Papulopustular skin lesions are seen more frequently in patients with Behçet’s syndrome who have arthritis: a controlled and masked study

E Diri, C Mat, V Hamuryudan, S Yurdakul, N Hızlı, H Yazıcı

Abstract
Objective—To determine the prevalence of acneiform skin lesions (comedones, papules, and pustules) in patients with Behçet’s syndrome (BS) with arthritis.

Methods—Study groups included 44 patients with BS with arthritis (32 men, 12 women, mean (SD) age 37.8 (8.9)), 42 patients with BS without arthritis (31 men, 11 women, mean age 35.5 (6.4)), 21 patients with active rheumatoid arthritis (five men, 16 women, mean age 48.8 (14)), and 33 healthy volunteers (28 men, five women, mean age 40.1 (8.1)). All probands and controls were examined by a rheumatologist and a dermatologist, in a prospective and masked protocol. An ophthalmological evaluation was performed if necessary. Skin lesions, including comedones, papules, and pustules, were counted and scored as 0: absent, 1: 1–5, 2: 6–10, 3: 11–15, 4: 16–20, and 5: >20.

Results—Although there was no significant difference between the four groups in the prevalence of comedones, the number of papules and pustules was significantly higher in patients with BS with arthritis (p=0.0037 for papules and p<0.0001 for pustules) than in the remaining three groups.

Conclusion—Acneiform skin lesions (papules and pustules) seem to be more frequent in patients with BS with arthritis. This suggest that the arthritis seen in BS may possibly be related to acne associated arthritis.

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Acneiform lesions and arthritis in Behçet’s syndrome

Table 1  Demographic features and the frequency and regional distribution of skin lesions in study groups. Results are given as mean (SD)

<table>
<thead>
<tr>
<th></th>
<th>BS* and arthritis (n=44)</th>
<th>BS without arthritis (n=42)</th>
<th>Rheumatoid arthritis (n=21)</th>
<th>Healthy controls (n=33)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female (n)</td>
<td>32/12</td>
<td>31/11</td>
<td>5/16</td>
<td>28/5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age (years)</td>
<td>37.8 (8.9)</td>
<td>35.5 (6.4)</td>
<td>48.8 (14)</td>
<td>40.1 (8.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>5.6 (1.6)</td>
<td>4.7 (1.2)</td>
<td>3.2 (2.1)</td>
<td>4.7 (1.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comedone</td>
<td>1.11 (1.4)</td>
<td>1.26 (1.8)</td>
<td>1.14 (1.7)</td>
<td>0.97 (1.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Papule</td>
<td>1.27 (1.3)</td>
<td>0.6 (0.8)</td>
<td>0.7 (1.6)</td>
<td>0.91 (1.1)</td>
<td>0.0037</td>
</tr>
<tr>
<td>Pustule</td>
<td>1.3 (1.3)</td>
<td>0.48 (0.6)</td>
<td>0.14 (0.4)</td>
<td>0.12 (0.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Face</td>
<td></td>
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<tr>
<td>Comedone</td>
<td>0.91 (1.1)</td>
<td>1.06 (1.7)</td>
<td>1.14 (1.7)</td>
<td>0.7 (1.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Papule</td>
<td>0.98 (1.3)</td>
<td>0.1 (0.3)</td>
<td>0.33 (0.9)</td>
<td>0.06 (0.2)</td>
<td>0.0011</td>
</tr>
<tr>
<td>Pustule</td>
<td>0.45 (0.9)</td>
<td>0.19 (0.5)</td>
<td>0.05 (0.2)</td>
<td>0.01 (0.1)</td>
<td>0.0004</td>
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<td>Back</td>
<td></td>
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<tr>
<td>Comedone</td>
<td>0.20 (0.5)</td>
<td>0.21 (0.5)</td>
<td>0.01 (0.1)</td>
<td>0.33 (0.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Papule</td>
<td>0.98 (1.3)</td>
<td>0.45 (0.7)</td>
<td>0.33 (1.1)</td>
<td>0.15 (1.4)</td>
<td>0.0038</td>
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<tr>
<td>Pustule</td>
<td>0.95 (1.2)</td>
<td>0.19 (0.4)</td>
<td>0.1 (0.3)</td>
<td>0.12 (0.4)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Chest</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Comedone</td>
<td>0.23 (0.8)</td>
<td>0.14 (0.8)</td>
<td>0.01 (0.1)</td>
<td>0.21 (0.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Papule</td>
<td>0.32 (0.7)</td>
<td>0.12 (0.3)</td>
<td>0.01 (0.1)</td>
<td>0.06 (0.2)</td>
<td>0.0067</td>
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<td>Pustule</td>
<td>0.43 (0.9)</td>
<td>0.17 (0.4)</td>
<td>0.01 (0.1)</td>
<td>0.01 (0.1)</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

