Prevalence and Outcome of Juvenile Idiopathic Arthritis-Associated Uveitis and Relation to Articular Disease

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ABSTRACT. ***Objective.*** To determine prevalence and complications of juvenile idiopathic arthritis (JIA)-associated uveitis, and to evaluate risk factors for uveitis and its relation to articular disease.

Methods. Records of 309 patients with JIA (244 female, 65 male, mean age at onset 4.9 yrs) were retrospectively reviewed. Occurrence of uveitis and complications were assessed among oligoarticular-onset JIA (193 patients), polyarticular-onset JIA (66 patients), and systemic-onset JIA (50 patients). The presence of antinuclear antibodies (ANA) was determined in patients with oligoarticular-onset JIA. Therapy and relapses of uveitis and arthritis were recorded at each visit during the followup (mean followup 7.6 yrs).

Results. Sixty-two patients developed uveitis (20.1%); 57 patients had oligoarticular-, 3 polyarticular-, and 2 systemic-onset JIA. Uveitis was asymptomatic in 56/62 cases. Fifty-five of the 62 patients (88.7%) developed uveitis within 4 years from disease onset. In patients with oligoarticular-onset JIA, an early age at disease onset and the presence of ANA ($p < 0.05$) and DRB1*11 ($p < 0.03$) were the best predictors of uveitis, while a polyarticular course was not associated to uveitis ($p > 0.05$). Active arthritis was present at the first episode of uveitis in 46/62 patients. Forty-four of the 62 patients experienced relapses of uveitis: in 20/62, relapses were concomitant to arthritis relapses; in 24/62 relapses presented without active arthritis. Complications of uveitis developed in 35.5% of the patients (22/62), leading to visual impairment in 13 patients.

Conclusion. Current guidelines provide early identification of uveitis in 90% of patients. With the exception of the first episode of uveitis, uveitis and arthritis seem to run different courses; close ophthalmologic scrutiny then should also be maintained during arthritis remission. (First Release Mar 1 2007; J Rheumatol 2007;34:1139–45)

Key Indexing Terms:
JUVENILE IDIOPATHIC ARTHRITIS
PEDIATRIC RHEUMATIC DISEASES
UVEITIS
OPHTHALMOLOGY

Chronic uveitis is one of the most threatening complications of juvenile idiopathic arthritis (JIA); its prevalence is variable in different series, ranging from 9.3% to 38% in the most recent studies[1-6]. JIA-associated uveitis is often asymptomatic and, if not treated early, it can lead to severe complications, such as cataract, glaucoma, and retinal detachment, that can cause reduction of visual acuity, from mild visual impairment to blindness[2,3,5-10].

The development of clinical algorithms for efficient screening of JIA populations at high risk of developing uveitis, with a view to early diagnosis and treatment, has been the mainstay of preventing or minimizing ocular complications of uveitis. Factors associated with a higher risk of developing uveitis in patients with JIA include early onset of JIA (before age 7 yrs), the presence of antinuclear antibodies (ANA), female sex, and the presence of HLA-A19, B22 and DR9 alleles. Conversely, a polyarticular course of oligoarticular onset disease is not associated with an increased risk, and HLA-DR1 appears to be protective[2,9,11-13].

We assessed the prevalence of uveitis and ocular complications in a large JIA population. Patients' clinical and biological characteristics were examined in order to evaluate the relation between uveitis and active arthritis episodes and to identify factors of prognostic value.

MATERIALS AND METHODS

Medical and ophthalmologic records of 309 patients (244 female, 65 male) with JIA were retrospectively reviewed. Clinical characteristics of the cohort are summarized in Table 1.

Patients were diagnosed or retrospectively reclassified according to the Edmonton criteria[14] and had subsequently performed their followup visits in the Rheumatology Centre of Milan over the last 20 years. All patients had been evaluated by the same team of ophthalmologists and pediatric rheumatologists from diagnosis through the course of their disease.

Our cohort included 193 patients with oligoarticular-onset JIA, 66 with

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Table 1. Clinical characteristics of 309 patients with JIA and prevalence of uveitis.

