A novel of optic neuritis: case series

Neurite óptica: série de casos

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ABSTRACT

Introduction: Optic neuritis is an inflammatory process of the optic nerve, considered the most common cause of subacute optic neuropathy in young adults. It can be classified as typical, meaning idiopathic or associated with multiple sclerosis, or atypical, associated with neuromyelitis optica spectrum disorder or even infectious or autoimmune cause. **Objectives:** Differentiate epidemiologically and anatomically typical and atypical optic neuritis. **Methods:** This is a descriptive, cross-sectional and observational study of 14 patients with a history of optic neuritis evaluated at the Hospital do Servidor Público Estadual de São Paulo – Iamspe. Patients with optic neuritis underwent a comprehensive ophthalmological examination, and retinal images were captured using optical coherence tomography. **Results:** Optic neuritis was more prevalent in females (78.57%) and in the left eye (71.43%), with a mean age of 51±15.88 years, with multiple sclerosis being the main etiology (42.86%). **Conclusion:** We demonstrated alignment of the present study with the literature regarding both epidemiological and anatomical data.

Keywords: Optic Neuritis; Multiple sclerosis; Epidemiology; Optical Coherence Tomography.

RESUMO

Introdução: A neurite óptica é um processo inflamatório do nervo óptico, considerada a causa mais comum de neuropatia óptica subaguda em adultos jovens. Pode ser classificada como típica, significando idiopática ou associada à esclerose múltipla, ou atípica, associada a distúrbio do espectro da neuromielite óptica ou mesmo de causa infecciosa ou autoimune. **Objetivos:** Diferenciar epidemiológica e anatomicamente neurite óptica típica e atípica. **Métodos:** Trata-se de um estudo descritivo, transversal e observacional de 14 pacientes com histórico de neurite óptica avaliados no Hospital do Servidor Público Estadual de São Paulo – Iamspe. Pacientes com neurite óptica foram submetidos a um exame oftalmológico completo e as imagens da retina foram capturadas por tomografia de coerência óptica. **Resultados:** A neurite óptica foi mais prevalente no sexo feminino (78,57%) e no olho esquerdo (71,43%), com média de idade de 51±15,88 anos, sendo a esclerose múltipla a principal etiologia (42,86%). **Conclusão:** Demonstramos alinhamento do presente estudo com a literatura tanto no que diz respeito aos dados epidemiológicos quanto aos anatômicos.

Descritores: Neurite Óptica; Esclerose múltipla; Epidemiologia; Tomografia de Coerência Óptica.

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Data de submissão: 10/12/2024
Data de aceite: 20/12/2024

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INTRODUCTION

Optic neuritis (ON) is an inflammatory process of the optic nerve, considered the most common cause of subacute optic neuropathy in young adults. It can be classified as typical, meaning idiopathic or associated with multiple sclerosis, or atypical, associated with neuromyelitis optica spectrum disorder or even infectious or autoimmune cause[1-2].

About 30% of patients with ON present at fundoscopy optic disc edema at onset, and the incidence is about 1.5 to 5.1 cases per 100,000 person-years[1, 3-7].

Optic neuritis associated with the neuromyelitis optica spectrum may or may not be mediated by aquaporin-4 (AQP4)-IgG antibodies (NMO) or associated with myelin oligodendrocyte glycoprotein (MOG)-related disease (MOGAD)[1, 8].

Autoimmune diseases, such as glial fibrillary acidic protein (GFAP)-associated autoimmunity and collapsin response mediator protein 5 (CRMP5) autoimmunity, as well as infectious diseases, should also be considered in patients with painless bilateral optic neuropathy associated with optic disc edema, especially if accompanied by neurological signs or symptoms[1].

This differentiation is important because of the different treatments and prognoses.

Chronically, optic neuritis may present persistent visual loss; relative afferent pupillary defect; Uhthoff phenomenon; optic atrophy; delay in the evoked visual potential and, in 85% of cases, characteristic thinning in the thickness of the retinal nerve fiber layer (RNFL)[2, 9-10].

