

VISUAL OUTCOME IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS RELATED UVEITIS

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SUMMARY

Purpose: To determine the incidence and characteristics of uveitis in a cohort of patients with juvenile idiopathic arthritis (JIA) as well as the nature of treatment and the risk factors for visual loss.

Patients and methods: Retrospective review of 52 patients with JIA, screened for uveitis between 1995 and 2005. The first group, presenting with symptoms of arthritis and uveitis, was diagnosed at screening. The second group presented with symptoms of uveitis, without any rheumatological complaints at the time of diagnosis. During follow-up, reactivation of uveitis and complications were registered and treated when indicated.

Results: Seventeen patients had symptoms of uveitis at time of presentation or developed uveitis at follow-up. Ten of this patient group had oligo-arthritis, 16 were antinuclear antibody (ANA) positive, 16 were girls. Three patients presented with ophthalmological symptoms without rheumatological complaints. In this group, complications were more pronounced. Treatment in all patients consisted of topical corticosteroids and dilating drops at different intervals. Visual acuity was good in most patients.

Conclusion: In this retrospective study, the risk of uveitis was higher in ANA-positive girls with oligo-arthritis. To reduce severe disease at presentation, earlier diagnosis of JIA, earlier referral for slit lamp examination and universal screening of vision in childhood are necessary.

RÉSUMÉ

But: Analyse de l'incidence, des caractères et du traitement de l'uvéite des patients souffrant d'arthrite juvénile idiopathique (AJI) et analyse des facteurs de risque d'une baisse de l'acuité visuelle.

Patients et méthodes: Analyse rétrospective d'une série de 52 patients ayant présenté une AJI, à la recherche d'une uvéite entre 1995 et 2005. Le premier groupe se présente avec des symptômes d'arthrite suivi d'uvéite. Le second groupe se présente avec une uvéite qui précède l'arthrite. Ces patients n'ont pas de plaintes rhumatologiques au moment du diagnostic. Les réactivations de l'uvéite et les complications sont notées et traitées si nécessaire.

Résultats: Dix-sept patients ont des symptômes d'uvéite au moment de la consultation ou au moment des contrôles suivants. Dix enfants ont une forme oligo-articulaire, 16 patients ont des anticorps antinucléaires (AAN), 16 patients sont des filles. Trois patients se présentent avec des symptômes ophtalmologiques sans plaintes rhumatologiques. Dans ce groupe, les complications sont plus prononcées. Le traitement local associe corticoïdes et mydriatiques. L'acuité visuelle est bonne pour la plupart des patients.

Conclusion: Dans cette étude rétrospective le risque d'uvéite est plus important chez les filles dont l'oligo-arthrite s'est déclarée tôt et en présence d'AAN. La détection précoce d'AJI et de l'uvéite, ainsi que des examens ophtalmologiques systématiques sont donc indispensables pour diminuer la sévérité de l'uvéite au moment de la première consultation.

KEY WORDS

uveitis, juvenile idiopathic arthritis

MOTS-CLÉS

uvéite, arthrite juvénile idiopathique

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INTRODUCTION

Juvenile idiopathic arthritis (JIA) covers a heterogeneous group of inflammatory conditions characterized by arthritis of unknown cause of at least six weeks duration starting before the patient's sixteenth birthday (7,17). The most frequent extra-articular manifestation of JIA is an insidious asymptomatic anterior uveitis with a chronic disease course (7). The risk of uveitis is highest in very young girls with the oligoarticular subtype of JIA and the presence of antinuclear antibodies (ANA), in up to 25% of those patients. The risk is much lower in the other subtypes of JIA (4,7). In view of the asymptomatic nature of the condition, routine screening of JIA patients at risk two to four times a year is crucial to prevent complications of uveitis (5,7). These complications include band keratopathy, posterior synechiae, cataract, secondary glaucoma, cystoid macular edema and cyclitic membrane with hypotony (3,7,19). The aims of this study were to determine the incidence and characteristics of uveitis in a cohort of patients with juvenile arthritis as well as the nature of treatment and the risk factors for visual loss.

