POLYMYALGIA RHEUMATICA: AN OVERVIEW

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ABSTRACT
Polymyalgia Rheumatica is a syndrome with a self-limited course, which affects mainly on the elderly persons. The chief complaints consist of pain and stiffness of the shoulders and the pelvic girdles with constitutional symptoms, plus a high erythrocyte sedimentation rate and C-reactive protein. The course can be shortened by corticosteroids.

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INTRODUCTION

Polymyalgia rheumatica (PMR) is a relatively common disease. It is characterized by proximal myalgia of the hip and shoulder girdles with significant morning stiffness (more than one hour)\(^1\). Approximately 15% to 30% of the patients with PMR develop giant-cell arteritis (GCA)\(^3\), while approximately 50% of the patients with GCA have associated PMR\(^1,2\) and the two disorders may represent different manifestations of a shared disease process.

EPIDEMIOLOGY

PMR has been described almost exclusively in white Caucasians, occasionally reported in African American persons, and is rarely seen in Asians. It is twice as common in females. The incidence of PMR increases with age\(^3\) but it rarely affects persons younger than 50 years\(^3\). The median age at diagnosis is 72 years\(^3\). The average incidence in the United States is 52.5 cases per 100,000 persons older than 50 years. The prevalence of the disease is 0.5-0.7\(^%\)\(^5\), although, it's prevalence is variable in other countries and higher in northern Europe\(^5,7\).

PATHOGENESIS

The exact causes of PMR are unknown. The disease is more common among northern Europeans, which may indicate a genetic predisposition\(^2\). The infectious process is characterized by fever, leukocytosis, high ESR and systemic symptoms\(^3,4\). An autoimmune process may play a role in the PMR development which is associated with the HLA-DR4 haplotype. High levels of IL-2 are associated with PMR, while high serum levels of IL-6 correlate with the increased disease activity\(^8\). Many investigators believe that non-erosive synovitis and tenosynovitis are responsible for many symptoms of PMR, where the macrophages and CD4+ T lymphocytes have been described in synovial membranes from involved joints\(^1\). Evidence of subclinical arterial inflammation can be detected in some patients, including the presence of activated dendritic cells, interleukin-1, and interleukin-6\(^3\). However, unlike GCA, interferon gamma producing T-cells are not prominent\(^1\). Hence, both PMR and GCA are associated with specific alleles of HLA-DR4. In addition, there is a sequence polymorphism within the hyper-variable region of the HLA-DRB1 gene that maps the antigen-binding cleft of the HLA-DR molecules, which suggests an important role for antigen selection and presentation. Patients with GCA and PMR share this sequence polymorphism, which are not shared by patients with rheumatoid arthritis\(^9,10\). Seasonal variation was suggested, indicating a possible environmental infectious triggering factor\(^4\).

MORTALITY/MORBIDITY

PMR is self-limited and often remits in 1-3 years. With appropriate treatment, the survival rate is similar to that of unaffected persons of the same age. However, some reports documented an increased mortality from vascular disease among men with PMR after the initial 2 years following diagnosis\(^16\).

DIAGNOSTIC CRITERIA\(^11\)

Diagnostic criteria include all of the following: Shoulder and pelvic girdle muscle pain without weakness; morning stiffness; symptom duration of more than two months, unless treated; erythrocyte sedimentation rate (ESR) greater than 30 mm per hour or C-reactive protein (CRP) level greater than 6 mg per L. With no rheumatoid arthritis, inflammatory arthritis or malignant neoplasm, no objective signs of muscle disease, plus a prompt and dramatic response to systemic corticosteroid therapy.

