

## Inflamed Shoulder Structures in Polymyalgia Rheumatica With Normal Erythrocyte Sedimentation Rate

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**Objective.** To investigate the inflammatory involvement of shoulder articular and extraarticular structures in polymyalgia rheumatica (PMR) patients with a normal erythrocyte sedimentation rate (ESR) at diagnosis.

**Methods.** This was a case–control study. All consecutive, untreated new outpatients diagnosed as having PMR with a normal ESR (<40 mm/hour) during a 6-month period were included in the study (case patients). Controls were 12 consecutive, untreated PMR outpatients with an ESR of >40 mm/hour who were observed after the case patients. Before starting corticosteroid therapy, all case patients and controls underwent bilateral shoulder ultrasonography (US) and magnetic resonance imaging (MRI). US and MRI scans were evaluated independently by two radiologists who were blinded to the reciprocal results.

**Results.** Six case patients (4 men and 2 women) and 12 controls (4 men and 8 women) were studied. Both US and MRI demonstrated bilateral subacromial/subdeltoid bursitis in all 6 case patients and in 11 of the 12 (92%) controls (*P* not significant [NS]). One control had unilateral bursitis. Glenohumeral joint synovitis was found in 4 of 6 case patients (67%) by MRI and in 3 of 6 case patients (50%) by US (*P* NS), as well as in 8 of 12 controls (67%) by MRI and in 7 of 12 controls (58%) by US (*P* NS). Both MRI and US detected biceps

tenosynovitis in 5 of 6 case patients (83%) and in 8 of 12 controls (67%) (*P* NS). The severity of bursitis did not differ significantly between the groups. US was as effective as MRI in detecting inflammatory changes of the shoulder.

**Conclusion.** MRI and US studies showed that PMR patients with normal or high ESRs have similar inflammatory shoulder lesions. Moreover, bilateral subacromial/subdeltoid bursitis represents the imaging hallmark in PMR patients with a high or normal ESR. MRI or US of the shoulder may facilitate the proper diagnosis in patients with the typical proximal symptoms of PMR who also have normal ESRs.

Polymyalgia rheumatica (PMR) is a common disease of the elderly, characterized by aching and stiffness in the neck, shoulder, and pelvic girdle, and is sometimes associated with giant cell arteritis (GCA). A systemic inflammatory reaction is usually associated with the disease, and an erythrocyte sedimentation rate (ESR) of at least 40 mm/hour has been included in the diagnostic criteria (1,2). However, some investigators have reported varying percentages (7–20%) of PMR patients who have a normal ESR (<40 mm/hour) at diagnosis (3).

Subacromial and subdeltoid bursitis is a hallmark of PMR (4), and in untreated patients, it can be easily demonstrated by magnetic resonance imaging (MRI) and ultrasonography (US) (5). Glenohumeral joint synovitis and long-head biceps tenosynovitis coexist in about 60–80% of patients (4,5). These findings rapidly improve after a few days of corticosteroid therapy (6). Inflammation of subacromial and subdeltoid bursae in association with synovitis of the glenohumeral joints and tenosynovitis of the biceps represents a likely basis for the diffuse discomfort in the shoulder girdle that is observed in PMR patients (4).

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Submitted for publication August 16, 2000; accepted in revised form January 16, 2001.

**Table 1.** Comparison of the findings of magnetic resonance imaging (MRI) and ultrasonography (US) of the shoulder in polymyalgia rheumatica (PMR) patients with a normal erythrocyte sedimentation rate (ESR) (case patients) and in PMR patients with a high ESR (controls)\*

Shoulder lesion	MRI			US		
	Case patients	Controls	<i>P</i>	Case patients	Controls	<i>P</i>
Bilateral bursitis	6/6	11/12	NS	6/6	11/12	NS
Grade 1†	5/12	11/24	NS	4/12	13/24	NS
Grade 2†	6/12	9/24	NS	7/12	6/24	NS
Grade 3†	1/12	3/24	NS	1/12	4/24	NS
Glenohumeral synovitis	4/6	8/12	NS	3/6	7/12	NS
Bilateral	2/6	4/12	NS	1/6	4/12	NS
Unilateral	2/6	4/12	NS	2/6	3/12	NS
Biceps tenosynovitis	5/6	8/12	NS	5/6	8/12	NS
Bilateral	3/6	6/12	NS	3/6	6/12	NS
Unilateral	2/6	2/12	NS	2/6	2/12	NS

\* Except where indicated otherwise, values are the number/total number of case patients or controls.