JIA	No. of Patients	Sex F (%)	Sex M (%)	Age at Onset*, yrs	Followup*, yrs	No. of Patients with Uveitis	Prevalence of Uveitis, %
Oligoarticular	193	161 (83)	32 (17)	4.2 ± 3.2	7.3 ± 5.1	57	29
Polyarticular	66	50 (76)	16 (24)	7 ± 4.2	6.7 ± 4.8	3	5
Systemic	50	33 (66)	17 (34)	5.2 ± 3.7	9.9 ± 7.4	2	4
Total	309	244 (79)	66 (21)	4.9 ± 3.6	7.6 ± 5.6	62	20

* Mean ± standard deviation.

polyarticular-onset JIA, and 50 with systemic-onset JIA. All patients had slit-lamp examinations every 3 to 6 months to assess the presence of uveitis and complications. Complications of uveitis were defined as having at least one of the following: synechiae, band keratopathy, iris atrophy, cataract, glaucoma, and retinal detachment. Visual acuity at last followup was recorded; visual impairment was defined as a corrected visual acuity worse than 20/40.

Patients with oligoarticular-onset JIA had ophthalmologic examinations every 3 months for the first 4 years from onset and then, if there had been no evidence of uveitis, every 6 months, regardless of the ANA status. Patients with polyarticular- or systemic-onset JIA had been screened for the presence of uveitis every 6 months for 2 years and then annually, if they had not developed uveitis. Patients with uveitis were examined more frequently at the discretion of the treating ophthalmologist.

Most patients were screened for the presence of HLA-DR1, DR9, DRB1*11, DRB1*08, A19, B22, and B27, and subsequently underwent controls including ANA testing (immunofluorescence method) and a thorough clinical evaluation. Arthritis relapse was defined as the presence of new inflamed joints possibly associated to elevated acute-phase reactants. Uveitis relapse was defined as the presence of cells and/or proteins in the anterior ocular chamber or keratitic precipitates on the corneal endothelium or lens in a previously quiescent eye.

The course of uveitis was defined according to the recommendations of the International Uveitis Study Group[15] as (1) single or (2) repeated episode(s); repeated episodes were further classified as (a) chronic (lasting > 4 mo) or (b) relapsing remitting (lasting ≤ 4 mo).

Statistical analysis in patients with and without uveitis was performed in the most homogeneous group, composed of subjects with oligoarticular JIA (193 patients).

The 2 tailed Fisher exact test was used to assess the role of potential prognostic factors between patients with and those without uveitis and between uveitis patients with and without ocular complications. Univariate odds ratios (OR) are presented along with their 95% confidence interval (CI). The significance level used in this study was $p < 0.05$. The statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) release 10.0 for Windows.

RESULTS

Prevalence. Sixty-two of 309 patients developed uveitis during the course of their disease, a prevalence of 20.1%. Of the 62 patients with uveitis, 27 had bilateral disease, with a total of 89 affected eyes.

Patients with uveitis had an earlier onset (mean 3.5 yrs) compared to those without uveitis (mean 4.9 yrs; $p < 0.001$). Patients with oligoarticular-onset JIA were more frequently affected (57/193, 29.6%), compared with polyarticular- and systemic-onset patients (3/66 and 2/50 patients, respectively). In most patients (56/62, 90.3%), uveitis was asymptomatic and ocular inflammation was detected by routine slit-lamp examinations. Six patients experienced symptomatic uveitis at diagnosis (4/57 patients with oligoarticular-onset and 2/3 with polyarticular-onset JIA): in these patients main symptoms were conjunctival hyperemia, pain, and blurred vision. Patients' characteristics and uveitis prevalence between groups are shown in Table 1.

In patients with oligoarticular-onset JIA, uveitis was detected before the onset of arthritis in 8 patients (14.4%) because uveitis was symptomatic (3 cases) or because slit-lamp examination was performed on suspicion of a rheumatologic disease (5 cases); in a further 9 cases (15.8%) asymptomatic uveitis was diagnosed at the first ophthalmological assessment immediately following the diagnosis of arthritis. In all, 30 patients out of 57 (52.6%) developed uveitis within the first 6 months of illness, 45 patients (78.9%) within the first 2 years of disease, and 52 patients (91.2%) within the fourth year from onset, while a late onset of uveitis was observed in 3 cases (after 8.2, 9, and 11.7 yrs from JIA onset, respectively); 50 patients of this group developed JIA before age 7 [87.1%, vs 97/136 (71%) patients with oligoarticular-onset JIA without uveitis].

