Original Article

Ophthalmic Manifestations of Multiple Sclerosis: A Case Series

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Abstract

Purpose: This case series study reports the ophthalmic manifestations observed in multiple sclerosis (MS) patients and their diagnostic implications.
Patients and Methods: A cross-sectional case series included 15 MS patients from Negah Eye Hospital, Tehran, Iran. Each patient underwent a comprehensive ophthalmic evaluation, including best-corrected visual acuity (BCVA), pupillary response, ocular motility, slit-lamp biomicroscopy, fundoscopy, visual field testing, optical coherence tomography (OCT), and visual evoked potentials (VEP). Patient demographics, systemic conditions, and treatment history were also analyzed.
Results: Our study included 15 patients with MS (11 females, 4 males, aged 18–56 years). BCVA ranged from 20/20 to 20/100, with objective color vision impairment in 6 % of cases. Relative afferent pupillary defect was observed in 6 % of patients. Optic neuritis and visual disturbances were common findings. Optic nerve atrophy was observed in 20 % of patients. Ocular motility disturbances, including internuclear ophthalmoplegia and diplopia, were present in 20 %. Visual field abnormalities were detected in 26 %, while VEP testing showed delayed latency in all tested eyes. OCT results were normal in 20 % of cases. Uveitis was noted in 6 %, and 13 % had concurrent COVID-19 infection.
Conclusion: This case series highlights the diverse ophthalmic manifestations of MS, with optic neuritis and ocular motility disturbances as key findings. VEP and OCT provide valuable diagnostic insights, especially for subclinical cases. A comprehensive ophthalmic assessment is crucial in MS management to improve diagnosis and prevent unnecessary treatments.

Keywords: Multiple sclerosis; Optic Neuritis; Ophthalmic Manifestations; Neuro-Ophthalmology.

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Introduction

Multiple sclerosis (MS) is a chronic autoimmune disease characterized by inflammatory demyelination of the central nervous system (CNS), leading to a broad spectrum of neurological symptoms [1]. Among these, ophthalmic manifestations are often the earliest indicators of the disease, significantly impacting visual function and quality of life. Optic neuritis, ocular motility disturbances, uveitis, and retinal changes are frequently observed in MS patients, offering valuable insights into disease progression and response to treatment [2-5].

Early recognition of ophthalmic involvement in MS is critical for timely diagnosis and appropriate management [6]. Advanced imaging techniques, such as optical coherence tomography (OCT) and visual evoked potentials (VEP), have emerged as important tools for detecting both subclinical and overt visual pathway involvement [7,8]. Moreover, as disease-modifying therapies for MS evolve, understanding their potential ocular side effects is crucial for optimizing patient care [9].

In this case series study, we present the ophthalmic manifestations observed in a cohort of MS patients evaluated at an ophthalmology referral center. Our findings show the importance of comprehensive ophthalmic evaluation in MS management, particularly in differentiating true optic neuritis from other causes of visual impairment, guiding treatment decisions, and preventing unnecessary interventions.

Patients and Methods

This case series study was conducted at Negah Eye Hospital, Tehran, Iran. This study was approved by the ethics committee of the Ophthalmic Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran, with the approval number of IR.SBMU.ORC.REC.1399.014. All patients provided written informed consent before participation.

A total of 15 patients from January 2020 to August 2021 (11 females, 4 males) aged 18 to 56 years with a confirmed diagnosis of multiple sclerosis (MS) were included in the present study. Patients were referred from neurology clinics for ophthalmic evaluation based on either visual complaints or routine monitoring of MS-related ocular involvement. Patients were included if they had a confirmed MS diagnosis based on clinical symptoms and MRI evidence of demyelinating plaques. Those with significant ocular comorbidities unrelated to MS, such as advanced glaucoma or severe cataract, were excluded. Individuals with a history of ocular trauma, prior intraocular surgery affecting vision (except for refractive surgery), or severe cognitive impairment preventing cooperation with testing were also excluded.

Each patient underwent a detailed ophthalmic examination, including best-corrected visual acuity (BCVA) measurement using a Snellen chart, pupillary response assessment for relative afferent pupillary defect (RAPD), color vision testing, and ocular motility evaluation to detect abnormalities such as internuclear ophthalmoplegia and diplopia. Slit-lamp biomicroscopy was performed to assess the anterior segment for signs of uveitis or other abnormalities, while fundoscopic examination was conducted to evaluate the optic nerve for atrophy, pallor, or retinal changes. Intraocular pressure was measured using applanation tonometry.

Paraclinical tests were performed in selected patients to assess visual pathway involvement. Visual field testing was conducted to detect MS-associated defects. Optical coherence tomography (OCT) was used to measure the retinal nerve fiber layer (RNFL) and macular thickness. Visual evoked potential (VEP) testing was performed to assess latency and amplitude changes indicative of demyelination. Systemic data, including disease duration, history of MS relapses, concurrent medical conditions such as diabetes, hypertension, and thyroid disorders, and ongoing treatments, including high-dose steroid therapy and disease-modifying drugs, were recorded.