NS = not significant.

† Number/total number of shoulders examined.

To our knowledge, the inflammatory involvement of the articular and extraarticular structures of the shoulder in PMR patients with a normal ESR has not yet been investigated. We therefore designed a case-control study in which we used MRI and US to assess the shoulder lesions in a series of patients with typical PMR findings, but with a normal ESR.

## PATIENTS AND METHODS

**Case patients.** All consecutive, untreated new patients diagnosed as having PMR with a normal ESR (<40 mm/hour) who attended the outpatient clinic of 3 secondary rheumatology centers (Hospitals of Prato, Reggio Emilia, and Potenza, Italy) during a 6-month period were included in the study. The diagnosis of PMR was accepted if all of the following were present: 1) persistent pain (for at least 1 month) involving two of the following areas: neck, shoulders, and/or pelvic girdle; 2) morning stiffness lasting for >1 hour; 3) rapid response to prednisone ( $\leq 20$  mg/day); 4) age >50 years; and 5) absence of other disease capable of causing the musculoskeletal symptoms.

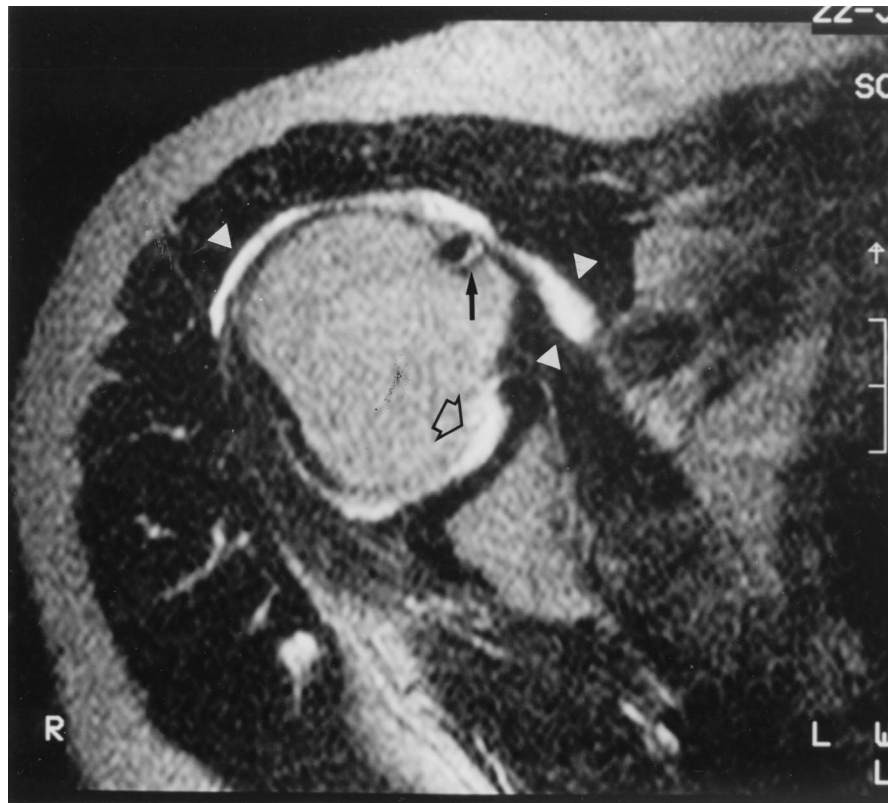
All patients were negative for rheumatoid factor (Rose-Waaler titer  $\leq 1:40$  or nephelometric determination  $\leq 20$  IU/ml on  $\geq 2$  occasions). Patients treated with corticosteroids prior to the clinical evaluation were excluded from the study. All patients were clinically assessed and prospectively followed up by the same rheumatologists (FC, CS, IO, and LN), who recorded medical information on a standardized data collection form at every visit. Temporal artery biopsies were only performed in patients with cranial signs and/or symptoms suggestive of GCA. At diagnosis and throughout followup, all patients were evaluated to determine whether they met the American College of Rheumatology (ACR; formerly, the American Rheumatism Association) 1987 revised criteria for rheumatoid arthritis (RA) (7).

