Characterisation of uveitis in patients with psoriatic arthritis

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Abstract

Objective—The purpose of this study is to describe the clinical characteristics of uveitis related to psoriatic arthritis (PsA), and also to compare the uveitis in PsA to the uveitis in spondyloarthropathy (SA).

Methods—Sixteen patients with uveitis and PsA were evaluated in a tertiary care uveitis clinic. These patients were compared retrospectively to a series of 89 patients with uveitis and SA.

Results—Eight (50%) of the 16 patients with uveitis had strictly peripheral arthritis, while two (12.5%) had axial, and six (37.5%) had axial and peripheral arthritis. Patients with uveitis and axial disease were more likely to be male (100% vs 38%) and HLA-B27 positive (6 of 6 typed positive vs 0 of 3 typed positive) when compared with those with uveitis and peripheral arthritis only. Compared with patients with SA, those with PsA were more likely to have insidious onset (19% vs 3%), simultaneously bilateral (37.5% vs 7%), chronic duration (31% vs 6%), or posterior (44% vs 17%) uveitis. Complications of uveitis were similar in the SA and PsA groups.

Conclusion—Uveitis in patients with PsA was more likely to be insidious in onset, continuous, posterior, and active bilaterally compared with uveitis in patients with SA. Patients with uveitis and axial involvement were most likely to be male and HLA-B27 positive compared with patients with uveitis and peripheral arthritis alone. Patients with seronegative arthritis and uveitis that begins insidiously, lasts longer than six months, is bilateral, or is posterior, should be carefully questioned about the presence of either psoriasis or inflammatory bowel disease.

Psoriatic arthritis (PsA) is a common disease in the rheumatology department, with early synovitis clinics reporting it as the second most frequent diagnostic category after rheumatoid arthritis.1 PsA affects 5% to 7% of patients with psoriasis and up to 30% of patients with severe skin disease.2

The arthritis associated with psoriasis follows different patterns, including oligoarticular disease (seen in 15% to 40% of patients), polyarticular disease (33% to 60%), distal interphalangeal disease (8% to 16%), arthritis mutilans (5%) and axial disease (20%).3 The axial disease often overlaps with the other four groups.

Uveitis, or intraocular inflammation, can occur in association with rheumatological conditions. The differential diagnosis for the combination of arthritis and uveitis is lengthy. Potential diagnoses include ankylosing spondylitis, Reiter’s syndrome, juvenile rheumatoid arthritis, inflammatory bowel disease, Behcet’s disease, Lyme disease, Whipple disease, vasculitides, Kawasaki disease, familial granulomatous uveitis and sarcoidosis. In each entity, the pattern of ocular involvement is frequently as distinctive as the pattern of joint disease. For example, ankylosing spondylitis is typically associated with a unilateral, sudden onset, recurrent, anterior uveitis, while juvenile rheumatoid arthritis is most often associated with a bilateral, insidious onset, continuous, anterior uveitis.

Clinical characterisation of uveitis associated with PsA is limited. The first report was a study of 112 patients with PsA by Lambert and Wright. This study included a broad spectrum of ocular inflammation associated with PsA.1 They found that conjunctivitis was the most common problem, affecting 35 patients (31.2%). Iritis (anterior uveitis) was found in 7.1%, episcleritis in 1.8% and keratoconjunctivitis sicca in 2.7%. They described 11 patients with axial involvement, three of them with anterior uveitis (33%), in comparison with uveitis occurring in only 6% of the patients with no axial disease.

It is not clear if the presence of PsA in patients with psoriasis increases their risk of uveitis. In a 1984 series of 101 patients with psoriasis who underwent ophthalmological evaluation7 the only three patients with uveitis also had arthritis. However, another series of 18 patients with psoriasis who developed uveitis showed that 11 of these patients (61%) also had PsA, but seven (39%) of them had only skin disease.8 Although we have not formally investigated the prevalence of psoriasis among patients with uveitis, our clinical impression based on evaluating approximately 1300 patients with uveitis is that psoriasis without arthritis is probably not a risk factor for developing uveitis. This hypothesis, however, should be submitted to a more rigorous epidemiological test.

