British Journal of Ophthalmology, 1989, **73**, 225–228

Screening for uveitis in juvenile chronic arthritis

JACK J KANSKI

From the Juvenile Rheumatism Unit, Canadian Red Cross Memorial Hospital, Taplow, and the Division of Rheumatology, Clinical Research Centre, Northwick Park Hospital, Harrow

SUMMARY Three hundred and fifteen patients with anterior uveitis associated with juvenile chronic arthritis (JCA) were studied in order to identify the various risk factors for uveitis. Girls were more susceptible to uveitis than boys by a ratio of 3:1. In 94% of cases the uveitis was diagnosed after the development of arthritis. The risk of uveitis was small after seven or more years had elapsed from the onset of arthritis. Patients with pauciarticular onset JCA had the highest risk of uveitis and systemic onset patients the least risk. The presence of circulating antinuclear antibody was also an important marker for an increased risk of uveitis. A regimen for routine screening of patients is suggested.

Juvenile chronic arthritis (JCA) is a rare idiopathic inflammatory arthritis occurring before the sixteenth birthday. The condition was formerly referred to as Still's disease, and in the United States it is frequently called juvenile 'rheumatoid' arthritis. About 20% of patients with JCA develop anterior uveitis, which is frequently bilateral.[1-8] The intraocular inflammation is typically asymptomatic, and, unless it is detected and treated at a relatively early stage, some patients are at risk of developing severe visual impairment.[9] It is therefore important to identify and screen patients who are at increased risk of ocular complications. Similarly, those with little or no risk should also be identified in order to spare the patients and parents the inconvenience of unnecessary and time wasting visits to the ophthalmologists.

The main purpose of this study is to describe the clinical and immunological characteristics of a large number of patients with JCA in relation to the likely risk of uveitis and to give guidelines to the necessity for routine screening.

Patients and methods

This study comprises 315 patients with anterior uveitis who fulfilled the criteria for the diagnosis of JCA. Special investigations included *x*-rays, synovial biopsy when indicated, and tests for IgM rheumatoid factor. Tests for circulating antinuclear antibodies (ANA) were performed on 277 patients. The author personally examined most of the patients over a 10-year period (January 1975 to December 1984). In most cases the diagnosis of uveitis was made when the patient attended a combined eye-joint clinic. The following information was obtained from the medical records: sex, age at onset of arthritis, age at time of diagnosis of uveitis, extent of arthritis during the first three months, subsequent course of joint involvement, presence of extraarticular systemic features, and presence of IgM rheumatoid factor and ANA.

Correspondence to Mr J J Kanski, FRCS, Prince Charles Eye Unit, King Edward VII Hospital, Windsor, Berkshire SL4 3DP.

Results

Of the 315 patients 234 (74%) were girls. The mean age of the patients at the onset of JCA was 3 years and 8 months (range 6 months to 16 years); 62% of children were under the age of 4 years when they developed arthritis and 90% were under the age of 8 years.

INTERVAL BETWEEN ONSET OF JCA AND DIAGNOSIS OF UVEITIS

In 295 patients (94%) JCA preceded the diagnosis of uveitis. Of these patients 158 (53%) developed uveitis within two years of the onset of JCA, and in 267 (90%) the interval was not longer than seven years. There were, however, three patients in whom the interval between the onset of JCA and the diagnosis of uveitis was over 20 years. In two of these the uveitis was first diagnosed on a routine slit-lamp examination when the patients were in their mid 20s, and in another the diagnosis was made at the age of 36 years when an optician noticed bilateral lens

opacities at a routine refraction. In 20 patients (6%) the diagnosis of uveitis antedated the development of JCA. Of these patients 17 developed JCA within four years, and in one patient joint involvement was delayed for nine years. When last examined 14 patients in whom uveitis antedated arthritis were aphakic in at least one eye, and of 29 eyes in 16 of these patients that had an adequate period of follow-up nearly half (14) had a visual acuity of counting fingers or less.

ARTICULAR FEATURES

The 315 patients were divided into three groups according to the mode of onset of JCA and the extent of joint involvement during the first three months. Table 1 shows the number of patients in each group and Table 2 shows the sex distribution in each group.

