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Neuro-Ophthalmological Evaluation in Patients with Multiple Sclerosis

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Research Article

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Abstract

Multiple Sclerosis (MS) is a chronic, autoimmune, inflammatory, demyelinating disease that affects the central nervous system. Objective. To evaluate the evolution of retinal and optic nerve ophthalmological manifestations in Multiple Sclerosis. Method. A prospective, descriptive, longitudinal study was carried out in a series of patients with MS, referred to the Neuro-ophthalmology clinic of the "Hermanos Ameijeiras" Hospital in the period from June 2021 to September 2022. Results. The average age was 43.1 years, with a predominance of the female sex (76.3%). The predominant clinical form was Relapsing-remitting (76.3%). Psychophysical studies (BCVA, CV test, CV) were normal in most cases except for contrast sensitivity (CS), detecting a significant decrease in the average values in the annual evolutionary study, especially in cases with greater clinical severity of the disease. OCT showed a decrease in the ganglion cell layer (OD. 42.1 and LE. 44.7%) and in the RNFL (26.3% in OA). Conclusions. In the series studied, women in the fourth decade of life with relapsing-remitting multiple sclerosis predominated. The annual follow-up of neuro-ophthalmological manifestations in patients with multiple sclerosis behaved in a stable manner, with no modifications detected in the psychophysical studies and diagnostic means except for the significant decrease in contrast sensitivity.

Keywords: Multiple Sclerosis; Neuro-Ophthalmological Study; Contrast Sensitivity

Abbreviations

WHO: World Health Organization; MSIF: Multiple Sclerosis International Federation; HAH: Hermanos Ameijeiras Hospital; BCVA: Best Corrected Visual Acuity; OCT: Optical Coherence Tomography; GCL: Ganglion Cell Layer; RNFL: Retinal Nerve Fiber Layer.

Introduction

Multiple sclerosis (MS) is a chronic, autoimmune, inflammatory, demyelinating disease that affects the entire

central nervous system. It is the main cause of non-traumatic neurological disability among young adults [1-3]. MS has been widely studied, but some aspects remain to be clarified, such as the risk factors for developing the disease, as well as the pathophysiology and treatment [3,4]. A study published by the World Health Organization (WHO) and the Multiple Sclerosis International Federation (MSIF) showed that between 2008-2013 there was a worldwide increase from 2.1 to 2.3 million, with a global prevalence of 33 cases/100,000 inhabitants6. The prevalence in Latin America ranges between 2 and 13 cases per 100,000 inhabitants [5-7].

Estrada4 published the first case in Cuba in 1965 and the first series of cases was described by Cabrera and Manero 10 years later. According to the studies by Cabrera Gómez and Rivera Olmos, the prevalence of MS in Cuba has been defined according to the national registry of this disease at 4.42 cases/100,000 inhabitants.

Some risk factors related to the disease have been identified, including: viral infections, especially by the Epstein-Barr virus, female sex, low exposure to sunlight (vitamin D deficiency), smoking, and family and personal history of MS [8-11].

MS is classified according to the clinical forms of its evolution, in: relapsing-remitting (85% of cases suffer from it), primary progressive, secondary progressive and relapsing progressive, which is the most serious and the one that occurs less frequently. Optic neuritis may be the onset in 30% of patients and in an even higher percentage (70-100%) during its course [8,9].

Magnetic resonance imaging (MRI) is essential for diagnosis. It is based on the presence of periventricular demyelination plaques and in the corpus callosum. Hyperintense lesions on T2 in the spinal cord at the cervical, thoracic or lumbar level are an expression of dissemination, which confirms the diagnosis of the disease (McDonald's criteria) [5].

The main objective of this research was to evaluate the annual evolutionary follow-up of psychophysical and structural ocular studies in patients with Multiple Sclerosis.

Methodological Design

A prospective descriptive study was conducted in the Ophthalmology Service of the "Hermanos Ameijeiras" Hospital (HHA). The universe was made up of MS patients who met the selection criteria. Patients considered for inclusion were those over 18 years of age with a diagnosis of MS, previously evaluated in the Neurology and Neuro-Ophthalmology clinic who agreed to participate in the study, with prior informed consent. Cases with psychiatric disorders or cognitive deficits who could not cooperate with the examination, with previous ophthalmological conditions, with use of drugs that can produce toxicity on the retina and optic nerve (chloroquine, ethambutol, antineoplasmatics, etc.) and pregnant patients were excluded.

The sample was left consisting of 38 patients (76 eyes) diagnosed with MS who met the inclusion criteria, who had an initial evaluation in the Neuro-Ophthalmology consultation (2019-2020) and who underwent annual follow-up, in the period from June 2021 to September 2022 [12-15].

