A population-based study on uveitis in juvenile rheumatoid arthritis

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ABSTRACT

Objective

To obtain information on the occurrence and characteristics of uveitis in a population-based survey of patients with juvenile rheumatoid arthritis (JRA).

Methods

The subjects in this study were entitled, under the nationwide sickness insurance scheme, to receive specially reimbursed medication for JRA in 5 of the 21 central hospital districts in Finland (population base about 270,000 children < 16 years of age) in 1980, 1985 and 1990.

Results

A total of 114 incident cases (34 boys and 80 girls) satisfied the criteria for JRA. Uveitis was diagnosed in 18 of these patients (16%). The mean age of uveitis patients at the diagnosis of JRA was 6.8 years (median 5.4 years) and the mean interval from the diagnosis of JRA to the detection of uveitis was 2.9 years. Silent (asymptomatic) anterior uveitis was found in 4 boys and 11 girls and acute anterior uveitis in 2 boys. One girl had marginal corneal ulceration with mild anterior uveitis. Uveitis was chronic (> 6 months) in 9 cases. Uveal inflammation was most severe in the 3 children whose uveitis was detected at the time of the diagnosis of JRA.

Conclusion

The study provides population-based information on the occurrence and characteristics of uveitis associated with JRA.

Introduction

Juvenile rheumatoid arthritis (JRA) is defined by the American Rheumatism Association (ARA) as chronic arthritis of unknown cause in a child younger than 16 years persisting for at least six weeks (1). Three subtypes of JRA are recognized: systemic, polyarticular and oligoarticular. The other set of criteria for children with juvenile chronic arthritis (JCA) presently in use was proposed by the European League Against Rheumatism. According to these criteria, a minimum duration of arthritis of 3 months is required. These criteria are widely used in Europe (2). The subtype is determined six months after the onset of joint symptoms.

Chronic uveitis is an important complication of JRA. Uveitis is usually asymptomatic and is often bilateral. In most instances, uveitis manifests itself within 7 years from the onset of arthritis (3). Chronic uveitis is stated to be particularly common in antinuclear antibody (ANA)-positive girls with early onset oligoarthritis (< 4 years of age) (3). In the systemic form of JRA it is rarely seen. If uveitis is not detected early and treated promptly, it can result in substantial morbidity and even blindness (3-5). Therefore an ophthalmologic evaluation is recommended every 3 to 6 months for the first 7 years of JRA (3).

There is great variation in the occurrence of uveitis in JRA in different series, ranging from 2% to 21% (3). The majority of previous studies on uveitis in JRA come from special pediatric or ophthalmologic clinics, and the duration of follow-up has varied greatly. Only a few epidemiological surveys have been published. In a community-based series from Rochester, Minnesota (6) consisting of 49 patients with JRA, uveitis was detected in two subjects (4%). In her epidemiological survey Andersson Gäre (7) reported uveitis in 11 out of 124 Swedish JRA patients (9%) and Moe (8) in a study from northern Norway found uveitis in 15/109 (14%) JCA patients.

In a recent report by Kaipiainen-Seppänen (9), the incidence of JRA in Finland was 14/100,000 in the population < 16 years of age. The purpose of our study was to obtain information on the occurrence of uveitis and its characteristics in this population-based series of JRA patients.

Patients and methods

Since 1966 the Sickness Insurance Act has provided for the prescription of drugs free of charge for certain chronic diseases, including chronic inflammatory rheumatic diseases (following an amendment in 1987, 90% of the costs have been reimbursed). The Finnish national sickness insurance scheme covers the entire population. Eligibility requires a com-

prehensive medical certificate written by the attending physician and approved by an expert adviser on behalf of the sickness insurance scheme.

The study population consisted of 114 JRA patients from an epidemiological study of juvenile rheumatic diseases in Finland (9). The diagnosis of JRA was confirmed by a pediatric rheumatologist according to the ARA criteria (cases of spondyloarthropathy, psoriasis or bowel diseases were excluded). All of these patients had been entitled to receive specially reimbursed medication for JRA in 5 of the 21 central hospital districts in Finland in 1980, 1985 and 1990. The study area covered 1,300,000 inhabitants (range 264,226 - 275,188 for those < 16 years of age), i.e. one-quarter of the population in Finland. The patient was defined as an incident case of JRA if his/her age at the time of diagnosis was under 16 years and if he/she met the ARA classification criteria for JRA (1), and had no prior entitlement to antirheumatic medication for a fixed period.

For the purposes of the present study, the clinical data on arthritis and uveitis in the patients were collected retrospectively from the drug reimbursement certificates and hospital records for the period up to the autumn 1997. All of the patients except one had been examined by an ophthalmologist at least once, and most 2 to 3 times a year. One of the authors (KK) had performed an ophthalmologic examination on 42 of the 114 patients, including 8 of the patients with uveitis.