Group 1—pauciarticular onset JCA. In 284 patients, of whom 75% were girls, the arthritis presented with and remained confined to fewer than five joints during the first three months of the disease. The most frequently involved joints were the knees, followed by the ankles and elbows. However, in one patient the disease presented with involvement of only one joint of the ring finger and in another with arthritis of a single toe.

According to the subsequent course of joint involvement the patients in this group were divided into the following three subgroups. (*a*) Persistently monoarticular JCA. In 29 patients the arthritis remained confined to one joint (invariably the knee). In some patients changes secondary to arthritis caused the affected leg to be slightly longer than the normal leg. In other patients the arthritis resolved without residua. Two patients in this subgroup developed uveitis prior to the onset of JCA. (*b*) Persistently pauciarticular JCA. In 133 patients between two and four joints became invovled subsequently. (*c*) Extended pauciarticular JCA. In 122 patients the arthritis subsequently spread to five more joints (that is, became polyarticular). In some patients severe joint deformities required surgical correction, and six patients developed secondary amyloidosis. In this subgroup six patients had uveitis prior to the onset of JCA.

Group 2—polyarticular onset of JCA. In 27 patients, of whom 70% were girls, the arthritis involved five or more joints during the first three months of the disease. The most frequently affected joints were the knees followed by the wrists and ankles.

Group 3—systemic onset JCA. In four patients (one girl) the disease was heralded by a high remittant fever which was characteristically at its height at night and normal next morning. In order to fulfil the criteria for systemic onset JCA at least one of the following signs was also present: a maculopapular (Still's) rash, generalised lymphadenopathy, splenomagaly, hepatomegaly, and pericarditis. All four patients in this group subsequently developed polyarthritis. It is important to emphasise that nearly half (153 of 315) the patients with JCA had a polyarthritis some time during the course of their disease.

SYSTEMIC FEATURES

Extrarticular systemic features, which are summarised in Table 3, were present at some time during the course of the illness in 35 out of 311 (11%) patients in groups 1 and 2. Several patients had more than one feature. Three patients died from complications of JCA. One died during sleep as a result of dislocation of his atlanto-occipital joint, another died from renal failure as a result of secondary amyloidosis, and the third was completely incapacitated and bedridden as a result of extremely severe polyarthritis and died of heart failure.

IMMUNOLOGICAL FEATURES

All patients gave negative results for IgM rheumatoid factor but 208 out of 277 (75%) were ANA positive. Table 4 shows that there was no difference between patients with pauciarticular and polyarticular onset JCA, though three patients with systemic onset JCA were all negative. There appeared to be no correla-

Table 1 *JCA subgroups*

JCA onset	*Number*	*Percentage*
Group 1 (pauciarticular)	284	90
Group 2 (polyarticular)	27	9
Group 3 (systemic)	4	1

Table 2 *Sex distribution in JCA subgroups*

JCA onset	*Girls*		*Boys*		*Total*
	Number	*Percentage*	*Number*	*Percentage*	
Group 1 (pauciarticular)	214	75	70	25	284
Group 2 (polyarticular)	19	70	8	30	27
Group 3 (systemic)	1	25	3	75	4

Table 3 *Systemic features*

Feature	*Number*		*Total (311)*
	Group 1 (284)	*Group 2 (27)*	
Cutaneous			
Still's rash	1	1	2
Morphea	1	1	2
Erythema nodosum	1	–	1
Psoriasis	8	3	11
Reticuloendothelial			
Hepatomegaly	2	–	2
Splenomagaly	6	1	7
Lymphadenopathy	3	1	4
Gastrointestinal			
Regional ileitis	1	–	1
Ulcerative colitis	1	1	2
Cardiovascular			
Pericarditis	1	–	1
Aortic incompetence	1	1	2
Secondary amyloidosis	6	–	6
Remittent fever	–	1	1
Enlarged salivary glands	1	–	1

tion between the level of ANA titre and the activity of either eye or joint inflammation.