CLINICAL PRESENTATION

PMR is typically characterized by the sub-acute or chronic onset of aching and morning stiffness in the shoulders, hip girdles, neck, and torso in patients over the age of 50\(^12,13\). In most patients, the shoulder girdle is the first to become symptomatic, though the hip or the neck is occasionally involved at onset. At presentation, symptoms may be unilateral, but usually become bilateral within a few weeks. Patients may have difficulty getting out of bed, rising from a chair and climbing the stairs. Most patients have systemic symptoms; fever is being the most common, plus other manifestations include weight loss, malaise and fatigue. Morning stiffness is most typical and lasts for at least 30 minutes. Carpal tunnel syndrome is found in 15% of patients. Examination is usually normal, but proximal muscle tenderness with normal power may be found. About half of the patients exhibit distal musculoskeletal manifestations in the form of synovitis or bursitis. Palpable synovitis appears to occur in more peripheral joints, such as the knees, wrists, and metacarpophalangeal joints\(^14-18\). Synovitis is usually mild and nonerosive, and can be asymmetric. Some patients develop swelling and pitting edema of the hands, wrists, ankles, and on top of the feet\(^14-17\). The edema usually occurs with other signs of PMR, but can be a presenting symptom. It appears to represent tenosynovitis and synovitis in regional structures\(^17\).

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of PMR is wide and includes amyloidosis, depression, osteoarthritis, fibromyalgia, paraneoplastic syndromes, GCA, polymyositis, hypothyroidism, multiple myeloma, fibromyalgia, and rheumatoid arthritis. Plus, acute or chronic infection, bursitis/tendinitis, cervical spondylosis, endocarditis, malignancy, Parkinson disease, remitting seronegative symmetrical synovitis with pitting edema (RS3PE). Additionally\(^18-20\) and shoulder disorders, such as shoulder synovitis, rotator cuff tendinitis, and subdeltoid bursitis.
LABORATORY STUDIES

Laboratory studies show that ESR is non-specific, but very sensitive for the diagnosis of PMR. It is usually higher than 40 mm/h (even > 100 mm/h)[21-23]. In 15-20% of the patients, ESR is slightly elevated or even normal. CRP is also elevated and may be parallel to the ESR. Some studies suggest that CRP is more sensitive than ESR for the diagnosis of PMR[24,25]. However, a complete blood count (CBC) can be normal or shows mild normocytic normochromic anemia, with mild leukocytosis and thrombocytosis. Alkaline phosphatase may be mildly increased while serum albumin levels could be slightly decreased. The creatine kinase level is usually normal (unlike polymyositis). Furthermore, antinuclear antibodies and rheumatoid factor levels are usually normal. Serum IL-6 levels are elevated and often closely parallel inflammatory activity of the disease. Radiographs of the painful joints are usually normal. MRI and bone scans are not normally used for the diagnosis of PMR[25]. However MRI of the shoulder reveals subacromial and subdeltoid bursitis and glenohumeral joint synovitis in the vast majority of patients. In addition, glenohumeral joint arthritis is also found in bone scans of most patients. Synovial fluid analysis is inflammatory; WBC counts are usually 1000-20,000 cells/µL, with 40-50% polymorphonuclear leukocytes. Temporal artery biopsy is not indicated in patients with isolated PMR.

TREATMENT

PMR is a chronic, self-limited disorder. Therapy is based on empiric experiences as few randomized clinical trials are available to guide treatment decisions. The therapeutic goals are to control painful myalgia, to improve muscle stiffness, and to resolve constitutional features of the disease. Corticosteroids are considered the treatment of choice as they often cause complete or near-complete symptom resolution with reduction of the ESR to normal. However, no definite evidence demonstrates that corticosteroids (or any other therapy) alter the natural history of PMR[26]. Non-steroidal anti-inflammatory drugs (NSAIDs) can be administered to some patients with mild symptoms; however, most patients require corticosteroids for total control of the symptoms. NSAIDs may be helpful in later stages of corticosteroid dosage tapering, and generally have no effect on ESR[26]. Methotrexate[27,28] have been used to limit the dosage and duration of corticosteroid therapy. At present, no clear cut data suggest that any of these drugs are superior to corticosteroid therapy. Furthermore, they seldom indicate the need to start antiresorptive therapy. An isolated increase in ESR (dual-energy X-ray absorptiometry [DEXA] scan) is an indication to start antiresorptive therapy. An isolated increase in ESR without symptoms during the course of treatment is often a valid reason to increase corticosteroid dose; however, a temporary delay in dosage reduction may be necessary. Because relapses are more likely to occur during the initial 18 months of therapy and within 1 year of corticosteroid withdrawal, all patients should be monitored for symptom recurrence throughout corticosteroid tapering and until 12 months after cessation of therapy. Approximately 50-75% of the patients can discontinue corticosteroid therapy after 2 years of treatment[29].

