

# Prevalence of the Spondyloarthritides in Patients with Uveitis

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**ABSTRACT.** *Objective.* To determine the prevalence of the spondyloarthritides in patients with uveitis and to establish criteria for certain subtypes of this group of diseases.

*Methods.* In a university-based prospective study, we examined 433 patients with different types of uveitis for signs of spondyloarthritides as defined by the classification criteria of the European Spondylarthropathy Study Group (ESSG).

*Results.* Forty-four of the 433 uveitis patients (36 with acute anterior uveitis and 8 with other types of uveitis) had spondyloarthritis according to the ESSG classification criteria. Nineteen of these 44 patients had ankylosing spondylitis (AS), 11 had undifferentiated spondyloarthritis, 9 reactive arthritis, and 5 psoriatic arthritis.

*Conclusion.* Uveitis is associated not only with AS and reactive arthritis, but also with undifferentiated spondyloarthritis and psoriatic arthritis. The ESSG criteria are helpful in identifying these spondyloarthritides in uveitis patients. (J Rheumatol 2004;31:2226–9)

*Key Indexing Terms:*

SPONDYLOARTHRITIS

UVEITIS

Uveitis is a heterogeneous group of diseases characterized by intraocular inflammation of the iris, ciliary body, and/or the chorioid<sup>1-3</sup>. It is associated with systemic diseases in 25% of patients<sup>1,4,5</sup>. While posterior uveitis is mostly associated with sarcoidosis and viral and bacterial infections, acute anterior uveitis (AAU) is known to be a prominent extraarticular manifestation of HLA-B27-associated joint diseases<sup>6</sup>. Distinguishing the different types of uveitis is of great practical relevance and would aid in the evaluation of new treatment strategies.

Twenty to 60% of patients with AAU exhibit signs and symptoms of spondyloarthritis<sup>2,8-10</sup>. Ankylosing spondylitis (AS) and reactive arthritis (ReA) manifesting as Reiter's syndrome, are observed in 34%–42% of unselected patients with AAU<sup>9</sup> and 73%–90% of HLA-B27-positive AAU patients<sup>1,4,11,12</sup>. Other spondyloarthritides, such as arthritis associated with chronic inflammatory bowel disease, psoriatic arthritis, and juvenile spondylitis, have also been reported in AAU<sup>3,12,13</sup>, but their prevalence in uveitis patients is less clear. In addition to these patients with well-defined spondyloarthritides, some patients have clinical or roentgenological signs or symptoms of spondyloarthritides

but do not fulfill diagnostic criteria for any specific disease of this group. Designated "undifferentiated spondyloarthritis"<sup>14</sup>, the frequency of this condition in uveitis patients has not yet been examined.

In 1991, the European Spondylarthropathy Study Group (ESSG) proposed a set of criteria for the classification of this group of HLA-B27-associated joint diseases<sup>15</sup>. These criteria can be used to identify patients with any one of the spondyloarthritides, including so-called undifferentiated spondyloarthritis<sup>14</sup>.

Our aim was use the ESSG criteria to determine the frequency of various types of spondyloarthritides, including undifferentiated spondyloarthritis, in patients with uveitis. In an ophthalmologic outpatient unit of the University Hospital of Cologne all patients admitted within a certain time period were observed.

## MATERIALS AND METHODS

All consecutive patients with uveitis (n = 443, male:female ratio 217:226, age range 14–72 years) who were seen between 1987 and 2000 by ophthalmologists (medical specialists) at the Department of Ophthalmology of the University of Cologne were referred for a rheumatologic examination. Four hundred and forty-three of these patients were included in the study. There were no exclusion criteria. Applying the International Uveitis Study Group (IUSG) criteria<sup>16</sup>, uveitis was classified according to the site of inflammation and onset of symptoms into the following subtypes<sup>17,18</sup>: acute anterior uveitis (AAU), chronic anterior uveitis (CAU), posterior uveitis, and panuveitis (Table 1).

Patients had clinical and roentgenographic examination for signs and symptoms of arthritis/spondylitis. Radiographs of sacroiliac joints were made in all patients with inflammatory lower back pain or at least one other symptom compatible with the presence of spondyloarthritis<sup>19</sup>. For all patients HLA-B27 typing was performed by the university's Institute of Transfusion Medicine using a standard microlymphocytotoxicity assay. The patients were screened for other systemic or infectious diseases (sar-

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**Table 1.** Anatomic classification of uveitis according to the International Uveitis Study Group (IUSG)<sup>16</sup>. Terms in bold refer to the main foci of inflammation. The meanings of the subsidiary points differ only slightly if at all.