Descriptive statistics were used to summarize patient demographics, ophthalmic findings, and systemic associations. The frequency of ophthalmic abnormalities was expressed as percentages. No inferential statistical analysis was performed, as this study aimed to describe clinical observations rather than establish causal relationships.

Results

A total of 15 patients were enrolled in the study, including 11 females (73 %) and 4 males (26), with an age range of 18 to 56 years.

Best-corrected visual acuity (BCVA) ranged from 20/20 to 20/100. Subjectively, all patients reported decreased color vision in the eyes with reduced visual acuity; however, objective color vision disturbance was detected in only one case (6 %). Seven female patients (46 %) had significant refractive errors. Three male patients (20 %) reported diplopia or demonstrated ocular motility disturbances.

A relative afferent pupillary defect (RAPD) was observed in one patient (6 %). Optic nerve atrophy was present in three cases (20 %), and one patient (6 %) presented with uveitis. Other ocular and systemic findings included ocular hypertension, a history of refractive surgery, and amblyopia in three cases (20 %). One patient (6 %) had a history of seizures. Neurological symptoms such as gait imbalance, difficulty walking, or speech difficulties were reported in eight patients (53 %). Two patients (13 %) had concurrent COVID-19 infection at the time of examination, while two others (13 %) had hypothyroidism. One patient (6 %) had hypertension, and two (13 %) had diabetes.

At the time of the ophthalmic examination, all patients except five (patients 1, 5, 13, 14, and 15) were undergoing pulse steroid therapy. MRI findings confirmed the presence of demyelinating plaques in the central nervous system (CNS) or spinal cord in all cases (100 %). Visual evoked potential (VEP) testing was available in nine patients (60 %), showing delayed latency in all tested eyes, including those considered clinically normal. Optical coherence tomography (OCT) of the optic nerve and macula was performed in four patients (20 %) and showed normal results. Visual field testing, conducted in four patients (26 %), revealed abnormalities, though none were specific for optic neuritis. Clinical and paraclinical findings of the patients are summarized in tables 1 and 2.

Table 1: Clinical findings of patients entering the study

Number	Age	Gender	Visual acuity	Pupillary Reflex	Ocular motility disturbance	History of optic neuritis	Uveitis	Fundoscopy	Extra ocular findings	Accompanying systemic disease
1	36	F	10/10 ou	Very mild questionable APD OS	-	-	-	Normal	-	-
2	27	F	10/10 4/10	Normal	-	Positive for the left eye	-	Normal	-	-
3	18	F	10/10 ou	Normal	-	Positive for the left eye	-	Normal	-	Epilepsy
4	35	M	10/10 ou	Normal	Right Internuclear ophthalmoplegia	-	-	Temporal optic Nerve pallor	Gait imbalance	-
5	43	F	10/10 ou	Normal	Exophoria	-	-	Normal	Difficulty walking and urinating	-
6	37	F	10/10 5/10 Severe left anisometropic amblyopia	Normal	-	-	Left anterior uveitis	Normal	History of severe pain in the left ear improved with steroids	-
7	26	M	10/10 ou	Normal	-	Complains of episodes	-	Normal	Difficulty walking and talking	-
8	55	F	10/10 2/10	Left APD	-	In acute attack left eye	-	Normal	Seems to be only real acute optic neuritis case	-
9	30	F	10/10 ou	Anisocoria with suspicious mild right APD	-	History of Right Optic Neuritis	-	Normal	Sensory motor limbal disturbance	-
10	37	F	5/10 7/10	-	-	History of Optic Neuritis	-	Normal	upper and lower Limbal paresthesia	Hyperthyroidism + blood hypertension
11	34	M	10/10 ou	-	Left exotropia + Diplopia	-	-	Normal	Difficulty walking –imbalance - limbal sensory and motor problems	diabetes
12	39	M	10/10 8/10	Suspicious mild right APD	Vertical diplopia	-	-	Normal	Left inf limb weakness	History of PRK
13	44	F	10/10 ou	normal	-	-	-	Normal	Lower limb unrest headache	-
14	34	F	One meter finger counting ou	Normal	-	History of Optic Neuritis	-	Bilateral optic atrophy	-	COVID-19
15	35	F	10/10 ou	normal	-	-	-	Normal	Temporal pallor	Diabetes Thyroid problems COVID-19

ou: Oculus uterque; APD: afferent pupillary defect

Table 2: Paraclinical findings of patients entering the study

No	IOP	OCT	VF	VEP	MRI
1	10 30	Normal	Normal	-	+
2	Normal	Normal	Field defect	disturbed	+
3	Normal	-	Field defect	disturbed	+
4	Normal	-	-	-	+
5	Normal	Normal	-	disturbed	+
6	Normal	Normal	-	-	+
7	Normal	-	-	disturbed	+
8	Normal	Normal	Left field defect	disturbed	+
9	Normal	-	-	-	+
10	Normal	-	-	disturbed	+
11	Normal	-	-	disturbed	+
12	Normal	-	-	disturbed	+
13	Normal	Normal	Normal	disturbed	+
14	Normal	-	-	-	+
15	Normal	-	-	-	+

