NMOSD (Doença do Especto da NMO): quais os sinais e sintomas

Thiago Fukuda PhD

Médico Neurologista

TELESSAÚDEBA

SUS

SESAB 100 anos

GOVERNO DO ESTADO BAHIA SECRETARIA DA SAÚDE

GOVERNO PRESENTE FUTURO PRA GENTE

Agenda da Aula

- Aspectos Históricos
- Epidemiologia no Mundo e no Brasil
- Fisiopatologia da NMO
- Principais sinais de sintomas (Síndromes típicas)
- Critérios diagnósticos
- Por que é importante fazer o diagnóstico de NMO?

Aspectos históricos da DENMO

Figura ilustrativa criada por IA (ChatGPT 4.0)

Aspectos históricos da DENMO

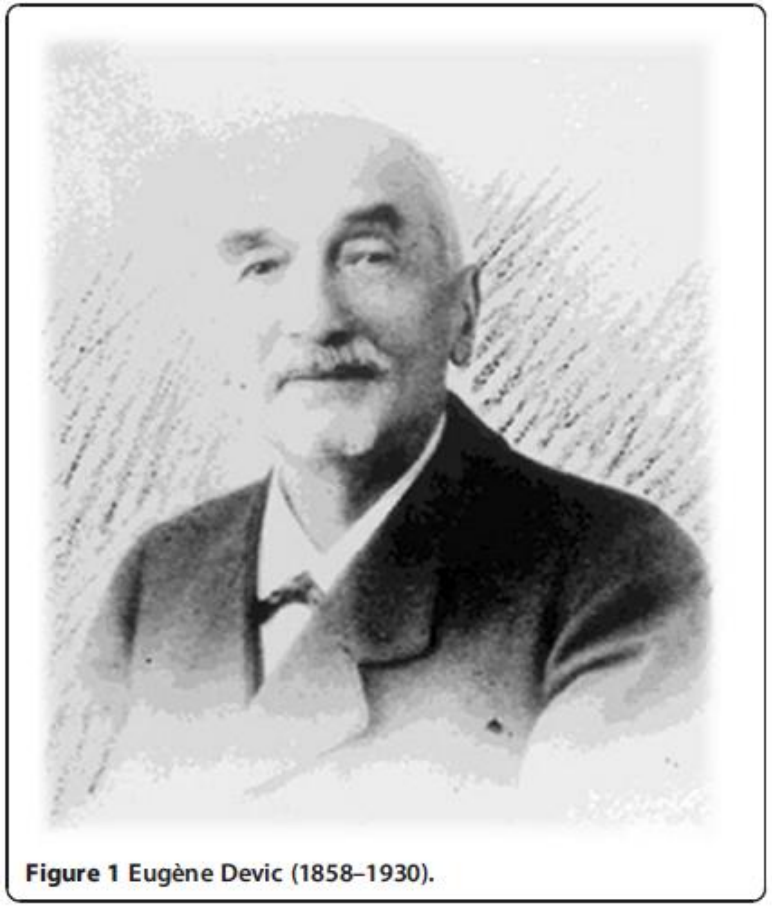
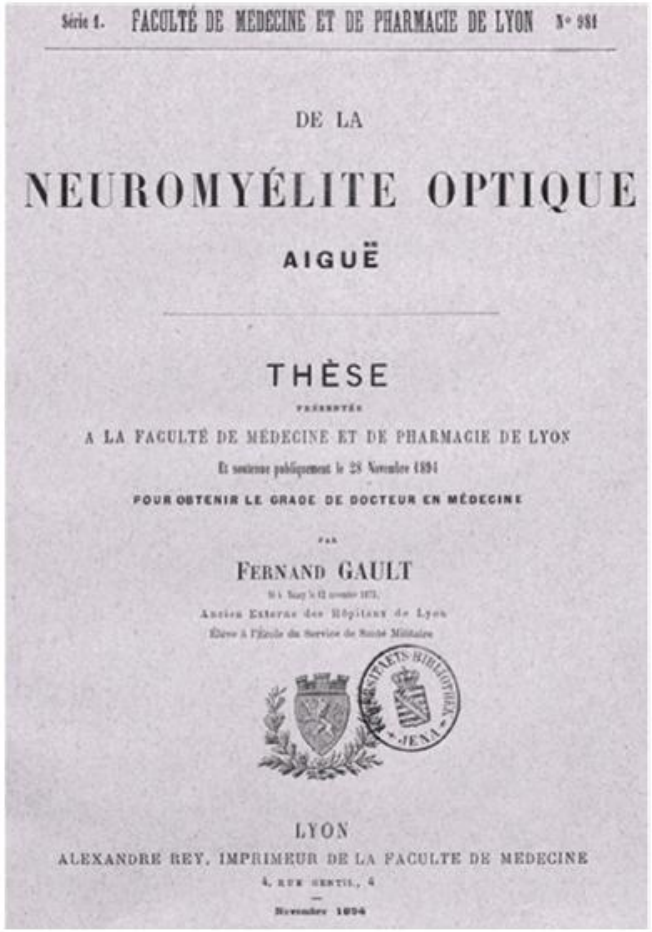


Figure 1 Eugène Devic (1858–1930).



Série t. FACULTÉ DE MEDECINE ET DE PHARMACIE DE LYON N° 981

DE LA

NEUROMYÉLITE OPTIQUE

AIGUË

THÈSE

PRÉSENTÉE

A LA FACULTÉ DE MÉDECINE ET DE PHARMACIE DE LYON

Et soutenue publiquement le 28 Novembre 1894

POUR OBTENIR LE GRADE DE DOCTEUR EN MÉDECINE

PAR

FERNAND GAULT

Né à Sury le 12 octobre 1871.

Ancien Externe des Hôpitaux de Lyon

Élève à l'École du Service de Santé Militaire

LYON

ALEXANDRE REY, IMPRIMEUR DE LA FACULTE DE MEDECINE

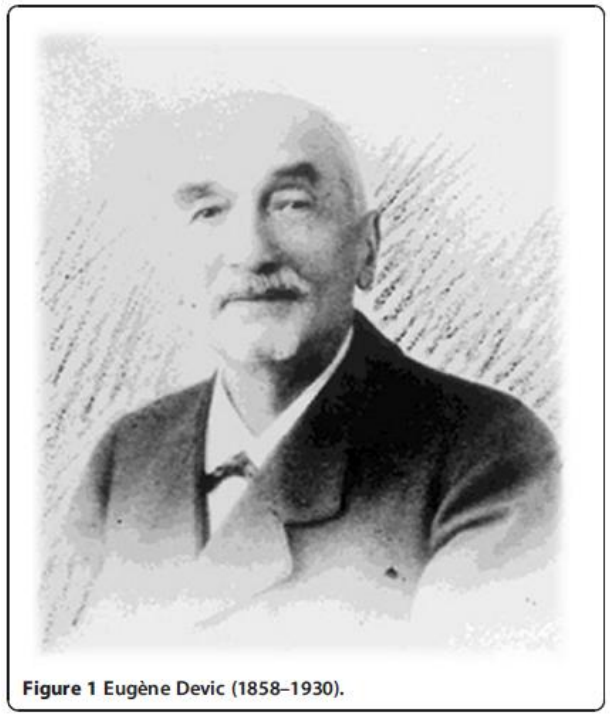
4, RUE GENTIL, 4

Novembre 1894

1894- (França) Eugene Devic e seu estudante Fernand Gault

Jarius S, Wildemann B. The history of neuromyelitis optica. J Neuroinflammation. 2013;10(1):1–12

Aspectos históricos da DENMO



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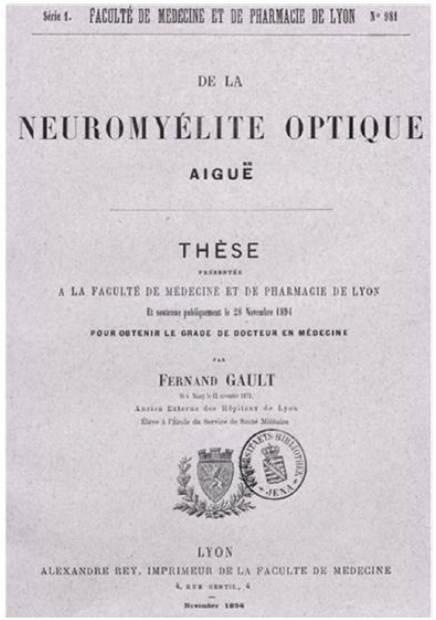

Série t. FACULTÉ DE MÉDECINE ET DE PHARMACIE DE LYON N° 981

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Novembre 1894

1894 (França)

Devic e seu estudante Fernand Gault

1930 -> Russel Brain

NMO e EM - A mesma doença ?

"...the clinical and pathological differences between neuromyelitis optica and disseminated sclerosis appear to be differences of acuteness and intensity only..."

