cell (WBC) count may be normal or slightly raised, but platelet counts are usually high.\(^{(2,18)}\) Of the liver function tests, serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) may be normal, while alkaline phosphatase may be slightly increased. Serum albumin may be slightly reduced. Creatinine kinase is usually normal, and this feature may be used for differentiating PMR from polymyositis and other myopathies. Antinuclear antibody and rheumatoid factor are usually normal. Serum IL-6 is raised and frequently parallels with the course of inflammation.\(^{(23)}\)

MRI of the shoulders shows subacromial and subdeltoid bursitis and glenohumeral synovitis in the majority of patients (Figure 1).\(^{(2)}\) MRI of the hands and feet reveals inflammation of the tendon sheaths in many patients.\(^{(24)}\)
On ultrasonography there is effusion in the bursa of the shoulder joint. (Figure 2). The findings on MRI are correlated with ultrasonographic findings, thus ultrasonography is indicated when the diagnosis is uncertain.

**Differential diagnosis**

The differential diagnosis may be divided into inflammatory and non-inflammatory disorders. Inflammatory disorders to be differentiated from PMR comprise rheumatoid arthritis; advanced spondyloarthropathy, including ankylosing spondylitis and psoriatic arthritis; systemic lupus erythematosus; scleroderma, Sjögren’s syndrome, and vasculitis; dermatomyositis and polymyositis. Of the non-inflammatory disorders may be mentioned osteoarthritis; spinal spondylosis; rotator cuff disease, adhesive capsulitis (frozen shoulder); drug-induced myalgia; infections, including viral infections, osteomyelitis, bacterial endocarditis, tuberculosis; malignancies (such as lymphoma, leukemia, myeloma, prostatic carcinoma); amyloidosis; Parkinson syndrome; chronic pain syndrome, fibromyalgia, depression; and endocrinopathies and metabolic bone diseases, such as hyperthyroidism, hypothyroidism, hyperparathyroidism, hypoparathyroidism, osteomalacia, and pseudogout with calcium pyrophosphate deposits.

**Associated disorders**

The diagnosis of GCA should be considered in all PMR patients. The symptoms of GCA are headache, claudication of the muscles of the jaw, and visual loss. The temporal artery is abnormal on palpation and vasculitis is detectable on biopsy.
Complications
PMR usually persists from several months to 5 years. Untreated patients frequently suffer from discomfort and decreased quality of life. The discomfort arises because the patients frequently experience difficulties in (i) getting up from their beds, standing up after sitting, getting out of a car; (ii) washing their hair (shampooing), or performing acts of personal hygiene; (iii) putting on clothes (shirts). Generally PMR is not accompanied by serious complications. Patients receiving long-term corticosteroid therapy are at risk of osteoporosis, corticosteroid myopathy, bruising, emotional symptoms (e.g., insomnia, restlessness, hypomania, depression), hypertension, diabetes, elevated cholesterol, and fluid retention. These complications have an impact on their health, social interaction, physical activity, and daily living.

Management
Management of PMR is oriented toward reduction of inflammation, mostly using low-dosage oral corticosteroids, such as prednisone or prednisolone, which characteristically produce a rapid and satisfactory response, not infrequently with a single one-day course. As a rule, however, the symptoms of PMR disappear within a few days of oral low-dosage prednisone (10 to 20 mg per day), although optimal responses may take more than two weeks to develop. Tapering of corticosteroid dosage should be started after the patient has been stabilized for two to four weeks, but the should be individualized. 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.

Although some patients with mild symptoms may recover on non-steroidal anti-
inflammatory drugs, such as aspirin or ibuprofen (Motrin, Advil), corticosteroids are currently considered the drug of choice for PMR, because they are capable of effecting a complete recovery and returning the ESR to normal levels. The addition of NSAIDs does not confer any additional advantages in duration of therapy or daily or cumulative prednisone doses, while producing more adverse events. However, some patients with PMR may achieve sustained remission with NSAIDs.\textsuperscript{(20, 31)}

Studies testing combinations of methotrexate and prednisone for a supposed corticosteroid-sparing effect have produced inconclusive results, although in one study the abovementioned combination was more effective than prednisone alone in preserving remission and reducing overall corticosteroid exposure.\textsuperscript{(32)} For prevention of corticosteroid-induced osteoporosis vitamin D and calcium have been found to be effective. 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 preventing glucocorticoid-induced osteoporosis, and suggests bone-density assessment for patients receiving long-term glucocorticoid therapy.\textsuperscript{(33)}

No limitation on movements is necessary.

In connection with the foregoing, the management principles of PMR may be taken to be as follows: \textsuperscript{(18)} (i) glucocorticosteroids constitute the most effective treatment and non-steroidal anti-inflammatory drugs offer very few benefits; (ii) in case of lack of response to prednisone (younger persons, muscle weakness, peripheral joint disease, and pain with or without stiffness), alternative diagnoses should be considered; (iii) there is scant evidence for the efficacy of steroid substitutes such as methotrexate or anti tumor necrosis factor; (iv) retraining of the remaining physical and psychosocial capabilities in collaboration with physiotherapists and occupational therapists. Monitoring of responses to treatment should be done by managing morning stiffness, pain and disability of proximal hip muscles, and the possibility of osteoporosis that might result in fractures. Occasionally, patients may suffer from relapses of PMR several years after the symptoms have disappeared. Several studies have demonstrated that relapses of PMR occur in 23\% to 29\% of patients during the entire follow-up period and, according to other studies, in 33\% of patients during the first year.\textsuperscript{(13)} A higher relapse rate (55\%) was reported by a retrospective study using prednisone at wide dose ranges (1-100 mg/d; median dose, 15 mg/d).\textsuperscript{(22)} Relapses of PMR may be treated by returning to previous high doses of prednisolone. Duration of therapy and occurrence of relapses have been related to high baseline inflammatory markers,\textsuperscript{(34,35)} older age, female gender, low initial steroid dose, faster tapering, longer duration of symptoms,\textsuperscript{(36)} and human leukocyte antigen (HLA) alleles.\textsuperscript{(37)}

**Prognosis**

PMR is usually a self-limited disease, but the progress and prognosis of PMR is extremely variable, although with prompt diagnosis and adequate treatment the prognosis is frequently very good. For recalcitrant cases, response to systemic corticosteroids is rapid and dramatic, but the treatment should be continued for 1-2 years and some patients need low doses for a relatively long period. Although relapses frequently occur within 1-3 years, the patients still respond to higher doses of systemic corticosteroids. PMR is not associated with increased mortality, but morbidity and mortality may occur as a result of immunosuppression or side effects of steroids.\textsuperscript{(38)}

**CONCLUSIONS**

There is an urgent need for standardized diagnostic and classification criteria for PMR.
In general, PMR remission occurs on a prednisone dose of 15 mg/d, and dose reductions to less than 10 mg/d should be done by tapering at a rate of less than 1 mg/mo. Treatment produces relief of pain and other symptoms and a return to previous function. The prognosis depends on the underlying condition and control of corticosteroid-associated complications.

REFERENCES