Proliferative Synovitis of the Shoulder Bursae is a Key Feature for Discriminating Elderly Onset Rheumatoid Arthritis Mimicking Polymyalgia Rheumatica From Polymyalgia Rheumatica

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ABSTRACT: Semiquantitative scoring for subacromial bursa (SAB), subdeltoid bursa (SDB), and subcoracoid bursa by both gray-scale (GS) and power Doppler (PD) ultrasonography was performed in 15 patients with polymyalgia rheumatica (PMR) (72.6 ± 7.7 years old) and 15 patients with elderly onset rheumatoid arthritis with PMR-like onset (pm-EORA) (70.7 ± 7.0 years old) before starting treatment. The GS grades of SAB were significantly higher in the shoulders with pm-EORA than in the shoulders with PMR. The GS and PD scores of SAB and the PD scores of SDB were significantly higher in pm-EORA than in PMR cases. The sums of GS and/or PD scores for the three bursae were significantly higher in pm-EORA than in patients with PMR. The sums of GS and PD scores for SAB were significantly higher in pm-EORA than in PMR cases. Moderate to severe proliferative synovitis of the shoulder bursae, especially in SAB, is a key feature for discriminating pm-EORA from PMR.

KEYWORDS: Polymyalgia rheumatica, elderly onset, rheumatoid arthritis, ultrasound, shoulder, bursitis

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Introduction
Polymyalgia rheumatica (PMR), which presents with strong pain and stiffness around the shoulder and hip girdles, is a common disorder among adults aged 50 years and older.1 Because patients with elderly onset rheumatoid arthritis (EORA) often present with polymyalgic symptoms that mimic PMR at onset, it is sometimes necessary to distinguish these two diseases in daily practice. We previously reported the differences in synovial and extrasynovial shoulder lesions between PMR and EORA with PMR-like onset (pm-EORA) by semiquantitatively analyzing musculoskeletal ultrasound (US) findings.2 In this previous study, we demonstrated that the inflammation in PMR is more dominantly localized in extrasynovial soft tissues compared with that in pm-EORA. Our previous study also revealed that the synovial lesions, including glenohumeral joint synovitis, tenosynovitis of the long head of the biceps tendon, and shoulder bursitis, were more severe in the patients with pm-EORA than in the patients with PMR. Although shoulder bursitis had been reported as the hallmark of the synovial lesion in patients with PMR,3 the bursitis was more severe in the shoulders with pm-EORA than in the shoulders with PMR. For such a comprehensive comparison of shoulder synovial lesions, the degree of bursitis was represented by the largest value among the scores for three kinds of bursal lesions: subacromial bursa (SAB), subdeltoid bursa (SDB), and subcoracoid bursa (SCB). In this study, we focus on the differences between PMR and pm-EORA in the severity of these bursal lesions.

Methods
A comprehensive US assessment of shoulder synovial lesions was performed in 15 patients with PMR (mean [standard deviation] age: 72.6 [7.7] years, disease duration: 1.7 [0.8] months, 5 women) and 15 patients with pm-EORA (mean [standard deviation] age: 70.7 [7.0] years, disease duration: 2.7 [1.1] months, 7 women) as previously described (see also Supplemental Table).2 Ultrasonography was performed to evaluate persistent inflammatory pain and stiffness in the neck and shoulder girdle before starting treatment with corticosteroids or antirheumatic drugs. A final diagnosis was confirmed for all patients based on the 1-year follow-up clinical data. Ultrasound image acquisition and scoring of shoulder bursitis were performed as previously described.2 In brief, SDB and SCB were scanned with the shoulder in a neutral position, whereas SAB was scanned with the shoulder in a modified Crass position. The gray-scale (GS) US grading of shoulder bursitis was subjectively determined (0 = absent, 1 = mild, 2 = moderate, and 3 = severe), whereas the power Doppler (PD) signal of bursitis was subjectively graded (0 = absent or minimal flow, 1 = mild or single-vessel signal, 2 = moderate or confluent vessels, and 3 = severe or vessel signals in >50% of the synovial area). The κ value of intra- and interobserver reliability was evaluated by blindly rescoring images as previously described.2 Intra- and interobserver agreement for the grading of shoulder bursitis was excellent and good, respectively.
Table 1. Distribution of GS and PD grades for three sites of shoulder bursitis.

| Grade (Score) | PMR N=30 | pm-EORA N=30 | Fisher's exact test |
|---------------|----------|--------------|--------------------|
|               | 0  1  2  3 | 0  1  2  3 | P Value            |
| SAB GS (%)    | 86.7 10.0 3.3 0.0 | 66.7 3.3 10.0 20.0 | 0.0173             |
| SAB PD (%)    | 93.3 0.0 6.7 0.0 | 73.3 10.0 6.7 10.0 | 0.0848             |
| SDB GS (%)    | 80.0 16.7 3.3 0.0 | 63.3 13.3 13.3 10.0 | 0.152              |
| SDB PD (%)    | 90.0 6.7 3.3 0.0 | 66.7 13.3 13.3 6.7  | 0.132              |
| SCB GS (%)    | 90.0 3.3 3.3 3.3 | 73.3 13.3 10.0 3.3  | 0.357              |
| SCB PD (%)    | 90.0 6.7 3.3 0.0 | 73.3 10.0 13.3 3.3  | 0.276              |

Abbreviations: GS, gray scale; PD, power Doppler; pm-EORA, elderly onset rheumatoid arthritis with PMR-like onset; PMR, polymyalgia rheumatica; SAB, subacromial bursa; SCB, subcoracoid bursa; SDB, subdeltoid bursa.