Jarius S, Wildemann B. The history of neuromyelitis optica. J Neuroinflammation. 2013;10(1):1–12

Aspectos históricos da DENMO

2004 -> Anti-AQP4-IgG: Síndromes distintas

Dra.Vanda Lennon (Mayo Clinic)

Articles

A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis

Lancet 2004; 364: 2106–12

Vanda A Lennon, Dean M Wingerchuk, Thomas J Kryzer, Sean J Pittock, Claudia F Lucchinetti, Kazuo Fujihara, Ichiro Nakashima, Brian G Weinshenker

Department of Neurology, Mayo Clinic Rochester, Rochester, MN, USA (Prof V A Lennon MD, S J Pittock MD, C F Lucchinetti MD, Prof B G Weinshenker MD); Department of Neurology, Mayo Clinic Scottsdale, Scottsdale, AZ, USA (D M Wingerchuk MD); Departments of Immunology (Prof V A Lennon) and Laboratory Medicine and Pathology (Prof V A Lennon, T J Kryzer MS, S J Pittock), Mayo Clinic College of Medicine, Rochester, MN, USA; and Department of Neurology, Tohoku University School of Medicine, Sendai 980-8574, Japan (K Fujihara MD, I Nakashima MD)

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Summary

Background Neuromyelitis optica is an inflammatory demyelinating disease with generally poor prognosis that selectively targets optic nerves and spinal cord. It is commonly misdiagnosed as multiple sclerosis. Neither disease has a distinguishing biomarker, but optimum treatments differ. The relation of neuromyelitis optica to optic-spinal multiple sclerosis in Asia is uncertain. We assessed the capacity of a putative marker for neuromyelitis optica (NMO-IgG) to distinguish neuromyelitis optica and related disorders from multiple sclerosis.

Methods Indirect immunofluorescence with a composite substrate of mouse tissues identified a distinctive NMO-IgG staining pattern, which we characterised further by dual immunostaining. We tested masked serum samples from 102 North American patients with neuromyelitis optica or with syndromes that suggest high risk of the disorder, and 12 Japanese patients with optic-spinal multiple sclerosis. Control patients had multiple sclerosis, other myelopathies, optic neuropathies, and miscellaneous disorders. We also established clinical diagnoses for 14 patients incidentally shown to have NMO-IgG among 85 000 tested for suspected paraneoplastic autoimmunity.

Findings NMO-IgG outlines CNS microvessels, pia, subpia, and Virchow-Robin space. It partly colocalises with laminin. Sensitivity and specificity were 73% (95% CI 60–86) and 91% (79–100) for neuromyelitis optica and 58% (30–86) and 100% (66–100) for optic-spinal multiple sclerosis. NMO-IgG was detected in half of patients with high-risk syndromes. Of 14 seropositive cases identified incidentally, 12 had neuromyelitis optica or a high-risk syndrome for the disease.

Interpretation NMO-IgG is a specific marker autoantibody of neuromyelitis optica and binds at or near the blood-brain barrier. It distinguishes neuromyelitis optica from multiple sclerosis. Asian optic-spinal multiple sclerosis seems to be the same as neuromyelitis optica.

Introduction

Neuromyelitis optica (Devic's syndrome) is a severe idiopathic inflammatory demyelinating disease that selectively affects optic nerves and spinal cord, typically spares the brain, and generally follows a relapsing course.[1–4] Within 5 years, 50% of patients lose functional vision in at least one eye or are unable to walk independently. In North America, the proportion of non-white individuals is higher among patients with neuromyelitis optica than among those with classic multiple sclerosis.[5,6] In Asia, an optic-spinal form of multiple sclerosis is a common inflammatory demyelinating disease. It accounts for 15–40% of multiple sclerosis cases in Japan.[7,8] Is the Asian optic-spinal form of multiple sclerosis the same entity as neuromyelitis optica seen in western populations?

When fully developed, neuromyelitis optica can be distinguished from multiple sclerosis by a combination of clinical, neuroimaging, and spinal-fluid findings.[3] Characteristics typical of neuromyelitis optica include episodic myelitis—commonly severe and frequently accompanied by paroxysmal tonic spasms—with longitudinally extensive spinal-cord lesions spanning three or more vertebral segments, absence of clinical evidence of brain involvement, and usually lack of multiple-sclerosis-type lesions on MRI of the brain.[3] During acute attacks, the spinal fluid contains inflammatory cells but there is no evidence of intrathecal IgG synthesis (panel). However, many patients showing initial symptoms of neuromyelitis optica are diagnosed with multiple sclerosis. Neither disorder has a specific diagnostic marker, but the prognosis and optimum treatments for the two diseases differ. Immunosuppressive drugs (eg, azathioprine and corticosteroids) are regarded as the best treatment for neuromyelitis optica,[9] whereas immunomodulatory treatments (eg, interferon beta and glatiramer acetate) are presently recommended for early treatment of multiple sclerosis.[3] When severe exacerbations of myelitis do not respond to corticosteroid therapy, plasmapheresis is more beneficial for patients with neuromyelitis optica than for those with multiple sclerosis.[10]

Early diagnosis and treatment are very important to reduce the morbidity of neuromyelitis optica. Early use of appropriate immunosuppressive therapy would be justified if this disorder could be reliably distinguished from multiple sclerosis at the initial onset of optic neuritis or transverse myelitis, before progression and fulfilment of all clinical diagnostic criteria. We describe a newly identified IgG autoantibody (NMO-IgG) that localises to the blood-brain barrier and seems to be a specific serological marker for neuromyelitis optica. We have assessed the diagnostic accuracy of this autoantibody for neuromyelitis optica and other high-risk syndromes that could lead to a diagnosis of the disorder (eg, longitudinally extensive transverse myelitis or recurrent optic neuritis).

Aspectos históricos da DENMO

2004 -> Anti-AQP4-IgG: Síndromes distintas

A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis

Lancet 2004; 364: 2106–12 Vanda A Lennon, Dean M Wingerchuk, Thomas J Kryzer, Sean J Pittock, Claudia F Lucchinetti, Kazuo Fujihara, Ichiro Nakashima, Brian G Weinshenker

Conceito Unificado em 2015

"Doença do Espectro da Neuromielite" Optica"

VIEWS & REVIEWS

International consensus diagnostic criteria for neuromyelitis optica spectrum disorders

OPEN

Dean M. Wingerchuk, MD, FRCP(C)
Brenda Banwell, MD, FRCP(C)
Jeffrey L. Bennett, MD, PhD
Philippe Cabre, MD
William Carroll, MD
Tanuja Chitnis, MD
Jérôme de Seze, MD
Kazuo Fujihara, MD
Benjamin Greenberg, MD
Anu Jacob, MD
Sven Jarius, MD
Marco Lana-Peixoto, MD
Michael Levy, MD, PhD
Jack H. Simon, MD
Silvia Tenembaum, MD
Anthony L. Traboulsee, MD, FRCP(C)
Patrick Waters, PhD
Kay E. Wellik, MLS
Brian G. Weinshenker, MD, FRCP(C)

Editorial, page 118

Supplemental data at Neurology.org

ABSTRACT

Neuromyelitis optica (NMO) is an inflammatory CNS syndrome distinct from multiple sclerosis (MS) that is associated with serum aquaporin-4 immunoglobulin G antibodies (AQP4-IgG). Prior NMO diagnostic criteria required optic nerve and spinal cord involvement but more restricted or more extensive CNS involvement may occur. The International Panel for NMO Diagnosis (IPND) was convened to develop revised diagnostic criteria using systematic literature reviews and electronic surveys to facilitate consensus. The new nomenclature defines the unifying term NMO spectrum disorders (NMOSD), which is stratified further by serologic testing (NMOSD with or without AQP4-IgG). The core clinical characteristics required for patients with NMOSD with AQP4-IgG include clinical syndromes or MRI findings related to optic nerve, spinal cord, area postrema, other brainstem, diencephalic, or cerebral presentations. More stringent clinical criteria, with additional neuroimaging findings, are required for diagnosis of NMOSD without AQP4-IgG or when serologic testing is unavailable. The IPND also proposed validation strategies and achieved consensus on pediatric NMOSD diagnosis and the concepts of monophasic NMOSD and opticospinal MS. *Neurology*® 2015;85:177–189

GLOSSARY

ADEM = acute disseminated encephalomyelitis; **AQP4** = aquaporin-4; **IgG** = immunoglobulin G; **IPND** = International Panel for NMO Diagnosis; **LETM** = longitudinally extensive transverse myelitis lesions; **MOG** = myelin oligodendrocyte glycoprotein; **MS** = multiple sclerosis; **NMO** = neuromyelitis optica; **NMOSD** = neuromyelitis optica spectrum disorders; **SLE** = systemic lupus erythematosus; **SS** = Sjögren syndrome.

Neuromyelitis optica (NMO) is an inflammatory CNS disorder distinct from multiple sclerosis (MS).[1,2] It became known as Devic disease following a seminal 1894 report.[3,4] Traditionally, NMO was considered a monophasic disorder consisting of simultaneous bilateral optic neuritis and transverse myelitis but relapsing cases were described in the 20th century.[5] MRI revealed normal brain scans and ≥3 vertebral segment longitudinally extensive transverse myelitis lesions (LETM) in NMO.[6–8] The nosology of NMO, especially whether it represented a topographically restricted form of MS, remained controversial.