Since the retina is a highly accessible structure for noninvasive imaging, optical coherence tomography (OCT) has been widely employed, using low-coherence light to capture high-resolution, cross-sectional images of the retinal and choroidal layers[11].

A finding well illustrated by OCT is the reduction in the thickness of the ganglion cell layer (GCL) and the inner plexiform layer (IPL) in multiple sclerosis (MS) even without previous ON, different from that documented by Walter et al., and this decrease correlates more significantly with visual function, being considered a more sensitive clinical structural marker than the thickness of the RNFL in early MS[2, 12-13].

The coherence tomography angiography (OCT-A) demonstrated reduction in peripapillary vascular density corresponding to areas of decreased RNFL, regardless of their etiology in chronic optic neuropathies, and appears to be a consequence of RNFL thinning, which tends to occur three to six months after ON[2,14-15].

This study aims to characterize the epidemiology of optic neuritis evaluated at the Hospital do Servidor Público Estadual de São Paulo – Iamspe (HSPE-Iamspe) and compare the findings of these patients with the anatomy, through OCT and OCT-A.

METHODS

The main outcome measures of this descriptive, cross-sectional, observational study were a comprehensive ophthalmological examination and OCT and OCT-A imaging. The study protocol was approved by the Research Ethics Committee of HSPE-Iamspe and conducted in accordance with national and international resolutions, and the Informed Consent Form (ICF) was obtained from patients before the start of treatment.

The inclusion criterion involved the definitive diagnosis of optic neuritis, and patients under 18 years of age, with visual acuity worse than 20/400 in both eyes (AO), refractive error with spherical equivalent above +/- 5 spherical diopters, previous ocular or neurological trauma, ocular media opacities, such as corneal leukoma and cataract > 2+/4+, concomitant ocular diseases, especially

glaucoma or suspected glaucoma, previous ocular or neurological surgery, and patients unable to perform the proposed examinations or remain in the study for any reason were excluded.

A comprehensive ophthalmic examination, which included an external eye examination, ocular motility assessment, biomicroscopy, refraction, and fundus assessment with indirect binocular ophthalmoscopy, was performed before OCT exam.

The data obtained in the study were summarized using descriptive statistics, such as mean, standard deviation, median, percentage, and presented in the form of tables, in addition to images from complementary OCT and OCT-A exams belonging to the research patients.

RESULTS

The fourteen patients in this sample underwent ophthalmological evaluation, OCT and OCT-A, 78.57% of whom were female, with a mean age of 51±15.88. Six cases (42.86%) presented with a diagnosis of optic neuritis as EM, four cases (28.57%) with no defined etiology, three cases related to NMO (21.43%) and one case secondary to MOGAD (7.14%). The majority presented with ON in the left eye (71.43%) – Chart 1.

Chart 1 - Demographic and diagnostic data of the patients evaluated.

Case	Age	Gender	Etiology of ON	Laterality of ON
1	52	F	MS	LE
2	44	F	MS	LE
3	81	F	NMO	LE
4	43	F	NMO	RE in 2019, LE in 2020
5	48	F	MS	RE
6	60	F	Unclear (AE)	LE
7	25	M	MS	RE
8	69	F	MS	LE
9	46	M	NMO	LE
10	44	F	Unclear (AE)	LE
11	68	F	MOGAD	BE in 2024, first LE
12	25	F	MS	LE
13	62	M	Unclear (AE)	LE
14	47	F	Unclear (AE)	LE

Legend: ON: optic neuritis MS: multiple sclerosis NMO: neuromyelitis optica MOGAD: Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease LE: left eye RE: right eye BE: both eyes

Chart 2 shows the descriptive statistical analysis based on the mean and standard deviation, in addition to the minimum and maximum values, for each variable studied.

Chart 2 - Descriptive statistics for each variable studied.

