·Clinical Research·

Uveitis associated with multiple sclerosis: complications and visual prognosis

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Abstract

• **AIM: To determine the frequency, subtype, complications, treatment and visual prognosis of uveitis in patients with multiple sclerosis (MS).**

• **METHODS: A total of 1702 MS patients´ medical records were reviewed for a history of uveitis both with a neurologist and an ophthalmologist.**

• **RESULTS: Nine patients (0.52%) with uveitis were detected. Eight of them were female, one was male. The mean age was 42.0±14.1y (range 22-66). Seven patients were relapsing remitting MS, two were secondary progressive MS. The mean duration of MS was 10.8±10.3y, and the mean duration of uveitis 10.3±9.9y. The onset of uveitis preceded that of MS (four patients) by a mean of 5.0±4.3y (range 1-11). MS diagnosed prior to the onset of uveitis (five patients) by an interval of 0.75-16y (mean 4.95±6.24y). There were 16 affected eyes of nine patients. The most common types of uveitis were panuveitis and intermediate uveitis. Uveitis was bilateral in most patients. The most common complications were cataract and glaucoma, and patients with such complications were surgically treated. The range of visual acuity of affected eyes was 20/800 to 20/22, with only six of 16 affected eyes better than 20/40. After treatment, the visual acuity of the affected eyes was better than 20/40 in 11 of 16 eyes.**

• **CONCLUSION: Uveitis should be considered when assessing an MS patient with visual loss, as surgical interventions other than medical treatments may be needed to improve visual function. Complications could be seen more often when posterior segment is involved.**

• **KEYWORDS:** complication; multiple sclerosis; uveitis; visual acuity

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INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory disorder of the central nervous system (CNS) white matter and a common cause of neurological disability in young adults [1,2]. Optic neuritis is the most frequent ophthalmic manifestation of MS, however intraocular inflammation may also occur. Uveitis is an intraocular inflammation involving the uveal tract, retina or vitreous body which appears unusually in MS [3]. The association between MS and uveitis is unclear. In patients with MS, the frequency of uveitis ranges from 0.4 to 26.9% and in patients with uveitis, the prevalence of MS is 1%-2%[4,5]. The most common type of uveitis has been reported to be intermediate uveitis which primarily involves the vitreous, peripheral retina and pars plana ciliaris [6]. Mild impairment in visual acuity (VA) may be seen at the time of initial presentation in patients with intermediate uveitis, in whom visual prognosis is related to the severity of the disease. Actually, macular involvement [cystoid macular edema (CME) and post-cystoid degeneration] is the most important prognostic factor for vision [7]. Patients with MS may also present with granulomatous anterior uveitis with development of extensive posterior synechiae and "mutton fat" keratic precipitates, that is highly suggestive of sarcoidosis [5,8-11]. Secondary changes due to uveitis such as cataract, CME, band keratopathy, glaucoma, retinal detachment, retinoschisis, vitreous hemorrhage and occlusive vasculitis may occur. Therefore, the management could be often difficult to achive [12,13]. We present herein the frequency, clinical features, complications and outcomes of uveitis in MS patients with a long follow-up.

SUBJECTS AND METHODS

The case records of 1702 consecutive patients with clinically definite MS treated at the Department of Neurology in Dokuz Eylul University between February 1976 and December 2008, were reviewed for a history of uveitis. This research was carried out in accordance with the Declaration of Helsinki and after obtaining approval from The local

Table 1 Demographic and clinical data of the patients

Patients	Age (a)/sex	Age at onset of		Type of MS	Type/laterality of UV	UV evolution	Follow up (a)
		UV (a)	MS (a)				
1	41/F	22	33	RR	Panuveitis/ BL	Chronic	3
2	22/M	17	20	RR	Intermediate/ R	Chronic	2
3	39/F	[1]34	34	RR	Panuveitis/ R	Chronic	4
4	42/F	40	37	RR	Intermediate/ BL	Chronic	5
5	37/F	29	34	RR	Posterior/ BL	Chronic	3
6	63/F	45	42	SP	Posterior/ BL	Chronic	18
7	66/F	36	34	SP	Panuveitis/ BL	Chronic	32
8	30/F	24	25	RR	Intermediate/ BL	Chronic	5
9	38/F	37	21	RR	Anterior/BL	Acute	17

BL: Bilateral; MS: Multiple sclerosis; UV: Uveitis; [1]The patient had uveitis after 9mo than MS onset.