In patients with polyarticular-onset JIA, uveitis was present at the onset of arthritis in all 3 patients with uveitis. Conversely, in patients with systemic-onset JIA, uveitis developed late in the course of the disease in both patients with uveitis (after 7 yrs and after 8.2 yrs from disease onset, respectively). Occurrence of uveitis in 62 JIA patients with reference to the onset of arthritis is shown in Figure 1.

The first episode of uveitis developed in 46 out of 62 patients (74.2%) in the acute phase of the articular disease; those patients with ongoing arthritis showed high values of erythrocyte sedimentation rate (ESR, mean 39 mm/h, range 1–119), while most patients whose first uveitis episode developed in the absence of active arthritis showed normal ESR values (mean 18 mm/h, range 1–65).

Course of uveitis. Eighteen patients (29%) had only a single episode of uveitis (Group 1). Forty-four patients (71%) presented repeated uveitis episodes, with chronic course in 36 (Group 2A) and relapsing remitting course in 8 cases (Group 2B). Uveitis relapses were more frequently observed in the years immediately following the first uveitis episode: after a mean followup of 9.1 years, 30 out of 44 (68.4%) Group 2 patients relapsed within 6 years from the first episode.

Prognostic factors. The characteristics of 193 (161 female, 32 male) oligoarticular-onset JIA patients with uveitis (n = 57)

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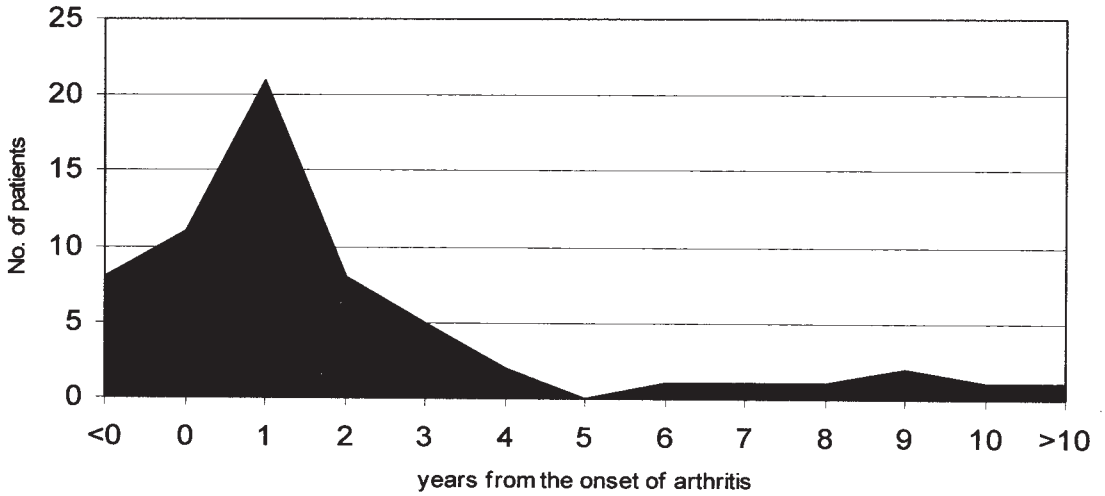

Figure 1. Occurrence of uveitis in 62 JIA patients with reference to the onset of arthritis.

and without uveitis (n = 136) were compared and the results are summarized in Table 2.

Patients with uveitis showed significantly earlier onset of JIA and higher rate of ANA positivity and ESR values at disease onset, while a polyarticular course, although more frequent in this group, was not associated with the occurrence of uveitis. HLA allele testing was performed in 148 patients: DRB1*11 allele was more frequent in patients with uveitis compared to those without uveitis (20/42 and 22/106, respectively; OR 3.47, 95% CI 1.16–7.47, p = 0.001). Conversely, the DRB1*08 allele was more frequent in patients without uveitis (64/106 vs 12/42 in the uveitis group; OR 0.26, 95% CI 0.12–0.57, p = 0.001).

