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Prognosis of juvenile rheumatoid arthritis-associated uveitis

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PURPOSE. *To evaluate the clinical characteristics and the visual prognosis of uveitis in juvenile rheumatoid arthritis (JRA).*

METHODS. *The authors examined 63 patients with uveitis and JRA observed from January 1985 to December 2000. The following characteristics of each patient were considered: age at first visit, age at onset of uveitis and arthritis, sex, laterality and localization of uveitis, ocular complications, antinuclear antibody (ANA) and human leukocyte antigen (HLA) DR11 positivity, and follow-up. A retrospective study on mid-time visual outcome and ocular complications was performed on 42 patients with more than 12 months of follow-up.*

RESULTS. *A total of 76.2% of the patients were female, with a mean age of 8.1 years. Chronic anterior uveitis was bilateral in 77.8% of the cases and unilateral in 22.2%. Arthritis was oligoarticular at onset in 87.3% of cases, and polyarticular in 12.7%. Mean age at arthritis onset was 4.5 years and mean age at uveitis onset was 5.4 years. ANA were positive in 92% of cases and HLA DR11 was present in 36 of the 43 patients tested (83.7%). Among the 42 patients with more than 12 months of follow-up, ocular complications occurred in 90.5% of cases and the most frequent were cataract (64.4% of eyes) and band keratopathy (59.2% of eyes). Secondary glaucoma (25% of eyes) was associated with the worst visual prognosis. A total of 64.5% of eyes maintained a visual acuity between 20/33 and 20/20 at the end of the follow-up.*

CONCLUSIONS. *Visual prognosis of uveitis associated with JRA is improving, owing to earlier diagnosis and intensive treatment. Ocular complications occurred frequently in patients with uveitis and JRA but they did not seem to seriously affect the final visual outcome. The authors did not observe any correlation between prognosis and sex, age at the onset of uveitis or arthritis, pattern of arthritis, or positivity for ANA or HLA DR11. In a percentage of cases, uveitis may develop before arthritis or years after the onset of arthritis; therefore, continuous ophthalmologic examinations are needed in young people with JRA. (Eur J Ophthalmol 2003; 13: 616-21)*

KEY WORDS. *Childhood, Uveitis, Juvenile rheumatoid arthritis, Visual prognosis*

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INTRODUCTION

Juvenile rheumatoid arthritis (JRA) represents the most frequent cause of chronic uveitis in childhood, causing 25 to 30% of pediatric anterior uveitis cases (1, 2). Diagnosis is often delayed owing to insidious and paucisymptomatic onset, chronic course, and young patient age. Uveitis is often detected too late in the presence of ocular complications. Risk factors for developing uveitis are early age at onset of arthri-

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tis, oligoarticular form, female sex, antinuclear antibodies (ANA), and human leukocyte antigen (HLA) DR11 positivity (1, 3-6).

Ophthalmologic screening in patients with JRA must be carried out at close intervals in patients at risk of developing uveitis. Visits must occur from once every 2 months to once a year for 8 years following arthritis onset. On average, most patients with JRA (53%) develop uveitis after 2 years from arthritis onset (6).

Visual prognosis of uveitis associated with JRA is improving, owing to earlier diagnosis and intensive treatment. Previous studies report poor visual acuity (VA) in almost half of the patients and blindness in 14 to 38% of cases (7-9). More recent works agree with an incidence reduction and a better prognosis of uveitis (10-17).

In this study, we evaluated the incidence of ocular complications and the presence of clinical, genetic, or therapeutic factors that might affect visual prognosis in a cohort of patients with uveitis and JRA observed over the past 15 years.

METHODS

We retrospectively examined the charts of 63 patients with uveitis and JRA observed from January 1985 to December 2000 at Immunovirology Ocular Service of the University of Roma "La Sapienza."

Each patient underwent a full ophthalmologic examination, including VA measurement using Snellen charts, slit-lamp biomicroscopy, intraocular pressure measurement, and ophthalmoscopy. Bulbar echography was performed in the presence of media opacities.

Uveitis diagnosis and classification and ocular complications evaluation were performed according to the International Uveitis Study Group criteria (18).

JRA diagnosis and classification as oligoarticular, polyarticular, or systemic pattern were made according to the American College of Rheumatology criteria (19). Patients were classified on the basis of the pattern of arthritis observed for 6 months after onset.

Every patient underwent HLA I and II class typing and serologic rheumatoid factor (RF) and ANA research.

For each patient, the following were considered: age at first visit, age at onset of uveitis, age at onset of arthritis, sex, laterality and localization of uveitis, ocular complications, ANA and HLA DR11 positivity, and follow-up.

Subsequently, a retrospective study on mid-time visual outcome was performed on 42 patients with more than 12 months of follow-up (mean follow-up, 55.4 months; range 12 to 185 months) considering VA at first and last visit, uveitis duration, and ocular complications. These 42 patients were then subdivided into two groups on the basis of the worst eye's VA at the end of follow-up (>20/100 or ≤20/100). Onset of arthritis and uveitis were then subdivided into six classes (0-2 years, 2-4 years, 4-6 years, 6-8 years, 8-10 years, >10 years). In order to evaluate the risk factors on long-term visual outcome, we evaluated final VA in relation to sex, onset of arthritis and uveitis, pattern of arthritis, ANA positivity, and HLA DR11 in these patients.