Uveitis is also reported in juvenile PsA. In a series of 49 children with chronic uveitis and arthritis, 13% of the children had juvenile PsA. These patients had a worse visual prognosis than children with juvenile rheumatoid arthritis.7

The relation of PsA with specific HLA types is still under scrutiny, but HLA-B27 seems to be implicated in 30%–40% of patients, especially those with axial disease.1 The B51 gene

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was implicated in the presence of uveitis in patients with psoriasis only.9

The clinical characteristics of uveitis in association with PsA are a potential aid in differential diagnosis. In addition consistent patterns of ocular disease could suggest the contribution of potentially identifiable environmental or genetic factors. Accordingly, we sought to characterise the pattern of eye inflammation associated with psoriatic arthritis, to compare this eye inflammation with that associated with spondyloarthritis, and to determine if the pattern of eye inflammation varied dependent on the pattern of arthritis associated with psoriasis.

Methods

We included all patients with the diagnosis of uveitis and PsA who underwent evaluation in the uveitis clinic in the Casey Eye Institute at the Oregon Health Sciences University, Portland, Oregon.

Patients were seen from 1985 to 1997. A total of 16 patients with PsA and uveitis were identified. The uveitis clinic database has been described previously.9 10 The OHSU inflammatory eye disease clinic is a collaboration between a rheumatologist (JTR) and members of the Department of Ophthalmology at the OHSU. Most patients are referred to this clinic by ophthalmologists for differential diagnosis or treatment recommendations and therefore usually have complicated or chronic disease. All patients underwent a comprehensive evaluation concerning their ocular and systemic diseases, as previously described.11 All patients provided a detailed medical history and received a thorough, dilated ophthalmological examination. Laboratory tests were ordered selectively based on clues provided by either history or examination.

The diagnosis of PsA was made by clinical judgment, based on the presence of different patterns of inflammatory polyarthritis in patients with psoriasis. As axial disease often overlaps with the other four types of PsA, for this study the patients were classified based on the presence of axial disease. Axial arthritis was defined as clinical and/or radiographic involvement of sacroiliac joints, spine or both. Clinical involvement was based on a history of inflammatory low back pain.12 Patients with ankylosing spondylitis, Reiter’s syndrome and incomplete Reiter’s syndrome composed the spondyloarthropathy (SA) group. These patients have been described in previous reports.7 13

For the purposes of this report, uveitis has been classified on the basis of type of onset, location, symmetry, continuity, and associated complications. Patients with sudden onset uveitis could identify the onset of eye disease within hours to days while patients with an insidious onset could not precisely identify the time the disease began. Patients with anterior uveitis had inflammation primarily anterior to the lens while patients with posterior uveitis had inflammation primarily posterior to the lens or both anterior and posterior inflammation. Symmetry was classified as unilateral (affecting only one eye), alternating (affecting either eye but not both simultaneously), or bilateral (both eyes involved simultaneously). The continuity of uveitis was classified as recurrent, meaning inflammation for less than six months with complete resolution between episodes and then at least one recurrent episode, or continuous, meaning inflammation persisting for six months or more. Patients with continuous inflammation are sometimes also described as having chronic inflammation. In this study we did not encounter patients with a single episode of uveitis lasting less than six months or with inflammation lasting greater than six months followed by a complete resolution and then a recurrence. Inflammation lasting greater than six months is a useful discriminator because episodes of uveitis in association with Reiter’s syndrome or ankylosing spondylitis rarely exceed six months in duration. Complications of uveitis include cystoid macular oedema, increased intraocular pressure, and posterior synechiae.

HLA testing was performed by lymphocytotoxicity either before referral or by the OHSU immunogenetics laboratory. Typing for HLA-B27 was not done routinely, but only if the clinician believed it would yield important diagnostic or prognostic information. Nine patients were tested in the PsA group, and 63 in the SA group.

For statistical analysis, a comparison of proportions was done using the χ² method or Fisher’s exact test. For means comparison (like age), a t test was performed.

