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Original Scientific Paper

SUBCLINICAL OPTIC NEURITIS

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SUMMARY – Acute optic neuritis is often associated with multiple sclerosis. It is considered to be the most common ocular symptom of multiple sclerosis. In addition to acute optic neuritis, in patients with multiple sclerosis, subclinical optic neuritis is also described. It is characterized by slow progression and bilateral involvement, thus being unnoticed by the patient. The purpose of the present study was to assess vision impairment in multiple sclerosis patients without a history of acute optic neuritis, using a number of functional tests including visual field testing by Octopus 101 perimetry N1 program, contrast sensitivity testing by Pelli Robson chart, and color vision by Ishihara pseudoisochromatic plates. The study included 35 multiple sclerosis patients aged 18-50 years, without subjective signs of vision impairment and visual acuity 1.0 according to Snellen. Visual field defects were found in 28 patients. The most common defects of visual fields were retinal sensitivity depression in peripheral zone and nerve fiber bundle defect. Reduced contrast sensitivity was found in 30 (86%) patients. Study results indicated multiple sclerosis patients free from signs of optic neuritis to suffer vision function impairment, as demonstrated by Octopus perimetry and contrast sensitivity testing with Pelli Robson charts.

Key words: *Optic neuritis; Multiple sclerosis; Vision tests*

Introduction

The association of multiple sclerosis and optic neuritis is very well known and thoroughly studied. Acute typical optic neuritis with visual acuity and visual field impairment is considered as the most common ophthalmologic manifestation of multiple sclerosis. Lesions of the optic nerve and optic pathway have been detected by histopathology in a great proportion of patients with multiple sclerosis, including those that have never suffered acute optic neuritis. Other forms of visual function impairment such as subclinical optic neuritis have also been described in multiple sclerosis patients. Unlike the acute form, subclinical optic neuritis is characterized by slow progression and bilateral involvement, thus being unnoticed by the patient[1-6].

Patients and Methods

This prospective study was conducted at Division of Neuroophthalmology, Department of Ophthalmology, Zagreb University Hospital Center, as part of the project entitled Ophthalmologic Deficits in the Early Diagnosis and Follow up of Multiple Sclerosis (project no.: 108-1081874-1984), Ministry of Science, Education and Sports, Republic of Croatia. The study included 35 multiple sclerosis patients aged 18-50 years, without subjective signs of vision impairment and visual acuity 1.0 according to Snellen. There were no data on vision loss in patient histories. Con-

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trol group included 35 age- and sex-matched healthy subjects. Both groups showed female predominance (Table 1).

Table 1. Patient distribution according to gender

Gender	Multiple sclerosis patients, n	Control group, n
Male	11	12
Female	24	23
Total	35	35

The diagnosis of multiple sclerosis was made by a neurologist[7,8]. Subjects with ophthalmologic lesions leading to impaired visual function, such as blurred optic media, retinal detachment, glaucoma, inflammatory changes, degenerative chorioretinal changes, etc., were excluded. Patients with refraction error greater than 3 diopters were also excluded. Each examination began with taking history data, followed by ophthalmologic examination, contrast sensitivity and color vision testing, and visual field testing by automated Octopus 101 perimetry. Visual acuity was assessed by the subjective method using standard optotypes according to Snellen at 6-m distance[9]. Pelli Robson test was used on contrast sensitivity testing[10,11]. This test was performed at 1-m distance and 85 cd/m^2 sensitivity, first monocular for each eye in separate, and then binocular. A +0.75 diopter lens was added in subjects older than 40. The logarithm unit of contrast sensitivity for the group of letters in which 2 of 3 letters from a particular group were recognized was taken as test result. Color vision was tested by use of Ishihara pseudoisochromatic plates, version 1977, which consist of 38 plates[12]. Vision field was tested on Octopus 101 perimeter using N1 program[13].

Tübingen classification of visual field defects was used to determine category of visual field defect[14], as follows: 1) normal finding; 2) central scotoma; 3) paracentral scotoma; 4) cecocentral scotoma; 5) nerve fiber bundle defect; 6) diffuse depression of retinal sensitivity 7) blind spot expansion; 8) sector defect; 9) hemianopic visual field defect; and 10) retinal sensitivity depression in peripheral zone.

Retinal sensitivity depression was categorized according to the mean defect value as follows: normal finding: -2.00 to 0.0 dB; grade I: 0.1-4.9 dB; 3) grade II: 5.0-9.9 dB; grade III: 10.0-14.9 dB; grade IV: 15.0-19.9 dB; grade V: 20.0-24.9 dB; grade VI: 25.0-29.9 dB; and grade VII: ≥30 Db.

Results

All study patients and control subjects had visual acuity 1.0 according to Snellen, normal anterior and posterior segment findings, and mean intraocular pressure 16 mm Hg. Results of contrast sensitivity testing are shown in Table 2. All control subjects submitted to contrast sensitivity testing had logarithm value of 1.80 for the right and left eye, whereas binocular test yielded a logarithm value of 1.95.

