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
many kinds of glaucoma medications, a conservative treat-
ment 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 diag-
nosis 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 exami-
nation of the fundus of the eye with 90 dioptre lens. The
diagnosis of uveitis was made according to the IUSG rec-
ommendations (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 examina-
tion 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 dis-
cussion 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 |
|---------------------------------------------------------------|
| Number of patients | All patients with uveitis | Patients with elevated IOP | p value |
|---------------------|---------------------------|---------------------------|---------|
| Gender M/F | n 104 | n 14 |
| 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.

**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
of glaucoma medication. There may be decreased by postoperative fibrosis causing a need for additional glaucoma surgery. In one case, the Molteno tube had to be removed 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, the Molteno tube had been reimplanted, 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.

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, the Molteno tube had been reimplanted, 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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**References**

Allingham RR, Damji KF, Freedman S, et al. 2005. Shields’ textbook of glaucoma. 5th ed. Philadelphia: Lippincott Williams and Wilkins. vol 3:p 626–43.

Auer C, Mermoud A, Herbort CP. 2004. Deep sclerectomy for the management of uncontrolled uveitic glaucoma: preliminary data. *Klin Monatsbl Augenheilkd*, 221:339–42.

### Table 3 Management of ocular hypertension/secondary glaucoma in 14 patients with juvenile idiopathic arthritis associated uveitis.

| 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 treatment 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                   | IOI/IOI                    | 0.9/0.1           | ++             | 11.9                 | Molteno/No              | +/-                  |
| 4. F                   | 18/17        | No/No                    | IOI/Cataract               | 0.1/0.5           | ++             | 10.8                 | Molteno x2              | +/-                  |
| 5. F                   | 26/19        | Yes/Yes                  | IOI/IOI                    | 0.2/0.6           | ++             | 9.4                  | Molteno/No              | +/-                  |
| 6. F                   | 28/14        | Yes/Yes                  | Cataract/Cataract          | 0.5/0.5           | +/-            | 6.2                  | No/No                  | +/-                  |
| 7. F                   | 9/12         | Yes/Yes                  | IOI/–                      | 1.0/1.0           | ++             | 13.3                 | Sclerectomy/No          | –/–                  |
| 8. F                   | 21/13        | Yes/Yes                  | IOI/IOI                    | 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                 | Molteno/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                 | Trabeculectomy+MM       | +/+                  |
| 13. F                  | 13/13        | Yes/Yes                  | IOI/IOI                    | 0.9/0.1           | –/+            | 9.3                  | No/Molteno              | –/–                  |
| 14. M                  | 13/13        | Yes/Yes                  | IOI/IOI                    | 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.
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Bloch-Michel E, Nussenblatt RB. 1987. International Uveitis Study Group recommendations for the evaluation of the intraocular inflammatory disease. *Am J Ophthalmol*, 103:234–5.

Ceballos EM, Beck AD, Lynn MJ. 2002. Trabeculectomy with antiproliferative agents in uveitic glaucoma. *J Glaucoma*, 11:189–96.

Freedman SF, Rodriguez-Rosa RE, Rojas MC, et al. 2002. Goniotomy for glaucoma secondary to childhood uveitis. *Am J Ophthalmol*, 133:617–21.

Foster CS, Havelková K, Baltatzis S, et al. 2000. Secondary glaucoma in patients with juvenile rheumatoid arthritis-associated iridocyclitis. *Acta Ophthalmol Scand*, 78:576–9.

Heinz C, Koch JM, Heiligenhaus A. 2006. Transscleral diode laser cyclophocoagulation as primary surgical treatment for secondary glaucoma in juvenile idiopathic arthritis: high failure rate after short term follow up. *Br J Ophthalmol*, 90:737–40.

Ho CL, Wong EY, Walton DS. 2004. Goniosurgery for glaucoma complicating chronic childhood uveitis. *Arch Ophthalmol*, 122:838–44.

Kanski JJ. 1990. Juvenile arthritis and uveitis. *Surv Ophthalmol*, 34:253–67.

Kotaniemi K, Kautiainen H, Karma A, et al. 2001. Occurrence of uveitis in recently diagnosed juvenile chronic arthritis. A prospective study. *Ophthalmology*, 108:2071–5.

Kotaniemi K, Savolainen A, Karma A, et al. 2003. Recent advances in uveitis of juvenile idiopathic arthritis. Major review. *Surv Ophthalmol*, 48:489–502.

Melamed S, Askennazi I. 2000. Juvenile-onset open-angle glaucoma. In Albert DM, Jakobiec FA, eds. Principles and Practice of Ophthalmology. Vol 4. 2nd ed. Philadelphia: WB Saunders. p 2678–82.

Merayo-Lloves J, Power JW, Rodriguez A, et al. 1999. Secondary glaucoma in patients with uveitis. *Ophthalmologica*, 213:300–4.

Molteno AC, Ancker E, Van Biljon G. 1984. Surgical technique for advanced juvenile glaucoma. *Arch Ophthalmol*, 102:51–7.

Neri P, Azuara-Blanco A, Forrester JV. 2004. Incidence of glaucoma in patients with uveitis. *J Glaucoma*, 13:461–5.

Ozctal PC, Vianna RN, Deschenes J. 2005. Ahmed Valve implantation in glaucoma secondary to chronic uveitis. *Eye*, 11[epub ahead of print].

Petty RE, Southwood TR. 1998. Revision of the proposed classification criteria for juvenile idiopathic arthritis: Durban, 1997. *J Rheumatol*, 25:1991–4.

Raivio VE, Immonen JJ, Puska PM. 2001. Transscleral contact krypton laser cyclophotocoagulation for treatment of glaucoma in children and young adults. *Ophthalmology*, 108:1801–7.

Sijssens KM, Rootho A, Berendschot TJTM, et al. 2006. Ocular hypertensive and secondary Glaucoma in children with uveitis. *Ophthalmology*, 113:853–9.

Sung VC, Barton K. 2004. Management of inflammatory glaucomas. *Curr Opin Ophthalmol*, 15:136–40.

Quintyn JC, Grenard N, Hellot MF, et al. 2003. Intraocular pressure results of contact transscleral cyclophotocoagulation with Neodymium YAG laser for refractory glaucoma. *Fr Ophthalmol*, 26:808–12.

Walton DS. 1994. Glaucoma in childhood. In Albert DM, Jakobiec FA, eds. Principles and practice of ophthalmology. Vol 4. Philadelphia: Saunders. p 2771–2.

Wolf MD, Lichter PR, Ragsdale CG. 1987. Prognostic factors in the uveitis of juvenile rheumatoid arthritis. *Ophthalmology*, 94:1242.

Välimäki J, Airaksinen PJ, Tuulonen A. 1997. Molteno implantation for secondary glaucoma in juvenile rheumatoid arthritis. *Arch Ophthalmol*, 115:1253–6.