Variable	Mean	Standard Deviation	Minimum	Maximum
AGE	51.00	15.88	25	81
VA RE (LogMAR)	0.06	0.12	-0.1	0.4
VA LE (LogMAR)	0.07	0.12	-0.1	0.3
CENTRAL MACULAR THICKNESS	179.13	13.78	160	209
INFERIOR RNFL	107.00	30.39	71	174
SUPERIOR RNFL	105.75	38.24	48	171
NASAL RNFL	83.88	18.32	54	113
TEMPORAL RNFL	57.00	10.54	43	73
INFERIOR TEMPORAL GCL	39.56	12.13	22	61
SUPERIOR TEMPORAL GCL	36.19	8.88	24	54
INFERIOR NASAL GCL	37.50	11.12	26	60
SUPERIOR NASAL GCL	36.88	10.53	22	57
SUPERIOR GCL	41.56	12.15	26	64
INFERIOR GCL	40.88	13.39	21	64

Legend: VA: visual acuity RE: right eye LE: left eye RNFL: retinal nerve fiber layer GCL: ganglion cell layer

Chart 3 presents the descriptive statistical analysis of each variable studied in relation to the diagnosis of optic neuritis.

Chart 3 - Descriptive statistical analysis of each variable related to the diagnosis of optic neuritis.

Variable	Multiple Sclerosis	MOGAD	Neuromyelitis Optica	Undefined Etiology	P-value
Gender					
Female (F)	5 (45.5%)	1 (9.1%)	2 (18.2%)	3 (27.3%)	1.000
Male (M)	1 (33.3%)	0 (0.0%)	1 (33.3%)	1 (33.3%)	
Side of Neuritis					
Both Eyes (BE)	0 (0.0%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	0.116
Right Eye (RE)	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Left Eye (LE)	4 (40.0%)	0 (0.0%)	2 (20.0%)	4 (40.0%)	
Laterality					
Bilateral	0 (0.0%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	0.073
Unilateral	6 (50.0%)	0 (0.0%)	2 (16.7%)	4 (33.3%)	

Chart 4 shows statistically worse visual acuity in NMO and in neuritis without defined etiology (being worse in NMO). It also shows that the thickness of the superior nasal perimacular ganglion cell layer is statistically thinner in NMO and in neuritis without defined etiology (being worse in NMO).

Chart 4 - Descriptive statistical analysis of each variable related to the diagnosis of optic neuritis

Variable	Multiple Sclerosis	MOGAD	Neuromyelitis Optica	Undefined Etiology	P-value
Age	46.0 ± 21.2	68.0 ± 0.0	46.0 ± 19.0	53.5 ± 14.2	0.616
VA RE	0.01 ± 0.0	0.04 ± 0.0	0.14 ± 0.0	0.00 ± 0.0	0.166
VA LE	0.00 ± 0.1	0.06 ± 0.0	0.14 ± 0.0	0.18 ± 0.2	0.031
CMT	168.5 ± 12.5	206.0 ± 3.0	174.0 ± 5.0	178.5 ± 5.2	0.070
Inferior RNFL	134.5 ± 40.5	97.0 ± 2.0	87.5 ± 9.2	97.0 ± 49.2	0.566
Superior RNFL	129.0 ± 55.8	89.5 ± 3.5	75.5 ± 32.8	121.0 ± 32.0	0.238
Nasal RNFL	96.0 ± 23.2	72.0 ± 2.0	71.5 ± 13.5	90.0 ± 14.5	0.298
Temporal RNFL	65.0 ± 18.8	53.5 ± 4.5	52.5 ± 9.8	52.0 ± 13.8	0.782
Inferior Temporal GCL	43.5 ± 16.8	46.0 ± 10.0	38.0 ± 9.2	29.0 ± 17.2	0.630
Superior Temporal GCL	44.0 ± 15.5	32.5 ± 5.5	35.0 ± 2.2	32.0 ± 5.8	0.555
Inferior Nasal GCL	39.5 ± 17.0	42.5 ± 0.5	28.5 ± 2.5	30.0 ± 13.2	0.160
Superior Nasal GCL	41.5 ± 14.8	44.0 ± 1.0	28.5 ± 2.2	36.0 ± 4.8	0.017
Superior GCL	51.0 ± 21.8	48.0 ± 6.0	30.0 ± 8.8	36.5 ± 7.0	0.267
Inferior GCL	50.5 ± 25.5	45.5 ± 0.5	35.0 ± 7.2	33.0 ± 13.8	0.679

Legend: VA: visual acuity RE: right eye LE: left eye RNFL: retinal nerve fiber layer GCL: ganglion cell layer

There is no statistical significance when analyzing the type of neuritis and laterality of involvement with the patient's gender – Chart 5.