PATIENTS AND METHODS

We retrospectively reviewed the charts of 52 patients, with juvenile idiopathic arthritis, as defined by the classification of the International League of Associations of Rheumatology (ILAR), examined between 1995 and 2005 at a combined rheumatology and ophthalmology clinic at the University Hospitals Leuven, Belgium. We recorded patient's gender, age at diagnosis of arthritis and uveitis, rheumatologic diagnosis, results of ANA testing and details of systemic and topical treatment. Our patient population was subdivided into two groups: in the first group, patients presented with symptoms of arthritis. Uveitis was diagnosed at screening. Screening in patients with ANA positive oligoarthritis was performed every three months for the first five years after diagnosis, and every six months for the following seven years as recommended. For patients with polyarticular arthritis who have a lower risk of uvei-

tis, screening 2 times a year was advised (1). Patients with systemic onset of JIA were instructed to have an ophthalmological examination once a year. All parents were instructed to evaluate the pupils of their child regularly with a flashlight to search for a poorly reacting pupillary response, suggesting the formation of synechiae. In some cases, parents having difficulty to evaluate the pupils, tropicamide 0.5% was administered once a week. The second group included patients presenting with uveitis, without any rheumatological complaints at the time of diagnosis. In this group, more ocular complications were evident at diagnosis, because uveitis with its complications had been unnoticed for a long time. Whenever active uveitis was detected, intense and close follow-up with short intervals was performed. All patients had a complete ophthalmological examination, including best corrected visual acuity in the distance and for near, tonometry, slitlamp examination and fundoscopy after dilatation. During follow-up, reactivation of uveitis and complications were registered and treated when indicated. Treatment consisted of dilating drops to prevent or cure formation of synechiae and consisted of corticosteroids in topical, subconjunctival or oral form. Surgical treatment of complications included lensectomy, trabeculectomy, iridectomy and chelation of band keratopathy.

RESULTS

Our patient group includes 52 patients, 42 girls and 10 boys. Twenty-eight patients were diagnosed with oligoarthritis, sixteen patients with polyarthritis, three patients with systemic onset arthritis, two patients with psoriatic arthritis and three patients without any signs of arthritis at the time of diagnosis of uveitis. Seventeen of those patients had uveitis at time of presentation or developed uveitis at follow-up (32.7%). (Table 1) Age ranged from 2 to 8 years at the time of the first presentation of ophthalmological symptoms, with a median age of 4. Ten of them had oligoarthritis (59%), 3 patients had polyarthritis (17.6%), one of them had psoriatic arthritis (5.8%), and 3 patients had no arthritis at the time of diagnosis of uveitis (17.6%). Sixteen uveitis patients were ANA positive. Sixteen uveitis patients were girls. Four-

Table 1: Visual acuity, ophthalmological findings, treatment and complications of JIA patients with uveitis.

Patient	Gender	Type JIA	Age RS	Age OS	Age LV	FU	ANA	VA diagnosis		VA last visit		Oft R/	Complications	R/complications
								RE	LE	RE	LE			
BD	F	O	3	3	10.5	7.5	+	0.2	0.2	1	0.12	N,D,T,SC	GL, CAT, BKP	I, CS, CB
CH	F	O	5.5	5.5	6.5	1	+	1	1	1	1	D,T	-	-
DL	F	OE	2	2	6.5	4.5	+	0.9	0.9	1	1	N,D,T	GL	TG
DJ	F	OE	3	4	9	5	+	1	0.7	ND	ND	D,T	-	-
KT	M	O	2	2	7	5	+	ND	ND	0.8	1	D,T	-	-
KK	F	O	2	3	14	11	+	1	1	1	1	N,D,T	-	-
RM	F	O	2.5	5	12	7	+	1	1	1	1	N,D	-	-
WN	F	O	5	5.5	7	1.5	+	0.8	0.7	0.9	0.8	D,T	GL, KP	TG, T
CS	F	O	2	2	12	10	+	0.25	0.25	1	0.9	D,T,SC	GL	TG
BF	F	P	8	8	15	7	+	1	1	1	1	D,T	-	-
DE	F	P	2.5	3.5	5	1.5	+	1	1	0.8	0.9	D,T	-	-
LA	F	P/Ps	2	5	15	10	+	0.3	1	0.7	1	D,T,SC	CAT, MO	C
SV	F	P	1	4	8	4	+	1	1	1	1	T	-	-
DM	F	-	-	4	8.5	4.5	+	0.5	0.6	0.7	0.9	TSC	CAT, BKP	I, CS, CB
YI	F	-	-	5	9.5	4.5	+	0.12	HM	0.6	LP	D,T,SC,O,MTX	CAT, BKP, Ph	CS, CB
DF	F	O	0.8	5	8	3	ND	0.08	0.6	0.8	0.9	D,T	BKP, PPM, MO	CB, RPM
VM	F	-	-	9	9.5	0.5	+	1	1	1	1	D,C,MTX	GL	TG

