Uveitis as a Cause of Visual Loss in Arthritides and Comparable Conditions

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ABSTRACT. ***Objective.*** To examine the role of inflammatory rheumatic diseases and comparable conditions in the etiology of severe uveitis leading to visual impairment and blindness.

Methods. A retrospective study based on the Finnish Register of Visual Impairment. At the end of 1996, the Finnish Register of Visual Impairment included 296 uveitis patients in whom uveitis was the main cause of visual impairment. The patient records were examined retrospectively to investigate the etiology of severe uveitis. Due to the incompleteness of data obtained of the patients blinded a long time ago, we included only 174 uveitis patients whose visual handicap (best corrected visual acuity in the better eye < 20/60 or severe visual field loss) was stated during 1980–1996.

Results. A total of 174 uveitis patients were found, 72 male and 102 female. A diagnosed or presumed inflammatory rheumatic disease or comparable condition was found in 38/174 (22%) patients: juvenile rheumatoid arthritis in 14 (8%), spondyloarthropathy (ankylosing spondylitis or reactive arthritis) in 10 (6%), sarcoidosis in 5 (3%), seronegative rheumatoid arthritis in 4 (2%); Behçet's disease was diagnosed in 2 (1%), 1 patient had polymyositis, 1 polyarteritis nodosa, and 1 juvenile systemic lupus erythematosus. In addition to the above, 10 (6%) patients had chronic back pain and 5 (3%) patients various noninflammatory joint problems. Diverse other ophthalmologic or systemic disease was detected in 38 (22%) cases. Trauma or surgery caused uveitis in 9 (5%) patients. For 74/174 (43%) uveitis patients no specific associating condition could be shown. Legal blindness was documented in 65/174 (37%) patients, including 8 totally blind persons.

Conclusion. This study provides first data on the relative importance of inflammatory rheumatic diseases and comparable conditions in the etiology of severe uveitis leading to visual handicap and blindness. (J Rheumatol 2001;28:309–12)

Key Indexing Terms:
UVEITIS BLINDNESS ETIOLOGY ARTHRITIS

Uveitis is an umbrella term used for intraocular infections and inflammations that frequently occur in characteristic locations and patterns[1]. Most often uveitis involves the anterior structures of the eye, i.e., the iris and/or the ciliary body. Less often uveitis affects the intermediate and posterior segments of the eye, including pars plana, vitreous, choroid, and retina. The term panuveitis refers to a disease that involves all segments of the eye[2].

Uveitis can be caused directly by infectious agents, e.g., toxoplasma and herpesviruses, or may accompany systemic diseases such as sarcoidosis and certain arthritides, juvenile rheumatoid arthritis[3] (JRA) and spondyloarthropathies (SpA) in particular. Many patients with anterior uveitis carry the HLA allele B27 without symptoms and signs of SpA. Uveitis remains without a clear-cut etiology or disease association in about one-third of the cases[4,5].

In the majority of cases, uveitis is acute, with symptoms (duration < 3 mo), and the prognosis is good. Uveitis in ankylosing spondylitis (AS) is usually unilateral and symptomatic, and resolves in 4 to 6 weeks with local corticosteroid treatment without complications. In chronic and recurrent cases, visual acuity may be impaired due to complications such as cataract, secondary glaucoma, or cystoid macular edema. It has been estimated that in western societies uveitis causes about 5% of blindness[6,7]. Due to increasing life expectancy, the proportion of senile degenerative conditions as a cause of blindness will likely continue to increase and, correspondingly, the share of most other conditions including uveitis decreases, particularly in incidence series.

Scarce information is available on the relative importance of different uveitis entities as a cause of visual impairment[4,8]. We therefore approached the issue using the Finnish Register of Visual Impairment. Special emphasis was given to the role of various rheumatic diseases and comparable conditions in the etiology of severe uveitis.

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MATERIALS AND METHODS

The study was based on the Finnish Register of Visual Impairment, founded in 1983. Its function is regulated by law and it is technically maintained by the Finnish Federation of Visually Impaired under the supervision of a governmental office (National Research and Development Centre for Welfare and Health). Specialists in ophthalmology (about 420 in the population of 5.1 million at the end of 1997) and the ophthalmologic hospital units are obliged to document patients in whom the corrected visual acuity is permanently less than 20/60 in the better eye or if the patient for some other reason (e.g., visual field defects) is regarded as comparable to the above visual impairment. The notification form provides information on the patient's details, diagnoses, and severity of the visual impairment (visual acuity and visual field). Additional information was sought from patient records. The coverage of the register is not complete, but during the last few years, the annual number of new cases of visual handicap in different age groups has been quite stable. At the end of 1996, the register covered 11,022 live persons. The most common causes of visual impairment in 1996 were senile macular degeneration 35%, hereditary retinal degeneration and diabetic retinopathy 10% each, glaucoma and other diseases of optic pathways 9%, and congenital developmental defects 6%.

In 1996, the register consisted of a total of 296 subjects (2.9%) diagnosed as uveitis. In the present study all information of uveitis cases was gathered from hospital records. Because data obtained were frequently and greatly incomplete on subjects blinded a long time ago, we included only those 174 subjects who had been registered during 1980-1996.