Chart 5 - Type of neuritis and laterality of involvement with the patient's gender.

Variable/Category	Female	Male	P-value
DIAGNOSIS			
Multiple Sclerosis	5 (45.5%)	1 (33.3%)	1.000
MOGAD	1 (9.1%)	0 (0.0%)	
Neuromyelitis Optica	2 (18.2%)	1 (33.3%)	
Undefined Etiology	3 (27.3%)	1 (33.3%)	
SIDE OF NEURITIS			
Both Eyes (BE)	4 (30.8%)	0 (0.0%)	0.472
Right Eye (RE)	1 (7.7%)	1 (33.3%)	
Left Eye (LE)	8 (61.5%)	2 (66.7%)	
LATERALITY			
Bilateral	4 (30.8%)	0 (0.0%)	0.529
Unilateral	9 (69.2%)	3 (100.0%)	

Chart 6 shows that the thickness of the inferior retinal nerve fiber layer is statistically thinner in women than in men, and the thickness of the superior perimacular ganglion cell layer is thinner in men.

Chart 6 - Thickness of the retinal nerve fiber layer and perimacular ganglion cell layer according to gender.

Variable	Female	Male	P-value
Age	48.0 ± 24.0	46.0 ± 18.5	0.544
VA RE	0.02 ± 0.0	0.10 ± 0.2	0.339
VA LE	0.00 ± 0.1	0.14 ± 0.2	0.576
Inferior RNFL	104.0 ± 50.0	76.0 ± 4.5	**0.015**
Superior RNFL	104.0 ± 43.0	63.0 ± 41.0	0.252
Nasal RNFL	89.0 ± 22.0	69.0 ± 24.0	0.788
Temporal RNFL	50.0 ± 21.0	57.0 ± 7.0	0.500
Inferior Temporal GCL	40.0 ± 13.0	25.0 ± 14.0	0.346
Superior Temporal GCL	35.0 ± 11.0	33.0 ± 6.5	0.346
Inferior Nasal GCL	37.0 ± 14.0	28.0 ± 4.0	0.137
Superior Nasal GCL	39.0 ± 9.0	26.0 ± 2.5	0.069
Superior GCL	46.0 ± 17.0	27.0 ± 3.5	**0.031**
Inferior GCL	45.0 ± 20.0	31.0 ± 4.5	0.106

Legend: VA: visual acuity RE: right eye LE: left eye RNFL: retinal nerve fiber layer GCL: ganglion cell layer

Figures 1 to 4 show the changes found in the retinal nerve fiber layer and in the perimacular ganglion cell layer with their corresponding angiographic findings.

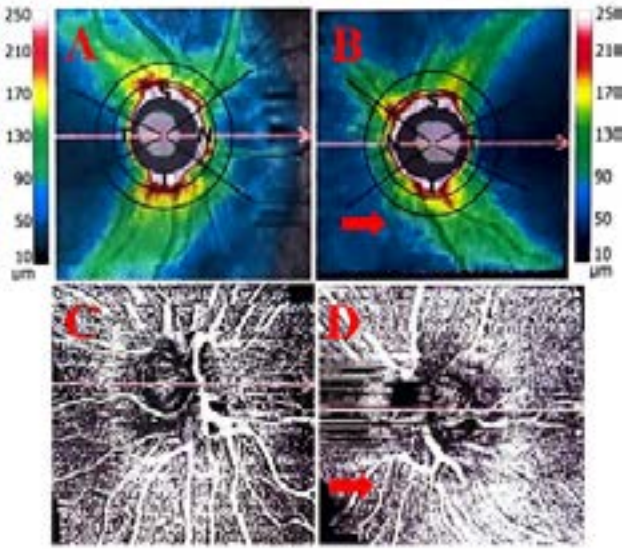


Figure 1 - Study patient showing the changes found in the peri-optic disc retinal nerve fiber layer and its corresponding OCT-A.

