Polymyalgia rheumatica: clinical picture and principles of treatment*

Irena Zimmermann-Górska
Department of Rheumatology, Rehabilitation and Internal Medicine, Poznań University of Medical Sciences, Poznań, Poland

Abstract: Polymyalgia rheumatica (PMR) is a common disease of the elderly. It is characterized by pain and stiffness in the neck, shoulders and the pelvic girdle. In most cases erythrocyte sedimentation rate and C-reactive protein levels are highly elevated. Polymyalgia rheumatica is frequently associated with giant cell arteritis. Steroids are the standard treatment for PMR but their dosage requires adjustment depending on clinical picture, co-morbid conditions and adverse effects. The most prominent features of the disease as well as the main principles of treatment are presented.

Key words: giant cell arteritis, polymyalgia rheumatica

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Polymyalgia rheumatica (PMR) is a syndrome characterized by pain and stiffness in the neck, shoulder and/or pelvic girdles, affecting older adults. The first description of symptoms similar to PMR was published in 1888 [1] by Bruce who defined them as "senile rheumatic gout". The term "polymyalgia rheumatica" was suggested by Barber in 1957 [2]. In 1960 Paulley and Hughes found evidence pointing to the relationship between PMR and giant cell arteritis (GCA) [3].

Polymyalgia rheumatica affects elderly people and is seldom diagnosed below the age of 50 years. Its incidence increases with age and it ranges from 20 to 50 new cases in 100,000 people of the general population per year with a fourfold higher risk to women compared with men [1].

The etiology and pathogenesis of PMR as well as GCA are not clear. Environmental (infections) [4,5], and genetic (HLA-DR4, HLA-DRB1*04) [6-8] factors are linked to an increased susceptibility to both diseases.

Proinflammatory cytokines – mainly tumor necrosis factor α, interleukin-1α and interleukin-6 (IL-6) have a potential role in the pathogenesis of PMR [9-11]. Moreover, in patients with PMR the reduced production of adrenal hormones (cortisol and dehydroepiandrosterone) was observed [9,12].

Morphological examinations have demonstrated that muscle biopsy specimens of patients with PMR were normal. A number of reports has revealed the presence of lymphocytic synovitis in joints [13]. Recent studies have suggested that the PMR synovitis is related to vasculitis. The authors observed peripheral small vessel vasculitis defined as mononuclear inflammatory cells around the capillary wall surrounding the non-inflammatory temporal artery in patients with PMR [14].

Clinical features

Characteristic symptoms of PMR are aching and pain in the muscles of the neck, the shoulder and/or pelvic girdle, hips and thighs. Severe stiffness after periods of inactivity is a typical feature. Night pain is common. Joint inflammation – particularly of knees and sternoclavicular joints, is frequently observed as well as diffuse edema of the hands and feet [1,15,16].

The onset may be abrupt or insidious and diagnosis may be delayed until the patient has been extensively evaluated for other causes. Systemic manifestations, i.e. low-grade fever, malaise, weight loss and depression, occur in 50% of cases.

Laboratory abnormalities

The elevation of erythrocyte sedimentation rate (ESR) of often over 100 mm/h, is very frequent. Only occasionally PMR may occur with normal or only mildly elevated ESR.

Mild or moderate normochromic or hypochronic anaemia, thrombocytosis, eosinophilia, hypergammaglobulinemia, elevated C-reactive protein (CRP) level, liver-associated enzyme abnormalities (increased alkaline phosphatase!) are common. Synovial fluid is inflammatory [17,18].

Imaging techniques

Joint and periarticular synovitis may be visualized by ultrasound examination and particularly by magnetic resonance imaging [19].

Correspondence to:
Professor Irena Zimmermann-Górska, MD, PhD, Katedra i Klinika Reumatologiczno-Rehabilitacyjna i Chorób Wewnętrznych, Uniwersytet Medyczny im. Karola Marcinkowskiego, ul. 28 czerwca 1956 r. 135/147, 61-545 Poznań, Poland, phone/fax: +48-61-831-03-17, e-mail: zimmermanngorska@hotmail.com
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Table 1. Healey's diagnostic criteria for polymialgia rheumatica (PMR) [20]

– Age >50 years
– Pain involving at least 2 of the following areas: neck, shoulders, pelvic girdle, persisting for at least 1 month
– Morning stiffness >1 hour
– ESR >40 mm/h
– Absence of other diseases capable of causing the musculoskeletal symptoms
– Rapid response to prednisone (20 mg/24 h or less)
Definite PMR = a patient must meet all of the above criteria

ESR – erythrocyte sedimentation rate

Table 2. Differential diagnosis of polymyalgia rheumatica

Joint diseases
– rheumatoid arthritis (particularly in the early stage!)
– osteoarthritis
– connective tissue diseases
– remitting seronegative symmetric synovitis with pitting oedema
– "soft tissue rheumatism", fibromialgia
Muscle diseases
– polymyositis, dermatomyositis
– myopathies (treatment with statins!)
Neoplastic diseases
– multiple myeloma
– lymphoma
– carcinoma (kidney, lung, colon)
Infections (bacterial endocarditis!)
Bone diseases
Hypothyroidism
Parkinsonism
Depressive illness
Functional myalgias

Diagnosis

Diagnosis of PMR is based on the clinical signs and symptoms, elevated ESR and CRP. Additionally a rapid response to small doses of corticosteroids (CS) is taken under consideration.