FURTHER OUTPATIENT CARE

Typically PMR is treated in an outpatient setting. The objective means of determining prognosis and decisions concerning duration of treatment remain empiric and often need careful supervision. Calcium and Vitamin D supplementation should be initiated in all patients with PMR who are starting corticosteroid therapy. Osteopenia or osteoporosis discovered with a bone mineral density study (dual-energy X-ray absorptiometry [DEXA] scan) is an indication to start antiresorptive therapy. An isolated increase of ESR without symptoms during the course of treatment is not a valid reason to increase corticosteroid dose; however, a temporary delay in dosage reduction may be necessary. Because relapses are more likely to occur during the initial 18 months of therapy and within 1 year of corticosteroid withdrawal, all patients should be monitored for symptom recurrence throughout corticosteroid tapering and until 12 months after cessation of therapy. Approximately 50-75% of the patients can discontinue corticosteroid therapy after 2 years of treatment[29].

COMPLICATIONS

The disease usually has a limited course of several months to 5 years. Untreated patients with PMR often feel unwell.

CORTICOSTEROIDS

Oral corticosteroids are the first line of treatment since these agents’ cause profound and varied metabolic effects. The exact mechanism of action in PMR is not well-known, although, the effect of corticosteroids on disease may be caused by their general anti-inflammatory and immunomodulatory properties. In addition, corticosteroids down-regulate cytokine production. Controversy remains regarding dose and duration of treatment. Dose depends on patient’s weight and severity of symptoms, which is expected to subside in 24-72 hours after initiating therapy[31]. Dose should be increased if symptoms are not well controlled within 1 week, and a diagnosis of GCA may need to be pursued. The initial goal of therapy is to rapidly achieve symptomatic control using a relatively low dose of glucocorticoids. After a period of quiescence, initiate to slowly taper the glucocorticoid dose. Most patients require treatment for one to two years, and relapses are common with tapering. A higher ESR, larger initial doses of prednisolone, and rapid tapering may be associated with earlier relapse[32]. Therefore, tapering should be guided by clinical response. Normalization of laboratory values are helpful, but should not set the guidelines for decreasing or stopping the treatment[31]. In contrast to other rheumatic diseases, alternate-day administration of corticosteroids in PMR has been largely unsuccessful. The usual initial dose is between 10-15 mg/d, this is usually enough to relief symptoms within 72 hrs. Asymptomatic patients should maintain this dose for 4 weeks, and then slow tapering until complete discontinuation within 2 years.
and have an impaired quality of life. Generally, PMR is not associated with serious complications; however, patients treated with corticosteroids are at risk for long-term complications of corticosteroid therapy. Relapses are common and may occur in up to 25% of all treated patients. Arteritic relapse in a patient who presented exclusively with PMR is unusual. Every patient should be considered at risk for GCA. Additionally, several cases of systemic amyloidosis-associated PMR have been reported.[11,33]

**PROGNOSIS**

PMR is usually self-limited, thus, with prompt diagnosis and adequate therapy, the condition has an excellent prognosis.

**PATIENT EDUCATION**

Educate and inform the patient about the potential benefits, the risks of corticosteroid treatment, and to encourage the patient to participate in choosing the treatment plan. Emphasize the importance of healthy dietary habits, and ensure adequate calcium and vitamin D supplementation. Also to emphasize compliance with the long-term treatment plans and to follow-up care in order to prevent relapses, flares, and subsequent morbidity secondary to corticosteroid therapy. Basically, advise patients to immediately seek medical care if symptoms recur.

**REFERENCES**


