Occurrence and management of ocular hypertension and secondary glaucoma in juvenile idiopathic arthritis-associated uveitis: An observational series of 104 patients

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Aims: To describe the development and management of ocular hypertension (OHT) and secondary glaucoma (SG) in patients with juvenile idiopathic arthritis (JIA)-associated uveitis.

Patients and methods: A series of 104 patients with newly diagnosed JIA and associated uveitis was collected in 1989–1996. A re-evaluation was made after mean 9.7 years (range 0.8–15.6 years) follow-up. OHT was diagnosed if intraocular pressure (IOP) had been ≥22 mmHg for longer than 3 months or when a single IOP was ≥30 mmHg despite normal visual field and optic disc. SG was diagnosed in a patient who had optic disc changes and/or visual field defects compatible with glaucoma.

Results: OHT or SG developed in 14 patients (14%, 22 eyes). IOP was under control (<22 mmHg) in 2 patients without treatment and in 3 patients with medication. Filtering surgery was performed in 9 patients, 5 of them needed additional glaucoma medication. The binocular visual acuity was 0.5 or better in all patients; in five eyes vision was less than 0.5, but no eye blinded.

Conclusion: OHT or SG in JIA patients with uveitis is a diagnostic and therapeutic challenge, but if the medical and surgical treatment is timed correctly, the sight can be saved in most patients.

Keywords: JIA, uveitis, glaucoma

Introduction

In juvenile idiopathic arthritis (JIA) chronic insidious uveitis develops in 20% of patients. The prevalence of glaucoma in JIA-associated uveitis ranges from 14%–27% (Wolf et al 1987; Kanski 1990; Kotaniemi et al 2001, 2003).

Secondary glaucoma (SG) is one of the most common causes of blindness in children and young adults with chronic uveitis (Merayo-Lloves et al 1999; Foster et al 2000; Sijssens et al 2006). Uveitic glaucoma may be a diagnostic problem. The elevation of intraocular pressure (IOP) may be oscillating, transient and innocuous, or persistent and severely damaging. On the other hand, exacerbation of uveitis may cause shutdown of the ciliary body and lead to hypotony, thus masking the underlying glaucoma. Multiple mechanisms may be involved in the elevation of IOP; closure of the anterior chamber angle with or without pupil block, and mechanism of open-angle glaucoma. Additionally, a patient may be a steroid-responder (Melamed et al 2000; Allingham et al 2005).

Topical steroids and systemic immunosuppressive drugs are the mainstay of uveitis treatment together with the best possible management of the underlying disease. Despite

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many kinds of glaucoma medications, a conservative treatment of SG is often inadequate (Melamed et al 2000; Sung and Barton 2004; Allingham et al 2005). In cases of a pupillary block, laser iridotomy is performed. Trabeculectomy with or without adjunctive antimetabolites may be required in patients with a permanent trabecular dysfunction. Goniotomy, viscocanalostomy or deep sclerectomy have been performed in some refractory cases. Cycloablation with the diode laser, free running YAG laser or cycloprobe may be necessary in some cases of treatment-resistant glaucoma (Raivio et al 2001; Ceballos et al 2002; Freedman et al 2002; Quintyn et al 2003; Auer et al 2004; Ho et al 2004; Heinz et al 2006). However, in many children with chronic uveitis artificial filtering shunts (such as Molteno or Ahmed) work best (Molteno et al 1984; Välimäki et al 1997; Ozdal et al 2005).

We describe the occurrence and management of ocular hypertension (OHT) and SG in series of 104 children with JIA-associated uveitis.

Patients and methods

An observational series of 104 JIA patients with uveitis is described. The patients were drawn out of 426 children with newly diagnosed JIA during 1989–1996 at the Rheumatism Foundation Hospital, Heinola, Finland (Kotaniemi et al 2001).The Rheumatism Foundation Hospital is a tertiary center for patients with juvenile arthritis from the whole country, but also serves as a secondary center for those living nearby. A pediatric rheumatologist had confirmed the diagnosis of JIA for every patient according to the ILAR criteria (Petty and Southwood 1998).