A variety of criteria for diagnosis of PMR have been developed. These proposed by Healey are of value in everyday practice [20] (Tab. 1).

Differential diagnosis

Differential diagnosis of PMR ought to be started from the evaluation of signs and symptoms which may be related to GCA. These two disorders frequently occur synchronously or sequentially in individual patients. Polymyalgia rheumatica has been diagnosed in 40–60% of patients with GCA. About 10–15% of "clear" PMR patients have positive temporal-artery biopsy [13,15,18,21].

In practice this biopsy is not necessary unless the presence of temporal arteritis is suggested by symptoms or signs, i.e. headache, jaw claudication, visual disturbance, scalp tenderness. The arteries of the head, neck, torso and extremities should be examined for tenderness, enlargement, bruits and decreased pulsation. Laboratory values in PMR and GCA are similar [13].

Clinical symptoms of PMR can be mimicked by many other diseases (Tab. 2).

Seronegative, late-onset rheumatoid arthritis with large joint involvement may be indistinguishable from PMR [9].

Osteoarthritis of shoulders and hips can mimic PMR but usually radiological examinations and laboratory tests allow easy differentiation.

Inflammatory myopathy resulting in muscle weakness shows typical abnormalities in laboratory tests and electromyographic examination.

Several prospective studies have suggested that patients with "classical" PMR do not appear to be an increased risk group for malignancy [17,22,23]. Atypical features of PMR, e.g. limited or asymmetric involvement of typical sites, the ESR less than 40 mm/h or more than 100 mm/h, age below 50 years and poor or delayed responses to CS may suggest occult malignancy [24,25]. In such cases, after diagnosis and treatment of neoplasia, musculoskeletal symptoms may be completely resolved [26–28]. The association between PMR and malignancy is still controversial [29]. The cases of this coincidence have been frequently reported [24,25,27,30].

Treatment

The current recommendation is to initiate treatment with 15–20 mg of prednisone per day as quickly as possible [31,32]. Prompt relief from myalgias can be expected within hours or days. Afterwards, a gradual reduction in daily prednisone doses depending on clinical symptoms and ESR and CRP values is recommended.

There are various methods of tapering of prednisone.

Recently Dasgupta et al. [31] recommended that the initial prednisolone dose should be 15 mg/24 h for 3 weeks. This dose should be tapered to 12.5 mg/24 h for the next 3 weeks, and then to 10 mg/24 h for 4–6 weeks, followed by a 1 mg reduction (4–8 weeks) or alternate day reductions (e.g. 10/7.5 mg alternate on days). The rapid reduction often results in relapse.

Some patients cannot tolerate the outlined dose-reduction regime and the dose of prednisone ought to be increased. Over 50% of patients with PMR have relapsing disease and require CS therapy for several years [33]. Many studies indicate that CS treatment can only rarely be discontinued before 2 years [34].

Most relapses occur after the prednisone dosage is reduced to less than 7.5 mg/24 h [30]. In the cases of PMR relapse, increasing prednisone to the previous higher dose or a single I.M. injection of depot methylprednisolone are recommended [31].

We need the effective treatment that could reduce exposure to CS [35]. The possibility of starting the CS therapy at low doses is still controversial [36,37]. Combining prednisone with methotrexate (MTX) was effective when MTX was administered after at least 1 year from the onset of the disease at a dosage of at least 10 mg/week [38,39]. These effects are also controversial [37]. Infliximab combined with prednisone did not affect the course of the disease [34].

After discontinuation of CS some patients can be effectively treated with nonsteroidal anti-inflammatory drugs which, however, can induce many adverse effects in the elderly.

Long-term treatment with CS requires the assessment of co-morbid conditions and side effects, particularly osteoporosis, hypertension, diabetes and cataracts. Early bone protection by co-prescribing calcium and vitamin D supplementation with steroids is essential. Biphosphonates should be used early if other risk factors are present or if there is a risk of higher cumulative CS [31].

There is a subset of patients so-called "resistant cases", who fail to respond to prednisone in doses 20 mg/24 h and require higher doses. In these patients high values of ESR (>50 mm/h) as well as very high levels of IL-6 were observed at diagnosis [11]. It is always extremely important to determine that in these "resistant cases" the diagnosis of PMR is unquestionable.

The mechanisms underlying PMR are complex. The role of proinflammatory cytokines and other factors in pathogenesis of the disease remain unclear. We do not have a target for the treatment and PMR still remains a "therapeutic challenge". At present we can only recommend the CS therapy which usually leads to the "dramatic" improvement.

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