An analysis of 372 patients with anterior uveitis in a large Ibero-American cohort of spondyloarthritis: the RESPONDIA Group

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Abstract

Objectives

This study analysed the frequency of anterior uveitis (AU) and its correlations in a large cohort of patients with spondyloarthritis (SpA).

Methods

A common protocol of investigation was prospectively applied to 2012 SpA patients in 85 centres from 10 Ibero-American countries. Clinical and demographic variables and disease indexes were investigated. Categorical variables were compared by χ^2 and Fisher's exact test, and continuous variables were compared by ANOVA or Kruskal-Wallis test. A value of $p<0.05$ was considered significant.

Results

AU was referred by 372 SpA patients (18.5%). AU was statistically associated with inflammatory low back pain ($p<0.001$), radiographic sacroiliitis ($p<0.001$), enthesopathies ($p=0.004$), urethritis/acute diarrhoea ($p<0.001$), balanitis ($p=0.002$), hip involvement ($p=0.002$), HLA-B27 ($p=0.003$), and higher C-reactive protein ($p=0.001$), whilst it was negatively associated with the number of painful ($p=0.03$) and swollen ($p=0.005$) peripheral joints, psoriatic arthritis ($p<0.001$), psoriasis ($p<0.001$), nail involvement ($p<0.001$), and dactilitis ($p=0.062$; trend). No association with gender, race, and indices (disease activity, functionality and quality of life) was observed. Logistic regression showed that ankylosing spondylitis ($p=0.001$) and HLA-B27 ($p=0.083$; trend) was significantly associated with AU, while extra-articular manifestations (predominantly psoriasis) were negatively associated ($p=0.016$).

Conclusion

Anterior uveitis is a frequent extra-articular manifestation in SpA patients, positively associated with axial involvement and HLA-B27 and negatively associated with peripheral involvement and psoriatic arthritis.

Key words

anterior uveitis, ankylosing spondylitis, psoriasis, HLA-B27, spondyloarthritis

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Introduction

Uveitis is classically described as the most frequent extra-articular manifestation of the spondyloarthritides (SpA) (1, 2). Its prevalence can vary according to the type of SpA (2). In ankylosing spondylitis (AS), considered the prototype of SpA, this prevalence can reach 40% of the patients in a long-term follow-up, and it is frequently anterior, acute, and unilateral (1). This profile can be different in psoriatic arthritis and enteropathic arthritis (3-5). Uveitis clinics around the world have frequently diagnosed a SpA in patients with HLA-B27 anterior uveitis (6-14). For this reason, anterior uveitis (AU) was included in the recently proposed classification criteria of axial and peripheral SpA (15, 16).

The present study analysed the presence of AU and its correlations in a large cohort of 2012 SpA patients in Ibero-America.

Methods

Consecutive patients with the diagnosis of SpA, according to the classification criteria of the European Spondyloarthropathy Study Group (ESSG) (17), were included in this prospective, observational and multicentric cohort of SpA, known as RESPONDIA (Registro de ESPONDiloartrites de Ibero-America: Ibero-American Registry of Spondyloarthritis). This group was created in 2005 and included rheumatologists from different Ibero-American countries interested in the study, evaluation and follow-up of patients with SpA. The group was constituted by nine Latin-American countries (Argentina, Brazil, Chile, Costa Rica, Ecuador, México, Perú, Uruguay and Venezuela) and the two Iberian countries (Spain and Portugal). Patients included were attended in ambulatory care between June 2006 and December 2008. Data were transmitted online and stored in the databank of the Registry of Spondyloarthritis of the Spanish Society of Rheumatology (REGISPONSER) (18).

In this study, a common protocol of investigation was applied to 2012 SpA patients in 85 centres in 10 Ibero-American countries. Patients were considered as AS if they fulfilled the New York modified criteria (19), and as psoriatic arthritis in case they fulfilled Moll and Wright criteria (20); reactive arthritis was considered according to specific criteria (21) and enteropathic arthritis when the patient presented inflammatory axial and/or peripheral joint involvement associated to inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis). Juvenile SpA was considered when the patient started SpA symptoms before 16 years of age.

Uveitis was defined by a self-reported history of anterior uveitis confirmed by an ophthalmological examination. Patients with intermediate or posterior uveitis were not considered.

