

## **Polymyalgic Rheumatica (PMR) / Giant Cell Arteritis (GCA)**

### **Introduction:**

PMR and GCA are related conditions affecting adults over the age of 50. Both are inflammatory diseases, with PMR involving the large joints of the hips and/or shoulders and GCA involving large and medium sized blood vessels. PMR occurs in about 30 individuals over the age of 50 per 100,000 population per year, while GCA is roughly half as common. Both conditions are about twice as common in women as in men and are seen most commonly in those of Northern European descent. The average age of onset is about 70 for both conditions, and with the aging population the prevalence of these disorders is expected to increase in the next few decades.

While the cause of these conditions is unknown, the fact that they tend to occur in cooler climates and in clusters of cases every several years suggests that infections may trigger PMR and GCA. Having certain genes also seems to increase the risk of developing either of these disorders.

### **Features of PMR:**

Patients with PMR tend to experience widespread pain in the regions of the shoulders, upper arms, neck, hips, buttock, and thighs. These symptoms may be sudden in onset and are accompanied by up to several hours of morning stiffness. While swelling of knees, elbows, or wrists may occur, there is most often no visible joint swelling but only difficulty with movement of the larger joints. A small percentage of patients may experience swelling of the entire hand and foot with edema, or excess fluid accumulation. These individuals are difficult to distinguish from rheumatoid arthritis (RA).

Fever, fatigue, weight loss, and anemia are often encountered in PMR and seem to be the result of the inflammation present in the large joints. Patients typically find these symptoms quite debilitating and seek a physician's care within a few months of their onset. The good news is that PMR is not only highly treatable, but most cases last no longer than 2 years before resolving, and PMR leaves behind no noticeable joint damage.

About 15-30% of patients with PMR develop GCA, which can occur any time during the course of the illness. GCA can either occur before, after, or at the same time as PMR in a given individual.

### **Features of GCA:**

The most common symptom of GCA (also known as temporal arteritis) is headache, typically located around the temple, but any new headache in someone over the age of 50 could potentially be a sign of GCA. This symptom is the result of inflamed blood vessels in the scalp. These blood vessels may become swollen, tender, and blocked as the disease progresses. Involvement of other nearby blood vessels can cause pain in the jaw with chewing or pain in the tongue with talking. The most feared complication of GCA is loss of vision, which can occur suddenly and without warning. More frequently, patients will experience warning signs of temporary visual blackouts or double vision. Overall, up to 20 or 25% of those with GCA experience some form of vision loss, resulting from blood vessel inflammation leading to occlusion. Much less commonly, strokes can also occur. Fever, fatigue, weight loss, and many similar symptoms that can occur in PMR also may be seen in patients with GCA. Moreover, about 40-50% of GCA patients have PMR.

While the inflammation more commonly occurs in blood vessels located above the neck, 10-15% of patients can experience narrowing of blood vessels leading to the arms or dilation of the aorta, the large vessel leading out of the heart, as a result of GCA. In such patients, reduction of blood pressure in one arm or complete loss of pulse may occur. Other less common symptoms include sore throat, dry cough, and toothache, all of which pose a challenge to physicians attempting to diagnose this condition.

### **Diagnosis**

When evaluating someone who may have PMR or GCA, reviewing a history of the illness is the best place to begin. Anyone over the age of 50 who experiences new onset symptoms similar to those described above warrants further investigation.

Laboratory tests can provide some valuable clues to the diagnosis of both PMR and GCA. Markers of inflammation such as the sedimentation rate and C-reactive protein are usually elevated, often dramatically. Any other inflammatory or infectious disease,

however, can also cause elevations of these markers. Moreover, normal or only mildly elevated values on these tests are seen in about 15-20% of those with both PMR and GCA. For this reason, these tests are most meaningful when coupled with the patient's symptoms. Anemia and elevations of liver enzymes are less commonly observed findings. Antibodies seen in RA or systemic lupus erythematosus (SLE) are typically absent in PMR and GCA.

The importance of making an accurate diagnosis is greater for GCA than for PMR. Missing the diagnosis can result in serious complications, while incorrectly making the diagnosis can needlessly expose a patient to the side effects of therapy. For this reason, a more accurate method of either excluding or confirming GCA is essential. For most patients, this involves obtaining a temporal artery biopsy.