The main characteristics of the patients are shown in Table 1. At the re-evaluation point, the mean age of the patients was 14.5 years (range 4.1–24.4 years), the mean follow-up time from the diagnosis of JIA was 9.7 years (range 0.8–15.6 years) and the mean duration of uveitis was 6.9 years (range 0.1–14.9 years).

The ophthalmic examination included best corrected visual acuity, careful biomicroscopy of the eyes and examination of the fundus of the eye with 90 dioptre lens. The diagnosis of uveitis was made according to the IUSG recommendations (Bloch-Michel and Nussenblatt 1987). The IOP was measured by applanation tonometry, whenever possible. OHT was diagnosed in patients in whom the IOP had been ≥22 mmHg for longer than 3 months, or a single IOP was higher than 30 mmHg and glaucoma treatment had been initiated despite normal visual field (when an examination had been possible) and optic disc. SG was diagnosed if a glaucomatous cupping of the optic disc was seen or a glaucomatous visual field was detected and IOP was higher than 21 mmHg (Walton 1994; Merayo-Lloves et al 1999). Visual field examinations were not possible to all our patients because of young age and therefore the evaluation of the visual fields was not reasonable.

Glaucoma surgery was indicated, when IOP had been constantly higher than 21 mmHg for longer than 3 months despite 2 to 4 different glaucoma drugs. The decision of implantation of the filtering device was made after discussion with 2 to 3 specialists dealing with complicating uveitis. Trabeculectomy with or without mitomycin-C and deep sclerectomy were the method of surgery in a few

Table 1 Comparison of the characteristics of all patients with JIA-associated uveitis with those complicated with elevated IOP

	All patients with uveitis	Patients with elevated IOP	p value
Number of patients	**n 104**	**n 14**	
Gender M/F	35/69	2/12	0.13
Mean age at onset of JIA, years (SD)	4.8 (3.8)	3.7 (3.5)	0.25
Mean age at onset of uveitis, years (SD)	5.9 (3.6)	3.9 (3.2)	0.026
Mean age at onset of glaucoma, years (SD)		9.8 (3.2)	
Type of JIA			0.83
-Oligoarthritis (%)	76 (66)	10 (71)	
-RF negative polyarthritis (%)	25 (24)	4 (29)	
-RF positive polyarthritis (%)	1 (1)	0	
-Systemic onset arthritis (%)	1 (1)	0	
-Enthesitis related arthritis (%)	0	0	
-Psoriatic arthritis (%)	1 (1)	0	
ANA+ (%)	69 (66)	11 (79)	0.37
HLA B27+ (%)	20/74 (27)	2/9 (22)	0.81

Abbreviations: JIA, juvenile idiopathic arthritis; SD, standard deviation; RF, rheumatoid factor; ANA, antinuclear antibodies; HLA, human leukocyte antigen; IOP, intraocular pressure.

cases. In the most refractory cases cyclodestruction was made (Molteno et al 1984; Välimäki et al 1997; Raivio et al 2001; Quintyn et al 2003; Ho et al 2004; Sung et Barton 2004; Heinz et al 2006).

Results

Fifty-four out of the 104 patients with JIA-associated uveitis (52%) had ongoing insidious uveitis after the mean follow-up of 9.7 years. OHT or SG had developed in 14/104 patients (13.5%, 22 eyes) in mean 5.8 years (range 0–11.3) after the uveitis had been diagnosed. All of them still had active uveitis. The patients who developed OHT or SG were younger at the onset of uveitis than those who had not had elevated IOP ($p = 0.026$) (Table 1). The use of the disease modifying antirheumatic drugs of the glaucoma/OHT patients at last visit is shown in Table 2.

Table 3 shows the details of the ocular status and the management of the patients with elevated IOP. Elevated IOP had been detected in both eyes of 8 patients and in either eye in 6 patients (Table 3, patients 2, 6, 7, 11, 13 and 14).