Demographic and clinical data were collected, including disease duration, tender and swollen joint count, visual analogue scale for pain according to patient (VAS for pain) and disease activity according to patient and physician (patient and physician VAS for activity, respectively). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values were also registered. For clinimetric evaluation of the degree of the mobility of the spine, we used the Bath Ankylosing Spondylitis Metrologic Index (BASMI) (22), including the following measures: occiput-to-wall distance, chest expansion, finger-to-floor distance, modified Schober test and lumbar side flexion. The presence of pain at enthesis sites were evaluated dichotomically by the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) (23). Disease activity and functional status were evaluated according to Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (24) and Bath Ankylosing Spondylitis Functional Index (BASFI) (25) questionnaires, respectively. Quality of life data were recorded through Ankylosing Spondylitis Quality of Life (ASQoL) (26) questionnaires. All used questionnaires were previously validated and culturally adapted in each of the participating countries. Radiological evaluation was measured with Bath Ankylosing Spondylitis Radiologic Index (BASRI), including BASRI-spine (which includes lumbar and cervical spine evaluation and sacroiliac joints)

and BASRI-total (BASRI-spine and BASRI-hips) (27). Hip involvement was also assessed by clinical (presence of pain and/or limitation) and radiological evaluations (classified as normal, suspicious, mild, moderate or severe) regarding BASRI-hips.

Statistical analysis

Categorical variables were compared by χ^2 and Fisher's exact test, and continuous variables were compared by ANOVA or Kruskal-Wallis test. *Post hoc* analysis was performed using Tukey test or Games-Howell test, depending on variances distribution. A value of $p<0.05$ was considered significant, and $p>0.05$–$p<0.10$ was considered a statistical trend. The statistical package SPSS, version 15, was used for the analysis.

Results

The group of 2012 SpA patients presented the following diagnoses: AS in 1254 (62.9%), psoriatic arthritis in 397 (19.9%), undifferentiated SpA in 189 (9.5%), reactive arthritis in 69 (3.5%), enteropathic arthritis in 22 (1.1%), and juvenile SpA in 63 (3.2%).

Anterior uveitis was referred by 372 SpA patients (18.5%). When comparing patients with and without AU, there was positive association among AU and AS and reactive arthritis, as well as negative association with psoriatic arthritis (Table I).

Predominant axial disease was positively associated with AU ($p<0.001$), while predominant peripheral disease was negatively associated ($p<0.001$). The "mixed" involvement (axial and peripheral and/or enthesitis) was the most frequent pattern of SpA in the present series (Table II).

When analysing demographic variables, SpA patients with AU presented similar distribution related to gender, race and familial history. Positive HLA-B27 was associated with AU; 72.1% of the patients with AU were HLA-B27 positive, compared to 60.6% of the patients without AU ($p=0.003$). Although the mean age was similar in patients with and without uveitis, age at disease onset (26.62±11.09 years *vs*. 31.89±14.60 years; $p<0.001$) and age at diagnosis (34.49±12.97 years *vs*. 37.44±14.72 years; $p=0.002$) were earlier in patients with AU.

Table I. Diagnosis in 2012 SpA patients, according to the presence of anterior uveitis.

	Uveitis n=372	No Uveitis n=1640	*p*-value
Ankylosing spondylitis	278 (74.7%)	976 (60.2%)	**<0.001**
Psoriatic arthritis	19 (5.1%)	378 (23.3%)	**<0.001**
Undifferentiated spondyloarthritis	32 (8.6%)	157 (9.7%)	NS
Reactive arthritis	24 (6.5%)	45 (2.8%)	**<0.001**
Enteropathic arthritis	6 (1.6%)	16 (1.0%)	NS
Juvenile-onset spondyloarthritis	13 (3.5%)	50 (3.1%)	NS

NS: not significant.

Table II. Osteoarticular data in 2012 SpA patients, according to the presence of anterior uveitis.