A major advance was the discovery that most patients with NMO have detectable serum antibodies that target the water channel aquaporin-4 (AQP4–immunoglobulin G [IgG]),[9,10] are highly specific for clinically diagnosed NMO, and have pathogenic potential.[7–8,10] In 2006, AQP4-IgG serology was incorporated into revised NMO diagnostic criteria that relaxed clinical

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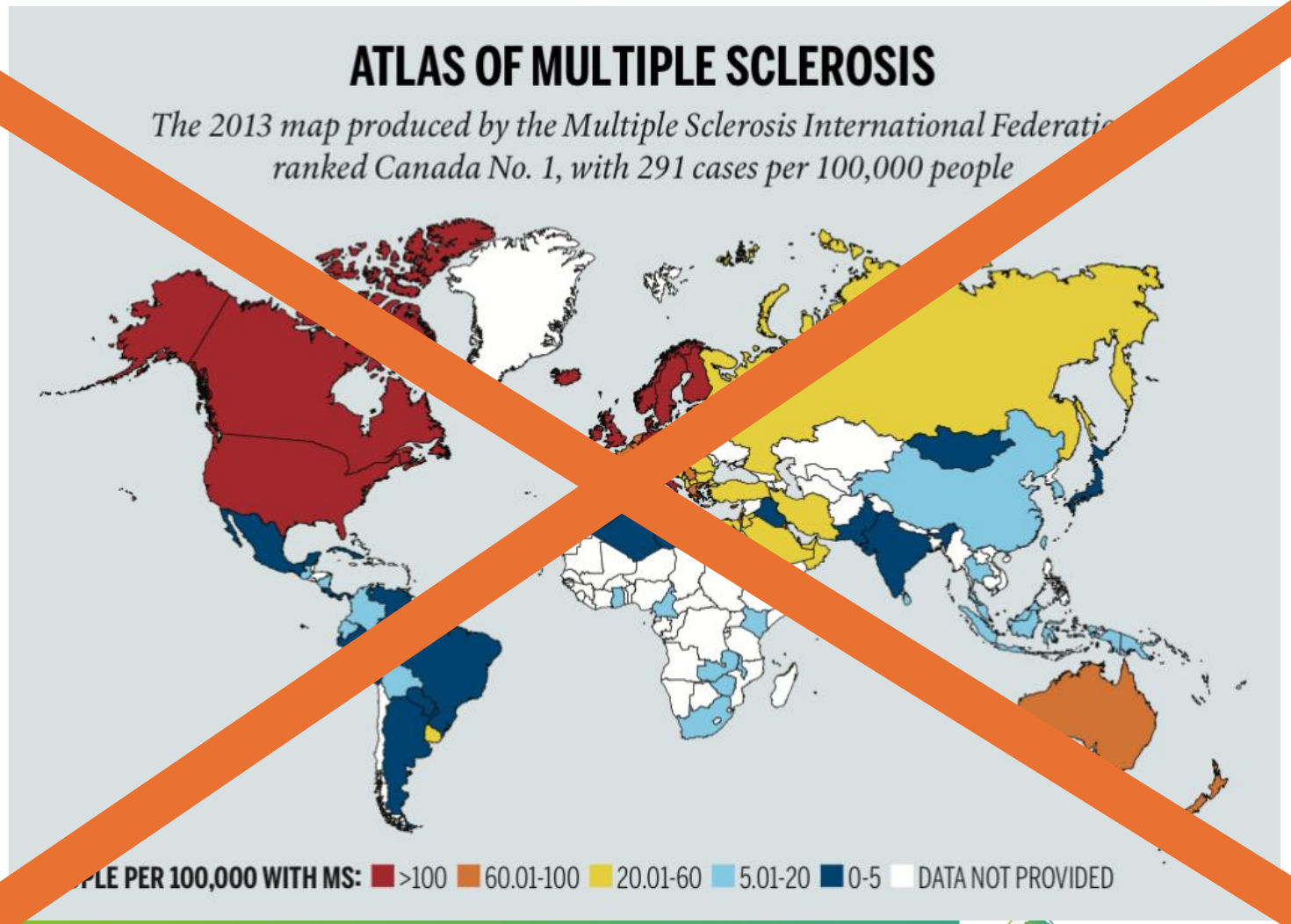
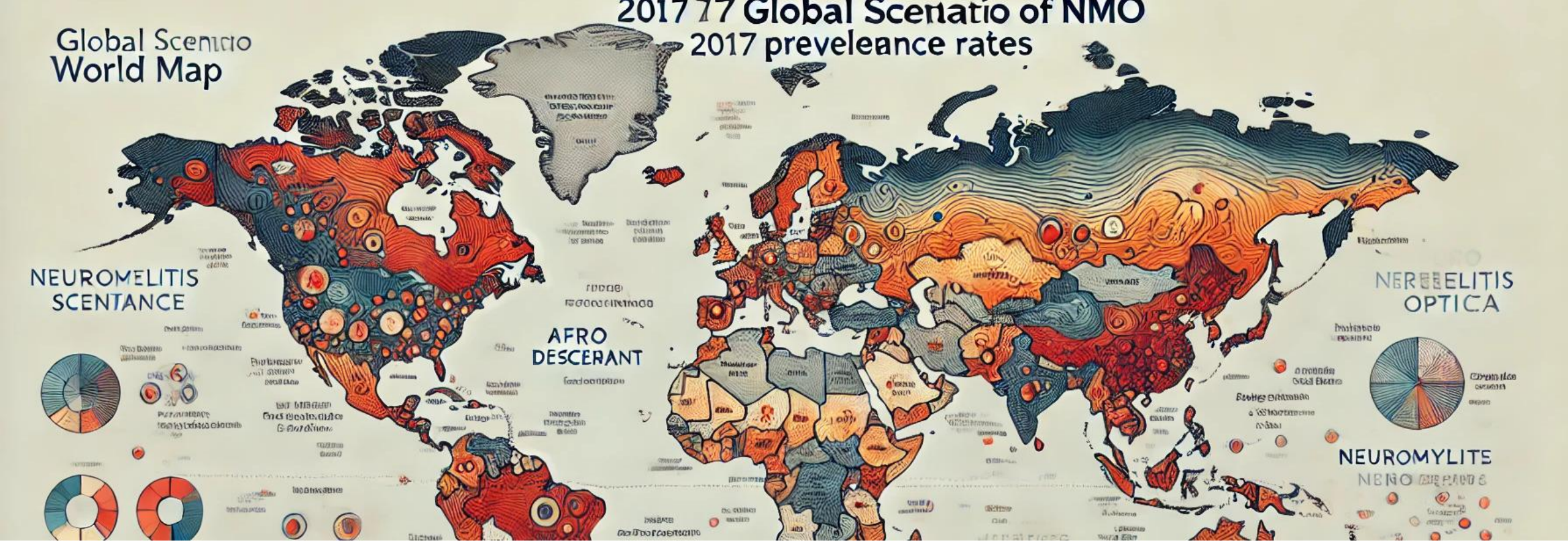
Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article. The Article Processing Charge was paid by the Guthy-Jackson Charitable Foundation.

Epidemiologia da Neuromielite Optica





Qual o Cenário da Doença do Espectro da NMOSD?

No Mundo

Figura Ilustrativa criada por IA (GPT 4.

No Mundo

2010

Neuromyelitis optica in France

A multicenter study of 125 patients

- Estudo observacional e retrospectico
- 26 centros de neurologia na França
- Entre os anos de 2007 e 2008

Table 1 Epidemiologic data derived from the 3 principal cohorts of patients with neuromyelitis optica

	American cohort[10]	Italian cohort[6]	Mexican cohort[9]
Diagnostic criteria	1999	1999	1999
Patients, n	80	46	34

2015

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

Neuromyelitis optica in Portugal (NEMIPORT) – A multicentre study

Joana Domingos[a,*,1], Luís Isidoro[b,1], Rita Figueiredo[c,1], Marisa Brum[d,1], Carlos Capela[e,1], Pedro Barros[f,1], Ernestina Santos[a,g], Maria do Carmo Macário[b], José Pinto Marques[d], Rui Pedrosa[e], José Vale[h], Maria José Sá[i,j]

- Unico estudo epidemiologico de NMO em Portugal
- 5 centros de neurologia, em 2012
- Incluido apenas 67 pacientes

Clinical Neurology and Neurosurgery 134 (2015) 79–84

2018

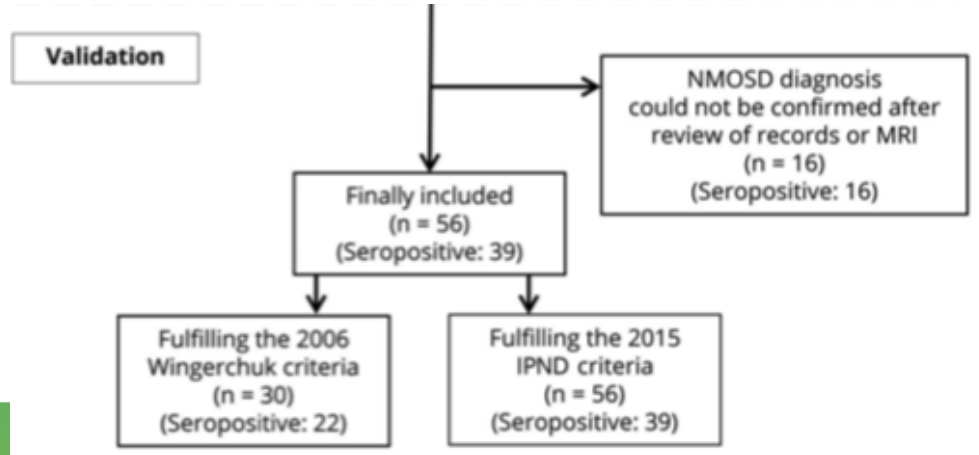
Nationwide prevalence and incidence study of neuromyelitis optica spectrum disorder in Denmark

