Polymyalgia rheumatica and its links with giant cell arteritis

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ABSTRACT – Polymyalgia rheumatica (PMR) was defined in 1957 and is linked with giant cell arteritis (GCA) in approximately 25% of cases. The peak incidence is between 60 and 75 years old and is increasing with the ageing population. Polymyalgia rheumatica is a clinical diagnosis without a 'gold standard' serological or histological test and there are other conditions that may mimic PMR. Treatment with a dose of 10–20 mg daily of prednisolone is suggested or 40–60 mg daily if GCA is also suspected. There are no absolute guidelines to the dose or its duration. The rate of reduction should be adjusted depending on the individual's response. Where temporal arteritis is suspected, this manifestation of GCA is a treatable medical emergency to prevent possible blindness, and steroids should be commenced immediately. There remain many unknowns in the cause, diagnosis and treatment of PMR and its overlap with GCA, and it is an ongoing challenge requiring further research.

KEY WORDS: arteritis, blindness, erythrocyte sedimentation rate, stiffness

Polymyalgia rheumatica (PMR) is an inflammatory disease which presents with symmetrical aching, tenderness and stiffness of the proximal muscles of the neck, shoulders and pelvis, particularly in the morning which may prevent a patient getting out of bed. Muscle strength is usually not impaired but is hindered by pain.[1] It is linked with giant cell arteritis (GCA) including temporal arteritis (TA) in approximately 25% or more of cases, where both conditions can occur in isolation of each other.[2] However, it has been argued that PMR and TA are clinical syndromes that from part of the spectrum of GCA and so different manifestations of the same disease process.[3,4] One author suggests that a generic term of 'polymyalgia arteritica' should be used where the 'relatively benign' PMR may later progress to GCA with its 'multi-system pathological process' including TA.[5] In GCA a syndrome of systemic inflammation accompanies the vascular manifestations. Arterial biopsies may reveal changes to the tunica media vasorum and tunica adventitia which cause narrowing or occlusion of the vessel leading to ischaemia distal to the lesion.

Distinguishing GCA and PMR is important because GCA can lead to blindness through TA and requires higher doses of steroid medication. Approximately 10% of patients initially presenting with PMR will have vasculitis on biopsy requiring a revision of their diagnosis. The standard treatment for PMR with low-dose steroids unfortunately has no prophylaxis against the blinding consequences of GCA.[6]

Clarity

The term PMR has an interesting history and it was not until 1957 that Barber tentatively suggested the term 'polymyalgia rheumatica' for this collection of symptoms and signs.[7] Prior to this, descriptions of the same clinical picture were given names such as anarthritic rheumatoid disease or myalgic syndrome of the aged with systemic reaction.[8] Although the definition of PMR is clearer, currently its overlap and distinction from GCA reinforce the statement in a paper as long ago as 1938 on the topic of temporal arteritis which refers to the condition of 'rheumatic arteritis':

> *There is great difficulty in making a confident separation of some of the forms of arteritis into groups on account of the lack of knowledge about the causation.*[9]

Caution

The need for clarity is relevant in current practice as GCA can be difficult to distinguish from, or may co-exist with, PMR, and can have the complications of blindness from its effect on the temporal arteries and cardiac ischaemia through its effects on the coronary arteries.[10] One paper makes this point well by suggesting that GCA could be an 'iceberg disease' with obvious classical forms distracting attention from the 'submerged mass of illness'.[11] In this paper the importance of palpation of the temporal arteries and auscultation of main arteries for bruits in the routine assessment of such patients is emphasised.

Cheung and Richards[12] cite the Scottish physicians Strachan *et al* in a 1980 issue of the *Lancet* and their proposed clinical classification of GCA to improve

the awareness of the diversity of this condition.[10] It is suggested that there is the 'classic GCA' and what is described as the concept of 'masked GCA'. This latter group is subdivided as follows where patients present with:

- anaemia
- weight loss and cachexia
- pyrexia of unknown origin
- aortic regurgitation
- ruptured aortic aneurysm
- cerebrovascular accident, myocardial ischaemia or intermittent claudication ('occlusive group').