The following data were obtained: sex and age of the patients, age at onset of uveitis and at detection of visual impairment, possible associations with systemic diseases, main complications of uveitis, and maximal visual acuity at the end of the study. The type of uveitis was recorded at the beginning and at the end of the study.

RESULTS

Uveitis was the main cause of visual handicap in 174 patients, 72 men and 102 women, during 1980–1996. The examination of their patient records revealed etiologic diseases or contributing factors of uveitis in 100 patients (57%); in 74 cases (43%) no clear-cut associations were found.

An inflammatory rheumatic disease or related condition was diagnosed or presumed in 38/174 (22%) uveitis patients: JRA in 14 patients (5 male, 9 female), SpA in 10 patients [7 with AS and 3 with reactive arthritis (ReA)], sarcoidosis in 5, seronegative rheumatoid arthritis (RA) in 4 (one of these had possible JRA), Behçet's disease in 2 patients and systemic lupus erythematosus in 1 patient, and 1 patient had polymyositis and 1 had polyarteritis nodosa.

The mean followup of uveitis was 24 years (range 0–74). The mean age of all the 174 uveitis patients was 36 years as their uveitis was diagnosed and the mean interval from the diagnosis to visual impairment was 18 years (Table 1).

Eleven of the 14 patients with diagnosed or presumed JRA had oligoarthritis; one of them later developed polyarthritis. In the remaining 3 cases oligoarthritis could not be established, but was highly probable. All the 7 patients who had been tested for antinuclear antibodies gave a positive result. The mean age at the detection of uveitis in JRA was 11 years (range 3–30) and the uveitis led to visual handicap within an average period of 11 years (range 1–41). Yet due to many years' treatment of uveitis, useful visual acuity could be saved in 6/14 patients with JRA.

The group of 38 patients with diverse ocular and systemic diseases associated with uveitis consisted of 10 patients with presumed toxoplasma retinochoroiditis, 8 patients with presumed tuberculous choroiditis, 3 patients with pars planitis, obvious vascular disease in 6 patients, 2 cases with multiple sclerosis, 2 cases with previous *Yersinia* infection without obvious arthritis, 1 borreliosis, 1 ulcerative colitis, and 5 miscellaneous cases.

Back pain was established in 10 patients, all of whom had complaints of lumbosacral spine, and another 5 patients had different noninflammatory joint problems. Trauma (6 patients) or surgery (3 patients) caused uveitis in 9 cases. In 74 patients no etiologic or contributing factors could be established. This group included 25 cases of choroiditis with unknown etiology.

At the end of the study, 11% of all the 174 uveitis patients retained normal central visual acuity of 20/40 or more in the better eye since their visual acuity had improved with proper treatment of uveitis and/or its complications after the statement of visual impairment, 13% had decreased visual acuity under 20/40 in the better eye but better than 20/60, 76% were visually impaired with acuity less than 20/60, including 37% legally blind with visual acuity under 20/200 in the better eye (Table 2). Cataract was the most frequent complication of uveitis, 80%, the second was cystoid macular edema, 42%, and the third was glaucoma, 38%. Posterior synechia and band keratopathy were also common findings, but they were not uniformly recorded.

DISCUSSION

The Finnish Register of Visual Impairment was founded in 1983, but is still far from complete. The coverage is probably better for new cases than for those blinded decades earlier. Similarly, it is reasonable to assume that young and middle aged patients are reported more accurately than very old ones.

Special problems occur with uveitis. Thus, the sequelae of uveitis such as cataract and glaucoma may be considered the cause of visual loss while the primary cause (uveitis) is not mentioned[8]. This error is likely to occur more frequently in idiopathic uveitis cases than in those with established etiology of uveitis or with well known disease associations.

Chronic uveitis is an important complication of JRA. Uveitis is usually insidious at the onset and is often bilateral. If not detected early and treated promptly, it can result in substantial morbidity and even blindness[9-12].

Uveitis occurring in conjunction with the HLA-B27 allele is a distinct clinical entity characterized typically by acute, unilateral, recurrent attacks of iridocyclitis[13,14]. This allele occurs in the Finnish more frequently (14%) than in most other populations of European origin. Occasionally, the inflammation becomes chronic, resulting in visually

Table 1. Age at onset of associating disease, age at diagnosis of uveitis, and years to visual impairment among 174 patients with chronic uveitis leading to severe visual impairment.