Statistical evaluation was done using chi-square analysis and Fisher exact test, and $p<0.05$ was considered significant.

RESULTS

Forty-eight (76.2%) of the 63 patients were female and 15 were male (23.8%); mean age was 8.1 years (range 2.5 to 40 years). Uveitis was detected in 112 eyes. Ocular involvement was bilateral in 49 cases (77.8%) and unilateral in 14 (22.2%). Fifty-five patients (87.3% of cases) had chronic anterior uveitis; in 8 patients (12.8% of cases), anterior uveitis that was acute at onset became chronic during follow-up. Arthritis was oligoarticular at onset in 87.3% of cases and polyarticular in 12.7%. In two cases, arthritis started as oligoarticular and became polyarticular after a mean of 13 months. Mean age at arthritis onset was 4.5 years (range 1 to 12) and mean age at uveitis onset was 5.4 years (range 1 to 12) without significant differences between males and females. ANA were positive in 92% of cases; RF was negative in all patients. HLA antigen DR11 was present in 36 of the 43 patients tested (83.7%). Among the 63 patients included in the study, 26.1 months (range -36 to +84) was the average time lapse between the onset of arthritis and that of uveitis. In 33 patients (52.4%), uveitis followed arthritis. In particular, in 16 cases (25.4%), uveitis was diagnosed within the first year after arthritis onset; in 12 cases (19%), after 1 to 5 years; and only in

5 cases (8%) after a 6- to 7-year time lapse. In 21 cases (33.3%), arthritis and uveitis started together or, on average, after a 1-month interval. In 9 patients (14.3%), uveitis occurred before arthritis (mean 14.1 months; range 3 to 36 months).

Among the 42 patients with more than 12 months of follow-up, 8 males and 32 females (mean age 8.1 years; range 2.5 to 19 years), uveitis mean duration from diagnosis to follow-up was 78.9 months (range 12 to 290), and ocular complications occurred in 38 cases (90.5%) (Tab. I).

TABLE I - OCULAR COMPLICATIONS IN PATIENTS WITH UVEITIS AND JUVENILE RHEUMATOID ARTHRITIS (38/42 patients, 90.5%)

Ocular complications	Patients	Eyes
Cataract	34 (80.9)	49 (64.4)
Band keratopathy	30 (71.4)	45 (59.2)
Papillitis/papilledema	20 (47.9)	30 (39.4)
Seclusio/synechiae	23 (54.7)	29 (38.1)
Secondary glaucoma	13 (30.9)	19 (25)
Hypotony	5 (11.9)	6 (7.8)
Cystoid macular edema	5 (11.9)	6 (7.8)
Retinal detachment	1 (2.3)	1 (1.3)

Values are n (%)

TABLE II - VISUAL ACUITY AT ONSET AND AT THE END OF THE FOLLOW-UP

Visual acuity	Initial	Final
20/20-20/33	51 (67.1)	49 (64.5)
20/40-20/100	14 (18.4)	14 (18.4)
20/200-20/500	3 (4.0)	6 (7.9)
<20/500	8 (10.5)	7 (9.2)

Values are n (%)

Posterior subcapsular cataract was the most frequent ocular complication (80.9% of cases, 64.4% of eyes). In most patients, it progressed slowly and asymmetrically in both eyes; surgery was needed in 16 patients and on 24 eyes (40.5% of cases, 30.3% of eyes).

Band keratopathy was found in 71.4% of the young patients and in 59.2% of eyes, but only 10 patients (12 eyes) needed corneal scraping.

Posterior synechiae were also observed in many patients, and affected more than two sectors, causing pupillary seclusio, in 54.7% of cases (38.1% of eyes).

Papilledema was very frequent (47.9% of cases, 39.4% of eyes), whereas secondary glaucoma was detected in 30.9% of cases (25% of eyes).

Visual prognosis was good. At the end of the study, 64.5% of eyes maintained a VA between 20/33 and 20/20, as at the beginning of follow-up; 18.4% of eyes had a VA between 20/40 and 20/100, whereas a lower percentage had a VA <20/50 (9.2%, versus 10.5% at the beginning of the study) (Tab. II).

Comparison of VA and uveitis duration did not show a significant impairment of visual function with time (Tab. III). This result confirms that improvement of visual prognosis in uveitis associated with JRA is related to early diagnosis and adequate therapy rather than to disease duration. We did not find any prognostic correlation with sex, age at onset of arthritis and uveitis, form of arthritis, ANA positivity, or presence of HLA DR11 (Tab. IV).

Final prognosis also depends on the timing and the choice of surgical treatment for ocular complications and on antiamblyopic measures adopted particularly in cases of unilateral or prevalently unilateral involvement of the eye.