In 20 patients uveitis and arthritis relapses were contemporary in at least one episode, while in 24 cases there was no association between them. When considering the whole num-

Table 2. Clinical data on 309 patients with JIA grouped according to occurrence of uveitis.

	Patients with Uveitis, n = 62	Patients without Uveitis, n = 247	p
Oligoarticular-onset JIA (no.)	57	136	—
Male/female	9:48	23:113	NS
Age at onset, yrs*	3.5 ± 2.6	4.5 ± 3.4	0.008**
Age at onset of uveitis, yrs*	4.9 ± 2.9	—	—
Mean interval to uveitis, yrs*††	1.3 ± 2.5	—	—
Patients with polyarticular course, no. (%)	19 (33.3)	31 (22.8)	NS
ESR at onset of the disease, mm/h	46	34	0.004†
ANA positive patients, no. (%)	50 (87.7)	100 (73.5)	0.04†
HLA-A19-positive, n	0 (43 tested)	3 (108 tested)	NS
HLA-B22-positive, n	1 (43 tested)	2 (108 tested)	NS
HLA-B27-positive, n	1 (43 tested)	14 (108 tested)	NS
HLA-DR1-positive, n	8 (42 tested)	21 (108 tested)	NS
HLA-DR9-positive, n	0 (42 tested)	1 (106 tested)	NS
HLA-DRB1*08-positive, n	12 (42 tested)	64 (106 tested)	0.001†
HLA-DRB1*11-positive, n	20 (42 tested)	22 (106 tested)	0.002†
Polyarticular-onset JIA (no.)	3	63	
Male/female	1:2	15:48	
Age at onset, yrs*	6.7 ± 3.8	6.7 ± 4.2	—
Age at onset of uveitis, yrs*	6.8 ± 3.8	—	
Mean interval to uveitis, yrs*††	0.05 ± 0.1	—	
Systemic-onset JIA (no.)	2	48	
Male/female	0:2	17:31	
Age at onset, yrs*	1.7 ± 0.8	5.3 ± 3.7	—
Age at onset of uveitis, yrs*	9.5 ± 0.2	—	
Mean interval to uveitis, yrs*	7.8 ± 1.1	—	

* Mean ± standard deviation. †† Interval between onset of arthritis and appearance of uveitis. ** t-test. † Chi-square test.

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ber of relapses (105 relapses of uveitis), relapses of arthritis and uveitis were contemporary in 37 episodes, while in the remaining 68 episodes the articular disease was inactive or stable.

In ANA-positive subjects, an increase in ANA titer was not associated with uveitis relapses. ANA were determined at the time of 84 uveitis relapses and were positive in 66/84 episodes and negative in 18/84; ANA titer was increased in 14 cases, decreased in 13, and unchanged in 18, while in the remaining 21 cases the preceding ANA titer was dated back to more than 4 months, thus preventing comparison.

Statistical analysis was not performed in patients with polyarticular- and systemic-onset JIA, because uveitis was rare among these subjects.

Complications. After a mean followup of 8.9 years, 22 uveitis patients out of 62 (35.5%) developed ocular complications; in 12 patients complicated uveitis affected both eyes. Seven patients in this group had their uveitis diagnosed before or at the same time as the arthritis; symptomatic uveitis also was more common in these patients: 4 out of 6 patients with symptomatic uveitis developed ocular complications.

Complications of uveitis and visual acuity at last followup are summarized in Table 3.

When patients with and without ocular complications were compared, no significant differences appeared in ESR values at onset (50 mm/h and 42 mm/h, respectively) and the presence of ANA (19/20 and 32/37 patients, respectively) and DRB1*11 allele (10/16 tested and 10/28 tested, respectively) in the patients with oligoarticular-onset JIA; uveitis patients with ocular complications relapsed more frequently (mean 4 relapses vs one relapse per patient).