Disease	No. of Patients	Age at Diagnosis of Rheumatic Disease, mean (range)	Age at Diagnosis of Uveitis, mean (range)	Years to Impairment, mean (range)
Juvenile arthritis	14	9 (1–30)	11 (3–30)	11 (1–41)
Ankylosing spondylitis	7	36 (15–60)	32 (22–46)	22 (12–34)
Reactive arthritis	3	42 (29–60)	48 (29–65)	6 (0–16)
Seronegative arthritis	4	22 (15–24)	29 (17–52)	19 (5–47)
Lupus erythematosus	1	8	9	0
Polyarteritis nodosa	1	59	27	37
Polymyositis	1	24	24	9
Behçet's disease	2	27 (22–31)	27 (23–31)	2 (1–2)
Sarcoidosis	5	53 (26–87)	43 (13–82)	17 (0–55)
Toxoplasma choroiditis	10	NA	19 (0–71)	31 (0–70)
Tuberculous choroiditis	8	NA	23 (10–34)	37 (14–60)
Miscellaneous diseases	20	NA	37 (1–78)	15 (0–55)
Back pain or arthralgia	15	43 (14–68)	49 (5–68)	7 (–3–26)*
Trauma or surgery	9	NA	46 (2–92)	14 (–1–46)*
No established etiology	74	NA	40 (0–78)	19 (–7–66)*
All patients	174	NA	36 (0–92)	18 (–7–70)*

*Visual impairment was detected in some cases before diagnosis of uveitis. NA: not available.

Table 2. The degree of visual impairment and number of patients in different etiologic groups.

Disease	No. of Patients	Final Visual Acuity			
		Normal or Decreased*	Visual Impairment**	Legal Blindness***	Total Blindness†
Juvenile arthritis	14	6	5	2	1
Ankylosing spondylitis	7	2		4	1
Reactive arthritis	3	1	1	1	
Seronegative arthritis	4	1	1	2	
Lupus erythematosus	1				1
Polyarteritis nodosa	1		1		
Polymyositis	1	1			
Behçet's disease	2				2
Sarcoidosis	5	1	2	2	
Toxoplasma choroiditis	10	2	4	4	
Tuberculous choroiditis	8	1	6	1	
Miscellaneous diseases	20	1	12	7	
Back pain or arthralgia	15	5	7	3	
Trauma or surgery	9	2		5	2
No established etiology	74	18	29	24	3
Total	174	41	68	57	8

*Visual acuity normal ≥ 20/40, decreased < 20/40 to 20/60; **visual acuity < 20/60 to 20/200; *** visual acuity < 20/200 to light perception; †no light perception.

impairing complications (cataract, glaucoma, cystoid macular edema, or band keratopathy). In some rare cases, there can be severe, sight-threatening posterior segment manifestations in patients with HLA-B27 associated uveitis[15]. There is occasional evidence that severe eye disease is more likely to accompany ReA than AS[16,17]. Yet to our knowledge no patient series has been published.

Our study series consisted of subjects whose visual loss had been established in 1980–96; cases from the earlier period were excluded. Thus our series is a cumulative incidence series rather than a prevalence series. About one-third of the patients in our series had some rheumatic complaints. It is highly probable that cases diagnosed as rheumatoid factor negative RA had a disease belonging to the SpA, with predominant peripheral joint involvement, and one patient probably had JRA. No case had rheumatoid factor positive RA.

The patients with JRA had longstanding disease, and most likely the diagnosis of arthritis and uveitis had been delayed. The number of cases diagnosed as SpA (AS or

ReA) was nearly the same as that of cases with JRA. Three out of the 10 patients with established SpA had ReA; the arthritis ran a chronic course in only one of them. Since the population based incidence of uveitis associated with AS is higher than the incidence of uveitis associated with ReA[5], it seems that uveitis associated with ReA might lead to visual loss in a higher percentage of cases and in a shorter time. The true prevalence of AS is probably much higher than the figures based on clinically significant disease[17]. The uveitis associated with SpA typically has an acute symptomatic onset, and the patients often carry the HLA-B27 allele. Yet the onset of uveitis was insidious and chronic in half of the present patients with AS or ReA, obviously due to selection of patients with poor prognosis of their disease.

A third group of the same order of magnitude as the group of JRA and SpA consisted of patients with ill defined back problems. It is probable that some of these patients had underlying SpA. Yet back complaints are very common in a middle-aged population; quite obviously their occurrence in conjunction with uveitis was often only coincidental.

The number of patients with sarcoidosis was appreciably lower than that of patients with JRA and SpA. This is in contrast to an earlier report where the most frequent systemic disorders associated with blinding uveitis were sarcoidosis and AS[8]. Beçhet's disease is very rare in Finland.

Most of the uveitis patients included in the present series represented treatment failures from a period prior to 1980. Systematic ophthalmologic screening for patients with JRA was instituted in Finland in the late 1970s. Since many cases of uveitis have proved refractory to glucocorticoids, antimetabolites and immunosuppressive drugs such as methotrexate and cyclosporin A, either alone or in combination, have been used to control endogenous noninfectious uveitis[1,18-20]. Similarly, technical advances have been made in cataract and glaucoma surgery[20,21]. Accordingly, the prognosis of uveitis in JRA is considered to be better today than it was a few decades ago[12]. The same is obviously true about many other uveitis entities[1].

Our study provides population based data on visual handicap associated with different uveitis entities. The importance of etiologic examination of uveitis patients cannot be overestimated and it is obvious that a continuous monitoring of the Finnish Register for Visual Impairment has yet to show marked changes in the etiology of blindness.

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