Results

The 16 patients with uveitis and PsA included eight with peripheral disease (50%), six with peripheral and axial disease (37.5%) and two with only axial disease (12.5%). Six patients who had only peripheral disease and all patients with peripheral and axial disease presented with the oligoarticular pattern of joint involvement. One patient had distal interphalangeal disease and another one had polyarticular disease. There were no cases of arthritis mutilans.

The 89 patients with SA included 35 with Reiter’s syndrome (usually incomplete Reiter’s syndrome) and 54 with ankylosing spondylitis.

Patients with PsA were more likely to receive a diagnosis of uveitis at an older age (39 years, range 19–64) than patients with SA (33 years, range 5–56) (p<0.001 by t test). For patients with PsA, the diagnosis of uveitis was made an average of 9.7 years after the onset of arthritis (range, 0–29).

The characteristics of the uveitis in association with psoriatic arthritis are compared with the uveitis in association with SA in table 1. Using a variety of parameters, the eye findings associated with PsA could often be distinguished from those seen in association with SA.

Compared with patients with SA, the uveitis associated with PsA was more likely to begin insidiously, was more likely to be continuous rather than episodic, was more likely to be bilateral, and was more likely to be posterior to the lens.

The rate of complications was not statistically different between the groups, with four
Table 1  Clinical differences between uveitis associated with PsA and SA

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PsA (n=16)</th>
<th>SA (n=89)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (y) (range)</td>
<td>39 (19–64)</td>
<td>33 (5–56)</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>
| Time between diagnosis of arthritis and uveitis (y) (range) | 9.7 (0–29) | 9 (2–27) | H
| Female | 5 (31) | 39 (44) | p=NS NS |
| HLA B-27 (+)* | 6 (67) | 56 (69) | p=NS NS |
| Insidious onset | 3 (19) | 3 (3) | p=0.064 |
| Continuous inflammation‡ | 5 (31) | 5 (6) | p=0.006 |

*The total number of patients with SA who underwent HLA-B27 typing was 63, and for those with PsA, nine. ‡Data not available. †Indicates active inflammation longer than six months. §Includes patients with either exclusively posterior inflammation or relatively equal anterior and posterior inflammation. NS = not significant.

Table 2  Differences between patients with axial and peripheral disease

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Peripheral (n=87)</th>
<th>Axial (n=8)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>5 (65)</td>
<td>0 (0)</td>
<td>p=0.01</td>
</tr>
<tr>
<td>HLA B27 (+)*</td>
<td>0 (0)</td>
<td>6 (100)</td>
<td>p=0.012</td>
</tr>
<tr>
<td>Sudden onset</td>
<td>6 (75)</td>
<td>7 (88)</td>
<td>p=NS NS</td>
</tr>
<tr>
<td>Episodic</td>
<td>5 (63)</td>
<td>6 (75)</td>
<td>p=NS NS</td>
</tr>
<tr>
<td>Age of onset uveitis (y)</td>
<td>5 (5)</td>
<td>33.6</td>
<td>p=0.001</td>
</tr>
<tr>
<td>PsA</td>
<td>3 (38)</td>
<td>4 (50)</td>
<td>p=NS NS</td>
</tr>
<tr>
<td>Anterior involvement</td>
<td>2 (25)</td>
<td>2 (25)</td>
<td>p=NS NS</td>
</tr>
</tbody>
</table>

*Three patients were tested in the peripheral group and six in the axial group for HLA-B27. NS = not significant.

(25%) developing cataract, three (19%) glaucoma, three (19%) with cystoid macular oedema and five (31%) with posterior synechiae in the PsA group versus 18 (28%), 12 (13%), 22 (25%), and 43 (48%) in the SA group, respectively.

We also compared the uveitis based on the presence or absence of axial disease (table 2). Although the numbers in each group are small, HLA-B27 typing does suggest that we are dealing with two distinct subsets. Considering all patients with axial disease in one group, all eight were male and of the six patients tested for HLA-B27 in this group, all of them were positive. In the peripheral arthritis group, there were five women and three men. Three of the eight patients were typed, and none were HLA-B27 positive. These differences were statistically significant (p=0.012). Type of onset, continuity, location, symmetry and complications were not significantly different. Patients with axial disease developed uveitis at a younger age (33.6 years ± 44.5 years, p<0.01), compared with patients with only peripheral arthritis.