	Uveitis n=372	No Uveitis n=1640	*p*-value
Axial involvement	125 (36.0%)	432 (28.1%)	
Peripheral involvement	21 (6.1%)	243 (15.8%)	**<0.001**
Enthesitic involvement	6 (1.7%)	54 (3.5%)	
Mixed involvement	195 (56.2%)	806 (52.5%)	
Inflammatory low back pain	273 (73.4%)	1026 (62.6%)	**<0.001**
Cervical spine involvement	128 (34.4%)	525 (32.0%)	NS
Hip involvement	98 (26.3%)	310 (18.9%)	**0.002**
Lower limb arthritis	186 (50.0%)	857 (52.3%)	NS
Upper limb arthritis	71 (19.1%)	484 (29.5%)	**<0.001**
Plantar fasciitis	42 (26.3%)	187 (24.1%)	NS
Dactilitis	40 (10.8%)	237 (14.5%)	**0.062**
No swollen joints	258 (70.5%)	961 (59.9%)	**<0.001**
Enthesopathies	233 (63.1%)	886 (54.9%)	**0.004**

NS: not significant.

Axial involvement variables (inflammatory low back pain [$p<0.001$], and radiographic sacroiliitis [$p<0.001$]) as well as hip involvement ($p<0.001$) were positively associated to the presence of AU (Table II).

Upper limb arthritis ($p<0.001$) was negatively associated with AU (Table II). Regarding peripheral arthritis, the negative statistical association was stronger as the number of swollen joints increased: although patients without swollen joints were more common in the AU group (70.5% *vs*. 59.9%), the frequency of ≥3 swollen joints was higher in the group without AU (18.5% *vs*. 10.7%) ($p<0.001$). Enthesopathies were frequent in the SpA patients in the present study (56.4% presented heel and/or Achillean enthesitis), and were positively associated with AU ($p=0.004$).

When analsing extra-articular manifestations, psoriasis ($p<0.001$), dactilitis (trend; $p=0.062$) and nail involvement ($p<0.001$) were negatively associated with AU (Table III). Patients with psoriatic spondylitis presented significant lower frequency of AU compared to AS ($p<0.001$). On the other hand, urethritis/diarrhoea preceding arthritis ($p<0.001$), and balanitis ($p=0.002$) were positively associated with AU (Table III).

Mean BASDAI, BASFI and ASQoL scores were similar in both groups (Table IV). Mean MASES ($p<0.001$), BASRI – total ($p<0.001$) and BASRI – hip ($p<0.001$) scores were higher in SpA patients with AU (Table IV). Mean CRP was significantly higher in the SpA group with AU ($p=0.001$), while mean ESR was similar in the two groups.

At the physical examination, AU was associated with lower Schober test ($p<0.001$) and lateral lumbar flexion ($p<0.001$), and higher occiput-to-wall distance ($p<0.001$) (Table IV). Visual analogue scale for pain, pain at night, patient and physician global health evaluation were similar in both groups (Table IV).

With reference to treatment, patients with AU were prescribed more frequently sulfasalazine (p=0.026), while patients without uveitis were prescribed methotrexate (p<0.001). The prescription of NSAIDs (continuous or on demand), corticosteroids, and anti-TNF was similar in both groups (Table V).

Logistic regression showed that ankylosing spondylitis (p=0.001) and HLA-B27 (p=0.083; trend) were significantly associated with AU and that extra-articular manifestations (predominantly psoriasis) were negatively associated with AU (p=0.016).

Table III. Extra-articular manifestations in 2012 SpA patients, according to the presence of anterior uveitis.

	Uveitis n=372	No Uveitis n = 1 6 4 0	*p*-value
Psoriasis	34 (9.3%)	488 (29.9%)	**<0.001**
Nail involvement	27 (7.5%)	292 (18.5%)	**<0.001**
Inflammatory bowel disease	20 (5.5%)	66 (4.1%)	NS
Urethritis / diarrhoea	38 (10.4%)	88 (5.4%)	**<0.001**
Balanitis	23 (6.2%)	44 (2.7%)	**0.002**
Lung involvement	9 (2.4%)	20 (1.2%)	NS
Heart involvement	8 (2.2%)	34 (2.1%)	NS
Kidney involvement	6 (1.7%)	30 (1.9%)	NS
Neurologic involvement	4 (1.1%)	14 (0.9%)	NS

NS: not significant.

Table IV. Indexes, metric and laboratory data in 2012 SpA patients, according to the presence of anterior uveitis.