Table 2. Distribution according to contrast sensitivity results in multiple sclerosis patients

Logarithmic value of contrast sensitivity	Right eye, n	Left eye, n	Both eyes, n
1.30	2	2	0
1.50	4	4	1
1.65	24	24	6
1.80	5	5	23
1.95	0	0	5

On visual field testing, the parameters of mean sensitivity and mean defect were analyzed. Results of visual field testing in multiple sclerosis patients with normal visual acuity and free from signs of acute optic neuritis are shown in Tables 3 and 4. Normal retinal sensitivity was found in 10 patients and reduced retinal sensitivity ranging to 4.9 dB in 25 patients. In control group, a mean sensitivity of 30-34.9 dB on the right eye was recorded in 18 (51%) and on the left eye in 25 (71%) subjects, while a mean sensitivity of ≥30 dB on

Table 3. Distribution of multiple sclerosis patients according to mean sensitivity results

Mean sensitivity	Right eye	Left eye
25.0-29.9 dB	5 (14%)	5 (14%)
30.0-34.9dB	29 (83%)	29 (83%)
<35.0 dB	1(2.8%)	1 (2.8%)

Table 4. Distribution of multiple sclerosis patients according to mean defect results

Mean defects	Right eye	Left eye
-2.0-0.0 dB	10 (28%)	10 (28%)
0.1-4.9 dB	25 (71%)	25 (71%)

the right eye was found in 17 (49%) and on the left eye in 10 (29%) subjects. All control subjects had the mean defect ranging from -2.00 to 0 dB on both eyes.

Color vision testing by use of Ishihara pseudoisochromatic plates revealed normal color vision both in patient and control groups. All plates were correctly read by all study subjects.

Discussion

Literature reports on autopsy histopathology studies show a high prevalence of optic nerve and optic pathway involvement in patients with multiple sclerosis[15]. In addition, postchiasmatic lesions and lesions to optic radiation detectable by magnetic resonance of the brain were also found in multiple sclerosis patients[15]. These changes can cause subclinical vision loss unnoticed by the patient but detectable by functional and electrophysiological visual function testing. There are literature reports on subclinical vision deficits identified by use of visual evoked potentials[16,17].

The aim of the present study was to assess vision impairment in multiple sclerosis patients without a history of acute optic neuritis, using a number of functional tests including visual field testing by Octopus 101 perimetry N1 program, contrast sensitivity testing by Pelli Robson chart, and color vision by Ishihara pseudoisochromatic plates.

In the group of multiple sclerosis patients with normal visual acuity and without signs of vision loss, visual field testing showed normal retinal sensitivity in 10 (28%) and slight retinal sensitivity depression in 25 (71%) patients. These findings are consistent with those reported by Chorazy *et al.* on visual field defect in 73.1% of their ophthalmologically asymptomatic patients with multiple sclerosis. The same authors found concentric narrowing in 46.2% and defect in the upper part of visual field in 26.9% of their patients[18]. In our study, impairments in the form of nerve fiber bundle defects (n=9), retinal sensitivity depression in peripheral zone (n=7) and paracentral scotomata (n=5) were most common. Blind spot expansion and sector defects were found in two patients each. Defects in the form of diffuse depression, central or cecocentral scotoma, or hemianopic form of visual field defect were not present in any of our patients. In this group, the mean value of retinal sensitivity was 32.0 dB and 32.14 dB on the right and left eye, respectively. The greatest loss of retinal sensitivity was 4.90 dB on the right eye and 4.20 dB on the left eye. In their study, Sisto *et al.* report on visual field defects in 64% of their patients, predominantly diffuse visual field depression, whereas central defect within 10° and 20° was found in 4 patients[19]. Other authors also detected visual field defects in patients with multiple sclerosis free from optic neuritis in their history. Many authors report on the presence of arcuate scotoma in these patients. Honan *et al.* found visual field defects in 9 of 24 multiple sclerosis patients, including arcuate scotoma in 5, focal constriction in 2, and peripheral constriction in 2 patients[20]. Meienberg *et al.* report on the majority of their patients to have scotoma in the 15°-30° eccentrically[21]. Frisén and Hoyt describe the occurrence of arcuate scotoma with subclinical loss of axons in the layer of retinal fibers[22]. On the other hand, Wildberger[23] found lesions in the mid-periphery of visual field, while Faschinger *et al.*[24] report on peripheral depression and disseminating scotomata. Nizankowska *et al.* found lesions in all quadrants, however, with considerable variation in the loss of sensitivity in the upper part of visual field[25].

In our study, nerve fiber bundle lesions of variable grade, including arcuate scotoma in 5 (14%) patients, were the most common defects, followed in prevalence by depression of retinal sensitivity in peripheral zone. Although different methods of visual field testing were used in some other studies, our results could still be considered consistent with their reports.