Only two patients had pure axial disease; both were HLA-B27 positive and developed sudden onset, unilateral and episodic uveitis, as is characteristic of either ankylosing spondylitis or Reiter’s syndrome. Of the 16 patients with uveitis and PsA, eight (50%), had unilateral or alternating, anterior uveitis typical of SA. Of this subset of eight, four were HLA typed and three were B27 positive. Seven were male and four had some component of axial disease. These numbers are small, but suggest that male patients with PsA tend to develop uveits that is more similar to that present in SA, and female patients with PsA tend to develop peripheral arthritis and uveitis more typical of inflammatory bowel disease.

Table 3  Summary of uveitis in Reiter's disease, ankylosing spondylitis (AS), inflammatory bowel disease (IBD) and psoriatic arthritis (PsA)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Age of onset of eye disease</th>
<th>Male:female</th>
<th>HLA B27+</th>
<th>Lifetime chance of uveitis</th>
<th>Pattern of uveitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reiter’s or AS</td>
<td>33</td>
<td>2:1</td>
<td>89%</td>
<td>20% to 40%</td>
<td>Sudden onset, anterior, unilateral, episodic</td>
</tr>
<tr>
<td>IBD</td>
<td>37</td>
<td>1:4.5</td>
<td>46%</td>
<td>3% to 11%</td>
<td>Frequently bilateral, posterior, insidious onset, continuous*</td>
</tr>
<tr>
<td>PsA</td>
<td>39</td>
<td>2:2.1</td>
<td>67%</td>
<td>7%</td>
<td>Frequently bilateral, posterior, insidious onset, continuous*</td>
</tr>
</tbody>
</table>

*Some patients with PsA or IBD have uveitis that follows the pattern seen with SA. Axial arthritis, male sex, and the presence of HLA B27 might be factors that predispose to the sudden onset, unilateral, anterior, episodic pattern.

Discussion

Our series revealed that as a general group, patients with PsA who develop uveitis were more likely to have a disease more insidious in onset, continuous (compared with episodic), posterior, and bilateral when compared with patients with uveitis and SA. Patients with uveitis and PsA with axial involvement were more likely to be male and HLA-B27 positive than PsA patients with uveitis and peripheral arthritis alone. Axial disease affects about one fifth of patients with PsA but accounted for 50% of our patients with PsA and uveitis.

We have previously reported that patients with uveitis and inflammatory bowel disease tend to have eye disease that is more often posterior, bilateral, insidious in onset, and chronic in duration compared with patients with uveitis and SA.10 The uveitis with PsA frequently resembles the uveitis associated with inflammatory bowel disease (table 3), although 50% of our patients had uveitis that was sudden in onset, anterior, and either unilateral or alternating as is characteristic of uveitis in association with SA.

Our study has several limitations. As a referral based centre, patients with mild or self limited disease may be more likely not to be referred. We did not HLA type all patients and we did not obtain radiographs of the pelvis on all patients. The diagnosis of axial disease was often based on history and may underestimate the true incidence of sacroiliitis. As a centre for the diagnosis and treatment of ocular disease, some details about skin and joint disease activity and treatment were not always available. A larger study may have revealed differences that could not be demonstrated statistically in our patient groups.

Despite these limitations, this study is the largest study of uveitis in association with PsA published to date. Our results indicate clearly that many patients with uveitis in association with PsA have eye disease that can be distinguished from that associated with SA. The presence of axial disease and uveitis has an HLA B27 association while such is not the case with peripheral arthritis and uveitis. At least two patterns of eye disease in association with PsA can be distinguished: a sudden onset, unilaterally active anterior disease indistinguishable
from what is classically associated with SA; and a more variable uveitis that is often insidious in onset, bilateral, and/or posterior as is frequently seen with inflammatory bowel disease.

Our study indicates that careful description of ocular disease can contribute to the differential diagnosis of the seronegative spondyloarthropathies. Further work needs to be done to clarify the role of specific genetic and environmental factors that contribute to the development of uveitis in a subset of patients with seronegative arthritis.

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