	Uveitis n=372	No Uveitis n=1640	*p*-value
BASDAI (SD)	4.32 ± 2.43	4.30 ± 4.45	NS
BASFI (SD)	4.47 ± 2.87	4.17 ± 2.87	0.076
MASES	2.35 ± 3.47	2.89 ± 3.79	**0.03**
Schober test (cm) (SD)	2.71 ± 1.79	3.42 ± 1.91	**<0.001**
Occiput-to-wall distance (cm) (SD)	6.01 ± 7.64	4.27 ± 6.46	**<0.001**
Lateral lumbar flexion (cm) (SD)	39.85 ± 19.60	46.0 ± 14.31	**<0.001**
Chest expansion (cm) (SD)	3.15 ± 1.78	3.26 ± 1.68	NS
Finger-to-floor distance (cm) (SD)	25.08 ± 19.26	23.34 ± 20.41	NS
VAS pain at night (last week)	4.09 ± 3.08	3.87 ± 3.19	NS
VAS pain (last week)	4.28 ± 2.94	3.94 ± 3.07	0.059
VAS patient global	4.85 ± 2.81	4.90 ± 3.99	NS
VAS physician	3.72 ± 2.58	3.68 ± 2.53	NS
ASQoL (SD)	7.63 ± 5.15	6.99 ± 5.29	NS
BASRI – TOTAL (SD)	7.73 ± 4.45	6.15 ± 4.30	**<0.001**
BASRI – HIP (SD)	6.50 ± 3.57	5.25 ± 3.51	**<0.001**
ESR	25.33 ± 21.19	24.03 ± 19.75	NS
CRP	11.43 ± 18.34	7.98 ± 14.46	**0.001**

ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASRI: Bath Ankylosing Spondylitis Radiologic Index; CRP: C reactive protein; ESR: Erythrocyte Sedimentation Rate; MASES: Maatricht Enthesitis Index; NS: not significant; VAS: Visual Analogue Scale.

Table V. Treatment in 2012 SpA patients, according to the presence of anterior uveitis.

	Uveitis n=372	No Uveitis n=1640	*p*-value
NSAID, on demand	31.6%	27.7%	NS
NSAID, continuous	60.1%	58.0%	NS
Corticosteroids	24.8%	24.7%	NS
Methotrexate	27.2%	42.8%	**<0.001**
Sulfasalazine	34.8%	25.8%	**0.024**
Leflunomide	4.5%	7.3%	NS
Infliximab	4.5%	4.0%	NS
Etanercept	3.8%	5.3%	NS
Adalimumab	2.0%	1.9%	NS

NSAID: non-steroidal anti-inflammatory drugs; NS: not significant.

Discussion

This study confirms in a multicentric Ibero-American cohort that the presence of AU, the most frequent extra-articular manifestation in patients with SpA (occurring in almost 20% in the present study), is associated with axial involvement and the presence of HLA-B27. On the other hand, our study showed that AU is less prevalent in patients with psoriatic arthritis or peripheral arthritis.

The modern concept of SpA, including the various extra-articular manifestations observed in the group, including uveitis, suggests that SpA should be considered as systemic diseases associated with HLA-B27 and not just as a group of musculoskeletal inflammatory diseases (1, 28, 29). Reinforcing this concept, there are several studies that showed that AU can be associated with the presence of HLA-B27, even without axial or peripheral joint involvement (9, 30).

The prevalence of uveitis in our study was similar to other studies (2, 31). Although the present study observed an association between AU and axial involvement, an Indian study found that extra-articular manifestations such as AU were more prevalent in patients who had peripheral arthritis (29). Genetic and environmental factors could explain these different results.

AU, characterised by sudden onset of eye pain, conjunctival hyperaemia, photophobia and blurred vision, is the most common form of uveitis, responsible for 90% of all cases (32). Half of the cases of AU is associated with the presence of HLA-B27 and in these cases, uveitis is typically unilateral, alternating between eyes, and has a good prognosis (2, 14, 33, 34). Male gender and history of unilateral acute AU in the same eye can be associated with a shorter time interval between relapses (35). AU in patients with HLA-B27 is rarely chronic (34). In fact, uveitis that occurs in patients with some SpA such

as psoriasis or inflammatory bowel disease may have a chronic course, can be bilateral and may involve the posterior uveal tract (4, 5).