A, B: Mapa de espessura da CFNR em olho direito (OD) (A) e em olho esquerdo (OE) (B). Há redução mais localizada em topografia nasal inferior em OE (seta). **C, D:** OCT-A do PCPR em OD (C) e em OE (D). A despeito de artefato de movimento e falha na captação, nota-se redução da densidade capilar peripapilar correspondente à área de afinamento da CFNR em OE (seta), quando comparada ao OD.

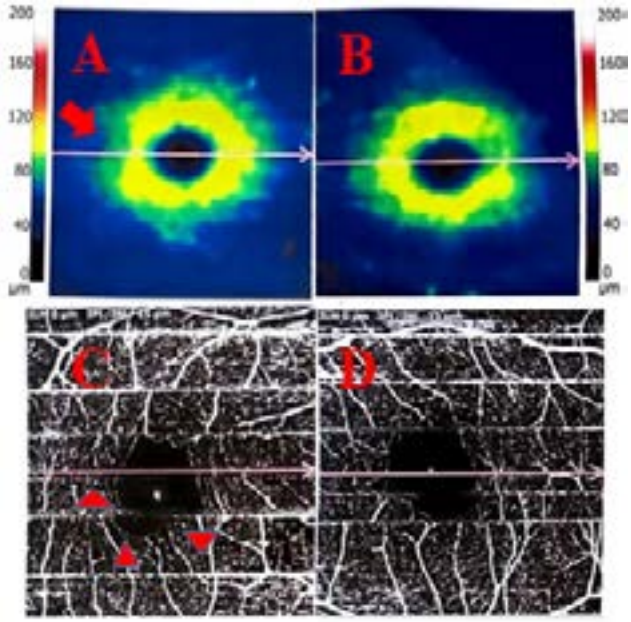


Figure 2 - Study patient showing the changes found in the perimacular ganglion cell layer and its corresponding OCT-A. **A, B:** Mapa de espessura da CCG e CPI em OD (A), onde nota-se uma redução (seta), e em OE (B). **C, D:** OCT-A do PCS em OD (C) e em OE (D) com artefato de movimento em ambos os olhos (AO). Há atenuação da rede capilar próximo a zona avascular foveal (ZAF) em OD (pontas de seta).