Repeated uveitis episodes, all with chronic course, were observed in 20/22 patients with ocular complications; patients without ocular complications showed repeated episodes in 24/40 cases, chronic in 16 patients and relapsing remitting in 8 patients.

Table 3. Ocular complications in JIA patients with uveitis.

	No. of Patients (no. of eyes)	%
Uveitis	62 (89)	
Complicated uveitis	22 (34)	35.4
Synechiae	12 (20)	19.3
Band keratopathy	8 (12)	12.9
Cataract	6 (10)	9.7
Glaucoma	2 (4)	3.2
Retinal detachment	1 (1)	1.6
Iris atrophy	1 (1)	1.6
Visual outcome at last followup of all eyes with complicated uveitis		
20/20–20/40	7	
20/50–20/100	7	
20/200 or worse (including blindness*)	12	
*Blindness, no. patients (eyes)	4 (5)	
No perception of light	3 (4)	
Light perception only	1 (1)	

All patients with ocular complications were not responsive to topical eye treatment with steroids and mydriatics and received other therapies: oral steroids (8 patients), intravenous steroids (7 patients), subconjunctival steroid injections (3 patients), and cyclosporine A (CSA, 4 patients). Most patients with ocular complications also received oral nonsteroidal antiinflammatory drugs (NSAID, 19 patients), plus methotrexate (MTX, 9 patients), slow-acting antirheumatic drugs (SAARD, 5 patients), or chlorambucil (one patient) for their articular disease.

Ocular complications led to visual impairment (i.e., corrected visual acuity worse than 20/40) in 13 patients out of 22 (21%; 19 eyes with impaired vision); 8 subjects (12 eyes) experienced severe visual loss (i.e., corrected visual acuity 20/200 or worse). Blindness was present in 4 patients, one of whom is legally blind ("no perception of light" in 3 cases/4 eyes; "light perception only" in 1 case/1 eye). Characteristics and disease activity at last followup of the 13 patients with visual impairment are presented in Table 4.

Surgical procedures were needed in 7/62 patients (in 3 patients multiple procedures were required): cataract extraction (5 patients), EDTA chelation scrub for band keratopathy (3 patients), glaucoma filtering surgery (1 patient), vitrectomy (2 patients), retinal photocoagulation (1 patient), and corneal transplant (1 patient).

Therapy. All patients were treated with topical eye drops (short acting mydriatics, particularly tropicamid or cyclopentolate or homatropine, and/or corticosteroid, such as dexamethasone). Nonresponder patients also received: oral steroids (14/62, 22.6%), subconjunctival steroid injections (4/62, 6.5%), intravenous steroid pulses (7/62, 11.3%), CSA (6/62, 9.7%), oral cyclophosphamide (1/62), and NSAID injections (1/62).

Forty-three out of 62 patients with uveitis were still receiving therapy for arthritis at the time of uveitis onset: most of them were receiving NSAID (40 patients), and/or MTX (9 patients), oral steroids (8 patients), intraarticular steroid injections (3 patients), SAARD (8 patients), chlorambucil (1 patient).

Local therapy was well tolerated by all patients. Both patients with bilateral glaucoma and 4 out of 6 patients with cataract had received topical and oral steroids.

Disease activity at last followup. At last visit, 7 out of 62 patients showed active uveitis. Twenty-three uveitis patients were in remission without any therapy, while 32 uveitis patients were in remission with local therapy (3 patients), systemic therapies such MTX, CSA, SAARD or steroids (20 patients), or both local and systemic therapies (9 patients). Active arthritis was present in 19 patients at last followup; in a single patient ocular and articular disease both were active, while uveitis was in remission in the remaining 18 patients with ongoing arthritis.

DISCUSSION

Uveitis remains a frequent complication of oligoarticular-

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Table 4. Characteristics of 13 uveitis patients with visual impairment.