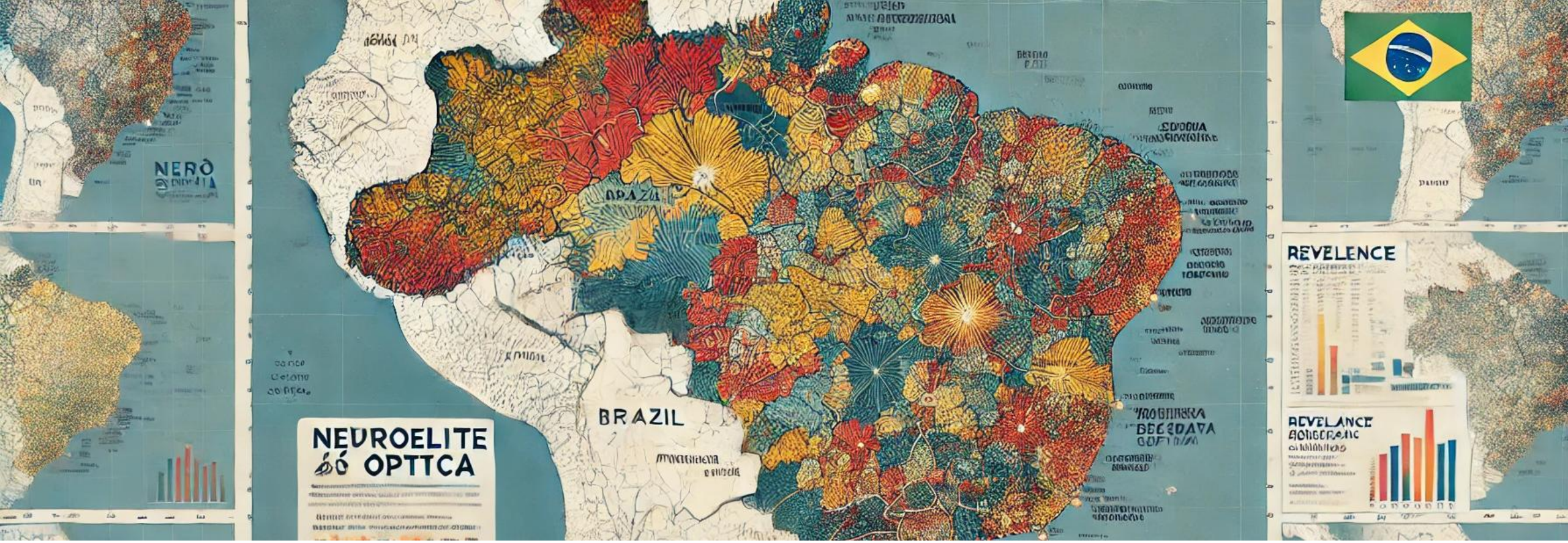
Viktoria Papp, MD, Zsolt Illes, MD, PhD, Melinda Magyari, MD, PhD, Nils Koch-Henriksen, MD, PhD, Matthias Kant, MD, PhD, Claudia Christina Pfleger, MD, PhD, Shanu Faerch Roemer, MD, PhD, Michael Broksgaard Jensen, MD, PhD, Annett Evelyn Petersen, MD, Helle Hvilsted Nielsen, MD, PhD, Lene Rosendahl, MD, Zsolt Mezei, MD, PhD, Tove Christensen, PhD, Kristina Svendsen, MD, PhD, Poul Erik Hyldgaard Jensen, MD, PhD, Magnus Christian Lydolph, MD, PhD, Niels Heegaard, MD, PhD, Jette Lautrup Frederiksen, MD, PhD, Finn Sellebjerg, MD, PhD, Egon Stenager, MD, PhD, and Thor Petersen, MD, PhD

Correspondence
Dr. Papp
papp.vittoria@gmail.com

Neurology® 2018;91:e2265-e2275. doi:10.1212/WNL.0000000000006645

- Estudo de base populacional
- 14 centros de neurologia na Dinamarca
- Período de 01 de janeiro de 2007 até 31 de dezembro de 2014





Qual o Cenário da Doença do Espectro da NMOSD?

No Brasil

Figura Ilustrativa criada por IA (GPT 4.

No Brasil

2017

http://doi.org/10.1590/0004-282X20160193

ARTICLE

Neuromyelitis optica: phenotypic characteristics in a Brazilian case series

Neuromielite óptica: características fenotípicas em uma série de casos brasileiros

Maria Cristina Del Negro[1], Patricia Beatriz Christino Marinho[1], Regina Maria Papais-Alvarenga[2]

Table 4. Characteristic of Brazilian NMO case series.

Variable	Papais-Alvarenga 2002	Alves-Leon 2008	Adoni 2008	Bichuetti 2009	Del Negro 2014
Number of cases	24	28	28	41	34
Study period	1995–2001	2003–2005	NR	1994–2007	2009–2012
female:male ratio	05:01	03:01	08:01	2.4: 1	7.5: 1
Age of onset	32.8	29.3	26	32.6	34.6
Disease duration years	7.7	12.3	7	7.4	8.0
Final EDSS	6	3.2	5.5	5.2	6.5

Del Negro MC, Marinho PBC, Papais-Alvarenga RM. Neuromyelitis optica: phenotypic characteristics in a Brazilian case series. Arq Neuropsiquiatr.

Experiência do mundo real de centro único na Bahia

"Salvador, capital da Bahia, é reconhecida como a cidade com a maior população de afrodescendentes fora da África."

Fukuda *et al. BMC Neurology* (2022) 22:95
https://doi.org/10.1186/s12883-022-02621-5

BMC Neurology

RESEARCH Open Access

Clinical and prognostic aspects of patients with the Neuromyelitis Optica Spectrum Disorder (NMOSD) from a cohort in Northeast Brazil

Thiago Gonçalves Fukuda[1,2,3*], Ivã Taiuan Fialho Silva[2], Tayla Samanta Silva dos Santos[2], Marcos Baruch Portela Filho[3], Fernanda Ferreira de Abreu[2] and Jamary Oliveira-Filho[1,2]

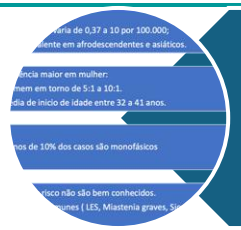
Retrospective Cohort
Single Center
UFBA University Hospital
Data from 2017 - 2019

Table 1 General characteristics of 91 patients with neuromyelitis optica spectrum disorders

Characteristics	Total
Age at onset (years), average ± SD	36.3 ± 13.6
Female, n (%)	72 (79.1)
Afro-descendants, n (%)	67 (73.6)
EDSS, median, (interquartile)	4 (2.62–6.50)
AQP4-IgG + , n (%)	55 (73.3)*
Autoimmune disease, n (%)	9 (10.2)
Recurrence, n (%)	71 (83.5)
Number of attacks, average ± SD	4.0 ± 3.6
Disease time (years), average ± SD	7.8 ± 6.9
Relapse rate, average ± SD	1.3 ± 1.6
Type of treatment, n (%)	
Azathioprine and glucocorticoid	37 (50.7)
Azathioprine	30 (41.1)
Rituximab	6 (8.2)

- A grande maioria dos pacientes são mulheres negras.
- Quase todos os pacientes com medicamentos com baixa evidência científica "off-label" e a maioria com suposta baixa eficácia.
- Falta de acesso a tratamentos e diagnósticos específicos.

Epidemiologia



É uma doença rara;

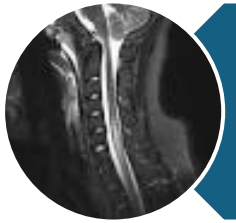
A prevalência varia de 0,37 a 10 por 100.000;

Mais prevalente em afrodescendentes e asiáticos.

Incidência maior em mulher:

Homem em torno de 5:1 a 10:1.

Média de inicio de idade entre 32 a 41 anos.



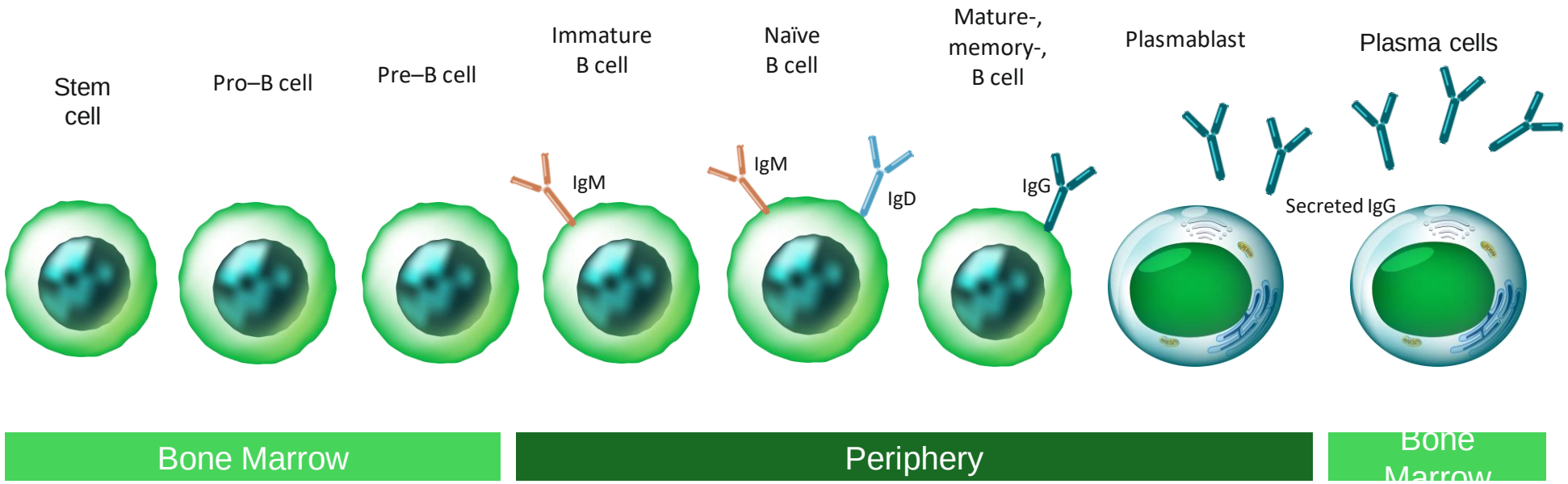
Menos de 10% dos casos são monofásicos

Fatores de risco não são bem conhecidos.