In 3 eyes of 2 patients a glaucomatous excavation of the optic nerve head and respective visual field defects were seen and SG was diagnosed. Twelve patients had OHT and glaucoma treatment had been initiated because of their continuously high IOP values (>21 mmHg). In all the patients the OHT/SG was open angle type and no one had pupillary block. Because of the young age of the patients, the gonioscopy was rarely possible to perform.

In two patients the elevated IOP had normalized with watchful waiting during the follow up and no treatment was needed. In 3 patients IOP was controlled with medical treatment. Filtering surgery was performed in 9 patients because of constantly high IOP (>21 mmHg) despite maximal medical treatment: Molteno filtering device in 7 (in one patient twice), trabeculectomy without Mitomycin in 1 patient and with Mitomycin in both eyes in 1 patient. In spite of that, glaucoma medication was needed in 5 of the 9 patients after surgery. None of them was a corticosteroid responder.

In the re-evaluation examination IOP was assessed to be under control (<22 mmHg) in all but 3 eyes (Table 3). Binocular visual acuity was at least 0.5 in all patients, in five eyes visual acuity ended up between 0.1 and 0.4. Impairment of the visual acuity was due to cystoid macular edema (2 eyes), retinal detachment (1 eye) and a secondary opacification of posterior capsule after IOL implantation (1 eye). In one eye (patient 4, Table 3) a corneal transplantation was performed after implantation of the second Molteno and the filtering devices were removed; the visual acuity was 0.2.

Table 2 Disease modifying antirheumatic drugs of the glaucoma/ocular hypertension patients alone or in combination at the last visit

Antirheumatic drug	Number of patients on the drug
Immunosuppressive/immunomodulatory drugs	
-Methotrexate	8
-Cyclosporin A	6
-Azathioprine	2
-Leflunomide	3
-Prednisolon	10
Biologic drugs	
-Etanercept	4
-Infliximab	4
-Adalimumab	2
Other drugs	
-Hydroxychlorokine	3
-Aurathiomalate	1

Discussion

Uveitic glaucoma in childhood is a diagnostic and therapeutic challenge. We have followed our series of 104 patients from the very beginning of arthritis and uveitis for nearly 10 years, on the average. Initially, we did not specifically look after the development of elevated IOP and that is why the data are in some degree deficient. On the other hand, frequently the ophthalmologic examination of small children is challenging and examination of visual fields or chamber angle is not possible. In our series of patients the diagnosis of OHT or SG was mostly based on constantly high IOP values and the treatment had to be initiated before the SG criteria were fulfilled.

Recently, Sijssens and colleagues (2006) reported that 38% of their 24 patients with JIA-associated uveitis had developed secondary glaucoma after 5 years. The interval between the diagnosis of uveitis and elevation of ocular pressure was only 1 year. Neri and colleagues (2004) detected glaucoma in 11% of their uveitis patients after 5 years follow-up. In our observational series 26% (14/54) of those with ongoing uveitis developed OHT/SG. However, the median length of time from uveitis to glaucoma in our series was markedly longer, 5.8 years. The majority of the children in our series were seen by the same ophthalmologists every 1–3 months from the very beginning of uveitis and thus their uveitis was diagnosed at an early stage. The patients were carefully monitored and the treatment of uveitis and arthritis was

Table 3 Management of ocular hypertension/secondary glaucoma in 14 patients with juvenile idiopathic arthritis associated uveitis. Data of the ocular status at the re-evaluation time point.

