

Characteristics of double seronegative optic neuritis in tertiary center in Brazil: Neuro-ophthalmological and clinical features

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INTRODUCTION

Optic neuritis is the leading cause of visual loss in young adults (18-45 years), often associated with Multiple Sclerosis (MS). Neuromyelitis Optica Spectrum Disorder (NMOSD) and Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), can also present with optic neuritis.¹

Clinically, it is characterized by low visual acuity, generally unilateral, color vision deficiency, eye pain that worsens with eye movement, and an afferent pupillary defect. The visual prognosis is usually favorable, with visual recovery occurring within 3-12 weeks, and less than 10% of patients retaining visual acuity (VA) of 20/50 or worse. These characteristics define typical optic neuritis.²

This retrospective study, conducted at a Brazilian tertiary center, investigated 40 patients with double seronegative optic neuritis (negative anti-MOG and anti-AQP4 antibodies), aiming to describe their clinical, radiological and ophthalmological profile.

METHODS

The study assessed epidemiological data, brain magnetic resonance imaging (MRI), analysis of cerebrospinal fluid (CSF), prognosis, recurrence rate and therapeutic failures throughout follow-up. The neuro-ophthalmological evaluation included visual acuity (VA), fundoscopy, optical coherence tomography (OCT), computerized perimetry, and Visual Evoked Potential (VEP).

RESULTS

The sample (40 patients) was predominantly female (75%) and white (68%), with a mean age of symptom onset at 38 years. The course was acute in 63% cases, and unilateral involvement was noted in 80%. Visual blurring predominated among the initial symptoms (45%), with a high frequency of association with eye movement pain (68%) and optic nerve edema (58%).

MRI were normal in 20%, and revealed hyperintensity, edema, and gadolinium enhancement mainly in the canicular segment of the nerve, with 30% chiasmatic involvement and 5.1% optic tract involvement. Oligoclonal bands in CSF were found in 10% of cases. Eight patients had increased cellularity in the CSF and only 4 cases of elevated proteins.

OCT reported most atrophy in the ganglion cell and inner plexiform layers (GCL-IPL), with an increase in the inner nuclear layer (INL), probably due to retraction.

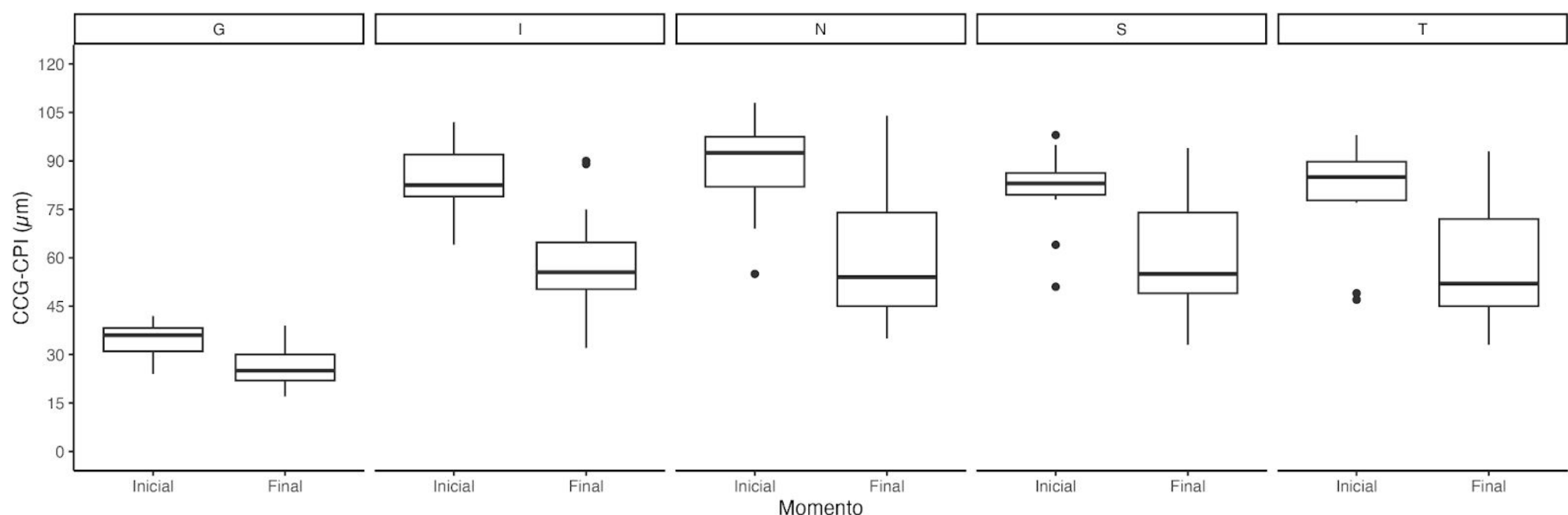


Figure 1 - Initial and final thickness of the ganglion cell layer (GCL) and the inner plexiform layer (IPL)

Fourteen patients had a VA outcome $\geq 20/200$. Half of the patients were treated chronically, with a good response to azathioprine and therapeutic failure in 15%. Recurrences occurred in 29% of patients, more frequently in whom had worse visual outcomes.

DISCUSSION

Visual blurring predominated among the initial symptoms (45%), corroborating the classic presentation of optic neuritis.¹

The rare occurrence of bilateral optic neuritis and longitudinally extensive lesions, suggests a less aggressive presentation. On the other hand, involvement of the optic chiasm, recorded in 30% of patients, is consistent with what is described in the literature for optic neuritis associated with NMOSD.³

The evidence suggests that the GCL is more susceptible to early atrophy in optic neuritis compared to the RNFL, highlighting its potential as a biomarker to monitor disease progression and visual outcomes.⁴

A worse outcome in visual acuity is associated with the absence of treatment or delays in initiating it. The main medications that effectively controlled the disease are the same ones prescribed in cases of NMOSD and MOGAD.⁵

CONCLUSION

We concluded that double seronegative optic neuritis has its own characteristics that differ from MS and resemble neuritis caused by NMOSD and MOGAD. The demographic data, clinical symptoms, MRI, CSF, and drug therapies were similar to MOGAD. However, chiasmatic involvement and prognosis were similar to NMOSD.

LITERATURE

1. Toosy AT, Mason DF, Miller DH. Optic neuritis. *The Lancet Neurology*. 2014;13(1):83-99.
2. Petzold A, Fraser CL, Abegg M, et al. Diagnosis and classification of optic neuritis. *Lancet Neurol*. 2022;21(12):1120-1134.
3. Carnero Contentti E, Delgado-García G, López PA, et al. Acute optic nerve lesions in first-ever NMOSD-related optic neuritis using conventional brain MRI: A Latin American multicenter study. *Mult Scler Relat Disord*. 2020;46:102558.
4. Syc SB, Saidha S, Newsome SD, Ratchford JN, Levy M, Ford E, Crainiceanu CM, Durbin MK, Oakley JD, Meyer SA, Frohman EM, Calabresi PA. Optical coherence tomography segmentation reveals ganglion cell layer pathology after optic neuritis. *Brain*. 2012;135(Pt 2):521-33.
5. Kemchoknatee P, Singhakul C, Arjkonharn N, Chainakul M, Tangon D, Srisombut T. A 10-Year Single-Center Study of the Clinical Characteristics of Optic Neuritis-Related NMOSD, MS, and Double Seronegative Optic Neuritis, Together with Factors Predicting Visual Outcomes. *Vision*. 2023; 7(1):16.