Doenças autoimunes (LES, Miastenia graves, Sjogren) são comumente associados.

Fisiopatologia

O CD19 é mais amplamente expresso nas superfícies das células B à medida que amadurecem em plasmablastos / plasmócitos

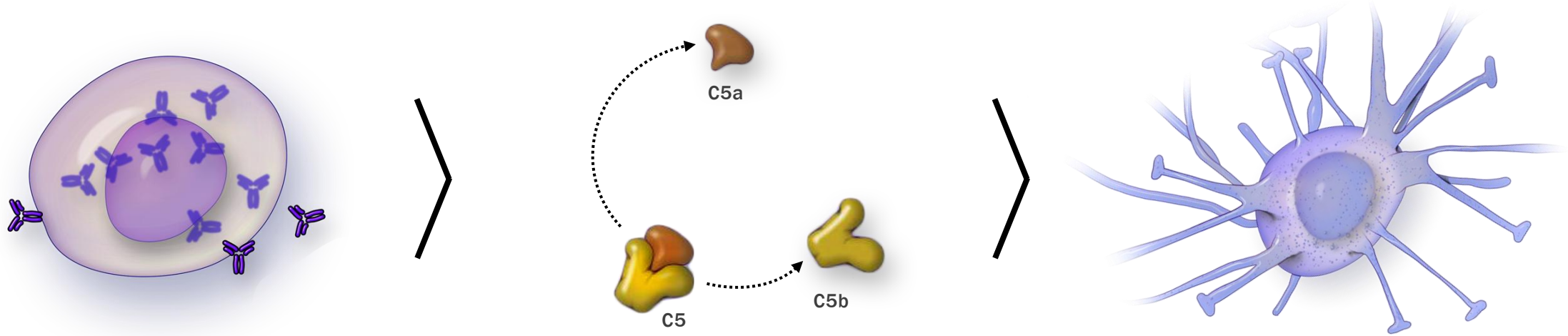


***3-5% of circulating T cell also express CD20[1]**

Ig, immunoglobulin.

1. Schuh et al. J Immunol, 2016; 197(4):1111-7

AVANÇO NO ENTENDIMENTO DA FISIOPATOLOGIA DA NMOSD



ANTICORPO AQP4 [1-3]

Anticorpos anti-AQP4 atravessam a barreira hematoencefálica e se ligam ao AQP4 nos pés dos astrócitos

ATIVAÇÃO DO COMPLEMENTO [2-4]

A ligação do anticorpo anti-AQP4 ativa o complemento, levando à inflamação e formação MAC

ASTROCITOPATIA LEVANDO À DESTRUIÇÃO NEURONAL [2,4]

Como visto na NMOSD, o complemento ativado leva à necrose de astrócitos, dano inflamatório e morte neuronal

Patogênese da NMOSD

MAC, complexo de ataque à membrana

1. Weinshenker BG, et al. *Mayo Clin Proc* . 2017;92(4):663-679. 2. Papadopoulos MC, et al. *Nat Rev Neurosci* . 2013;14(4):265-277. 3. Piatek P, et al. *Front Immunol* . 2018;9:1694.4. Wingerchuk DM, et al. *Lancet Neurol* . 2007;6(9):805-815.