<b>Anterior uveitis</b>
Iritis
Anterior cyclitis
Iridocyclitis
<b>Intermediate uveitis</b> (formerly known as pars planitis)
Posterior cyclitis
Hyalitis
Basal retinochoroiditis
<b>Posterior uveitis</b>
Focal, multifocal, or diffuse choroiditis,
chorioretinitis, retinochoroiditis, or neuroveitis
<b>Panuveitis</b>

coidosis, Behcet's disease, neurological diseases, viral or bacterial infection) by consultants or ourselves after appropriate diagnostic investigations. If the chest radiograph revealed a bihilar lymphadenopathy then a bronchoalveolar lavage was performed for diagnosing sarcoidosis.

The following criteria were used for classification of rheumatic diseases: spondyloarthritides were defined according to the ESSG criteria<sup>15</sup>, AS according to the New York criteria<sup>20</sup>, and psoriatic spondyloarthritis as proposed by Wright and Moll<sup>21</sup>. ReA was defined as the presence of rheumatoid factor-negative peripheral arthritis in at least one joint associated with clinical or microbiological evidence of a causative extraarticular infection<sup>22</sup>. Reiter's syndrome is a special form of ReA and characterized by a combination of arthritis, redness of the eyes, and urinary tract signs. Advances in the diagnosis of ReA/Reiter's syndrome are considered by Sieper and Braun<sup>23</sup>. Undifferentiated spondyloarthritis was defined as arthritis in adults which fulfilled the ESSG criteria but did not meet the criteria for the established disease categories AS, psoriatic arthritis, ReA, or arthritis associated with chronic inflammatory bowel disease<sup>14,21,22,24</sup>. Other rheumatic disorders, such as rheumatoid arthritis and connective tissue diseases, were classified according to established American College of Rheumatology (ACR-ARA) criteria.

## RESULTS

Forty-four of the 433 (10%) patients with uveitis were found to have spondyloarthritides according to the ESSG classification criteria. The prevalence of spondyloarthritis and other systemic diseases in the various uveitis groups is shown in Table 2. Spondyloarthritis was observed in 36 of 93 (39%) AAU patients, 3 of 90 (3%) patients with CAU, and 5 of 250 (2%) patients with other types of uveitis (AAU versus other types of uveitis:  $p < 0.001$ ; chi-square test).

Table 3 shows the distribution of each of the ESSG criteria in the uveitis patients with spondyloarthritis. Forty of the 44 (91%) ESSG criteria-positive patients with spondyloarthritides were HLA-B27 positive compared with 30 of 389 (8%) ESSG criteria-negative uveitis patients ( $p < 0.001$  chi-square test). Forty-eight of the 93 (52%) AAU patients typed for HLA-B27 were positive. Thirty-two of these 48 (67%) B27-positive AAU patients had ESSG criteria-positive spondyloarthritis. The spondyloarthritis had been diagnosed before the study in 18 of the 44 (41%) uveitis patients, but was diagnosed during the study in the remaining 26 (59%) patients.

**Table 2.** Prevalence of various systemic diseases in 433 patients with uveitis at a university-based eye clinic.

	AAU	CAU	PostU	PanU	Total
Spondyloarthritis	36	3	3	2	44
Connective tissue disease	0	1	1	3	5
Rheumatoid arthritis	0	0	0	1	1
Juvenile rheumatoid arthritis	0	5	0	0	5
Sarcoidosis	1	8	1	6	16
Behcet's disease	0	0	7	2	9
Multiple sclerosis	0	0	0	10	10
Vogt Koyanagi Harada	0	2	0	0	2
Interstitial nephritis	1	0	0	0	1
Inflammatory bowel disease	0	2	0	0	2
Total	93	90	128	122	433

AAU: acute anterior uveitis; CAU: chronic anterior uveitis; PostU: posterior uveitis; PanU: combined posterior/anterior uveitis.

Thirty-six patients had a specific subtype of spondyloarthritis, as described in Table 4. Rheumatic disease was not diagnosed before the study in 11 patients with AS, in 4 patients with ReA/Reiter's syndrome, and in 3 patients with psoriatic arthropathy.

Eleven AAU patients fulfilled ESSG criteria but not diagnostic criteria for the above mentioned well-defined types of spondyloarthritis. These patients were therefore classified as having undifferentiated spondyloarthritis. The pattern of arthritis in these patients was characterized by asymmetrical oligoarthritis, radiological evidence of sacroiliitis with or without inflammatory low back pain, and enthesopathy, but it lacked further features of specific types of spondyloarthritides. Eight patients were HLA-B27 positive. Three patients presented with the first attack of uveitis, while 5 patients reported earlier episodes of AAU. The ophthalmological picture of uveitis in all patients showed typical signs and symptoms of uveitis, but no specific ocular manifestations were associated with undifferentiated or other forms of spondyloarthritis.