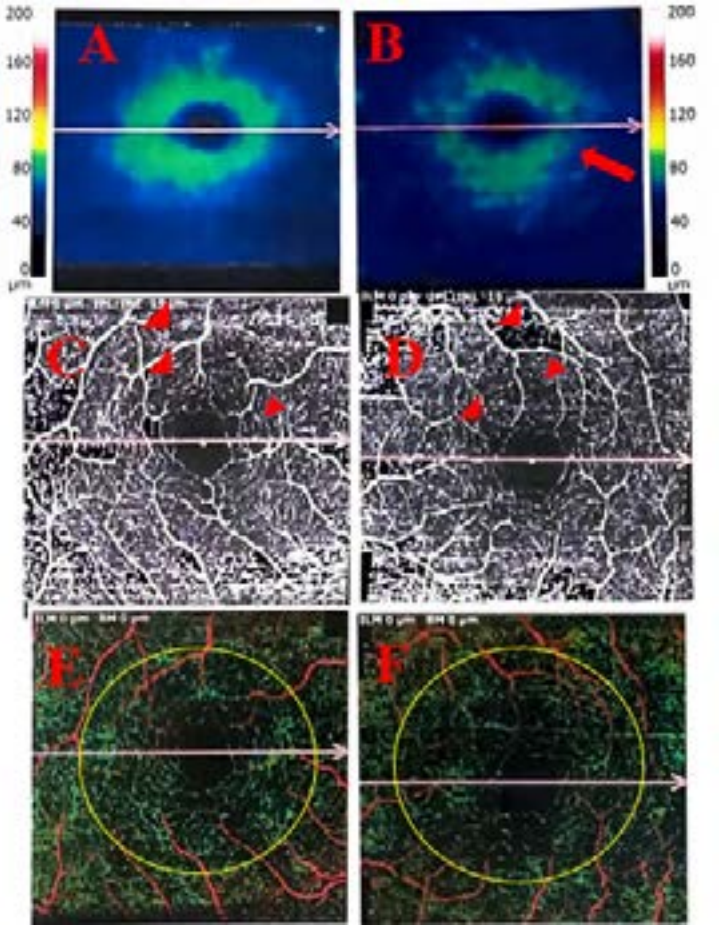


Figure 3 - Study patient showing the changes found in the perimacular ganglion cell layer and its corresponding OCT-A. **A, B:** Mapa de espessura da CCG e CPI em OD (A) e em OE (B), mostrando importante redução em OE (seta). **C, D:** OCT-A do PCS da retina em OD (C) e em OE (D), que demonstra uma restrição na distribuição dos capilares em OE, quando comparada ao OD (pontas de seta). **E, F:** Mapa da OCT-A com codificação de profundidade em OD (E) e em OE (F), reiterando a diminuição difusa da vascularização em OE em relação ao OD (círculos).

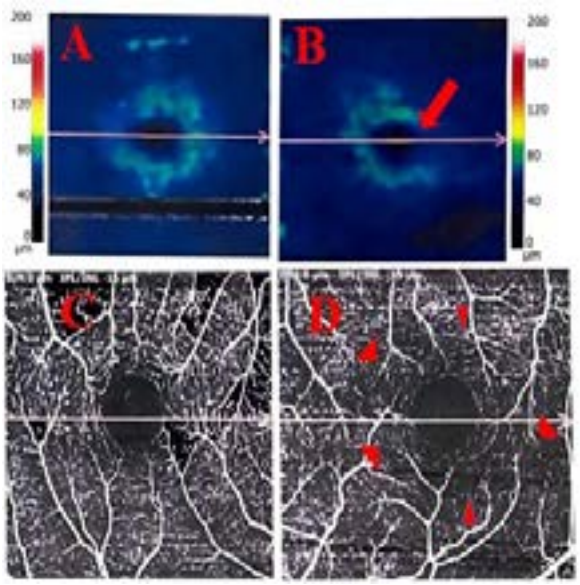
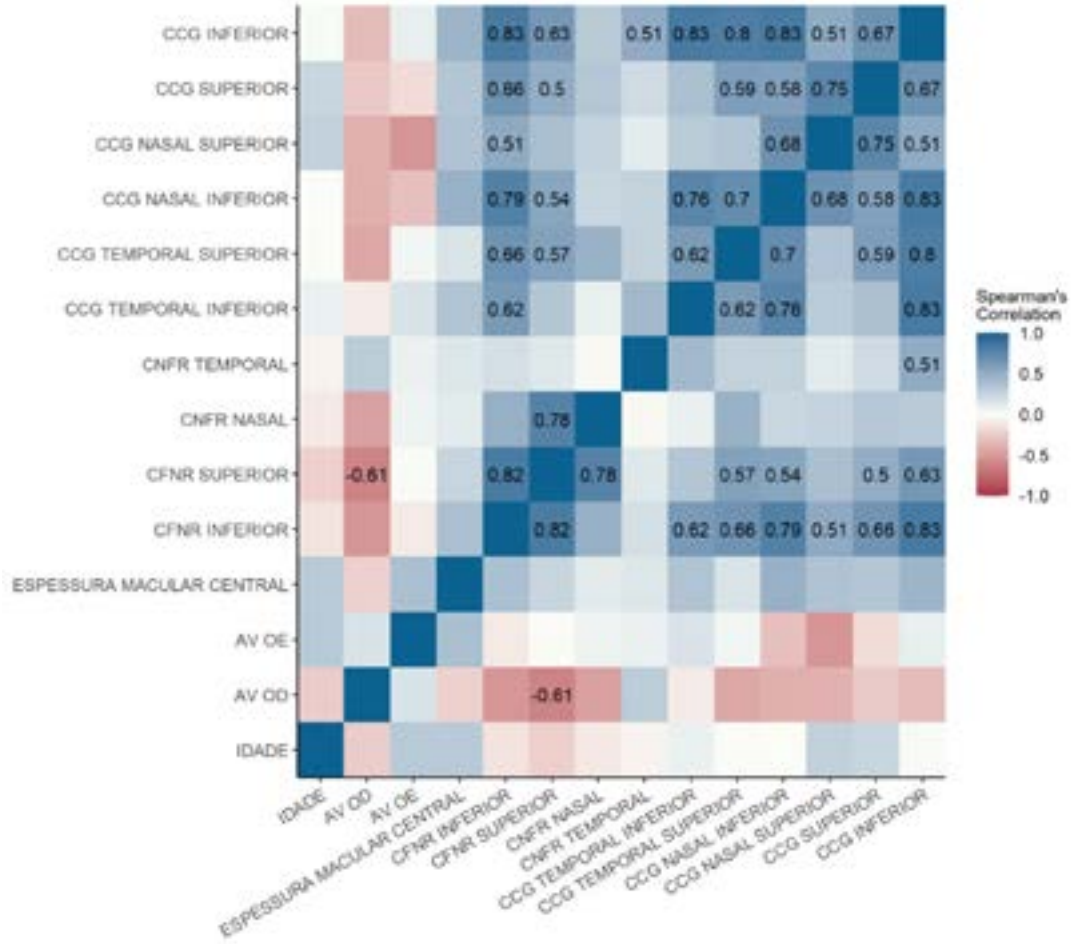