The variables were: age, sex, MS classification, time of evolution. Best corrected visual acuity (BCVA), color vision (CV)), contrast sensitivity (SC)) and static perimetry (PE). The fundus of the eyeIt was performed with the pupil dilated and light-free, biomicroscopy with an aerial lens (+90). Optical coherence tomography (OCT) was performed with the CIRRUS 5000 HD. The thickness of theretinal fiber layer (RNFL). It was considered normal when the values were between 75 and 107.2 microns.He Ganglion cell layer (GCL) thickness, nnormal. between72.9 and 92.5 microns.

A database was created in Microsoft Office Excel 2007, where all the variables described above were recorded. The SPSS package, version 11.5, was used.

Results

Table 1 shows the predominance of the female sex (76.3%). The average age in the series studied was 43.2 years. It is noteworthy that this value was higher in women (44.6 ± 10.4) compared to men (38.6 ± 18.5).

Demographic aspects	Sex				Total	
	Female		Male			
	No.	%	No.	%	No.	%
	29	**76**	**9**	**24**	**38**	**100**
Age in years (Mean ± SD)	(44.6 ± 10.4)		(38.6 ± 18.5)		(43.2 ± 12.8)	

SD: Standard deviation.

Table 1: Distribution of patients by age and sex.

Clinical forms of MS evolution		No.	%
Clinical diagnosis	Recurring Sender	29	76
	Primarily progressive	7	18
	Secondarily progressive	2	5.3
	Total	38	100

Table 2: Distribution of patients according to the clinical form of presentation of Multiple Sclerosis.

The predominant clinical form was Relapsing-remitting (76.3%). This clinical variant of MS is the least severe compared to the progressive ones (Table 2).

The average evolution time of the studied cases was 9.4 years with a standard deviation of 6.9. The systemic and ocular manifestations are less serious with respect to the progressive forms.

The above is evidenced in Tables 3 & 4, in which the average values of the BCVA of the right eye (RE) and left eye (LE) are recorded.

In most of the cases evaluated, BCVA remained within the normal range in both eyes (BE) in the initial study, which is shown in the last column of the table (total average value). Within this normal vision range (0.9 –1), (76.3%) and (63.2%) were found for OD and LE, respectively. In the annual follow-up, which is shown in the center of the table, a slight decrease is observed, without statistical significance in OD and LE (p=0.059), (p=0.096) respectively.

Initial MCVA	Annual evolutionary AVMC				Total
	<0.4	0.4 – 0.6	0.6 – 0.8	0.9 - 1	
<0.4	1 (2.6%)	0(0.0)	0(0.0)	0(0.0)	1 (2.6%)
0.4 – 0.6	1 (2.6%)	5(13.2%)	0(0.0)	0(0.0)	6(15.8%)
0.7 – 0.8	0(0.0)	0(0.0)	2(5.3%)	0(0.0)	2(5.3%)
0.9 - 1	0(0.0)	1(2.6%)	2(5.3%)	26(68.4%)	29(76.3%)
Total	2(5.3%)	6(15.8%)	4(10.5%)	26(68.4%)	38(100%)

Table 3: Result of the evolutionary study of the OD MCVA.

Initial MCVA	Annual evolutionary AVMC				Total
	<0.4	0.4 – 0.6	0.6 – 0.8	0.9 - 1	
<0.4	1 (2.6%)	0(0.0)	0(0.0)	0(0.0)	1(2.6%)
0.4 – 0.6	1 (2.6%)	5(13.2%)	0(0.0)	0(0.0)	6(15.8%)
0.7 – 0.8	0(0.0)	2(5.3%)	4(10.5%)	1(2.6%)	7(18.4%)
0.9 - 1	0(0.0)	1(2.6%)	1(2.6%)	22(57.9%)	24(63.2%)
Total	2(5.3%)	8(21.1%)	5(13.2%)	23(60.5%)	38(100%)

Marginal homogeneity test: p=0.096.

Table 4: Result of the evolutionary study of the OI MCVA.

Examination of pupillary light reflexes was normal in AO (92.1), with only a low percentage of involvement. In the three cases with partial bilateral optic atrophy, a decrease in reflexes was observed. The study of color vision behaved in a similar waysimilar. A low percentage of involvement was observed in 7 cases (18.4%). He The fundus was normal in AO in most cases, only in some cases signs of optic nerve damage were seen in OD and OI (28.95) and (26.3%) respectivelyand even lower with optic atrophy (7.9%).

Static perimetry in AO was normal in most cases. (65.8%). According to the OCT study, a decrease in the retinal nerve fiber layer (RNFL) was observed in the minority of the cases studied. (26.3%) in AO. The decrease in average valuesof the internal plexiform complex-ganglion cells was seen in a higher percentage (42.1%) and (44.7%) for OD and

OI respectively.

No modifications foundin the annual follow-up, both in the neuro-ophthalmological examination and in the diagnostic methods described above.

The use of steroids, immunosuppressants and biological therapy that these patients have received could influence the results of the neuro-ophthalmological examination, however, the most frequent conditions such as lens opacity and ocular hypertension were not found.