JIA: juvenile idiopathic arthritis; RS: rheumatological symptoms; OS: ophthalmological symptoms; LV: last visit; FU: follow-up; ANA: antinuclear antibody; VA: visual acuity; O: oligoextended arthritis; P: polyarthritis; Ps: psoriatic arthritis; ND: no data; HM: hand movement; LP: perception of light; N: NSAID; D: dilating drops; T: topical corticosteroids; SC: subconjunctival corticosteroids; O: oral corticosteroids; MTX: methotrexate; GL: glaucoma; CAT: cataract; BKP: band keratopathy; KP: keratic precipitates; MO: macular oedema; Ph: phthisis; PPM: pre-pupillary membrane; I: iridectomy; CS: cataract surgery; CB: chelation band keratopathy; TG: topical glaucoma treatment; T: trabeculectomy; C: corticosteroids; RPM: removal prepupillary membrane

teen patients presented with rheumatological symptoms and uveitis became apparent at follow-up screening. Three patients presented with ophthalmological symptoms, without any signs of arthritis. Ocular complications in this group were more pronounced. Every patient was treated with topical corticosteroids and dilating drops at different intervals. Five patients needed subconjunctival corticosteroid injection to control uveitis activity and 1 patient was treated with oral corticosteroids. Two patients with isolated severe uveitis were systemically treated with methotrexate. Complications of uveitis included synechiae in 12 patients, bandkeratopathy in 4 patients, lensopacities in 6 patients, glaucoma in 5 patients, macular edema in 2 patients, prepupillary membrane in 1 patient and phthisis bulbi in 1 patient. This patient had undergone a lensimplantation elsewhere and developed consecutively phthisis. Treatment of complications consisted of chelation of bandkeratopathy in 4 patients, lensectomy in 3 patients, treatment of glaucoma by topical therapy in 4 patients and by trabeculectomy in 1 patient, removal of a prepupillary membrane in 1 patient. If we compared visual acuity (VA) at presentation with VA at last evaluation, VA remained normal in 16 eyes, there was improvement of VA in 9 eyes, mainly due to treatment with lensectomy and chelation of bandkeratopathy. In two eyes a further decrease of vision occurred: one phthisic eye, and one with already serious cataract and bandkeratopathy at presentation. Results are depicted in table 1.

DISCUSSION

JIA is characterized by arthritis of unknown cause of at least six weeks duration starting before the patient's sixteenth birthday (7,17). The different terminology in chronic childhood arthritis can be confusing for ophthalmologists. Whereas the term juvenile chronic arthritis has been proposed by the European League of Associations of Rheumatology (EULAR), in the United States the name juvenile rheumatoid arthritis was put forward by the American College of Rheumatology (ACR). The main differences between the EULAR and the ACR criteria were the duration of joint symptoms necessary for the diagnosis of chronic arthritis (three months versus six weeks) and inclusion versus