Pt no.	Age at Onset (yrs)	Type of JIA Onset	Onset with Arthritis/ Uveitis [1]	Symptomatic Uveitis	Unilateral/ Bilateral Uveitis	ESR Value at Onset (mm/1st h)	Ocular Complications	Surgical Procedures	Final Visual Acuity	Therapy Arthritis/ Uveitis	Last Followup (therapy)	
											Uveitis	Arthritis
1	2.33	Oligo-articular	Arthritis	YES	Bilateral	36	Synechiae	None	20/50 20/50	TED [2] NSAID [3] Ia-SI [4]	**Active** (TED)	None
2	1.16	Oligo-articular		No		11	Synechiae, left pupil seclusion	None	20/40 20/200	TED, Ia-SI, NSAID, ScSI [5] MTX [6], SAARD [7]	None	**Active** (NSAID)
3	2.5	Oligo-articular	Uveitis	YES	Bilateral	101	Synechiae, cataract	Cataract extraction	20/40 20/50	TED,NSAID, CSA [8], oral S [9], i.v. S [10],	None (TED, CSA, oral S)	**Active** (Ia-SI)
4	1.6	Oligo-articular	Arthritis	No	Bilateral	89	Synechiae, band keratopathy, glaucoma	Glaucoma filtering surgery	20/200 NLP [11]	TED, oral S, CSA,ScSI SAARD, NSAID, Ia SI	None	None
5	1.75	Oligo-articular	Arthritis	No	Bilateral	62	Right band keratopathy	None	20/200 20/20	TED,MTX, NSAID, oral S, i.v. S	None (MTX, TED)	None (MTX)
6	1.83	Oligo-articular	Uveitis	No	Bilateral	12	Band keratopathy, synechiae	Vitrectomy, EDTA chelation scrub	20/200 LPO [12]	TED, oral S, i.v. S, Sc SI, CSA, NSAID	None (TED, CSA)	None (CSA)
7	1.92	Oligo-articular	Arthritis	No	Unilateral (left)	25	Synechiae, band keratopathy, cataract	Cataract extraction	20/20 20/200	TED, Ia SI NSAID	None	**Active** (NSAID)
8	7.83	Oligo-articular	Arthritis	No	Bilateral	Not performed	Synechiae, cataract	None	20/50 20/50	TED,IaSI NSAID, oral S, i.v. S	None (oral S)	None (oral S)
9	4.25	Oligo-articular	Arthritis	No	Unilateral (left)	36	Synechiae	None	20/20 20/50	TED, NSAID, MTX, Ia-SI	**Active** (TED)	None
10	3	Oligo-articular	Arthritis	No	Unilateral (right)	78	Synechiae, band keratopathy, pupil seclusion, cataract	Cataract extraction	20/200 20/20	TED, CSA, MTX, NSAID, IaSI	None	None
11	1.58	Oligo-articular	Contempo-rary	No	Bilateral	48	Synechiae, band keratopathy, cataract, retinal detachment	Cataract extraction, EDTA chelation scrub, retinal photo – coagulation, corneal transplant	NLP NLP	TED, CSA, oral S, i.v. S, NSAID	Legally blind	None
12	6.42	Oligo-articular	Contempo-rary	No	Unilateral (right)	8	Synechiae, band keratopathy	None	20/50 20/20	TED, NSAID	None	None
13	2.33	Systemic	Arthritis	No	Bilateral	53	Synechiae, cataract, glaucoma, phtysis bulbi	EDTA chelation scrub, vitrectomy, cataract extraction	NLP 20/200	TED, oral S, SAARD	None	None

(1) Arthritis = onset of arthritis preceded onset of uveitis; uveitis = onset of uveitis preceded onset of arthritis; contemporary = diagnosis of arthritis and uveitis were contemporary; (2) topical eye drops (mydriatics plus steroids); (3) nonsteroidal antiinflammatory drugs; (4) intraarticular steroid injections; (5) subconjunctival steroid injections; (6) methotrexate; (7) slow-acting antirheumatic drugs; (8) cyclosporine A; (9) oral steroids; (10) intravenous steroid pulses; (11) no light perception; (12) light perception only.

onset JIA, while it is uncommon in patients with polyarticular- and systemic-onset JIA. Patients referred to the Rheumatology Centre of Milan were submitted to slit-lamp evaluations every 3 to 6 months; we then assumed that every case of uveitis could be identified in our cohort.