*BS = Behçet’s syndrome.
†p Values indicate the difference among study groups; p<0.05 indicates that the group with the highest value had a significantly increased number of lesions compared with the other groups. (Kruskal-Wallis—one way analysis of variance).

Discussion

The results support our hypothesis that skin papules and pustules are associated with arthritis in BS.

The prevalence of other disease manifestations was similar in patients with BS with or without arthritis. Furthermore, the drugs used at the time of study were similar in both groups, suggesting that disease severity was also similar in both groups. On the other hand, the probability remains that both the presence of arthritis and the pustular lesions simply reflected more severe disease within the organs affected. Our clinical impression was that this was not the case. However, a formal assessment of disease severity in the two groups was not made and we must add that currently there is no widely accepted severity index available for BS.

The patients with RA in this study were examined so that the prevalence of papulopustular lesions in patients with BS could be compared with that in another group of patients with a chronic inflammatory condition. However, the prevalence of acne, in general, decreases with age and our patients with RA were somewhat older than the patients with BS, even though they were well beyond early adulthood when acne lesions are most common. In retrospect, it would have been preferable to have had a control group strictly

Figure 2  The prevalence of clinical features other than the acneiform skin lesion in the patients with Behçet’s syndrome with (solid bars) and without arthritis (open bars). OU = oral ulcers; GU = genital ulcers; EN = erythema nodosum; TP = thrombophlebitis; EI = eye involvement; PA = pathergy test.
comparable in age and sex. Furthermore, in such studies in the future the inclusion of control groups with psoriasis or SAPHO, or both, would also be desirable, especially in the light of the following discussion.

The association of arthritis and papulopustular lesions has been well described in both SAPHO syndrome and psoriatic arthritis. In the pathogenesis of psoriatic arthritis streptococcus species⁶⁷ and in SAPHO syndrome Propionibacterium acnes⁸ have been implicated. Edlund et al carried out an open biopsy study of affected joints and para-articular bone and found that in seven of 15 patients with palmoplantar pustulosis and sternocostoclavicular arthro-ostitis, Propionibacterium acnes was grown in least two of five cultures.⁹ The role of micro-organisms in the pathogenesis of BS has also been studied. Lehner et al analysed serum samples from patients with BS by immunoblot assay and found that IgA antibodies to the recombinant 65 kDa mycobacterial heat shock protein and to soluble protein extracts of Streptococcus sanguis, ST3, KTH-1, KTH-2, and KTH-3, were significantly increased.¹⁰ A Japanese group reported that patients with BS showed significantly higher antibody titres to Streptococcus sanguis strains 113–20, 114–23, and 118–1 than control groups.¹¹ Finally, Çalgüneri et al found that prophylactic penicillin treatment significantly reduced the number of arthritis episodes.¹² Taken together, these findings suggest an infectious cause in the pathogenesis of BS, akin to a “reactive” arthritis. However, unlike the reactive arthritides, enthesitis and the HLA-B27 association are absent in BS. The nature of the genital lesions is quite different and, as was true for our patients, sacroiliitis is usually not present in BS.

The association of arthritis with acne and not with the other manifestations also raises the intriguing possibility that more than one pathogenetic mechanism might be operative in BS. This contention is also supported by the observation that one agent, thalidomide, is uniformly effective for almost all the skin mucosa manifestations of BS except the erythema nodosum lesions, which it actually exacerbates.¹³

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