The study of contrast sensitivity (SC) in AO is shown in tables 5 and 6. In the initial evaluation, the average values behaved within the normal range and above it ((over 1.85) In most cases, however, a significant decrease (p=0.014) in the interval was found1.65-1.85andgreater than 1.85in the annual evolutionary follow-up (Table 5).

Initial contrast sensitivity	Contrast sensitivityannual evolutionary				Total
	Less than 1.35	1.35-1.65	1.65-1.85	Over 1.85	
Less than 1.35	1 (2.6%)	0(0.0)	0(0.0)	0(0.0)	1(2.6%)
1.35-1.65	2 (5.3%)	8 (21.1%)	0(0.0)	0(0.0)	10(26.3%)
1.65-1.85	0 (0.0)	3(7.9%)	2(5.3%)	0(0.0)	5(13.2%)
Over 1.85	0 (0.0)	0(0.0)	1(2.6%)	21(55.3%)	22(57.9%)
Total	3 (7.9%)	11((28.9%)	3(7.9%)	21(55.3%)	38(100.0%)

Marginal homogeneity test: p=0.014.
Table 5: Patients according to contrast sensitivity (Right eye).

Discussion

MS is a debilitating neurological disease in young adults, manifesting with a wide variety of symptoms: weakness, spasticity, urination disorders, cognitive impairment, fatigue, among others. Visual disturbances may be the first manifestation of the disease1-14. In the present study, there was a clear predominance of women in the fourth decade of life, which coincides with most of the published series1-11.

The Relapsing-Remitting clinical form was the most frequent in the present study with a short average evolution time (9.4 years). All the authors consulted agree that it is the most frequent and least severe clinical variant, both in its systemic and ocular manifestations [1,2,4,5]. The above explains the preservation of visual function in the initial examination and in the annual evolutionary follow-up of the psychophysical studies, however, in the SC studies, with the Pelli-Robson test, alterations were detected, with a decrease in the average values in the annual follow-up [10-14].

Most of the authors consulted6,89,10,11 state that this test is of low contrast, with high sensitivity and specificity to detect visual alterations, even subclinical, in patients with MS and preservation of BCVA, which is a high contrast test and may be normal in patients with a decrease in the retinal fiber layer and the optic nerve in the range of 40% or more [10].

In 2014, Soler et al.11 considered that contrast sensitivity changes according to the degree of impairment in patients with Multiple Sclerosis. Based on the above, they conducted research to determine the relationship between the contrast sensitivity test and the level of severity in 62 patients with MS. The aforementioned authors came to the following conclusion: Contrast sensitivity, analyzed by the Pelli-Robson test, decreases significantly as the level of severity increases in patients with Multiple Sclerosis.

The series studied in the present investigation was smaller (38 cases) with a predominance of the Relapsing-Remitting clinical form and only 9 cases with the progressive forms, two of these with the Secondarily Progressive form, which are the most serious and with a longer evolution time of the disease (19 years).Statistical analysis was not possible to arrive at conclusions as accurate as those of Soler, et al. [11,12] however, the author performed an individualized analysis with the most affected patients (9 cases) and obtained similar results, based on clinical evidence.

OCT is an objective test, several authors Garcia S, Soler García A, Ossa-Calderón C, Petzold A, et al. [11-14] agree on its importance for early determination of alterations in nervous structures and long-term visual prognosis in patients with MS.The alterations ofthenervous structure isThey begin tofrom thedecreaseof the thickness of CCG, ydafter the RNFL, so the involvement of the GCC may precede the visual deficit [1,13-15]. The magnitude of the thinning of the inner retinal layers seems to reflect quite accurately that of the underlying neurodegenerative processes at the level of the central nervous system.

In 2017, Petzold, et al. [14] published the results of a systematic review of the literature and subsequently a meta-analysis in patients with MS: The authors concluded the following: the difference between patients with multiple sclerosis compared to healthy subjects is found in the measurement of the peripapillary nerve fiber layer and the inner plexiform ganglion cell layer at the macular level. The magnitude of the thinning of the inner retinal layers seems to accurately reflect that of the underlying neurodegenerative processes at the level of the central nervous system.

In the present investigation, RNFL alterations were detected, but the highest percentage was found in the CCG, which coincides with the aforementioned publications.

There were no changes in the annual follow-up of the OCT. The authors of this study considered that a short-term evaluation was carried out, which can be modified over a longer period of time. In the bibliography consulted to date 7-15, no evolutionary studies of clinical examinations supported by diagnostic means in patients with MS have been found. In the study carried out by Gonzales, et al. [6] in patients with relapsing-remitting MS in a 6-year follow-up period, only BCVA and SC were analyzed.

It is concluded that in the series studied, women in the fourth decade of life with Relapsing-Remitting Multiple Sclerosis predominated and that the annual evolutionary follow-up of neuro-ophthalmological manifestations behaved in a stable manner, because no major variations were found in the clinical examination, in the diagnostic means and in the psychophysical studies, except for the significant decrease in Contrast Sensitivity.

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