TABLE III - COMPARISON BETWEEN VISUAL ACUITY AND UVEITIS DURATION

	Uveitis duration			
Visual acuity	**1-2 years**	**3-4 years**	**5-6 years**	**>7 years**
20/20-20/33	17 (56.7)	8 (61.7)	6 (85.7)	18 (69.3)
20/40-20/100	6 (20)	1 (7.7)	—	6 (23.1)
20/200-20/500	4 (13.3)	1 (7.7)	1 (14.3)	1 (3.8)
<20/500	3 (10)	3 (23.1)	—	1 (3.8)

Values are n (%)

TABLE IV - COMPARISON BETWEEN CLINICAL FEATURES AND WORST EYE'S FINAL VISUAL ACUITY (VA)

Characteristics	VA >20/100 (25 patients)	VA ≤20/100 (17 patients)
Female	21	13
Male	4	4
Oligoarticular pattern	20	15
Polyarticular pattern	5	2
ANA +	21	17
ANA -	4	0
DR11 +	16	13
DR11 -	7	1
Arthritis onset		
0-2 yr	3	1
2-4 yr	7	5
4-6 yr	9	7
6-8 yr	3	3
8-10 yr	3	0
>10 yr	0	1
Uveitis onset		
0-2 yr	0	1
2-4 yr	5	3
4-6 yr	8	6
6-8 yr	3	4
8-10 yr	6	1
>10 yr	3	2

*p>0.05 In all cases (range 0.123 to 1)
ANA = Antinuclear antibody

DISCUSSION

Visual prognosis in uveitis associated with JRA historically has been poor owing to the high incidence of ocular complications and the high risk of blindness. The importance of early and adequate diagnosis has been stressed only in the last few years, and studies conducted in the 1970s and 1980s reported a <20/40 VA in 66% of cases, blindness in 14 to 38% of patients, and ocular complications in 75% of affected eyes (7-9). In more recent reports, visual prognosis has improved, ocular complications are reported in less than 50% of cases, and VA <20/40 is reported only in 9 to 30% of affected eyes (10-17). Sherry et al (10), Malagon et al (11), and Candell-Chalom et al (13) did not report blindness in any of their patients; Cabral et al (12) and Eldesten et al (17) reported blindness in 10% and 6% of cases, respectively.

Current studies also reveal an improvement in visual prognosis and a reduction in uveitis prevalence. Sherry et al (10) report reduction in uveitis prevalence from 45% to 13%; Candell-Chalom et al (13) report a 9.3% prevalence; Kotaniemi et al, 16% to 24% (16, 20); Berk et al, 12.2% (14); and Oren et al, 13% (15).

In JRA, a reduction in the severity and prevalence of uveitis seems to be related to improved knowledge and diffusion of ophthalmologic screening and to more suitable topical and systemic treatment.

In our study of 63 children with uveitis and JRA, ocular complications occurred frequently (82.5% of patients). The percentage rises if we consider a group of 42 patients with more than 12 months of follow-up, where complications occurred in 38 cases (90.5%), but complications often did not seriously affect the final visual outcome.

Cataract and band keratopathy were the most frequent ocular complications we observed (in 64.4% and 59.2% of eyes, respectively). Secondary glaucoma, occurring in 25% of eyes, was associated with the worst visual prognosis. These results agree with the literature (17).

In our patients, we did not observe any statistical correlation between prognosis and sex, age at onset of uveitis or arthritis, form of arthritis, ANA positivity, or HLA DR11.

Uveitis usually has a chronic course and different clinical expressions. In most cases, it is associated with oligoarticular JRA (87.3% of cases) and with ANA positivity (92% of cases). According to other authors (14), in patients with JRA ocular involvement occurs more frequently in females (female to male ratio = 3:1).

In our study, uveitis started before arthritis in 14.3% of cases, with a mean interval of 14.1 months, as only rarely reported by other authors (6, 14, 21, 22). About 33% of patients developed uveitis at the same time as arthritis or within 1 month from the onset of arthritis, and 60.6% of cases developed uveitis within 2 years from arthritis. The risk of developing uveitis decreases during the years following the onset of arthritis, and seems to be low after 7 years. These results agree with Kanski (6, 23); Chaylack et al (8) report that 30% of their patients developed uveitis after 16 years of age and Akduman et al (22) state that three of seven patients developed uveitis 10 years after the onset of arthritis.

This evidence highlights that children with JRA may

develop uveitis in the second decade of life, more than 7 years after the onset of arthritis. Therefore, continuous ophthalmologic examinations are needed in adolescence.

In children with JRA, the visual prognosis of uveitis is improving with time owing to earlier diagnosis, which is made possible by rigorous ophthalmic monitoring (10, 13-16, 23), and prolonged and adequate ocular topical and systemic therapy (mydriatics, steroids, and nonsteroidal anti-inflammatory drugs) together with specific treatment for JRA (e.g., steroids, methotrexate).

At the end of the follow-up period, 64.5% of eyes had a prevalent >20/33 VA and only 17.1% of eyes had VA ≤20/200. These results agree with more recent studies (13-17, 24). We stress the importance of treatment of amblyopia for a better visual outcome, mainly after surgery, in patients with unilateral or asymmetric complicated cataract (25).

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