Epidemiology of uveitis in children over a 10-year period

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Abstract

Objectives

The aim of the present study is to investigate the demographics, aetiologies, complications, treatments and visual outcomes in paediatric uveitis patients in the French-speaking part of Switzerland.

Methods

Chart review of all patients diagnosed with uveitis before the age of 16 years, presenting to two tertiary referral centres (uveitis and paediatric rheumatology clinics) in Lausanne, Switzerland, between 2000 and 2009.

Results

Seventy-nine children (37 girls) were identified, 62 living in Switzerland, 15 in Europe and 2 in North Africa. Median age at first symptoms was 9.0 years (range 1.5–15.8 years), with a median follow-up time of 1.8 years (0–8 years). Both eyes were involved in 51 patients (64.6%). The course was acute in 30.4%, chronic in 60.8% and recurrent in 8.9%. Anterior uveitis occurred in 39.2%, intermediate in 32.9%, posterior in 22.8% and panuveitis in 5.1%. The three main diagnoses were idiopathic uveitis (34.2%), JIA-related uveitis (22.8%) and toxoplasmic retinochoroiditis (15.2%). During the last follow-up visit, the visual acuity (VA) was ≥8/10 in 72% of all eyes with a measurable VA. Cataract (8%), ocular hypertension/glaucoma (8%) and macular fibrosis (4%) were the three most common severe complications. Systemic steroids were given to 56% and biological agents to 24% of patients with inflammatory uveitis.

Conclusion

Uveitis in children can be a devastating disease. A strict classification of aetiologies and a tight collaboration between paediatric rheumatologists and ophthalmologists are important to ensure early control of ocular inflammation and improve long-term visual prognosis.

Key words

uveitis, epidemiology, children, visual outcome

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Introduction

With an incidence of about 4.9/100.000 in Europe (1), paediatric uveitis is a rare but devastating disease, leading to unilateral legal blindness in 17% of patients (2). Besides, being a diagnostic challenge, it remains a therapeutic one. Biological agents have recently been introduced for the treatment of cases refractory to systemic steroids and immunosuppressants. Despite serious potential side effects, biological agents are considered to be safe for use in children (3, 4), but this new trend in uveitis therapy has not yet been subjected to epidemiological evaluation.

Few studies have been published on the epidemiology of uveitis in children this last decade in Europe (1, 2, 5). Paroli *et al*. observed changes in the visual prognosis over time (5), emphasising the importance of updated data. Two Swiss studies observed a high complications rate in JIA-related uveitis, especially in preschool children with positive ANA antibodies (6, 7). One of the two showed a good visual outcome despite the complications (6).

The aim of this study is to evaluate the demographics, aetiologies, complications, treatments and visual prognosis of childhood uveitis in French-speaking Switzerland.

Materials and methods

Medical records of all patients under the age of 16 years, presenting for the first time with uveitis between January 2000 and December 2009 to the uveitis clinics of the Jules-Gonin Eye Hospital and the paediatric rheumatology clinic of the Lausanne University Hospital, were retrospectively and systematically reviewed. These two hospitals are the tertiary referral centres for a population of about 220.000 children under the age of 16.

Seventy-nine children were identified and classified according to the SUN classification of the International Uveitis Study Group, based on the location of the inflammation (8). The diagnosis of juvenile idiopathic arthritis (JIA) was established following the ILAR classification (9). Other diagnoses were based on previously published criteria and the opinion of experts.

General data retrieved included date of birth, sex, place of residence, ages at first symptoms and at first visit to the referral centre, follow-up time and systemic disease association. Uveitis data considered were anatomical location, duration, course, laterality, aetiology, complications, ocular surgery and treatments. All patients underwent a complete ophthalmic examination, including visual acuity (VA), intraocular pressure, slit-lamp biomicroscopy and fundus examination. We retrieved these data for the first and the last visit, as well as systemic symptoms and relevant laboratory tests (ANA, HLA-B27, rheumatoid factor, ANCA, HLA-B51, angiotensin converting enzyme). Systemic diseases were diagnosed by a paediatric rheumatologist. Aetiologies were divided into two groups: infectious and inflammatory (associated with a systemic or specific ocular disease, or idiopathic).

Our database was used for descriptive statistics (percentages, medians, standard deviation). Approval for the study was obtained from the Ethics Committee of the University Hospital in Lausanne.

Results

Over a ten-year period, 79 children, diagnosed with uveitis before their sixteenth birthday, were seen for the first time in our referral centres (Table I). Sixty-two patients were living in Switzerland, whereas 15 came for treatment from other European countries (Italy, France, Macedonia, Portugal, Romania) and 2 from Algeria. The male-female ratio was 1.14:1. The inflammation was often bilateral (51/79 patients), especially in intermediate uveitis (23/26). The median follow-up was 1.8 years (range: 0–8 years). Anterior uveitis cases were much younger at disease-onset compared to all patients (median age 4.6 *versus* 9 years). They were also more common (39.2%) than other locations. Among all types of uveitis, the course was more often chronic (48 patients) than acute (24) or recurrent (7).