Prevalence and aetiology

Polymyalgia rheumatica is twice as common in women and rare under the age of 50 years with a peak incidence between ages 60–75.[13] The disease is almost always confined to Caucasians with a higher incidence in Scandinavia and northern Europe. The incidence therefore varies between 10–50 cases/100,000 of the population aged over 50.[3] The number of persons at risk is expected to double in the next 25 years as the average age of the population increases.[14] The cause of PMR is unknown as is the relationship between PMR and GCA. In a seminar on the subject it was reported:

> *Few population-based studies have assessed the epidemiological aspects of polymyalgia rheumatica because there is a lack of a diagnostic hallmark and universally accepted diagnostic and classification criteria.*[15]

As the onset of symptoms can be quite sudden, a possible viral aetiology has been proposed. However, 'A well-defined infectious agent has never been found.' Nevertheless genetic factors appear to be important and HLA-DR4 has been associated with PMR but the aetiology remains unclear.[15]

Symptoms

The onset of PMR is usually acute. However, symptoms are generally present for longer than a month before patients seek advice. Many authors refer to 'proximal girdle involvement' and the word 'girdle' may be interpreted as muscles that encircle the neck, shoulders or pelvis. Two cardinal features of PMR are girdle pain and morning stiffness, lasting for over 30 minutes.[1] The aching pain and stiffness is usually of sudden onset and quickly becomes bilateral. There may also be systemic symptoms such as low-grade fever, fatigue and weight loss. Transient peripheral synovitis of the wrists, knees and sternoclavicular joints has also been documented.[2]

Giant cell arteritis most commonly affects the branches of the internal and external carotid arteries which can lead to symptoms such as headache or symptoms of the associated anatomy such as pain chewing food, jaw pain, sinus or tongue pain.[14] For dentists, GCA should be considered in the differential diagnosis if a patient has puzzling symptoms that are not explained by oral findings.[16] Giant cell arteritis often manifests as a new-onset headache or a headache that is different from previous headaches. If the patient has a headache, particularly a temporal headache or develops visual symptoms or scalp tenderness, GCA affecting the extracranial arteries, eg the temporal arteries, should be considered. A temporal artery biopsy may be indicated to confirm the diagnosis but steroids should be commenced urgently with this degree of suspicion in what is a treatable medical emergency to prevent potential loss of vision.

In GCA, inflammation in the walls of the smaller vessels leads to a narrowing of the lumen and eventual occlusion where pain is a result of ischaemia. Jaw claudication and headache occur in 30–80% of cases and visual disturbances such as amaurosis fugax, hallucinations, diplopia, or irreversible visual loss occur in less than 20% of cases.[17] The loss of vision results from ischaemia and infarction of the optic nerve and this results in the appearance of a pale and swollen optic nerve head on fundoscopy.[6] Appreciable visual loss occurs in 30–50% of patients with untreated GCA, but it is very difficult to predict which patients with GCA will go on to develop ocular complications.[18] Occasionally large arteries are also affected where conditions such as aortic dissection have been reported.[19]

Differential diagnosis

Many conditions may mimic the symptoms of PMR and these should also be considered, for example an occult malignancy or sepsis which can present with muscle pains. Similarly fibromyalgia, osteoarthritis and rheumatoid arthritis or systemic lupus erythematosus should also be considered. A combination of osteoarthritis with a systematic problem such as intercurrent infection may appear to be PMR.[2] Metabolic conditions should be excluded including thyroid disease and hyperparathyroidism. The likelihood of such conditions is greater with a normal erythrocyte sedimentation rate (ESR) on presentation, a poor response to corticosteroids, age of onset less than 50 years, an absence of upper limb involvement and a slow onset. Polymyalgia rheumatica is a clinical diagnosis without a 'gold standard' serological or histological test.[2]

Diagnostic parameters

A raised ESR continues for many to be the universal diagnostic parameter and the parameter by which response to treatment with steroids is judged and the condition monitored. The 'lack of a gold standard bedevils the establishment' of an accurate diagnosis.[20] If it appears that clinically a patient has PMR, a C-reactive protein (CRP) should be measured as this may be raised in patients with a normal ESR. Measurement of the plasma viscosity (PV) may also be considered.[21,22] Studies vary, but an ESR of at least 40 mm/h supports the diagnosis with associated symptoms. However, 5–20% of cases may have an ESR within the normal range.[12,15] There may be a mild normocytic anaemia which is frequently associated with chronic disease but tests for rheumatoid factor and antinuclear antibodies are generally negative. A rapid response to steroids is an important diagnostic pointer.[1,3] In GCA, arteries may be thickened, tender and nodular with pulsation being absent or reduced.[13] Temporal artery biopsy is not an investigation with

a high sensitivity and where GCA is suspected, despite a negative biopsy, steroid treatment should be started.[5,13] Also the problems of obtaining biopsies and their results quickly are impractical.[13]