Results

According to the data obtained, anterior uveitis had been detected in 18 patients. Consequently, the overall occurrence of uveitis in the JRA population studied was 18/114 (16%). The principal clinical characteristics of the whole group according to their onset type of JRA are shown in Table I and the main characteristics of the 18 patients with uveitis are shown in Table II. The mean age at the diagnosis of JRA was 7.4 years (range 0.8 - 15.8 yrs., median 6.7 yrs.) for whole series, and 6.8 years (range 1.2 - 15.8 yrs., median 5.5 yrs.) for the patients with uveitis. The mean age at the onset of uveitis was 9.7 years (range 1.3 - 18.2 yrs., median 10.6 yrs.). The mean follow-up period for the patients was 7.5 years (range 0.5 - 17 yrs., median 7.0 yrs.).

Among the 18 patients with uveitis the male/female ratio was 1:2. Thirteen patients had oligoarthritis and 5 had polyarthritis. None of the 7 patients with systemic onset JRA developed uveitis. The mean age at the onset of JRA was 5.7 years (range 1.5 - 13.7 yrs., median 5.1 yrs.) for those with oligoarthritis and 9.7 years (range 1.2 - 15.8 yrs., median 13.1 yrs.) for those with polyarthritis. The uveitis was diagnosed at the age of 8.8 (range 1.3 - 15.1 yrs., median 10.5 yrs.) and 12.0 (range 3.4 - 18.2 yrs., median 14.3 yrs.), respectively .

The onset of uveitis was asymptomatic in 15 patients (4 boys and 11 girls). Both eyes were affected in 8 children. In 6 patients anterior uveitis was detected in connection with the onset of arthritis, and in 5 the uveitis ran a chronic course. The mean interval from the diagnosis of JRA to uveitis was 2.9 years (range -0.7 - 11.7 yrs., median 0.3 yrs.). However, in 2 children the asymptomatic uveitis was de-

Table I. Main characteristics of the patients according to their type of juvenile rheumatoid arthritis.

Characteristics	Type of juvenile rheumatoid arthritis			
	Oligoarthritis n = 86	Polyarthritis n = 21	Systemic n = 7	All n = 114
Male/female	27 : 59	4 : 17	3 : 4	34 : 80
Patients with uveitis	13	5	0	18
ANA positive	42 (86)#	7 (20)	0 (7)	49 (113)
RF positive	0 (86)	3 (21)	1 (5)	4 (112)
HLA B27 positive	19 (51)	5 (13)	0 (2)	24 (66)

#Numerals in parentheses indicate the number of patients studied.
ANA: antinuclear antibody; RF: rheumatoid factor; HLA B27: HLA B27 antigen.

Table II. Main characteristics of the 18 juvenile rheumatoid arthritis (JRA) patients with uveitis in the population-based JRA group (n = 114).

Type of uveitis	Gender	Onset type	Age at JRA onset (yrs.)	Interval to uveitis# (yrs.)	Eye afflicted	ANA	B27
Chronic	F	oligo	3.3	8.2	left	-	-
	M	poly	1.3	2.2	both	+	NT
	F	oligo	6.4	0	left	-	+
	M	oligo	2.7	0	both	+	NT
	F	oligo	1.5	0	both	+	-
	M	poly	15.8	0	both	-	NT
Healed chronic	M	oligo	5.9	0	both	+	-
	F	oligo	5.2	5.6	both	+	-
	F	poly	4.0	4.5	both	-	-
Episodic	F	oligo	6.7	3.8	left	-	NT
	F	oligo	3.7	11.4	left	+	+
	F	oligo	1.6	0	left	+	NT
	F	oligo	3.4	11.7	right	+	NT
	F	poly	13.1	5.1	both	-	+
	F	oligo	7.1	0.6	left	+	NT
	F	poly (RF+)	14.3	0.1	right	NT	NT
Acute	M	oligo	13.6	-0.6	right	-	+
	M	oligo	13.1	-0.4	left	-	+

ANA: antinuclear antibody; B27: HLA B27 antigen; RF+: rheumatoid factor positive; NT: not tested.
#Interval to uveitis denotes the interval between the onset of arthritis and the appearance of uveitis; a negative value indicates that the uveitis was detected before the arthritis.

tected as late as 11.4 and 11.7 years after the onset of oligoarthritis. One girl had marginal corneal ulceration and mild anterior uveitis in one eye a few weeks after her polyarticular rheumatoid factor positive disease was diagnosed. Two boys whose oligoarthritis was diagnosed at the age of 13 both had an episode of acute anterior uveitis that preceded the diagnosis of JRA by 3 and 8 months, respectively. Both of them were HLA B27 positive and had developed spondyloarthropathy 10 years after the onset of the juvenile oligoarthritis.

In 6 patients with asymptomatic anterior uveitis, the eye disease ran a chronic course and they had active ocular inflammation at the end of the follow-up (local corticosteroid treatment was given in 5/6 cases). Three of these patients experienced complications: one patient had cystoid macular oedema, cataract and glaucoma in one eye; one had cataract and secondary glaucoma in one eye; and one patient had cataract in both eyes. In all of the cases with complications the uveitis had been detected at the onset of JRA. The patient with cystoid macular oedema had a visual acuity as low as 20/400 in the affected eye at the end of the follow-up.