The different aetiologies were classified into two groups, namely inflammatory (69.6%) and infectious (30.4%). The 3 most frequent diagnoses were

Table I. Demographic and medical characteristics at baseline examination at the referral centre for 79 children with uveitis.

Characteristics (n: number of patients)	All uveitis (n=79) (100%)	Anterior uveitis (n=31) (39.2%)	Intermediate uveitis (n=26) (32.9%)	Posterior uveitis (n=18) (22.8%)	Panuveitis (n=4) (5.1%)
Gender					
Male/female	42/37	14/17	18/8	8/10	3/1
Age (year) at first symptoms					
Median (range)	9.0 (1.5–15.8)	4.6 (2.1–15.8)	9.3 (1.5–15.3)	10.0 (3.2–15.6)	11.9 (4.9–15.1)
Course n (%)					
Acute	24 (30.4)	8 (25.8)	2 (7.7)	12 (66.7)	2 (50)
Chronic	48 (60.8)	20 (64.5)	22 (84.6)	4 (22.2)	2 (50)
Recurrent	7 (8.9)	3 (9.7)	2 (7.7)	2 (11.1)	
Ocular involvement n (%)					
Bilateral	51 (64.6)	16 (51.6)	23 (88.5)	10 (55.6)	2 (50)

Table II. Aetiologies of uveitis.

Aetiologies (n: number of patients)	All uveitis (n=79)	Anterior uveitis (n=31)	Intermediate uveitis (n=26)	Posterior uveitis (n=18)	Panuveitis (n=4)
Inflammatory uveitis					
Idiopathic	27 (34.2)	6 (19.4)	20 (76.9)	-	1 (25)
JIA	18 (22.8)	16 (51.6)	1 (3.8)	1 (5.6)	-
Behçet	3 (3.8)	1 (3.2)	-	1 (5.6)	1 (25)
Sarcoidosis	2 (2.5)	2 (6.5)	-	-	-
Post-streptococcal	2 (2.5)	1 (3.2)	-	-	1 (25)
Scleroderma	1 (1.3)	1 (3.2)	-	-	-
Lupus	1 (1.3)	-	-	1 (5.6)	-
Sympathetic ophthalmia	1 (1.3)	-	-	-	1 (25)
Infectious uveitis					
Toxoplasmosis	12 (15.2)	-	-	12 (66.7)	-
Herpes	4 (5.1)	3 (9.7)	-	1 (5.6)	-
Cat scratch disease	3 (3.8)	-	3 (11.5)	-	-
Lyme	2 (2.5)	-	2 (7.7)	-	-
Chickenpox	2 (2.5)	1 (3.2)	-	1 (5.6)	-
Toxocara canis	1 (1.3)	-	-	1 (5.6)	-

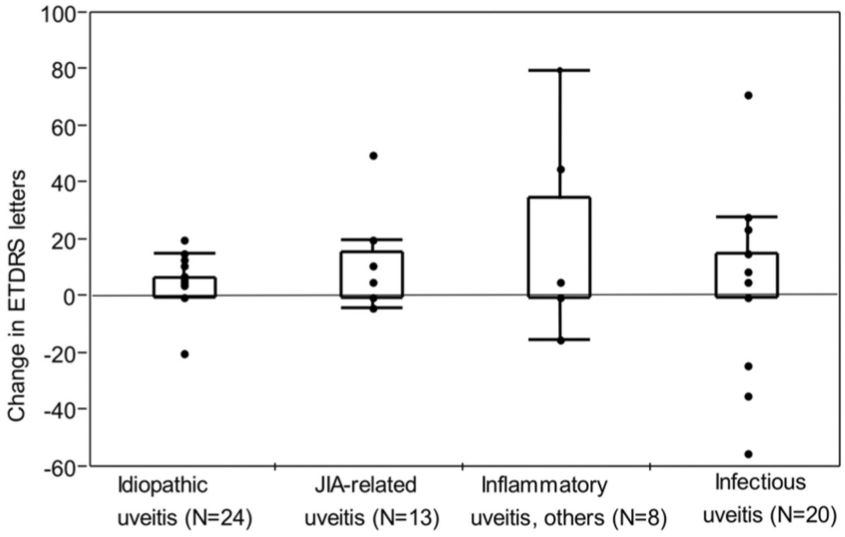

Fig. 1. Change in VA during the follow-up, in 65 eyes with a measurable VA at first and last visit. N: number of eyes. Boxes represent data between the 25th and 75th quartiles, and whiskers the distance from the boxes to the outermost points within the computed range (upper quartile +1.5*[interquartile range]; lower quartile -1.5*[interquartile range]). Many eyes showed the same change in VA during the follow-up, resulting in points superimposed on each other, most importantly those without change (idiopathic: 11, JIA-related: 6, inflammatory others: 4, infectious: 7).

idiopathic uveitis (27 patients), JIA-related uveitis (18 patients) and toxoplasmic retinochoroiditis (12 patients) (Table II). Most cases of JIA-related uveitis were anterior (16/18) and all cases of toxoplasmic uveitis were posterior. Idiopathic uveitis cases were mainly intermediate (20/27).