## DISCUSSION

The association of uveitis, especially AAU, with AS and Reiter's syndrome has been shown in a number of studies<sup>8,9,22,25-27</sup>. In a study of 236 patients with uveitis, Rosenbaum<sup>27</sup> found AS in 5.5% and Reiter's syndrome in 7.2%, especially when acute, unilateral anterior uveitis was present. The association was also confirmed by Rothova, *et al*<sup>28</sup>, who investigated 865 patients with various types of uveitis and observed AS or ReA/Reiter's syndrome in 44 of 471 (9.3%) AAU patients and 4 of 176 (2.3%) patients with panuveitis. AUU may sometimes occur for a long time in isolation as the only clinically apparent manifestation of the HLA-B27-associated disease process.

Other studies of rheumatic manifestations in uveitis patients, however, have suggested that not only typical AS

Table 3. Distribution of the ESSG criteria in uveitis patients with spondyloarthritis.

ESSG Criterion	Acute Anterior Uveitis n = 93					Other Types of Uveitis n = 340			
	AS n = 17	ReA n = 9	PsA n = 2	ESSG+ n = 8	ESSG- n = 57	AS n = 2	PsA n = 3	ESSG+ n = 3	ESSG- n = 332
Inflammatory back pain	16	7	2	4	6	2	2	1	16
Synovitis	4	9	1	5	2	0	1	3	12
Positive family history	6	3	1	5	4	0	0	2	7
Psoriasis	0	0	2	1	2	0	3	0	5
Inflammatory bowel disease	0	0	0	0	0	0	0	0	2
Urethritis diarrhoea	0	9	0	0	5	0	0	0	14
Alternate buttock pain	13	3	2	5	2	1	1	0	2
Enthesopathy	8	4	0	5	1	1	0	1	7
Sacroiliitis	17	2	2	0	0	2	1	0	0

AS: ankylosing spondylitis; ESSG+: ESSG criteria fulfilled; ReA: reactive arthritis/Reiter's syndrome; ESSG-: ESSG criteria not fulfilled; PsA: psoriatic arthritis.

Table 4. Subtypes of spondyloarthritis in 44 patients with positive ESSG criteria.

Subtypes of Spondyloarthritis	Acute Anterior Uveitis, n*
Ankylosing spondylitis	17
Reactive arthritis	9
Psoriatic arthritis	2
Undifferentiated spondarthritis	8
Total	36

\* ESSG criteria-positive patients with other types of uveitis: 8

and ReA/Reiter's syndrome, but also incomplete forms of spondyloarthritis may be associated with AAU<sup>2,4,5,8</sup>. These studies showed that inflammatory low back pain<sup>4</sup>, radiological sacroiliitis<sup>5</sup> or so-called possible AS<sup>8</sup> are present in a considerable proportion of patients with AAU.

Our results confirm these observations and show that AAU is associated with AS, ReA/Reiter's syndrome, as well as other spondyloarthritis such as psoriatic arthritis. The data further show that a considerable number of uveitis patients have incomplete forms of spondyloarthritis, a condition designated as undifferentiated spondyloarthritis<sup>14</sup>. We used ESSG criteria which, as they do not include uveitis, might be more appropriate than the Amor criteria<sup>22</sup> for the diagnosis of spondyloarthritis.

The rheumatological manifestations of undifferentiated spondyloarthritis observed in our uveitis patients included peripheral arthritis and/or inflammatory spinal pain, a positive family history for these diseases, the presence of buttock pain, enthesopathy, or sacroiliitis. It has been suggested that silent urogenital or gastrointestinal infections or subclinical gut inflammation may play a role in the pathogenesis of both AAU<sup>3</sup> and spondyloarthritis<sup>29</sup>. We did not examine our patients for asymptomatic urogenital or gut inflammation by urethral swabs or endoscopy. It therefore

remains to be determined whether AAU associated with undifferentiated spondyloarthritis may be accompanied by subclinical inflammation or locally asymptomatic infection with potentially arthritogenic bacteria. The clinical picture of uveitis in patients with associated arthritis in our study accords with previous reports showing an acute, mostly unilateral inflammation of the anterior eye chamber with numerous cells in the vitreous and frequently posterior synechiae and cystoid macular edema, but no mutton fat precipitates<sup>3,27,28</sup>. No specific ocular symptoms were identified which might suggest the presence of an associated rheumatic disease. However, our study suggests that the proposed ESSG classification criteria can be helpful in the diagnosis of spondyloarthritis in uveitis patients. The ESSG criteria can be useful in clinical practice as well as for classification in scientific studies.

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