Discussion

Although, in general, JCA is more common in girls than in boys by a ratio of 3:2,[10–12] it appears that girls carry a distinctly higher risk of ocular complications. In this study 74% (234 of 315) were girls, and the incidence in other studies ranges between 60% and 92%.[1 2 4 7 13–18] It is also evident that girls are more susceptible to chronic anterior uveitis than boys, irrespective of whether or not they have JCA.[19] At present no adequate explanation can be given for the increased susceptibility of girls to uveitis.

In 90% of cases the interval between the onset of JCA and the diagnosis of uveitis was less than seven years. It therefore appears that the risk of uveitis is small after seven or more years have elapsed from the time of onset of arthritis, so that the intervals between routine screening can be extended, but it is impossible to say with certainty when the risk of uveitis is nil. It is therefore recommended that an annual screening should still be performed even when the patients with JCA reach adulthood. Although only 20 (6%) of the patients were found to have uveitis prior to the onset of JCA, there is little doubt that the type of chronic iridocyclitis that is typically associated with JCA can occur in the absence of joint involvement, particularly in girls, and in fact the majority of children with chronic iridocyclitis do not develop arthritis.[18 19] Nevertheless, it should be stressed that, although 17 out of 20 patients in this study developed JCA within four years of the diagnosis of uveitis, in one patient joint involvement was delayed for nine years. It would therefore seem reasonable to exclude the possibility of subsequent JCA only after a prolonged period of follow-up.

Table 4 *ANA in subgroups of JCA (277 patients)*

JCA onset	*ANA positive*	
	Number	*Percentage*
Group 1 (pauciarticular)	189/248	76
Group 2 (polyarticular)	19/26	73
Group 3 (systemic)	0/3	3

Although there was no correlation between the activity of joint and eye inflammation, a striking association was apparent between the mode of onset of JCA and the subsequent risk of uveitis. Although about 30% of patients with JCA have a systemic onset,[12] in this study only four out of 315 patients had this mode of presentation. It is therefore apparent that uveitis is sufficiently rare in this group of patients for an annual screening to suffice.

About 20% of all JCA patients have a polyarticular onset,[12] and in this study 9% had this mode of presentation. It is difficult to compare these findings with those of other reports, because none enumerate the number of joints involved during the first three months of the disease but merely indicate the extent of arthritis when the patient was last examined. Because the risk of uveitis in the group with polyarticular onset JCA is higher than in the systemic onset group, a six-monthly slit-lamp examination would seem appropriate.

The most frequent mode of presentation of JCA, accounting for about 50% of cases, is monopauciarticular.[12] In some patients the disease remains monopauciarticular, while others subsequently develop polyarthritis. It is this group with monopauciarticular onset of JCA that is of particular importance to ophthalmologists because of the high risk of ocular complications. In this study 90% of patients had this mode of presentation. However, it should be emphasised that 43% subsequently developed polyarticular disease, which was complicated in six patients by secondary amyloidosis. From these findings it is recommended that, when assessing the risk factors of uveitis, the ophthalmologist should take a careful history of the mode of onset of arthritis and ignore the extent of joint involvement when he first examines the patient. This is because nearly half of all patients with JCA will have a polyarthritis some time during the course of their disease.

Table 5 *Screening regimen for uveitis in JCA*

Risk factor	*Frequency of screening*
Systemic onset	Annual
Polyarticular onset	6-monthly
Pauciarticular onset	3-monthly
Positive ANA	2-monthly

Conversely, in some patients the arthritis may be mild, transient, and confined to only one joint. These patients may present with uveitis and the past history of arthritis may be overlooked by the ophthalmologist or forgotten by the patient or parents. Because of the high risk of uveitis in patients with pauciarticular onset JCA, a three-monthly screening is recommended for at least seven years from the onset of JCA.

It is interesting to note that, although only four patients with uveitis had the typical systemic onset of JCA, there were several patients in groups 1 and 2 who had various combinations of systemic features but who did not fulfil the criteria for true systemic onset JCA. It therefore appears that the presence of systemic features does not necessarily indicate a low risk of uveitis as in the true systemic onset group.