We found a uveitis prevalence of 20.1%; such prevalence reaches 29% in the patients with oligoarticular-onset JIA, in accord with prevalence rates reported in different European studies[2,12,16,17].

As observed in other series[5,13], uveitis developed soon after the onset of arthritis in most patients of our study (48/62, 77.4%, within the first 2 yrs). In our cohort, 35.5% (22/62) of the patients developed uveitis within the first 2 months of disease; interestingly, uveitis preceded arthritis in 13% (8/62) of

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the patients and it was contemporary to onset of the articular disease in a further 19.4% (12/62) of the cases.

In our cohort, 88.7% (55/62) of patients with uveitis developed ocular inflammation by 4 years from disease onset, thus confirming the recommendations of the current guidelines[11].

Oligoarticular-onset JIA, an early onset of arthritis, and the presence of ANA appeared as the main risk factors for development of uveitis. Although few patients had HLA allele testing, the presence of HLA-DRB1*11 in oligoarticular-onset patients seemed more frequent in patients with uveitis compared to those without uveitis; in contrast, the presence of DRB1*08 seemed to confer protection. Additional studies with larger numbers of patients are needed to confirm this finding.

It was a common belief that articular and ocular inflammation ran different courses in patients with JIA[18]; more recently, in a series of 372 subjects with recently diagnosed JIA[17], greater disease activity has been observed, in terms of number of inflamed joints and laboratory measures, and less frequent achievement of clinical remission in patients with uveitis compared to patients without uveitis. In our cohort, the first episode of uveitis had developed more frequently in patients with ongoing arthritis, suggesting careful monitoring of eye disease is needed in JIA patients with active arthritis. On the other hand, relapses of uveitis presented in the absence of arthritis in two-thirds of the cases; this observation reinforced the need for a careful followup during remission, particularly in patients with antecedent uveitis episodes. We could not find laboratory measures significantly associated to relapses of uveitis; in particular, while the presence of ANA represents a risk factor for the development of uveitis, an increase in the ANA titer was not associated to uveitis relapses.

Polyarticular course in patients with oligoarticular-onset JIA was more common in patients with uveitis (33.3%), but it was not associated to a higher risk of developing uveitis, as also observed by other authors[17].

Despite recent advances in therapeutic options for both arthritis and uveitis, complications of uveitis are still common. In our series, 35.5% of the 62 patients developed complications. Prevalence of band keratopathy, cataract, and glaucoma appeared to be lower than in previous studies[6,19], while reduction in visual acuity still affected one patient out of 5 in our cohort and 16% of 163 patients with uveitis in a recent study from the UK[9].

In 7 out of 22 uveitis patients with ocular complications in our cohort, the diagnosis of uveitis preceded or was contemporary to the onset of arthritis and was asymptomatic in 6 cases; it is possible that complications occurred in these patients in consequence of a delay in the diagnosis of the asymptomatic uveitis.

Most patients with uveitis in our study improved with local therapy; nonresponding patients were treated with systemic therapies as well, particularly steroids, or CSA as a corticosteroid-sparing regimen. In refractory cases steroid pulses were used, while tumor necrosis factor inhibitors were avoided because of contradictory results in JIA-associated uveitis[20].

Until new and more effective therapeutic options for the treatment of uveitis in patients with JIA become available, prevention of ocular complications, particularly the reduction of visual acuity, should be focused on identification of subjects at high risk for the development of uveitis, and on close cooperation between ophthalmologists and rheumatologists in order to obtain the best results in the treatment of uveitis.

Oligoarticular-onset JIA patients with early onset disease who are ANA-positive may benefit from closer ophthalmologic followup, particularly during flares of the articular disease for the first 4 years of the disease, as recommended by current guidelines[11]. In patients with antecedent uveitis episodes, careful and periodic screening also is needed during remission of the articular disease. On the basis of our results, ophthalmologic controls every 3 months for the first 6 years from the first uveitis episode would confirm diagnosis of uveitis relapses in almost 70% of the patients with antecedent uveitis episodes. Nevertheless, longer uveitis relapses can occur beyond these time bounds; further studies on wide series of JIA patients with uveitis should be promoted in order to create screening guidelines for ophthalmologic followup in these patients.

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