The majority of the cases of AU in SpA respond very well to topical corticosteroids (36). Some cases of AU with difficult response, associated with frequent flares or chronic course, may require oral corticosteroids, sulphasalazine or methotrexate (36-38). TNF-α inhibitors can also be used and determine good response, especially monoclonal antibodies (39, 40). Extra-articular manifestations, mainly uveitis, have been recently included as an important topic in the ASAS / EULAR recommendations for the management of AS (41), and are considered in the indication of biologic agents for the treatment of SpA (42). A recent French study examined the reasons for switching biological agents in SpA patients and showed that the presence of peripheral arthritis and enthesitis were predictive of change, which did not occur by the presence of uveitis (43).

If AU is left untreated, anterior chamber inflammation can become serious, even leading to the emergence of hypopyon. However, the presence of hypopyon in patients with SpA has been less frequent nowadays, due to earlier diagnosis and treatment (44). Other complications of recurrent or chronic uveitis include pupil synechiae, cataract, and glaucoma (44).

It is important to observe that in the present study, the presence of AU was associated with inflammatory low back pain, radiographic sacroiliitis and enthesopathies, whereas these are classic characteristics that increase the chance of having SpA (16, 45). A recent Canadian publication, determining the prevalence of inflammatory back pain in a cohort of 167 patients with AU, found that 46.8% of the patients were classified as IBP (46). The same is true when we found an association between AU with hip involvement, but no upper limb joints. It is known that SpA has preference for affecting the large joints of the lower limbs (45). Our study also demonstrated that AU occurs in patients with SpA who started the disease in early age. The registry of Brazilian patients with SpA shows that patients with start of the disease in younger age exhibit more axial involvement and uveitis as compared to older patients (47).

In this study, the presence of AU did not affect the average values of disease indexes, like BASDAI, BASFI, and ASQoL. This is not unexpected, whereas flares of AU are not associated with the activity or severity of the SpA. We found association between AU and higher MASES scores, thus confirming the study that showed higher prevalence of enthesopathies in patients with AU and HLA-B27 (48).

Besides psoriatic arthritis, we emphasise the negative association between AU and psoriatic skin lesions and nail involvement. On the other hand, we found an association between reactive arthritis and AU as previously reported (34).

Conclusion

In conclusion, it is important to consider that AU in Ibero-American SpA patients occurs especially in the subgroup with positive HLA-B27 and predominant axial involvement, where it can occur as a minimal manifestation or initial symptom of SpA. All patients with AU should be submitted to a rheumatologic evaluation since undiagnosed SpA may be present in a significant percentage of cases.