University Hospital Medical Ethics Committee. Written informed constent from patients was obtained. Patients who fulfilled the criteria of Poser *et al* [14] for the diagnosis of clinically definite MS and who were examined for the occurrence of visual symptoms both by a neurologist and by an expert ophthalmologist on uveal disorders were included into the study. All patients were of caucasian origin. Patients whose uveitis were attributed to systemic vasculitis, chronic bacterial or viral infections and patients who had history of optic neuritis had been excluded. Also, records were checked if dermatological and urological examinations had revealed any evidence of aphthosis that is diagnostic for Behçet's disease and if neurosarcoidosis had been ruled out by chest X-ray, and angiotensin converting enzyme level in serum. After that, records were checked for a clinical opthalmological examination in order to determine clinical and anatomical pattern of uveitis as well as the treatment schedule. Uveitis was anatomically classified according to the International Uveitis Study Group criteria [6] as anterior (iridocyclitis), posterior (the primary site of inflammation is in the retina or in the choroid), intermediate uveitis (pars planitis) or panuveitis. Medical records were documented and summarized about treatment of uveitis as follows: 1) anterior uveitis was treated with topical corticosteroids and mydriatics; 2) bilateral active posterior uveitis with VA poorer than 20/40 in the better eye, was managed with systemic corticosteroids; 3) intermediate uveitis was treated with systemic and local steoroids in patients with VA poorer than 20/40, however patients with VA better than 20/40 were monthly followed-up. Panuveitis was treated with systemic and local steroids. Patients treated with immunosupressive agents when there was reactivation of uveitis following withdrawal or tapering of steroids, no response or tolerance to steroid treatment, or when there was a need for more intensive treatment due to high risk of blindness.

The complications of the uveitis were divided into three groups: cataract, glaucoma, and retinal neovascularization. Cataract surgery was performed when visually significant cataract had developed or where the fundus view was obscured due to lens opacity in patients with posterior segment inflammation. Cataract surgery technique was extracapsular cataract extraction (ECCE) in our patients with clinically significant cataract becuase they were performed before phacoemulsification surgery era. Elevated intraocular pressure (IOP) was treated by medical agents. Glaucoma surgery was undertaken when an IOP of <21 mm Hg could not be attained by the medical treatment. Retinal neovascularization was treated by argon laser panretinal photocoagulation.

RESULTS

Nine patients (0.52%) with uveitis were identified out of 1702 definite MS patients between February 1976 and December 2008. Eight of them were female, one was male. The mean age was 42.0±14.1y (range 22-66). Seven patients were relapsing remitting MS (RRMS), two were secondary progressive MS (SPMS). The mean annual number of MS relapses was 0.61±0.38 (0.15-1.4). The mean duration of MS was 10.8 ±10.3y (range 2-32), and the mean duration of uveitis 10.3 ±9.9y (range 1-30). The mean age at onset of uveitis was 31.7 ±9.2y (range 17-45), and the mean age at onset of MS 31.2 ±7.5y (range 20-42). Four patients had a history of uveitis prior to the onset of MS. The onset of uveitis preceded that of MS by an interval of 1-11y (mean 5.0±4.3y). MS was diagnosed prior to the onset of uveitis in our five patients by an interval of 0.75-16y (mean 4.95±6.24y). Median follow-up was 5y (range 2-32). No correlation was found between the type of MS and type of uveitis. The detailed clinical data of the 16 eyes of 9 MS patients with uveitis are summarized in Table 1.

Anterior uveitis (iridocyclitis) was present in two eyes, intermediate uveitis (pars planitis) in five, posterior uveitis in four and panuveitis in five eyes. Only one patient had acute course of uveitis, and the remaining eight suffered from chronic course. Uveitis was bilateral in most patients (77.8%). Granulomatous uveitis was present in four eyes of two patients. Three eyes were treated with topical steroids,

Table 2 The ophthalmologic findings and outcome of uveitis in our patients

Patient	Laterality	Type of uveitis	VA before treatment	VA after treatment	Causes of decreased final VA	Surgery
P1	R	Panuveitis	20/100	20/60	CAT	ECCE+PCIOL
	L	Panuveitis	20/250	20/200	CAT+ERM	ECCE+PCIOL
P2	R	Intermediate	20/30	20/25	CAT	ECCE+PCIOL
P3	R	Panuveitis	20/60	20/30	-	None
P4	R	Intermediate	20/25	20/22	-	None
	L	Intermediate	20/25	20/22	-	None
P5	R	Posterior	20/60	20/40	CAT+Glaucoma	ECCE+PCIOL+trab
	L	Posterior	20/100	20/40	CAT+Glaucoma	ECCE+PCIOL+trab
P6	R	Posterior	20/800	20/400	CAT+Glaucoma+ERM	Vitrectomy+trab+5FU
	L	Posterior	20/40	20/25	CAT	ECCE+PCIOL
P7	R	Panuveitis	20/100	20/35	CAT	ECCE+PCIOL
	L	Panuveitis	20/200	20/50	Vitreous haemorrhage	Vitrectomy+laser PRP
P8	R	Intermediate	20/100	20/60	CAT+RD+CME	ECCE+PCIOL+vitrectomy
	L	Intermediate	20/100	20/40	CME	None
P9	R	Anterior	20/25	20/20	-	None
	L	Anterior	20/22	20/20	-	None

CAT: Cataract; ECCE+PCIOL: Extracapsular cataract extraction with posterior chamber intraocular lens implant; trab: Trabeculectomy; RD: Retinal detachment; CME: Cystoid macular edema; PRP: Pan-retinal photocoagulation; ERM: Epiretinal membrane; 5FU: 5-fluorouracil; VA: Visual acuity.

two eyes were treated with intravitreal steroids, eight with systemic steroids, and 4 out of these 8 patients were treated with additional immnosupressive agents. Three eyes were followed-up without any medication for uveitis. The most common complication was cataract (9/16 eyes; 56%) and cataract surgery was performed in 8 eyes, because one patient (P6) did not want to have surgery. The visual outcome following surgery was satisfactory in all eyes except the left eye of P1. The second most common complication was glaucoma (3/16 eyes; 19%) and trabeculectomy was performed in all eyes as medical treatment was not able to lower IOP (Table 2).