IOP: intraocular pressure; OCT: optical coherence tomography; VF: visual field; VEP: visual evoked potential; MRI: magnetic resonance tomography

Discussion

Decreased visual acuity (VA) was the primary complaint in 10 patients (66 %), of whom 8 (80 %) were female and 2 (20 %) were male. Among the patients with reduced VA, 70 % had refractive errors and were not wearing corrective glasses, with one patient having amblyopia. Notably, some patients were reluctant to acknowledge their pre-existing visual problems and had already undergone pulse steroid therapy prescribed by their neurologists. They were subsequently referred to our clinic due to a lack of treatment response. This highlights the necessity of a comprehensive ophthalmic examination and thorough history-taking before initiating high-dose steroid therapy [10].

In one patient, reduced vision was associated with uveitis (6 %).Two female patients who were hospitalized for COVID-19 infection, along with one male patient (20 %), exhibited optic atrophy or temporal pallor.

Visual field testing was performed in four patients (26 %). Among these, one had a normal result, one exhibited a monocular defect, and two showed bilateral but asymmetric visual

field abnormalities. Visual pathway may be affected in MS and the severity of visual field defects vary based on the location and extent of demyelination [11-13]. In previous studies, visual field abnormalities have been reported to be present in as high as 90 % of MS cases [14-16].

Pupillary reflex abnormalities are often used as a clinical indicator of optic neuritis [17]. However, their reliability is limited due to natural variations in pupil size and response speed among healthy individuals [18]. In our study, only one patient (case 8) exhibited a clear afferent pupillary defect (6 %). Another patient (case 6) had anisocoria, with a larger pupil on the asymptomatic side, but demonstrated normal light reflexes.

A significant observation in our study was the overdiagnosis of optic neuritis. Ten of our patients (66 %) were undergoing high-dose steroid therapy prescribed by their neurologists without a confirmed diagnosis of optic neuritis. This aligns with the findings of Stunkel et al., [19] who reported a 60 % overdiagnosis rate for optic neuritis. It is important to note that high-dose steroid therapy offers no long-term visual benefits and should not be administered indiscriminately in neuro-ophthalmic complaints without confirmatory testing.

Ocular motility disturbances were observed in three patients (20 %), all of whom were young males. One had internuclear ophthalmoplegia (INO), another reported vertical diplopia, and the third had a history of transient diplopia. Efferent pathway disorders are more commonly seen in progressive MS and are associated with a worse neurological prognosis. Damage to nerve fibers in the brainstem often leads to persistent ocular motility disturbances, even when optic neuritis resolves [20]. INO has been reported in 15-52 % patients with MS, with bilateral involvement being highly suggestive of MS [21].

One patient (6 %) in our study had anterior uveitis. This patient also had amblyopia in the same eye and had already received high-dose steroid therapy for presumed optic neuritis before undergoing an ophthalmic examination. Uveitis and periphlebitis occur in 0.4 to 26.9 % of MS cases and is estimated to be 10 times more prevalent than in the general population [22-27].

MRI remains the most valuable diagnostic tool for MS, providing insights into disease progression and lesion localization [28]. In our study, all patients had MRI-confirmed demyelinating plaques.

VEP testing was available in 60 % of our cases and showed delayed latency in all tested eyes, including those considered clinically normal. Studies suggest that VEP is a reliable indicator of subclinical optic nerve dysfunction among patient with MS [29].

OCT, which measures structural changes in the retina and optic nerve, is gaining importance in MS management [30-31]. Although OCT was performed in only 20% of our cases, the results were within normal limits.

One patient (case 14), who had bilateral partial optic atrophy and decreased vision to finger counting, was also infected with COVID-19. This patient exhibited confusion, raising the possibility of cortical blindness or adverse effects of MS disease-modifying therapies. High-dose steroids, frequently used in MS relapses, can cause central serous chorioretinopathy (SCR) and lead to retinal atrophy [32].

Conclusion

This case series highlights the diverse ophthalmic manifestations of MS, with optic

neuritis and ocular motility disturbances as key findings. VEP and OCT provide valuable diagnostic insights, especially for subclinical cases. A comprehensive ophthalmic assessment is crucial in MS management to improve diagnosis and prevent unnecessary treatments.

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.