Figure 4 - Study patient showing the changes found in the perimacular ganglion cell layer and its corresponding OCT-A. **A, B:** Mapa de espessura da CCG e CPI em OD com falha de captação (A) e em OE (B). Há redução mais evidente em OE (seta) **C, D:** OCT-A do PCS da retina em OD (C) e em OE (D), que apresenta atenuação da rede capilar em OE - lado acometido (pontas de seta).

In table 1 we find Spearman's correlation showing the relationship between two variables based on the dependence between the positions of each one.

Table 1 - Spearman correlation between the variables studied.



DISCUSSION

Multiple sclerosis is the main cause of optic neuritis, more frequently affecting women and with a unilateral tendency, with the left eye being the most involved, as shown in Charts 3 and 5.

Although less frequent, cases related to MOGAD and NMO were more severe and tended to be bilateral[16-17]. This trend can be observed in Chart 2, where the two bilateral cases in the study were associated with both conditions.

Previously, NMO was defined as a monophasic episode characterized by bilateral and simultaneous optic neuritis. It is now recognized that the NMO spectrum manifests as a recurrent disease, including unilateral cases separated by weeks or even years. Early and accurate diagnosis is crucial, considering that NMO has a worse prognosis than multiple sclerosis and requires specific therapeutic approaches[17]. Within five years, about 50% of patients lose functional vision in at least one eye[18].

The study found, with statistical significance, a greater involvement of the retinal nerve fiber layer (RNFL) and ganglion cells in some quadrants in men. There are still few studies in the literature supporting this finding, but it is believed that late diagnosis in men, hormonal factors, and predisposition to vascular changes may be associated[19].

Previous studies have observed differences in magnetic resonance imaging (MRI) findings between men and women, suggesting that sex hormones influence the modulation of brain damage in multiple sclerosis. Men with MS tend to present more destructive lesions, and the degree of brain damage is associated with higher estradiol levels[19].

A study conducted with patients from the United Kingdom and Japan showed that men were significantly more likely than women to develop permanent visual impairment over time [20]. This correlates the more significant reduction in RNFL and ganglion cell layer (GCL) thickness in men with their final visual acuity.

It is known that optic neuritis leads to a reduction in RNFL thickness [9-10, 14-15, 21-22]. This reduction is linked to a decrease in the superficial capillary plexus (SCP) (an important finding in OCT-A for monitoring chronic diseases) [14-15], as illustrated by the representative case of a 44-year-old woman (Figure 1).

In addition to the classic changes in the RNFL and SCP, optic neuritis also leads to a reduction in GCL and inner plexiform layer (IPL) density, as well as in the deep capillary plexus (DCP) of the retina, as supported by Figures 2, 3, and 4 [2].

CONCLUSION

We demonstrated alignment of the present study with the literature regarding both epidemiological and anatomical data.

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