Figure 1. Comparison of the scores for respective mode or bursa between shoulders with PMR and pm-EORA by Mann-Whitney U test. (A) The sum of GS scores of SAB, SDB, and SCB. (B) The sum of PD scores of SAB, SDB, and SCB. The sum of GS and PD scores of (C) SAB, (D) SDB, and (E) SCB. GS indicates gray scale; PD, power Doppler; pm-EORA, elderly onset rheumatoid arthritis with PMR-like onset; PMR, polymyalgia rheumatica; SAB, subacromial bursa; SCB, subcoracoid bursa; SDB, subdeltoid bursa.
Results
The distribution of the GS US and PD US grades for the three kinds of bursitis are shown in Table 1. Analysis of the distribution of the grades by Fisher’s exact test revealed that the GS grades of bursitis of the SAB in the patients with pm-EORA were significantly higher than those in the patients with PMR. Comparison of the scores by Mann-Whitney U test showed that the GS and PD scores of bursitis of the SAB and the PD scores of bursitis of the SDB in the patients with pm-EORA were significantly higher than those in the patients with PMR (\(p = 0.0351\), \(p = 0.0414\), and \(p = 0.0245\), respectively).

Both the sum of GS scores and the sum of PD scores for the three bursae were significantly higher in the shoulders with pm-EORA than in the shoulders with PMR (\(p = 0.0166\) and \(p = 0.00751\), respectively) (Figure 1A and B). When we compared the sums of GS and PD scores for each bursa between the disorders, only the sums of GS and PD scores for the SAB were significantly higher in the shoulders with pm-EORA than in the shoulders with PMR (\(p = 0.0438\)) (Figure 1C to E).

Correlations between inflammatory markers and the sum of GS or PD scores for the three bursae of bilateral shoulders were examined using the Spearman’s rank correlation test. In the patients with pm-EORA, PD scores rather than GS scores were more positively correlated with serum C-reactive protein (CRP) rather than erythrocyte sedimentation rate. Correlation only between the sums of PD scores and CRP was statistically significant (\(R = 0.584, p = 0.0224\)). In contrast, GS or PD scores did not correlate with inflammatory markers in the patients with PMR, probably because the inflammation in PMR is more dominantly localized in extrasynovial soft tissues.

Discussion
We previously showed that bursitis was more severe in the shoulders with pm-EORA than in the shoulders with PMR by comparing the largest GS and PD scores among SAB, SDB, and SCB. In this study, the GS and/or PD scores of respective bursal lesions as well as the sum of the GS or PD scores of the three kinds of bursae were compared between patients with PMR and pm-EORA. Similar to the results of our previous report, it was revealed that shoulder bursitis was more severe in pm-EORA than in PMR cases. Among the three bursal lesions, the bursitis of SAB was significantly more severe in pm-EORA than in patients with PMR. Representative GS and PDUS images of SAB and SDB are shown in Figure 2.

We suspect that the difference in the degree of shoulder bursitis arises from a difference between the two disorders in the degree of synovial proliferation. Synovial proliferation is one of the most important features of rheumatoid arthritis (RA), and it is detected by GSUS as hyperechoic thickening of the articular synovium, tenosynovium, or bursal wall. In contrast, our previous data suggested that synovitis in PMR may be characterized as exudative synovitis rather than proliferative synovitis compared with synovitis in RA, a finding consistent with a previous report. This may explain the significant difference in the bursitis of the SAB between the two disorders in this study. Because the subacromial space is thought to be tighter than the subdeltoid or subcoracoid spaces, synovial fluid in the SAB may translocate into the SDB, and in some situations into the
SCB, due to pressure and gravity, whereas the proliferated synovium does not move.

**Conclusions**

Moderate to severe proliferative synovitis of the shoulder bursae, especially SAB, is a key feature for discriminating EORA mimicking PMR from actual PMR.

**Author Contributions**

TS conceived and designed the experiments, wrote the first draft of the manuscript, contributed to the writing of the manuscript. TS, RY, and YS analyzed the data. TS, RY, YH, and YS agree with manuscript results and conclusions. TS, YH, and YS jointly developed the structure and arguments for the paper. TS and YS made critical revisions and approved final version. All authors reviewed and approved the final manuscript.

**REFERENCES**

1. Soriano A, Landolfi R, Manna R. Polymyalgia rheumatica in 2011. *Best Pract Res Clin Rheumatol.* 2012;26:91–104.

2. Suzuki T, Yoshida R, Okamoto A, Seri Y. Semiquantitative evaluation of extrasynovial soft tissue inflammation in the shoulders of patients with polymyalgia rheumatica and elderly-onset rheumatoid arthritis by power Doppler ultrasound. *Biomed Res Int.* 2017;2017:4272560.

3. Salvarani C, Cantini F, Olivieri I, et al. Proximal bursitis in active polymyalgia rheumatica. *Ann Intern Med.* 1997;127:27–31.

4. Wakefield RJ, Balint PV, Szkudlarek M, et al. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. *J Rheumatol.* 2005;32:2485–2487.

5. Naredo E, D’Agostino MA, Wakefield RJ, et al. Reliability of a consensus-based ultrasound score for tenosynovitis in rheumatoid arthritis. *Ann Rheum Dis.* 2013;72:1328–1334.

6. Sakellariou G, Iagnocco A, Riente L, et al. Ultrasound imaging for the rheumatologist XLIII: Ultrasonographic evaluation of shoulders and hips in patients with polymyalgia rheumatica: a systematic literature review. *Clin Exp Rheumatol.* 2013;31:1–7.

7. Falsetti P, Acciai C, Volpe A, Lenzi L. Ultrasonography in early assessment of elderly patients with polymyalgic symptoms: a role in predicting diagnostic outcome. *Scand J Rheumatol.* 2011;40:57–63.