**Control group.** The 12 consecutive, untreated outpatients who were observed after the case patients and who were diagnosed as having PMR according to the Healey criteria (1) served as controls. Controls had ESRs of >40 mm/hour.

**Laboratory analysis.** At diagnosis, ESR and C-reactive protein (CRP) levels were determined in all patients concomitant with their clinical evaluation. ESR was determined using the Westergren method (normal <15 mm/hour), and CRP was measured by nephelometry (NA latex CRP kit; Behringwerke, Marburg, Germany) (with 0.5 mg/dl as the upper limit of the normal reference range). ESR and CRP level were measured twice in patients with normal values at diagnosis.

**Radiologic examination.** Before starting corticosteroid therapy, bilateral shoulder US and MRI were performed on all case patients and controls. The median interval between US and MRI evaluations was 4 days (range 1–8 days). The equipment used for US was an SSA 340A (Toshiba, Tokyo, Japan) with a high-resolution 7.5-MHz linear transducer. All US examinations were performed jointly by two radiologists (MM and GC) who had special training in musculoskeletal sonography. Both radiologists agreed on the US shoulder findings. Shoulder sonograms were obtained according to previously standardized techniques (8–10). MRI scans were also evaluated by two radiologists (AB and FR). To compare the findings, the radiologists evaluated the US and MRI scans independently and were blinded to the clinical diagnosis and to the reciprocal results. MRI examinations were performed as previously reported (4).

US and MRI were used to evaluate the glenohumeral joint space, subacromial and subdeltoid bursae, and synovial sheath of the long head of the biceps. Inflammatory involvement of these structures was defined by the presence of fluid collection. US diagnostic criteria were as follows. Bursitis was indicated by the presence of sonolucent fluid distending the bursa >1 mm (9). Glenohumeral joint synovitis was indicated by the presence of intraarticular effusion sufficient to cause a gap of >3 mm between the humeral head and the joint capsule



**Figure 1.** Magnetic resonance imaging scan of the shoulder of a patient with polymyalgia rheumatica and a normal erythrocyte sedimentation rate. Axial T2-weighted scan shows grade 2 bursitis, i.e., the presence of fluid within the subacromial and subdeltoid bursae (**white arrowheads**). A moderate amount of fluid is also present within the glenohumeral joint (**open arrow**) and within the tenosynovial sheath of the long head of the biceps (**black arrow**).

(scans were obtained with the transducer placed in the axilla and the arm in 90° of abduction) (10). Biceps tenosynovitis was indicated by the presence of fluid surrounding the bicipital groove, giving a “target image” on axial sonogram or a distance of >5 mm between the biceps tendon sheath and the tendon groove on longitudinal sonogram (8). As previously reported (4), for both US and MRI scans, measurement of fluid accumulation within the bursae was graded by using a semi-quantitative scale, where 0 = no accumulation, 1 = sufficient accumulation to allow visualization of the structure, 2 = moderate accumulation, and 3 = quantity of fluid sufficient to stretch the walls of the structure.

The study protocol was reviewed and approved by each of the 3 ethics committees of the participating centers. Written informed consent was obtained from all study subjects.

**Statistical analysis.** Statistical analysis was performed using the SPSS statistical package (SPSS, Chicago, IL). The chi-square test and *t*-test for independent values were used.