Patient number, Gender	IOP mmHg R/L	Optic disc unaffected R/L	Cataract and management R/L	Visual acuity R/L	Active Uveitis	Follow-up*, years R/L	Surgical treatment R/L	Medical reatment R/L
1. F	18/11	Yes/Yes	Aphakia/Aphakia	1.0/0.8	+/+	10	Molteno/Molteno	–/–
2. F	8/12	Yes/Yes	Aphakia/–	0.5/1.0	+/–	14.9	Molteno/No	–/–
3. F	17/21	Yes/No	IOL/IOL	0.9/0.1	+/+	11.9	Molteno/No	+/+
4. F	18/17	No/No	IOL/Cataract	0.1/0.5	+/+	10.8	Moltenox2, cycloablatio/Molteno	+/+
5. F	26/19	Yes/Yes	IOL/IOL	0.2/0.6	+/+	9.4	Molteno/No	+/+
6. F	28/14	Yes/Yes	Cataract/Catarat	0.5/0.5	+/+	6.2	No/No	+/–
7. F	9/12	Yes/Yes	IOL/–	1.0/1.0	+/–	13.3	Sclerectomy/No	–/–
8. F	21/13	Yes/Yes	IOL/IOL	0.7/0.2	+/+	12.8	Molteno/Molteno	–/+
9. F	21/21	Yes/Yes	Cataract/Cataract	1.0/0.9	+/+	14.7	No/No	+/+
10. F	13/17	Yes/Yes	Cataract/Cataract	1.0/1.0	+/+	14.4	No/No	–/–
11. F	7/12	Yes/Yes	Cataract/–	0.8/1.0	+/–	13.9	Trabeculectomy/No	–/–
12. M	27/9	Yes/Yes	Cataract/–	0.8/1.0	+/+	12.2	Trbeculectomy+MM /Trabeculectomy+MM	+/+
13. F	13/13	Yes/Yes	IOL/IOL	0.9/0.1	–/+	9.3	No/Molteno	–/–
14. M	13/13	Yes/Yes	IOL/IOL	0.5/1.0	+/+	13.5	No/no	–/–

Abbreviations: M, male; F, female; R, right eye; L, left eye; IOP, intraocular pressure; IOL, intraocular lens; *, follow up from the diagnosis of arthritis; Molteno, Molteno drainage device; MM, Mitomycin.

constantly changed according to the activity of both arthritis and uveitis. The elevated IOP was frequently detected before glaucomatous changes had developed in the eye.

According to Välimäki and colleagues (1997), the best treatment of uncontrolled secondary glaucoma in JIA- associated uveitis is implantation of the molteno filtering device, because the failure rate after trabeculectomy in JIA children was known to be high and the use of mitomycin in childhood was inconvenient. In our series the control of IOP was achieved by Molteno filtering device in 7 of the 14 patients. However, 5 of the patients who had been operated on, needed additional glaucoma medication. In one case, after the Molteno tube had been reimplantated, the cornea decompensated leading to removal of the filtering devices and to corneal transplantation. The effect of Molteno tube may be decreased by postoperative fibrosis causing a need of glaucoma medication.

In a large cohort of uveitis patients reported by Merayo-Lloves and colleagues (1999), 16% of the patients with JIA-associated uveitis ended up with chronic secondary glaucoma during the 10-year follow-up. Their choice of treatment was Mitomycin-C trabeculectomy or insertion of a drainage implant in patients with refractory glaucoma. Inadequate control of glaucoma was found in 9% of their JIA patients with uveitis despite aggressive treatment of uveitis and SG. The frequency of SG in the series of Merayo-Lloves and colleagues corresponds to that of ours: 14% of patients with JIA-associated uveitis developed OHT or SG. Also a great majority of our patients underwent filtering surgery.

In our series all the 14 patients with elevated IOP had binocular visual acuity >0.5, whereas 42% of the uveitis patients of Merayo-Lloves and 64% of the uveitis cases of Neri had visual acuity >0.5 after 5 years follow-up. The difference may be due to different patient series.Even if techniques of the modern glaucoma surgery have improved the prognosis of this severe disease, we still have treatment resistant cases. We agree with Merayo-Lloves and colleagues (1999) that by early recognition of uveitis and active treatment of uveitis and underlying arthritis, development of secondary glaucoma can be diminished. In this observational series of JIA patients with associated uveitis, drainage shunt implantation was frequently the choice of treatment of elevated intraocular pressure.

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