exclusion of certain disease conditions, such as juvenile ankylosing spondylitis and juvenile psoriatic arthritis. Recently, a new set of criteria was published by the ILAR covering all idiopathic childhood arthritides under the name juvenile idiopathic arthritis (7,17). This classification has now been widely accepted. JIA has been recognized since the early 1800s, extra-articular manifestations of JIA being first described at the end of that century (18). The association between intraocular inflammation and chronic arthritis in children was first documented by Ohm in 1910 (15). In our study, there was a difference in the presenting symptoms of uveitis. In the first group, uveitis was found during screening examination of patients who presented with rheumatological complaints. These children had no ophthalmological symptoms. In the second group, patients presented with ophthalmological symptoms, without rheumatological complaints. Within this group, more and serious complications at the time of presentation were found, because of unnoticed uveitis for a long time. In literature, we found that chronic uveitis occurs in about 20% to 30% of JIA patients with oligoarthritis, particularly in very young girls with the oligoarticular subtype of JIA and presence of ANA. In some small series, higher frequencies have been reported (6,7). In a retrospective study of 71 patients with juvenile arthritis, there was an incidence of uveitis of 38% (3). Another retrospective analysis of 760 patients showed a prevalence of uveitis of 9.3%. Uveitis occurred less frequently (5-10%) in patients with polyarthritis and virtually never in systemic onset disease (9). Patients with psoriatic arthritis not infrequently had chronic uveitis (7). So, risk factors of developing uveitis include the pattern of initial joint disease, the patient's sex, ANA status and age at onset (4,8,11,14,16). These findings are confirmed in our study. However, one study concluded that in Turkish children with JIA, the incidence of ANA positivity and uveitis was low (18.5%) (10). Our findings in three children with severe uveitis at presentation were also in agreement with the literature. Indeed, we found in one study that when arthritis preceded uveitis, 6% of patients had a poor visual outcome, compared to 67% of patients whose initial manifestation of JIA was uveitis (19). All three of our patients with se-

vere uveitis were ANA positive. Complications occur in consequence of a delay in the diagnosis of insidious uveitis (7,12,19) and with formation of synechiae. Another study showed that the visual prognosis of the children with JIA that developed uveitis was excellent, with only 30% experiencing less than 20/20 vision (16). In our study, visual outcome was good in most patients. Ten patients had final visual outcome of more than 0.8 in each eye. Phthisis had developed in one eye of one patient. Intraocular lens implantation is not advocated in children with JIA-associated active uveitis, as postoperative inflammation is especially exuberant (13). Few have reported favourable outcomes after cataract surgery with IOL in children with JIA-associated uveitis, and long term outcomes have not been reported. Factors that limited the postoperative visual outcome after IOL implantation in literature included posterior synechiae, macular edema, persistent inflammation and glaucoma. (13) Advice was given to have adequate long-term preoperative and postoperative control of intraocular inflammation with systemic immunosuppressive therapy in addition to intensive topical corticosteroid treatment (13). Another patient in our study had one eye with final visual acuity of 0.12, which had cataract and band keratopathy at presentation. Visual complications as synechiae, band keratopathy, cataract or glaucoma developed in 31% of the patients with uveitis (2). Treatment objectives in uveitis are reduction of inflammation, relief of discomfort and preservation or restoration of vision (16). Topical corticosteroids have been the standard treatment to decrease ocular inflammation (16). Topical mydriatics and cycloplegics relieve discomfort associated with ciliary spasm and prevent synechiae (16). It is important to instruct parents to evaluate the presence of synechiae, as they can develop in a week time. In our experience a personalized and fine tuned combination of mydriatics, local steroid drops and subconjunctival steroid injection in selected patients, was associated with an improvement of VA over time, except in those children who had already severe or complicated uveitis at presentation.

CONCLUSION

Uveitis is a frequent extraarticular manifestation of JIA. In our retrospective study, we found the risk of uveitis to be higher in ANA-positive girls with early onset oligoarthritis. Because of the insidious nature of uveitis, it is important to screen patients regularly and to motivate the parents to check pupillary response at home in order to prevent serious complications. The only way to reduce severe disease at presentation is by earlier diagnosis of JIA, earlier referral for slit lamp examination and, ultimately, by universal screening of vision in childhood.