The temporal artery is located just in front of the ear and leads to the scalp. It can be easily sampled under local anesthesia with minimal complications, and no impairment in circulation occurs once it is removed. When inflammatory cells are seen within the blood vessel wall, the diagnosis of GCA is secure. Overall, about 85% of patients with GCA have such findings when their temporal arteries are examined under the micro-scope. How to treat those remaining 15% with negative biopsies that have otherwise classic features of GCA is controversial, but these individuals seem to have fewer complications and could be treated less aggressively.

Those with GCA demonstrating inflammation in larger blood vessels may be best diagnosed by certain x-ray studies. An arteriogram, where dye is injected into blood vessels to detect abnormalities compatible with GCA is an appropriate study to pursue when there is any reason to suspect disease involving the vessels leading to the arms. Such patients have fewer positive temporal artery biopsies. Magnetic resonance imaging (MRI) studies or ultrasound are other options for imaging the vessels that do not involve needle sticks or dye, but the detail in blood vessel walls may not be as precise. Some recent studies have suggested that ultrasound of the temporal artery may one day be an alternative to biopsy, but this procedure still needs to be refined.

#### **Therapy for PMR:**

In many ways, the therapy for PMR is also part of the diagnosis. Corticosteroids at relatively low doses (10-20 mg/day of prednisone, for example) typically produce such a dramatic reduction in pain and stiffness within one week (or even within a day or two) that a prompt response helps to confirm the diagnosis of PMR. If such a response is seen in a patient with suspected PMR, the dose of steroids can be slowly reduced and eventually discontinued without a return of symptoms. In the majority of individuals, 1-2 years of therapy is necessary to adequately suppress disease activity.

In a minority, higher doses of corticosteroids may be required, reductions in the dose may result in a return of symptoms, or a longer duration of therapy may be required. In such patients, methotrexate (MTX) has been shown in a recent study to allow steroids to be decreased successfully. Some of these individuals with features of PMR that are resistant to therapy must be observed carefully for the development of GCA or progression to RA.

Corticosteroids may cause weight gain, elevation of blood sugars, cataracts, weakening of the bones, and increased susceptibility to infection. While steroid side effects are of concern when therapy is given for more than 6 months, the fact that low doses are sufficient to treat PMR minimizes these complications.

#### **Therapy for GCA:**

As with PMR, the treatment of choice for GCA is corticosteroids, but at a much higher dose. Prednisone at a dose of 40-60 mg/day is the recommended initial dose to suppress inflammation and prevent complications (vision loss, for example). This therapy can be started in a patient in whom GCA is strongly suspected before the temporal artery biopsy without affecting the results. Also as with PMR, the dose is gradually reduced over about 2 years, adjusting based on the presence of GCA symptoms, and eventually discontinued.

Unfortunately, the dose of steroids required to treat GCA frequently results in side effects in this age group that is typically being treated. Bone density measurement, calcium and vitamin D supplements, and additional therapies if needed can help prevent osteoporosis (see related section) and are recommended in steroid-treated patients. Other side effects listed above, however (see Therapy for PMR section), are more difficult to prevent.

To help reduce corticosteroid doses, other therapies have been sought. There have been conflicting reports about the effectiveness of MTX in treating GCA. Azathioprine (Imuran), another drug that suppresses the immune system, has been shown



to be helpful as a “steroid-sparing” drug. Newer medications known as TNF antagonists (namely, infliximab and etanercept) have been attempted in small studies and may be helpful but are expensive and must be given either intravenously or by weekly injection.

Strangely enough, the most promising “new” therapy for GCA may be aspirin! A recent study suggested that patients taking aspirin along with corticosteroids experience fewer complications, such as vision loss, as compared with those only on corticosteroids. Further research is needed, but it is reasonable at present to recommend low dose daily aspirin for treatment of GCA due to the low expense and relatively low rate of side effects of this therapy.

All in all, PMR and GCA are treatable illnesses with a good long-term outlook as long as the diagnosis is made and adequate therapy is initiated promptly.