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References

1. MIELANTS H, VAN DEN BOSCH F: Extra-articular manifestations. *Clin Exp Rheumatol* 2009; 27 (Suppl. 55): S56-61.
2. ZEBOULON N, DOUGADOS M, GOSSEC L: Prevalence and characteristics of uveitis in the spondyloarthropathies: a systematic literature review. *Ann Rheum Dis* 2008; 67: 955-9.
3. PAIVA E, MACALUSO DC, EDWARDS A, ROSENBAUM JT: Characterization of uveitis in patients with psoriatic arthritis. *Ann Rheum Dis* 2000; 59: 67-70.
4. DURRANI K, FOSTER CS: Psoriatic uveitis: A distinct clinical entity? *Am J Ophthalmol* 2005; 139: 106-11.
5. LYONS JL, ROSENBAUM JT: Uveitis associated with inflammatory bowel disease compared with uveitis associated with spondyloarthropathy. *Arch Ophthalmol* 1997; 115: 61-4.
6. ROSENBAUM JT: Acute anterior uveitis and spondyloarthropathies. *Rheum Dis Clin North Am* 1992; 18: 143-51.
7. LINSSEN A, MEENKEN C: Outcomes of HLA-B27-positive and HLA-B27-negative acute anterior uveitis. *Am J Ophthalmol* 1995; 120: 351-61.
8. PATO E, BAÑARES A, JOVER JA *et al*.: Undiagnosed spondyloarthropathy in patients presenting with anterior uveitis. *J Rheumatol* 2000; 27: 2198-202.
9. MONNET D, BREBAN M, HUDRY C, DOUGADOS M, BRÉZIN AP: Ophthalmic findings and frequency of extraocular manifestations in patients with HLA-B27 uveitis: a study of 175 cases. *Ophthalmology* 2004; 111: 802-9.
10. FERNÁNDEZ-MELÓN J, MUÑOZ-FERNÁNDEZ S, HIDALGO V *et al*.: Uveitis as the initial clinical manifestation in patients with spondyloarthropathies. *J Rheumatol* 2004; 31: 524-7.
11. LINDER R, HOFFMANN A, BRUNNER R: Prevalence of spondyloarthritides in patients with uveitis. *J Rheumatol* 2004; 31: 2226-9.
12. CHUNG YM, LIAO HT, LIN KC *et al*.: Prevalence of spondyloarthritis in 504 Chinese patients with HLA-B27-associated acute anterior uveitis. *Scand J Rheumatol* 2009; 38: 84-90.
13. JAKOB E, REULAND MS, MACKENSEN F *et al*.: Uveitis subtypes in a German interdisciplinary uveitis center - Analysis of 1916 patients. *J Rheumatol* 2009; 36: 127-36.
14. ACCORINTI M, IANNETTI L, LIVERANI M, CAGGIANO C, GILARDI M: Clinical features and prognosis of HLA B27-associated acute anterior uveitis in an Italian patient population. *Ocul Immunol Inflamm* 2010; 18: 91-6.
15. RUDWALEIT M, VAN DER HEIJDE D, LANDEWÉ R *et al*.: The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009; 68: 777-84.
16. RUDWALEIT M, VAN DER HEIJDE D, LANDEWÉ R *et al*.: The Assessment of SpondyloArthritis international Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis* 2011; 70: 25-31.
17. DOUGADOS M, VAN DER LINDEN S, JUHLIN R *et al*.: The European Spondyloarthropathy Study Group preliminary criteria for the classification of spondyloarthropathy. *Arthritis Rheum* 1991; 34: 1218-27.
18. COLLANTES E, ZARCO P, MUÑOZ E *et al*.: Disease pattern of spondyloarthropaties in Spain: description of the first national registry (REGISPONSER) – extended report. *Rheumatology* (Oxford) 2007; 46: 1309-15.
19. VAN DER LINDEN S, VALKENBURG HA, CATS A: Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984; 27: 361-8.
20. MOLL JMH, WRIGHT V: Psoriatic arthritis. *Semin Arthritis Rheum* 1973; 3: 55-78.
21. KINGSLEY G, SIEPER J: Third International Workshop on Reactive Arthritis, 23-26 September 1995, Berlin, Germany. *Ann Rheum Dis* 1996; 55: 564-84.
22. JONES SD, PORTER J, GARRETT SL, KENNEDY LG, WHITELOCK H, CALIN A: A new scoring system for the Bath Ankylosing Spondylitis Metrology Index (BASMI). *J Rheumatol* 1995; 22: 1609.
23. HEUFT-DORENBOSCH L, SPOORENBERG A, VAN TUBERGEN R *et al*.: Assessment of enthesitis in ankylosing spondylitis. *Ann Rheum Dis* 2003; 62: 127-32.
24. GARRETT S, JENKINSON T, KENNEDY LG, WHITELOCK H, GAISFORD P, CALIN A*:* A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994; 21: 2286-91.
25. CALIN A, GARRETT S, WHITELOCK H *et al*.: A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Functional Index. *J Rheumatol* 1994; 21: 2281-85.
26. DOWARD LC, SPOORENBERG A, COOK SA *et al*.: Development of the ASQoL: a quality of life instrument specific to ankylosing spondylitis. *Ann Rheum Dis* 2003; 62: 20-6.