At first visit, 58/102 eyes (57%) with a measurable VA had VA≥8/10. At last visit, the percentage with VA≥8/10 was higher (72%, 53/74 eyes). Twelve eyes

Table III. Systemic treatments used among patients with inflammatory diseases.

Systemic treatments (n: number of patients)	All patients with inflammatory uveitis (n=55)	Idiopathic uveitis (n=27)	JIA uveitis (n=18)	Inflammatory uveitis, others (n=10)
Steroids n (%)	31 (56)	14 (52)	11 (61)	6 (60)
Methotrexate	16 (29)	5 (19)	9 (50)	2 (20)
Azathioprine	10 (18)	5 (19)	2 (11)	3 (30)
Cyclosporine	4 (7)	1 (4)	–	3 (30)
Cyclophosphamide	2 (4)	1 (4)	–	1 (10)
Biologic drugs	13 (24)	2 (7)	10 (56)	1 (10)
Enbrel (Etanercept)	9 (16)	1 (4)	8 (44)	–
Humira (Adalimumab)	5 (9)	1 (4)	4 (22)	–
Remicade (Infliximab)	3 (5)	–	3 (17)	–
Rituxan (Rituximab)	1 (2)	–	–	1 (10)

Often more than one systemic drug/patient.

Table IV. Main complications encountered in the present and other studies.

Complications	By etiology				Compared to other studies					
	Idiopathic uveitis (N=48)	JIA-related (N=29)	Inflammatory uveitis, others (N=17)	Infectious uveitis (N=36)	Present study, 2012 (N=130)	Hamade, 2009 (14) (N=300)	Paroli, 2009 (5) (N=241)	Kump, 2005 (11) (N=469)	Rosenberg, 2004 (13) (n = 1 4 8)	de Boer 2003 (2)
~~(n=123)~~										
Posterior synechiae N/n (%)	8 (17)	13 (45)	3 (18)	–	24 (18)	129 (43)	70 (29)	164 (35)	81 (55)	–
Maculopathy (fibrosis, oedema)	10 (21)	-	1 (6)	8 (22)	19 (15)	24 (8)	35 (15)	1111 (24)	72 (49)	29 (24)
Ocular hypertension/glaucoma	4 (8)	6 (21)	–	1 (3)	11 (8)	81 (27)	31 (13)	71 (15)	49 (33)	23 (19)
Cataract	2 (4)	8 (28)	–	–	10 (8)	78 (26)	38 (16)	188 (40)	77 (52)	43 (35)
Papillitis/papilloedema	3 (6)	4 (14)	3 (18)	–	10 (8)	49 (16)	37 (15)	38 (8)	43 (29)	36 (29)
Band keratopathy	–	5 (17)	–	–	5 (4)	53 (18)	57 (24)	107 (23)	52 (35)	15 (12)
Epiretinal/neovascular membranes	1 (2)	–	–	3 (8)	4 (3)	16 (5)	38 (16)	52 (11)	15 (10)	–
Retinal detachement	1 (2)	–	–	2 (6)	3 (2)	10 (3)	3 (1)	14 (3)	28 (19)	3 (2)
Vitrous haemorrage	1 (2)	1 (3)	–	–	2 (2)	68 (23)	–	5 (1)	13 (9)	2 (2)
One or more complications	21 (44)	18 (62)	4 (24)	13 (36)	–	–	–	–	–	–

n: number of patients; N: number of eyes.
More than one complication/eye possible.

(12%) had a VA ≤1/10 at first visit, but only 8 (6%) at last visit. Figure 1 shows the changes in VA during the follow-up, in ETDRS letters, according to 4 main categories. Among 65 eyes, with measurable first and last VA, 31 improved their vision, 28 remained stable and only 6 got worse. Patients with a loss of vision during the follow-up were as follows (loss in ETDRS letters is shown followed by the loss in decimal notation – the two are not proportional): one cat scratch disease (-55, 9/10), one toxoplasmic retinochoroiditis (-35, 2.5/10), one chickenpox (-24; 2/10), one idiopathic (-20, 6/10), one Behçet (-15, 3/10) and one JIA-related (-4, 1/10). The ETDRS score gives a linear progression of VA and can easily be translated to decimal notations (10).