The range of visual acuity of affected eyes was 20/800 to 20/22, with six of 16 affected eyes better than 20/40 before treatment. The visual acuity of the affected eyes after treatment was better than 20/40 in 11 of 16 eyes.

DISCUSSION

In this study we identified that 0.52% of 1702 definite MS patients were associated with uveitis. This finding is consistent with several previous studies performed by Le Scanff *et al* [15] who found 0.65% of 4300 MS patients had uveitis, Thouvenot *et al* [16] who found 0.7% of 700 had uveitis, and Biousse *et al* [9] who found that approximately 1% of 1098 MS patients had uveitis, but seems to be little lower than Zein *et al* [17] who reported uveitis 1.3% in 1254 MS patients and Schmidt *et al* [18] 1.8% in 450 MS patients. This might be due to the difference in the diagnostic criteria of the diseases in the studies. There was a female preponderance (89%) which was also reported previously [9,11,17]. There were four patients with uveitis diagnosed before the onset of MS, and five patients vice versa. There was no patient that had both concurrently.

The most common types of uveitis were intermediate (pars planitis) and panuveitis. These findings are in line with Markomichelakis's and Biousse *et al*'s findings [4,9], but are not consistent with Le Scanff *et al* [15] who reported the most common type of uveitis as posterior uveitis, Schmidt *et al* [18] and Towler and Lightman[11] as anterior uveitis. It was shown that all types of uveitis could be seen in MS, however the HLA-DR15 allele was shown to cause a predisposition to MS and pars planitis [19-23]. Thus, diagnosis of multiple sclerosis should be considered preferably if there is bilateral pars planitis, particularly in females [24]. The majority of our patients with uveitis had bilateral involvement which is similar to other studies[9,17,25,26].

Most previous reports on MS-associated uveitis give relatively little information on visual prognosis. The present study is important for detecting complications associated with the type of uveitis and visual outcome that were seen in MS patients. In our patients, the VA was 20/200 or worse in 19% of affected eyes before treatment, whereas it was 13% of affected eyes after treatment. The VA was 20/40 or better in 37% of affected eyes before treatment and in 68% of affected eyes after treatment. It was observed that the poor visual prognosis was associated with the complications seen in the retina. There were epiretinal membrane in two eyes and vitreous haemorrhage in one eye of the patients who had a VA of 20/200 or worse. These findings reinforced that panuveitis and intermediate uveitis could give rise to permanent complications despite appropriate treatment. Nevertheless, the visual outcome following vitrectomy and panretinal photocoagulation for vitreous haemorrhage in our patient was very satisfactory as VA improved from 20/200 to

20/50. The VA improved to a higher level in the patients who had also relatively good VA before treatment.

The most common complication of uveitis was cataract. VA was considerably improved after surgery in patients with isolated cataract secondary to uveitis. On the other hand, poorer VA was achieved after surgery in patients with accompanying ocular complications such as epiretinal membrane, glaucoma and CME. The second most common complication was glaucoma. IOP below than 21 mm Hg was achieved in all eyes after trabeculectomy. Most of our patients had reached good visual prognosis after treatment, when we took into account that only six of 16 affected eyes were better than 20/40 in the beginning.

Our study has several limitations. First, our data were collected from the medical records, during which time the diagnostic criteria for MS and uveitis have been refined. Also, patients' reports might have not been noted down to the medical records. Consequently, it is possible that we have underestimated the true prevalence of uveitis. Second, although none of our patients had optic neuritis in this study, the baseline visual acuity was not exactly known. As such, subclinical deficits could not be accounted for. Third, we did not assess any magnetic resonance imaging (MRI) or cerebrospinal fluid analysis that might differentiate MS patients with uveitis from those without uveitis. However, it was reported that MRI features in patients with MS-associated uveitis had no convincing evidence of a special lesional distrubution[18].

It is important to recognize that underlying reason for visual impairment in patients with MS other than optic neuritis, the possibility of uveitis, may develope. On the other hand, uveitis could be a manisfestation of an underlying disease like MS. Therefore patients with uveitis should undergo a detailed neurological examination, and also presence of interval between uveitis and MS onset should be kept in mind for further follow-up. The patients with MS-associated uveitis may need to be treated as early as possible with appropriate surgical interventions for protecting their optimum vision and for improving the quality of life.

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