27. WANDERS AJ, LANDEWÉ RB, SPOORENBERG A *et al*.: What is the most appropriate radiologic scoring method for ankylosing spondylitis? A comparison of the available methods based on the Outcome Measures in Rheumatology Clinical Trials filter. *Arthritis Rheum* 2004; 50: 2622-32.
28. VAN DEN BOSCH F: A survey of European and Canadian rheumatologists regarding the treatment of patients with ankylosing spondylitis and extra-articular manifestations. *Clin Rheumatol* 2010; 29: 281-8.
29. SINGH G, LAWRENCE A, AGARWAL V, MISRA R, AGGARWAL A: Higher prevalence of extra-articular manifestations in ankylosing spondylitis with peripheral arthritis. *J Clin Rheumatol* 2008; 14: 264-6.
30. TAY-KEARNEY ML, SCHWAM B, LOWDER C *et al*.: Clinical features and associated systemic diseases of HLA-B27 uveitis. *Am J Ophthalmol* 1996; 121: 47-56.
31. VAN DER CRUYSSEN B, RIBBENS C, BOONEN A *et al*.: The epidemiology of ankylosing spondylitis and the commencement of anti-TNF therapy in daily rheumatology practice. *Ann Rheum Dis* 2007; 66: 1072-7.
32. WAKEFIELD D, CHANG JH, AMJADI S, MACONOCHIE Z, ABU EL-ASRAR A, MCCLUSKEY P: What is new HLA-B27 acute anterior uveitis? *Ocul Immunol Inflamm* 2011; 19: 139-44.
33. MAX R, LORENZ HM, MACKENSEN F: Ocular involvement in spondyloarthropathies: HLA-B27 associated uveitis. *Z Rheumatol* 2010; 69: 397-402.
34. DUMBRĂVEANU L, CUŞNIR V, GROPPA L, CALININA L: HLA B27 uveitis in ankylosing spondylitis and reactive arthritis. *Oftalmologia* 2010; 54: 29-35.
35. AGNANI S, CHOI D, MARTIN TM *et al*.: Gender and laterality affect recurrences of acute anterior uveitis. *Br J Ophthalmol* 2010; 94: 1643-7.
36. TAYLOR SR, ISA H, JOSHI L, LIGHTMAN S: New developments in corticosteroid therapy for uveitis. *Ophthalmologica* 2010; 224 (Suppl. 1): 46-53.
37. MUÑOZ-FERNÁNDEZ S, HIDALGO V, FERNÁNDEZ-MELÓN J *et al*.: Sulfasalazine reduces the number of flares of acute anterior uveitis over a one-year period. *J Rheumatol* 2003; 30: 1277-9.
38. GANGAPUTRA S, NEWCOMB CW, LIESEGANG TL *et al*.: Methotrexate for ocular inflammatory diseases. *Ophthalmology* 2009; 116: 2188-98.
39. RUDWALEIT M, RØDEVAND E, HOLCK P *et al*.: Adalimumab effectively reduces the rate of anterior uveitis flares in patients with active ankylosing spondylitis: results of a prospective open-label study. *Ann Rheum Dis* 2009; 68: 696-701.
40. CUNNINGHAM ET, ZIERHUT M: TNF inhibitors for uveitis: balancing efficacy and safety. *Ocul Immunol Inflamm* 2010; 18: 421-3.
41. BRAUN J, VAN DEN BERG R, BARALIAKOS X *et al*.: 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011; 70: 896-904.
42. TODOERTI M, PIPITONE N, MATUCCI-CERINIC M, MONTECUCCO C, CAPORALI R: ITALIAN SOCIETY FOR RHEUMATOLOGY: Recommendations for the use of biologic therapy from the Italian Society for Rheumatology: off-label use. *Clin Exp Rheumatol* 2011; 29 (Suppl. 66): S42-62.
43. DADOUN S, GERI G, PATERNOTTE S, DOUGADOS M, GOSSEC L: Switching between tumour necrosis factor blockers in spondyloarthritis: a retrospective monocentre study of 222 patients. *Clin Exp Rheumatol* 2011; 29: 1010-3.
44. ZAIDI AA, YING GS, DANIEL E *et al*.: Hypopyon in patients with uveitis. *Ophthalmology* 2010; 117: 366-72.
45. VAN DER HORST-BRUINSMA IE, LEMS WF, DIJKMANS BA: A systematic comparison of rheumatoid arthritis and ankylosing spondylitis. *Clin Exp Rheumatol* 2009; 27 (Suppl. 55): S43-9.
46. CHAN CC, INRIQ T, MOLLOY CB, STONE MA, DERZKO-DZULINSK L: Prevalence of inflammatory back pain in a cohort of patients with anterior uveitis. *Am J Ophthalmol* 2012; 153: 1025-30.
47. SKARE TL, LEITE N, BORTOLUZZO AB *et al*.; BRAZILIAN REGISTRY OF SPONDYLOARTHRITIS: Effect of age at disease onset in the clinical profile of spondyloarthritis: a study of 1424 Brazilian patients. *Clin Exp Rheumatol* 2012; 30:351-7.
48. MUÑOZ-FERNÁNDEZ S, DE MIGUEL E, COBO-IBÁÑEZ T *et al*.: Enthesis inflammation in recurrent acute anterior uveitis without spondylarthritis. *Arthritis Rheum* 2009; 60: 1985-90.