TELESSAÚDEBA

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FUTURO PRA GENTE

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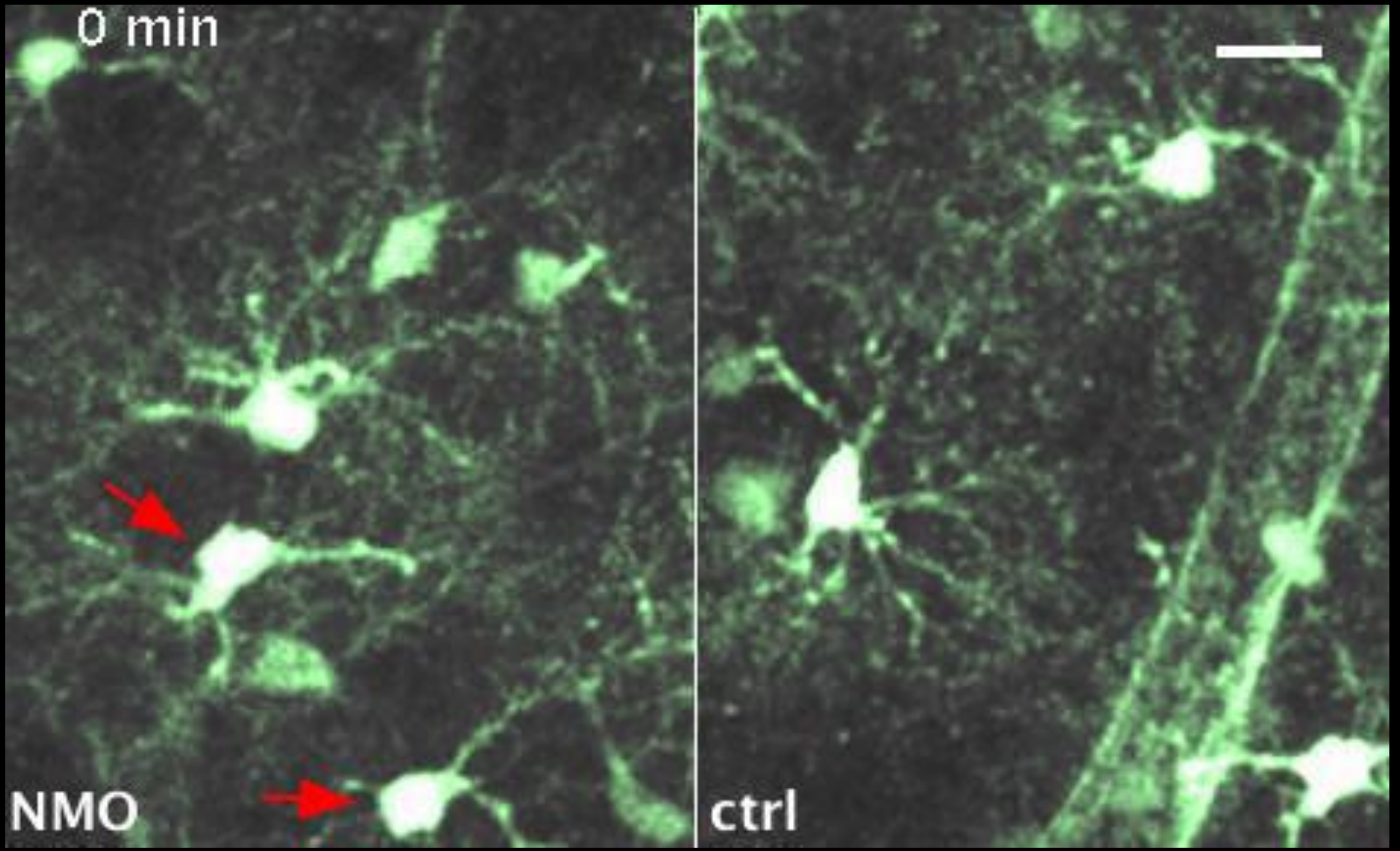
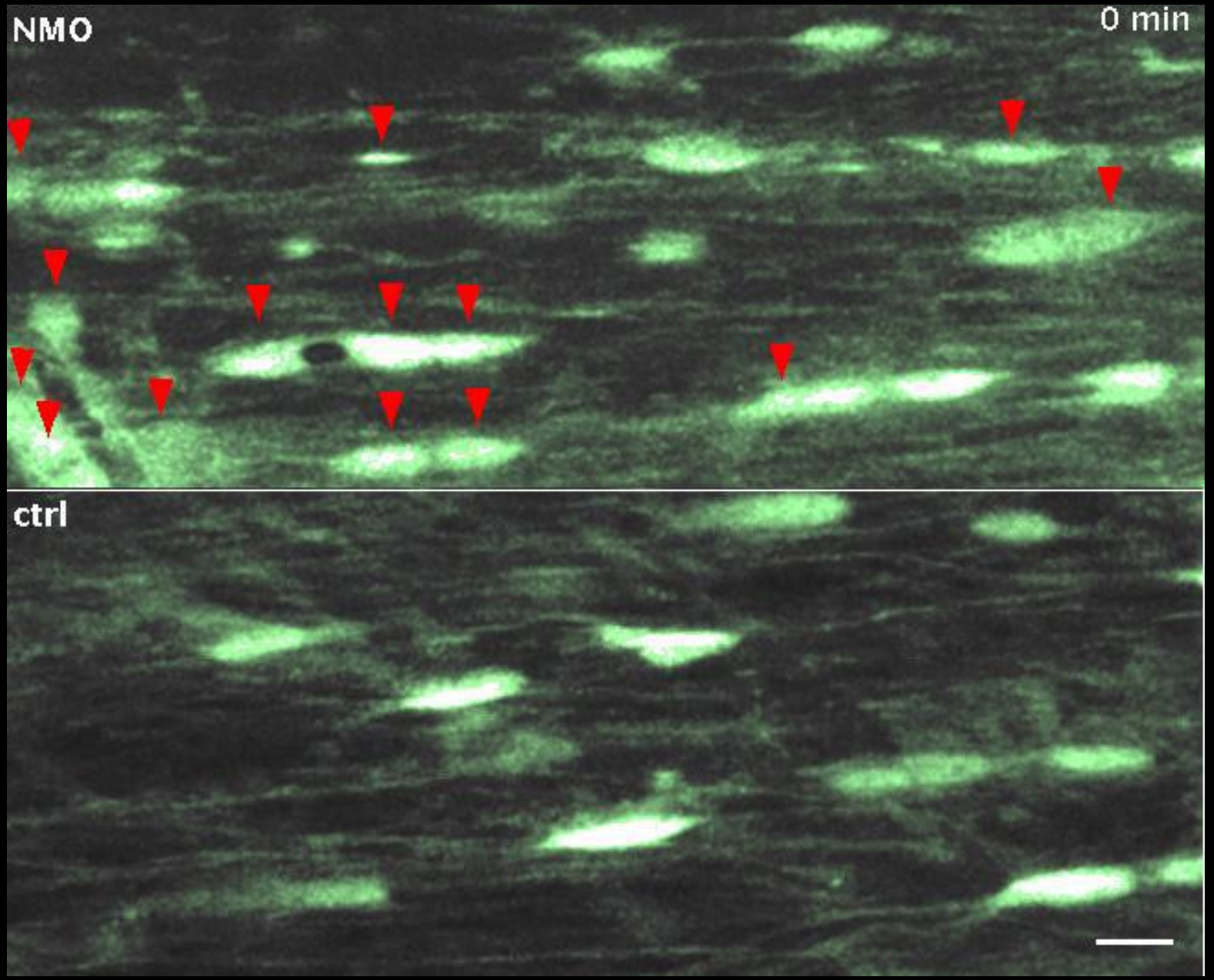
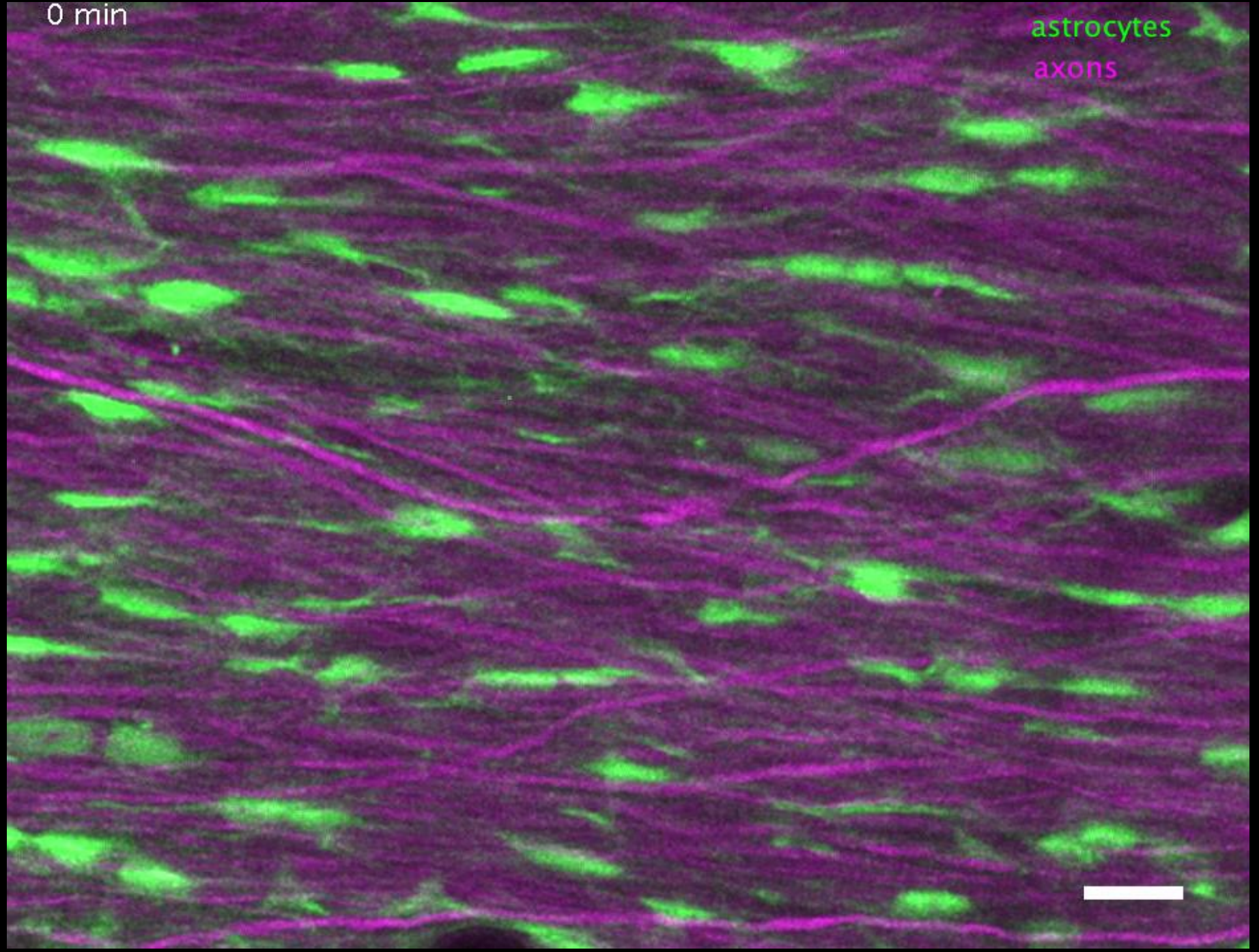


1. Herwerth M, Kalluri SR, Srivastava R, et al. In vivo imaging reveals rapid astrocyte depletion and axon damage in a model of neuromyelitis optica-related pathology. *Ann Neurol.* 2016;79(5):794-805. doi:10.1002/ana.24630



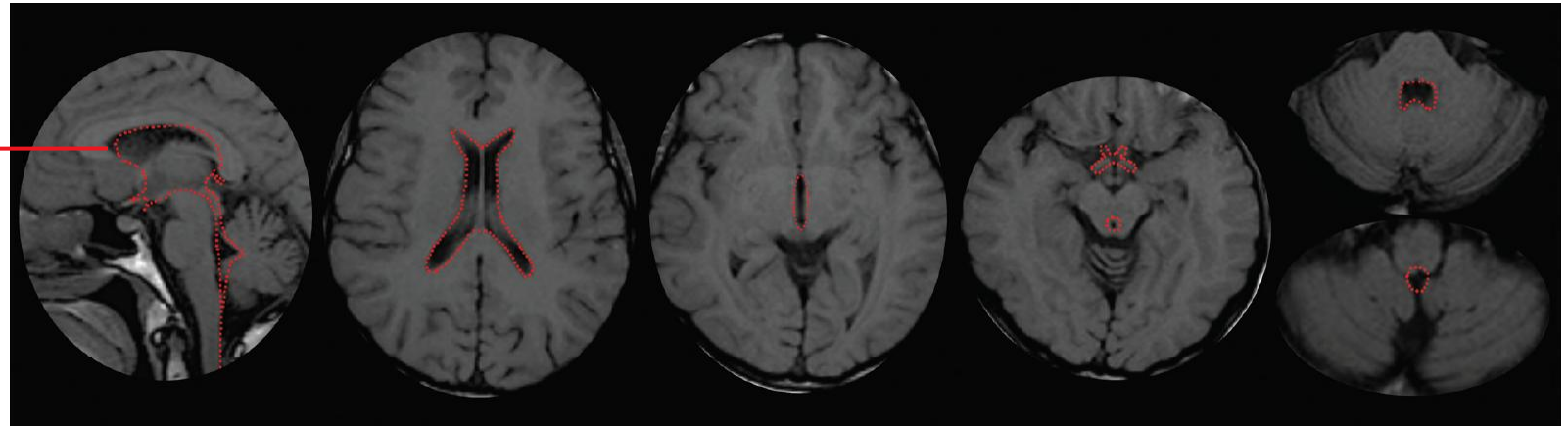
1. Herwerth M, Kalluri SR, Srivastava R, et al. In vivo imaging reveals rapid astrocyte depletion and axon damage in a model of neuromyelitis optica-related pathology. *Ann Neurol.* 2016;79(5):794-805. doi:10.1002/ana.24630