Treatment

Corticosteroids are the drug of choice. Salvarani and colleagues suggest a dose of 10–20 mg daily of prednisolone for PMR or 40–60 mg daily if GCA is also suspected as this is the dose necessary to suppress the disease.[14,15] There are no absolute guidelines for the dose or its duration, but the amount of prednisolone can be reduced once symptoms have eased which they usually do quickly and the ESR has normalised. If symptoms start to relapse then the reduction in dose has been too quick. In mild cases of PMR there may be a response to a non-steroidal anti-inflammatory drug without having to resort to steroids. Patients should be made aware of possible side-effects with steroids and also to alert other healthcare practitioners that they are on steroids with the increased risk of infection or gastrointestinal bleeding. As patients may be on steroids for some time it is appropriate to consider prophylaxis with calcium and vitamin D supplementation and other treatment such as a bisphosphonate for those found to have osteopenia or osteoporosis. Ideally concomitant bisphosphonate and calcium/vitamin D therapy should be prescribed from the onset of glucocorticoid treatment. This is particularly important as PMR and GCA may occur in older people who are already at greater risk of osteoporosis.

A patient presenting with sudden loss of vision in one or both eyes should be given an intravenous injection of 10 mg dexamethasone because of the risk of permanent blindness.[5] Treatment with corticosteroids is mandatory for GCA to prevent vascular complications and treatment may be required for three to four years and relapses are most likely in the first 18 months of treatment. During relapses which may occur in a third or more patients, the dose of prednisolone should be increased to the dose given before relapse or more, depending on the severity of symptoms.[13] Relapse is associated with rapid tapering of the dose.[2] For example, in order to prevent this, where a patient is on 15 mg this should be maintained for four weeks and then reduced to 12.5 mg for another four weeks. When a dose of 10 mg is reached it should be reduced by 1 mg every four to eight weeks and the rate of reduction should be adjusted depending on the response. The dose, length of treatment and rate of reduction are based largely on observational studies. There should, however, be a dramatic response to treatment within a few days and tapering of the dose should be individualised.[2,14] There are many other potential side-effects of steroids such as sleep disturbance, confusional states and corticosteroid myopathy which paradoxically can lead to weakness rising from a chair or falls.[14] Monitoring of blood glucose with ESR measurements should also be considered as diabetes may be precipitated.

An alternative treatment reported to oral prednisolone is intramuscular methylprednisolone acetate such as a regimen of 120 mg every three to four weeks for the first 12 weeks, followed by monthly injections with a dose reduction of 20 mg every three months. A reduction of lower incidence of glucocorticoid-related side-effects has been documented.[2] The use of steroid-sparing agents, such as methotrexate, azathioprine, cyclophosphamide and cyclosporine, is possibly useful in reducing the side-effects of steroids. Due to a lack of data, however, no conclusive recommendations can be made.[16]

Prognosis

Polymyalgia rheumatica and GCA are self-limiting conditions which usually last two years but cases have been recorded of persisting for up to seven.[23] It was reported in 1979 that 'the difficulty often lies not in starting treatment but in deciding how long it should continue'.[24] There is a need for a careful assessment to maintain an acceptable balance between the benefits and risks of long-term steroid therapy.[19]

Conclusion

There remain many unknowns in the diagnosis and treatment of PMR and its overlap with GCA. It remains a challenge and an area requiring further research. Steroids, however, remain the cornerstone of treatment.[17]

Conflict of interest

The author was the junior house officer in 1984 to Dr RW Strachan, Emeritus Consultant Physician, Dumfries and Galloway Royal Infirmary, who has been cited in this paper. Perhaps, this is not a conflict of interest, but the impact of a good teacher.

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