The finding that all patients with JCA were negative for rheumatoid factor confirms the fact that seropositive children with 'juvenile rheumatoid arthritis' resemble their adult counterparts and do not carry an increased risk of uveitis. Routine screening of asymptomatic patients in this group of patients is therefore unnecessary. However, the high incidence of positive findings for ANA in this study of 75% and an incidence of 71%[18] reported in other studies, as opposed to an incidence of 30% in JCA patients without uveitis,[20] serve to emphasise the need for frequent routine screening of all ANA positive patients. It is suggested that this group should be screened at two- to three-month intervals for at least seven years from the time of onset of JCA, particularly if they also have disease of pauciarticular onset. The recommended regimen for screening during the first seven years is summarised in Table 5.

This work formed part of an MD thesis accepted by the University of London.

References

1 Stewart AJ, Hill RH. Ocular manifestations in juvenile rheumatoid arthritis. *Can J Ophthalmol* 1967; **2:** 58–62.
2 Kazdan JJ, McCulloch JC, Crawford JS. Uveitis in children. *Can Med Assoc* 1967; **96:** 385–91.
3 Smiley WK. The eye in juvenile rheumatoid arthritis. *Trans Ophthalmol Soc UK* 1974; **94:** 817–29.
4 Key SN, Kimura SJ Iridocyclitis associated with juvenile rheumatoid arthritis. *Am J Ophthalmol* 1975; **80:** 425–9.
5 Kanski JJ. Anterior uveitis in juvenile rheumatoid arthritis. *Arch Ophthalmol* 1977; **95:** 1794–7.
6 Kanski JJ. Care of children with anterior uveitis. *Trans Ophthalmol Soc UK* 1981; **101:** 387–90.
7 Spalter HF. The visual prognosis in juvenile rheumatoid arthritis. *Trans Am Ophthalmol Soc* 1975; **3:** 554–70.
8 Kanski JJ, Shun-Shin GA. Systemic uveitis syndromes in childhood: an analysis of 340 cases. *Ophthalmology* 1984; **91:** 1247–52.
9 Wolf MD, Lichter PR, Ragsdale CG. Prognostic factors in the uveitis of juvenile rheumatoid arthritis. *Ophthalmology* 1987; **94:** 1242–8.
10 Schaller J, Wedgwood RJ. Juvenile rheumatoid arthritis: a review. *Pediatrics* 1972; **50:** 940–53.
11 Ansell BM, Wood PHN. Prognosis in juvenile chronic polyarthritis. *Clin Rheum Dis* 1976; **2:** 397–405.
12 Ansell BM. Chronic arthritis in childhood. *Ann Rheum Dis* 1978; **37:** 107–20.
13 Verterdal E, Sury B. Iridocyclitis and bandshaped corneal opacity in juvenile rheumatoid arthritis. *Acta Ophthalmol (Kbh)* 1950; **28:** 321–36.
14 Smiley WK, May E, Bywaters EGL. Ocular presentations of Still's disease and their treatment. *Ann Rheum Dis* 1957; **16:** 371–82.
15 Smiley WK. Iridocyclitis in Still's disease. *Trans Ophthalmol Soc UK* 1965; **85:** 351–6.
16 Kimura SJ, Hogan MJ, O'Connor GR, Epstein WV. Uveitis and joint disease. *Arch Ophthalmol* 1967; **77:** 309–16.
17 Chylack LT, Bienfang DC, Bellows AR, Stillman JS. Ocular manifestations of juvenile rheumatoid arthritis. *Am J Ophthalmol* 1975; **79:** 1026–33.
18 Ohno S, Char DH, Kimura SJ, O'Connor GR. HLA antigens and antinuclear antibody titres in juvenile rheumatoid arthritis. *Br J Ophthalmol* 1977; **61:** 59–61.
19 Perkins ES. Pattern of uveitis in children. *Br J Ophthalmol* 1966; **50:** 169–85.
20 Schaller JG, Johnson GD, Holborow EJ, Ansell BM, Smiley WK. The association of antinuclear antibodies with the chronic iridocyclitis of juvenile rheumatoid arthritis. *Arthritis Rheum* 1974; **17:** 409–16.

Accepted for publication 8 February 1988.