Thirty-three out of 55 patients with inflammatory uveitis (60%) received systemic treatment (Table III): 56% systemic steroids, 58% DMARDs and 24% biological agents. Eight patients with infectious uveitis were treated simultaneously with systemic steroids and anti-infectious agents. Etanercept was the biological agent most commonly prescribed. Among 13 patients treated with biological agents, 11 received methotrexate. JIA-related uveitis cases received more systemic treatments than other inflammatory cases, accounting for 77% of all patients treated with biological agents and 56% of those with methotrexate.

The main complications observed in our study are listed in Table IV. JIA-related uveitis was the diagnosis with the highest complication rate both at diagnosis and later (18/29 eyes). It included most of the cataracts (8/10) and ocular hypertension/glaucoma (6/10) as well as all the band keratopathies (5/10). The higher complication rate in JIA-related uveitis is partly due to the intensity, chronicity and type of inflammation, as well as sometimes a lack of symptoms leading to a greater delay before treatment. The use of etanercept alone or before switching to adalimumab or infliximab was not linked to more complications. Among maculopathies (19/130 eyes), macular oedema (reversible process) was more common (14/19) and mainly seen in idiopathic uveitis (10/14), whereas macular fibrosis (irreversible) was less common (5/19; of which 4 toxoplasmic retinochoroiditis). Epidemiological studies mentioned in Table IV showed a higher

percentage of cataracts and ocular hypertension/glaucoma than ours.

Discussion

Our cohort was comparable in demographics and aetiologies to previously published European and North American studies (5, 11, 12, 13). Our diagnoses were based on international criteria confirmed by an ophthalmologist and a rheumatologist. Our patients received more biological agents, and had less complications and a better visual outcome.

The median age at first symptoms (9.0 years) and median follow-up (1.8 years) were similar to most studies (5, 11, 12, 14). Anterior uveitis constituted the largest group (39.2%) in our population, as in most publications. Toxoplasmic retinochoroiditis (15.2%) was generally more frequent in our cohort (11-13), except for the Italian study (5). The VA of our patients was globally better at last (72% ≥8/10) than first visit (57% ≥8/10), with only 6 patients experiencing a decrease in VA in one eye. Infectious uveitis presented proportionally more eyes with a decrease in VA during the follow-up. The mean gain in visual acuity was 6.6±19.9 letters, showing a positive tendency but a large range of values. The percentage of VA at last visit ≥5/10 in our patients (77.7% of eyes) was similar to that found by Kump *et al*. (77%) (11), but higher than in 2 other studies (64 and 61,4%) (13, 14). The same three studies had approximately 3 times more eyes with a VA of ≤1/10 at last visit. Paroli *et al*. observed visual outcomes very similar to ours (5).

We have compared the use of systemic treatments in our population compared to previously published cohorts. Rosenberg *et al*. (13) described 48% of their patients with inflammatory uveitis treated with systemic treatments and 11% with etanercept. De Boer *et al*. (2) had 46% of all patients with systemic treatments, 32% with systemic steroids and one with an anti-TNF-α (initiated for the rheumatologic disease). In both studies, fewer patients were treated with systemic and/or biological drugs than in our population. The higher proportion of our patients with JIA-related uveitis receiving systemic treatments (61% steroids, 56% biological agents) may be due to the double use of these drugs for rheumatologic and ophthalmic purposes, and to the more aggressive nature of JIA-related uveitis, requiring more potent treatments. Infliximab and adalimumab have been described as more effective than etanercept in paediatric uveitis (3, 13, 14). Etanercept is currently the only TNF-alpha blocker approved by the Swiss health authorities for treatment of juvenile arthritis, and the inferior effectiveness of etanercept in uveitis became known only a few years ago, explaining its more frequent use. Off-label agents are now used more commonly. In Lausanne, the collaboration between the uveitis and the paediatric rheumatology clinics enables the use of strict ophthalmic and rheumatologic definitions, discussions of cases, and prompt and potent systemic treatments for ocular inflammation.

Fewer complications were seen in our study compared to those listed in Table IV. Rosenberg *et al*. had a longer follow-up, explaining partly their higher rate of complications (13). In comparison with previous series, our study shows a higher use of systemic treatments together with less complications and better visual outcome. These results emphasise the importance of early aggressive treatment for better long-term visual prognosis.

Limitations of our study include the size of the cohort and its retrospective design. Both referral hospitals being tertiary centres, more complicated cases have been seen (children referred locally or from abroad), resulting in biased data. Prospective studies are needed to confirm our observations.

Uveitis in children can be a devastating disease. A strict classification of aetiologies and a tight collaboration between paediatric rheumatologists and ophthalmologists are important to ensure early control of ocular inflammation and improve long-term visual prognosis.

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