0 min
astrocytes
axons

Expressão de AQP4 no SNC

- A AQP4 é altamente expressa no nervo óptico, medula espinhal, áreas periventriculares, hipotálamo e regiões subpiais, bem como no tronco encefálico e na área postrema

Expressão AQP4



Periependimário superfície do lateral Ventrículos

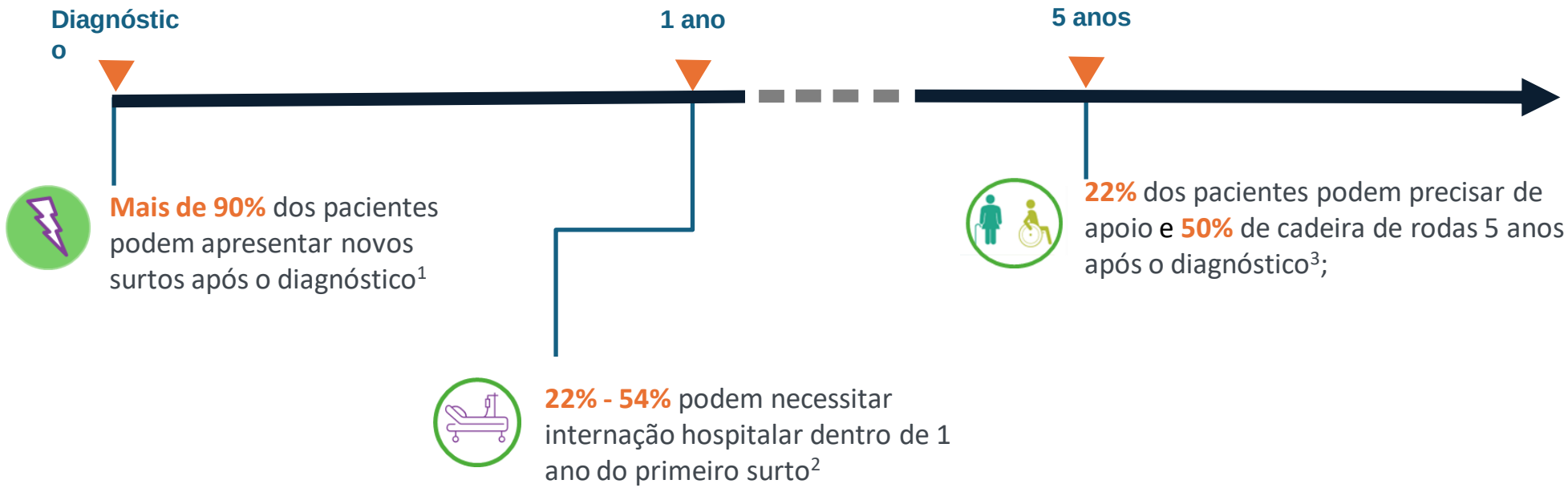
Periependimário superfície do terceiro ventrículo (região diencefálica)

Periaquedutal área e quiasma óptico

Periependimário superfície do quarto ventrículo e área postrema

AQP4, aquaporina-4; SNC, sistema nervoso central
Dutra BG, et al. Radiografia. 2018;38(1):169-193.

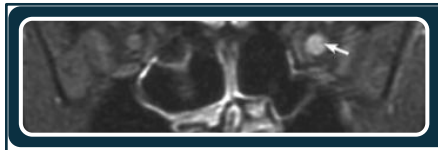
NMOSD: Uma doença imprevisível com desfechos que podem impactar a qualidade de vida dos pacientes[1]



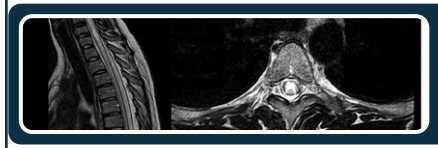
- Os surtos são **imprevisíveis** e associados a **danos neurológicos e incapacidades permanentes**[5,6,7].
- **83 %** dos casos de mielite transversa e **67%** dos casos de neurite óptica **não se recuperam** ou podem apresentar recuperação **incompleta**[2]

1.Wingerchuk, Dean M, and Claudia F Lucchinetti. *The New England journal of medicine* vol. 387,7 (2022): 631-639. 2.Marrie RA, et al. *Int J MS Care*. 2013;15:113-8; 3. Jiao Y, Fryer JP, Lennon VA, et al. *Neurology*. 2013;81(14):1197-1204. 4. Oh J, Levy M. *Neurol Res Int.* 2012;2012:460825. 5. Jarius, S., Ruprecht, K., Wildemann, B. *et al. J Neuroinflammation* **9**, 14 (2012). 6. Wingerchuk DM, Lennon VA, Lucchinetti CF, Pittock SJ, Weinshenker BG. *Lancet Neurol.* 2007;6(9):805–815. 7. Kessler RA, Mealy MA, Levy M. *Neurol Neuroimmunol Neuroinflamm.* 2016;3(5):e269.