We also tested contrast sensitivity as an important functional method of vision testing in various clinical conditions. Contrast sensitivity is one of the basic visual function characteristics. Defects in contrast sensitivity can cause difficulties in reading, recognizing faces and traffic signs, and in everyday activities. That is why contrast sensitivity testing is of great importance on assessing visual function and quality of life in these patients[11,26-28]. Studies have shown that contrast sensitivity may also be damaged in patients without a history of optic neuritis or subjective vision problems. In our group of multiple sclerosis patients without signs of vision loss and with normal visual acuity, the mean contrast sensitivity was 1.64±0.1 on both eyes.

Contrast sensitivity reduced to the logarithm value of 1.65 was recorded in 24 (69%) multiple sclerosis patients as compared with the logarithm value of 1.80 found in all control subjects. The more so, the logarithm value of contrast sensitivity of 1.50 was found in 4 and of 1.35 in 2 patients, although they reported no vision problems in their history. These findings are consistent with those reported by other authors having tested visual function in multiple sclerosis patients free from subjective signs of vision impairment. Contrast sensitivity was tested by different methods. So, Fahy *et al*. report on reduced contrast sensitivity in 33% of their study subjects[28]. Sisto *et al*. found 77.1% of their patients to have impaired contrast sensitivity[19]. Wender reports on the Pelli Robson test to be sensitive in detecting vision loss[29], and Balcer *et al*. found it to be highly useful in detecting visual function defects[30].

Impairment of color vision is known to occur during the course of acute optic neuritis. Many patients report on washed-out color perception during optic neuritis. On initial color saturation test, color vision differs between the affected and secondary eye[1,3]. Therefore, we included color vision testing by use of Ishihara plates in the present study. All plates were normally read by all study patients and control subjects.

Study results indicated multiple sclerosis patients free from signs of optic neuritis to suffer vision function impairment, as demonstrated by visual function tests. The afferent vision system, extending from the retina to the primary visual cortex, is frequently or even regularly affected in multiple sclerosis patients. As previously reported[15], histopathologic studies reveal visual system involvement in multiple sclerosis. Autopsy studies show optic nerve involvement in 94%-99% of multiple sclerosis patients, with retrochiasmatic pathways being also quite frequently affected. Multiple sclerosis is characterized by thinning of the nerve fiber and ganglial cell layers, while optic nerve and chiasm lesions are also caused by inflammation, demyelination, gliosis, axonal damage, and atrophy. Pathologic changes of the lateral geniculate body and visual cortex may also be found as foci of primary degeneration, secondary due to wallerian degeneration because of white matter thread lesions, or as the result of transsynaptic degeneration due to lesions in anatomically related distant regions. Thinning of the retinal nerve fiber layer, associated with axonal degeneration and leading to vision loss in multiple sclerosis patients, was demonstrated in clinical studies using structural diagnostic methods[31-34]. These lesions may manifest as acute loss or as subclinical, so-called clinically silent lesions without acute symptoms. Namely, visual field lesions involve peripheral segments of visual field, in the range of 10º to 30º eccentricity. These lesions involve visual field bilaterally and progress slowly, thus frequently being unnoticed by the patient.

Results of the present study suggest that the usual opinion on the acute form of optic neuritis as the most common ophthalmologic manifestation in multiple sclerosis and the initial symptom in 30% of patients should be reconsidered, as a significantly higher prevalence of the subclinical form of optic neuritis was demonstrated in the study population.

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Sažetak

SUPKLINIČKI OPTIČKI NEURITIS

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Akutni optički neuritis je često povezan s multiplom sklerozom. Smatra se najčešćom oftalmološkom manifestacijom te bolesti. Uz akutni optički neuritis opisani su i bolesnici sa supkliničkim oblikom. Svrha ovog istraživanja bila je procijeniti oštećenje vida kod bolesnika s multiplom sklerozom bez povijesti akutnog optičkog neuritisa primjenom brojnih funkcionalnih testova uključujući testiranje vidnog polja pomoću programa perimetrije Octopus 101 N1, testiranje kontrastne osjetljivosti Pelli Robsonovim tablicama i ispitivanje kolornog vida pseudoizokromnim tablicama prema Ishihari. Ispitivanje je uključilo 35 bolesnika s multiplom sklerozom u dobi od 18-50 godina bez subjektivnih znakova oštećenja vida i oštrine vida 1,0 prema Snellenu. Oštećenje vidnog polja pronađeno je u 28 bolesnika. Najčešća oštećenja su depresija osjetljivosti mrežnice u perifernoj zoni i defekt snopa živčanih vlakana. Smanjena kontrastna osjetljivost pronađena je u 30 (86%) bolesnika. Rezultati ispitivanja pokazali su da se u bolesnika s multiplom sklerozom bez subjektivnih znakova oštećenja vida mogu naći supklinička oštećenja pomoću perimetrije Octopus i Pelli Robsonovim tablicama za ispitivanje kontrastne osjetljivosti.

Ključne riječi: *Optički neuritis; Multipla skleroza; Testovi vida*