REFERENCES

- (1) CASSIDY J.T., PETTY R.E. – Juvenile Rheumatoid Arthritis. Textbook of Pediatric Rheumatology, fourth edition, 2001, 218-321. Edited by W.B. Saunders Company.
- (2) CHALOM E.C., GOLDSMITH D.P., KOEHLER M.A., BITTAR B., ROSE C.D., OSTROV B.E., KEENAN G.F. – Prevalence and outcome of uveitis in a regional cohort of patients with juvenile rheumatoid arthritis. *J Rheumatol*, 1997; 24: 2031-2034
- (3) CHEN C.S., ROBERTON D., HAMMERTON M.E. – Juvenile arthritis-associated uveitis: visual outcomes and prognosis. *Can J Ophthalmol*, 2004; 6: 614-620
- (4) EDELSTEN C., VICKIE L., BENTLEY C.R., KANSKI J.J., GRAHAM E.M. – An evaluation of baseline risk factors predicting severity in juvenile idiopathic arthritis associated uveitis and other chronic anterior uveitis in early childhood. *Br J Ophthalmol*, 2002; 86: 51-56
- (5) FOSTER C.S. – Diagnosis and treatment of juvenile idiopathic arthritis-associated uveitis. *Curr Opin Ophthalmol*, 2003; 14: 395-398
- (6) GORI S., BROGLIA A.M., RAVELLI A. – Frequency and complications of chronic iridocyclitis in ANA-positive pauciarticular juvenile chronic arthritis. *Int Ophthalmol*, 1995; 18: 225-228
- (7) KAISU K., ANNELI S., ANNI K., KIMMO A. – Recent advances in uveitis of juvenile idiopathic arthritis. *Surv Ophthalmol*, 2003; 5: 489-502
- (8) KANSKI J.J. – Screening for uveitis in juvenile chronic arthritis. *Br J Ophthalmol*, 1989; 73: 225-228
- (9) KANSKI J.J., PETTY R.E. – Chronic childhood arthritis and uveitis. *Ocular Infection and Immunity*; 1996: 485-493

- (10) KASAPCOPUR O., YOLOGLU N., ÖZZYAZGA Y. – Uveitis and antinuclear antibody positivity in children with juvenile idiopathic arthritis. *Indian Pediatrics*, 2004; 41: 1035-1039
- (11) KOTANIEMI K., KAUTIAINEN H., KARMA A., AHO K. – Occurrence of uveitis in recently diagnosed juvenile chronic arthritis: a prospective study. *Ophthalmology*, 2001; 108: 2071-2075
- (12) KOTANIEMI K., SAVOLAINEN A., AHO K. – Severe childhood uveitis without overt arthritis. *Clin Exp Rheumatol*, 2003; 21: 395-398
- (13) LAM L.A., LOWDER C.Y., BAERVELDT G., SMITH S.D., TRABOULSI E.I. – Surgical management of cataracts in children with juvenile rheumatoid arthritis-associated uveitis. *Am J Ophthalmol*, 2003; 135: 772-778
- (14) LEAK A.M., ANSELL B.M., BURMAN S.J. – Antinuclear antibody studies in juvenile chronic arthritis. *Arch Dis Child*, 1986; 61: 168-172
- (15) OHM J. – Bandförmige Hornhauttrübung bei einem neunjährigen Mädchen und ihre Behandlung mit subconjunctivalen Jodkaliumeinspritzungen. *Klin Monatsbl Augenheilkd*, 1910; 48: 243-246
- (16) OREN B., SEHGAL A., SIMON J.W., LEE J., BLOCKER R.J., BIGLAN A.W., ZOBAL-RATNER J. – The prevalence of uveitis in juvenile rheumatoid arthritis. *J AAPOS*, 2001; 5: 2-4
- (17) PETTY R.E., SOUTHWOOD T.R., BAUM J. – Revision of the proposed classification criteria for juvenile idiopathic arthritis. *J Rheumatol*, 1998; 25, 1991-1994
- (18) STILL G.F. – On a form of chronic joint disease in children. *Am J Dis Child*, 1978; 132: 195-200
- (19) WOLF M.D., LICHTER P.R., RAGSDALE C.G. – Prognostic factors in the uveitis of juvenile rheumatoid arthritis. *Ophthalmology*, 1987; 10: 1242-1248

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