Three additional patients had long-standing silent uveitis (> 6 months) in both eyes that healed in 2.6, 1.8 and 0.7 years, respectively. Among the remaining 6 patients, 4 had one short episode of anterior uveitis in one eye (duration of uveitis 1 - 4 months), one had bilateral anterior uveitis of one month's duration and one patient had two short episodes of anterior uveal inflammation in one eye (no symptoms in any of these cases). A visual acuity of 20/40 or better in both eyes was recorded in all cases except the one with macular edema in one eye.

ANA were tested in 113 of the 114 JRA patients and 49 (43%) of them were found to be ANA positive. In the uveitis group 17/18 children were tested for ANA and 9 (53%) were ANA positive, 8 of whom had oligoarthritis.

HLA B27 antigen was tested in 66/114 cases and was positive in 24 (36%) patients; 5/10 of the patients with uveitis were positive. Two of the HLA B27 positive patients ten years later developed spondyloarthropathy.

Discussion

The nationwide sickness insurance scheme provides a good basis for epidemiological studies in Finland. The detected incidence of JRA, 14/100,000 in the pediatric population by Kaipiainen-Seppänen (9), was in agreement with earlier studies and remained constant during the three years of the study. The sensitivity of the inclusion criterion, i.e. drug reimbursement in JRA, was good (10, 11).

Our JRA patients had all been treated at the central hospitals of their districts or at the Rheumatism Foundation Hospital (a tertiary care centre for the entire country). Accordingly, the patients' records were readily available. Most of our patients had been evaluated by ophthalmologists at the onset of their JRA and thereafter one or two times a year for several years. We assumed that most, if not all, of the uveitis cases in our JRA patient series could be identified. This population-based study is unique due to the nationwide comprehensive registers available in Finland (9).

In an early hospital-based study from Finland, Laaksonen reported the occurrence of rheumatic iritis in 5.5% of her patients < 15 years of age, but the patients had not been evaluated by an ophthalmologist (12). In a community-based Finnish study Kunnamo detected uveitis in 6/29 (21%) JRA patients (13). In a community-based study carried out in Rochester, Minnesota only 4% of the patients had uveitis, but ophthalmologic consultations had not been performed in all the JRA patients (6). In the population-based cohort study of Andersson Gäre (7), uveitis was found in 9% of children with JCA and the type of uveitis was chronic in 3/11 cases. In a recent epidemiological report from Norway (8), uveitis was detected in 14% of JCA patients, with 5/15 cases displaying complications. In our study the occurrence of uveitis was 16% and in 9/18 patients the uveitis ran a chronic course. A more thorough case detection protocol and a different study design could perhaps explain the differences seen in the various studies.

Most of our patients (86/114) had oligoarticular disease and 15% of them developed uveitis. These findings are comparable with the results of Sherry (14), who in 1991 reported a 13% prevalence of uveitis among 134 patients with oligoarticular JRA. As in earlier reports (3, 4), the majority of our patients with uveitis had oligoarthritis, and 8 of them (62%) were ANA positive. About half of the patients were tested for HLA B27 antigen, which was found to be positive in 36% of them, including the two who developed acute uveitis and several years later spondyloarthropathy. The overall frequency of HLA B27 in the Finnish population is 14.5%.

Uveitis is usually detected in patients during the first years from the onset of arthritis (3). In a recent report from pediatric centres in Philadelphia (15), 90% of patients developed uveitis during the first four years of arthritis, on the average within 1.8 years. In our series the mean interval from the diagnosis of JRA to the onset of uveitis was 2.9 years and two-thirds of the uveitis cases were diagnosed during the first 4 years of arthritis.

Sometimes the onset of uveitis may be delayed by more than a decade after the onset of arthritis (16). In our study as well, two children developed asymptomatic anterior uveitis more than 11 years after the diagnosis of the joint disease. Thus, there are strong reasons to continue a systematic follow-up of patients with JRA beyond the first years of the joint disease.

We share the opinion that the prognosis of uveitis is worst in patients in whom the uveitis is diagnosed before or at the onset of JRA (3, 15). Six of our patients had silent uveitis at the onset of JRA and all 3 of the patients with severe complications belonged to this group. However, the uveitis is still active in 6 of the 18 patients in our series (including the 3 with complications), and the figures regarding complications could increase with a longer follow-up.

The prognosis of uveitis in JRA is considered to be better today than it was a few decades ago (4, 17). Interestingly, in most of our patients the uveitis resolved, remaining active in only 6/18 patients. The overall visual prognosis was also good, perhaps because of early ophthalmologic evaluation and proper treatment of the detected uveitis cases.

During these systematic eye examinations several short episodes of asymptomatic uveitis were found, some of which resolved without treatment.

As a rule patients with particular joint problems are referred to rheumatologists and those with special eye problems are referred to ophthalmologists. Thus, patient series collected from specialised rheumatologic or ophthalmologic centres may provide a biased view of the frequency and types of uveitis present in the population; only a population-based study can give reliable information on ophthalmologic problems in JRA patients.

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