## RESULTS

During the 6-month period, we observed a total of 72 PMR patients. We studied 6 case patients (4 men

and 2 women, mean  $\pm$  SD age at diagnosis  $72 \pm 4.1$  years, mean  $\pm$  SD followup period of  $11 \pm 3.8$  months) and 12 controls (4 men and 8 women, mean  $\pm$  SD age  $73 \pm 6.2$  years, mean  $\pm$  SD followup period  $10 \pm 2.4$  months). The groups did not differ significantly in clinical characteristics (duration of symptoms before diagnosis, duration of morning stiffness, presence of systemic signs and symptoms, pelvic girdle involvement, distal musculoskeletal manifestations, and associated GCA). Mean  $\pm$  SD ESR and CRP levels at diagnosis were  $25 \pm 6.5$  mm/hour and  $2.4 \pm 1.1$  mg/dl in case patients and  $67 \pm 22.6$  mm/hour and  $4.6 \pm 3.7$  mg/dl in controls.

Rapid improvement of symptoms was observed in all PMR patients after corticosteroid therapy was given. None of the patients met the ACR 1987 criteria for RA or developed articular erosions during the followup period.

MRI and US findings are summarized in Table 1.



**Figure 2.** Ultrasonography of the shoulder of the same patient as in Figure 1, confirming the presence of sonolucent fluid within the subacromial bursa (**open arrows**) and surrounding the long biceps tendon groove (**black arrows**).

Subacromial/subdeltoid bursitis was detected by both MRI and US in all case patients and controls, with no significant differences. This finding was bilateral in all 6 case patients (100%) and in 11 of the 12 controls (92%) (*P* not significant). Glenohumeral joint synovitis and long head biceps tenosynovitis were observed less frequently, with no statistically significant differences between the groups. US was as effective as MRI in assessing the frequency and severity of bursitis (Figures 1 and 2), glenohumeral joint synovitis, and biceps tenosynovitis in both groups.

### DISCUSSION

A high ESR (>40 mm/hour or >30 mm/hour, depending on the chosen cutoff value) represents one of the diagnostic criteria for PMR (1,2). Confirming the findings of our previous report (3), in the present study, we found that 6 of 72 PMR patients (8.3%) had an ESR of <40 mm/hour.

Previous MRI and US studies demonstrated that subacromial/subdeltoid bursitis is the most frequent shoulder lesion in PMR patients with a high ESR (4,5).

We therefore suggested that proximal bursitis might represent a hallmark of PMR.

MRI is considered the gold standard in depicting both the articular and extraarticular inflammatory lesions of arthritic shoulders (11). However, US may be a valid and less expensive alternative for detecting soft tissue inflammatory changes in the shoulder (12).

Patients with the clinical picture of classic PMR but a normal ESR may present some diagnostic difficulties for clinicians. The similarity of clinical findings suggests that PMR patients with a normal ESR have the same pathologic process but with a blunted inflammatory reaction. There are no studies showing the shoulder lesions in these patients.

In this case-control study, we used MRI and US to evaluate the inflamed shoulder structures in 6 PMR patients who had a normal ESR at diagnosis. Both MRI and US showed subacromial/subdeltoid bursitis in all case patients (normal ESR) and control patients (high ESR). Bursitis was bilateral in 100% of the case patients and in 92% of the controls, with no statistically significant between-group differences. In addition, no

between-group differences in the severity of bursitis or the frequency of glenohumeral joint synovitis and biceps tenosynovitis were observed. Confirming previous observations (5,12), we found that shoulder US was as effective as MRI in detecting articular and extraarticular inflammatory changes in this series of PMR patients.

The blunted inflammatory reaction may make it difficult to distinguish PMR from other pathologic processes of the shoulder that can produce US or MRI findings of bursitis, such as rotator cuff injury, tendinosis, and tendinitis (13). However, unlike PMR, these disorders occur unilaterally in the majority of patients (14,15).

In conclusion, our study confirms that bilateral subacromial/subdeltoid bursitis represents the imaging hallmark of PMR, both in patients with a high ESR and in those with a normal ESR. The inflammatory shoulder involvement in PMR patients with a normal ESR, which resembles that in patients with a high ESR, accounts for the similarity of clinical findings. The small number of patients studied does not allow us to draw definitive conclusions. However, our data suggest that shoulder MRI or US examination may be useful for supporting the diagnosis of PMR in patients presenting with the typical proximal symptoms and a normal ESR.

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