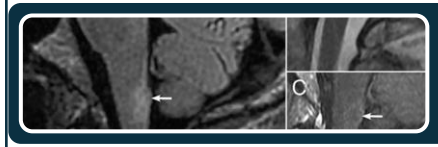
Síndromes típicas ou Síndromes Core



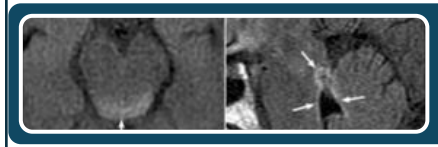
•Neurite óptica aguda



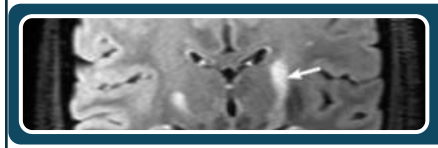
Mielite aguda



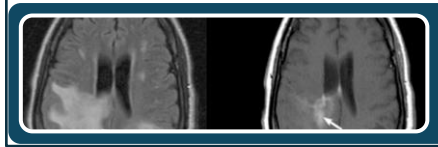
Síndrome da área postrema



Síndrome aguda de tronco encefálico



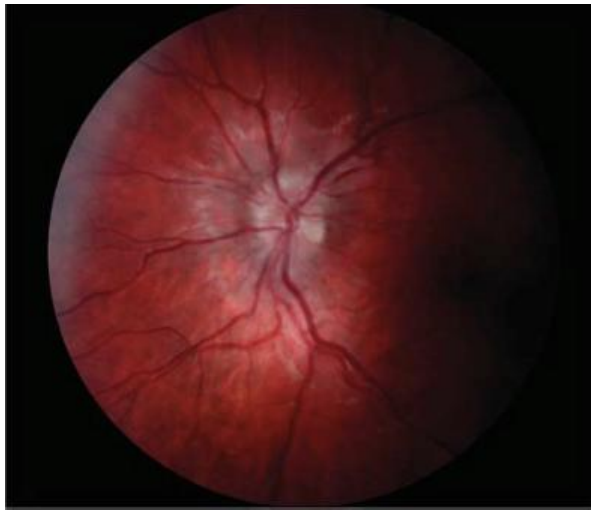
Síndrome Diencefálica

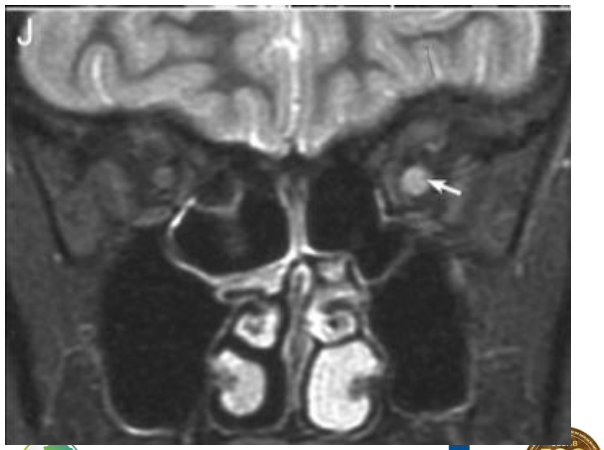


Síndrome cerebral sintomática

Neurite Óptica

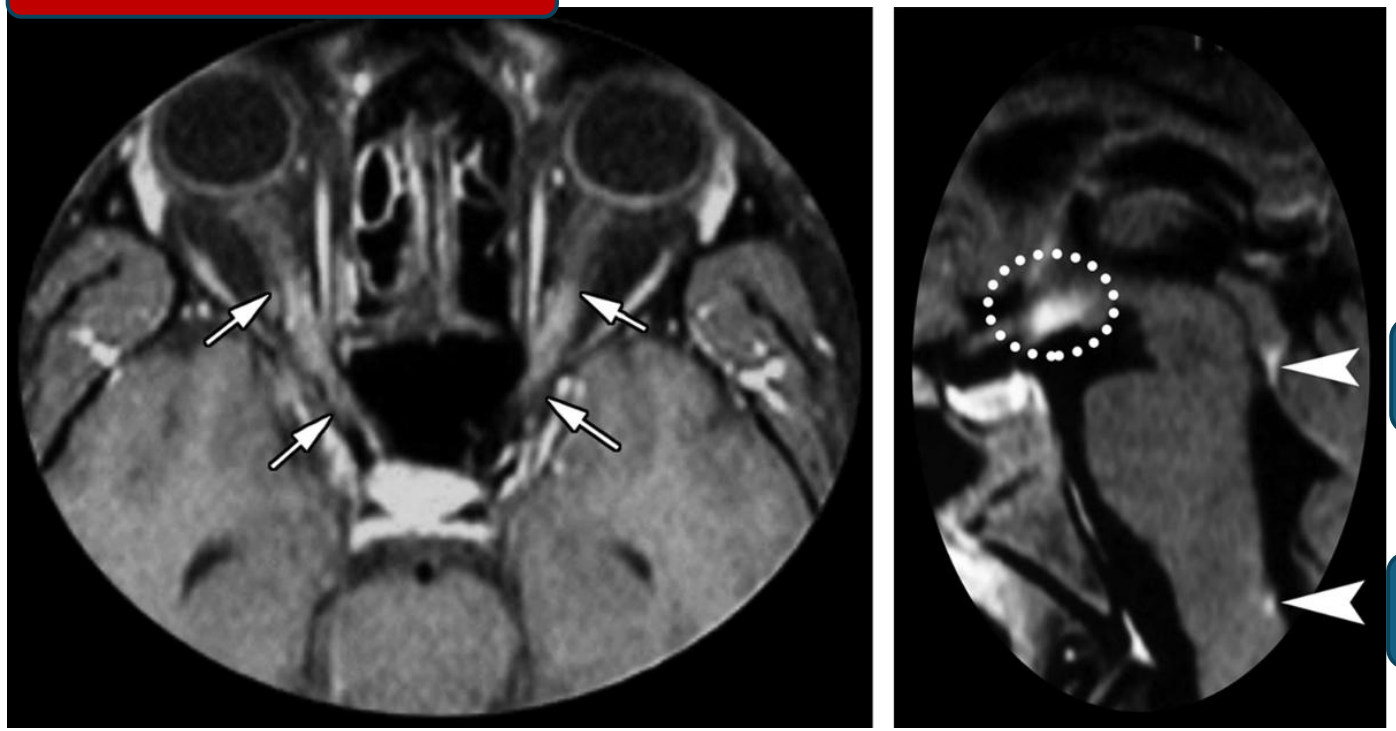
- Ocorre em torno de 50% dos pacientes
- Dor ocular com BAV
- Redução grave de acuidade visual (< 20/200)
- Geralmente longitudinalmente extensa
- Neurite óptica sequencial numa sucessão rápida ou neurite óptica simultânea bilateral é altamente sugestiva





Neurite óptica Bilateral

RM T1 GD



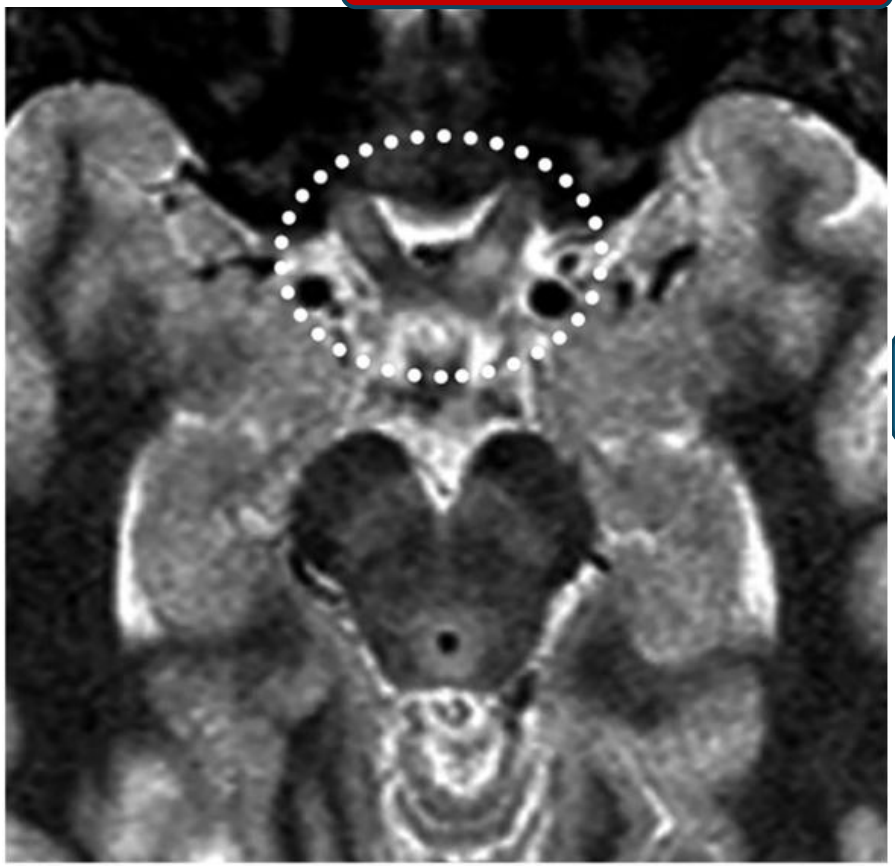
Periarqueductal

Área póstrema

Neuromyelitis Optica Spectrum Disorders: Spectrum of MR Imaging Findings and Their Differential Diagnosis
Rocha, Renato Hoffmann Nunes, and Antônio Carlos Martins Maia Júnior.RadioGraphics 2018 38:1, 169-193

Neurite óptica

RM T2 axial



Quiasma óptico

Neuromyelitis Optica Spectrum Disorders: Spectrum of MR Imaging Findings and Their Differential Diagnosis
Rocha, Renato Hoffmann Nunes, and Antônio Carlos Martins Maia JúniorRadioGraphics 2018 38:1, 169-193

Neurite Óptica

Contents lists available at ScienceDirect

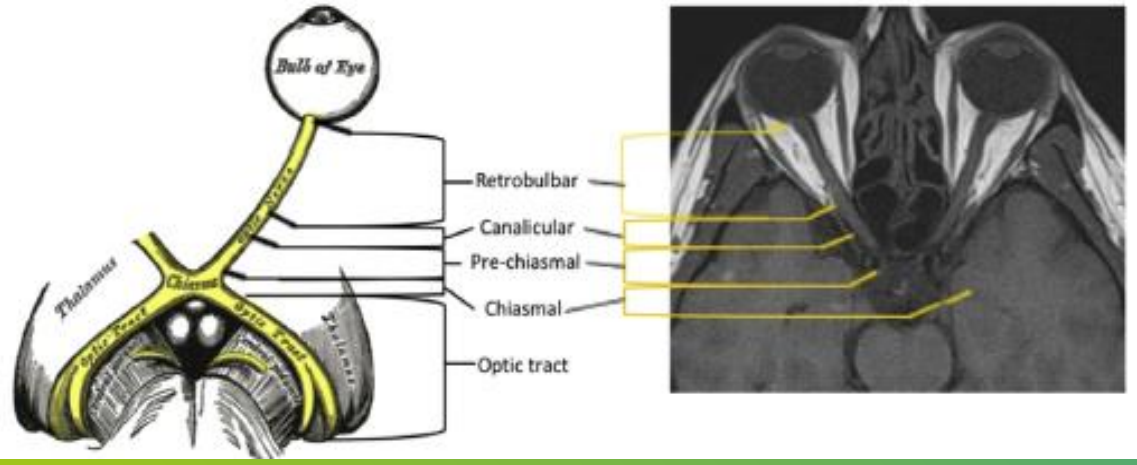
Journal of the Neurological Sciences

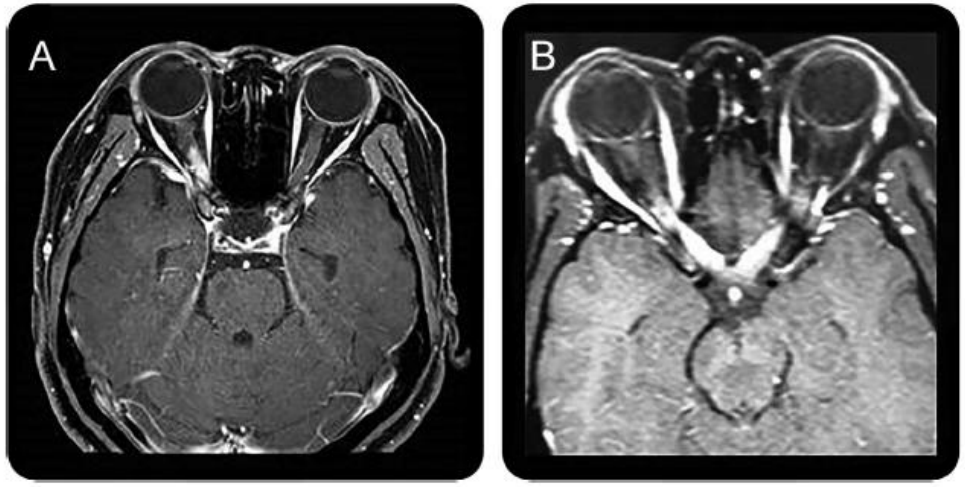
journal homepage: www.elsevier.com/locate/jns

Longitudinally extensive optic neuritis as an MRI biomarker distinguishes neuromyelitis optica from multiple sclerosis

Maureen A. Mealy [a], Anna Whetstone [a], Gunes Orman [b], Izlem Izbudak [b], Peter A. Calabresi [a], Michael Levy [a,*]

[a] Department of Neurology, Johns Hopkins University, Baltimore, MD, USA
[b] Department of Radiology, Johns Hopkins University, Baltimore, MD, USA





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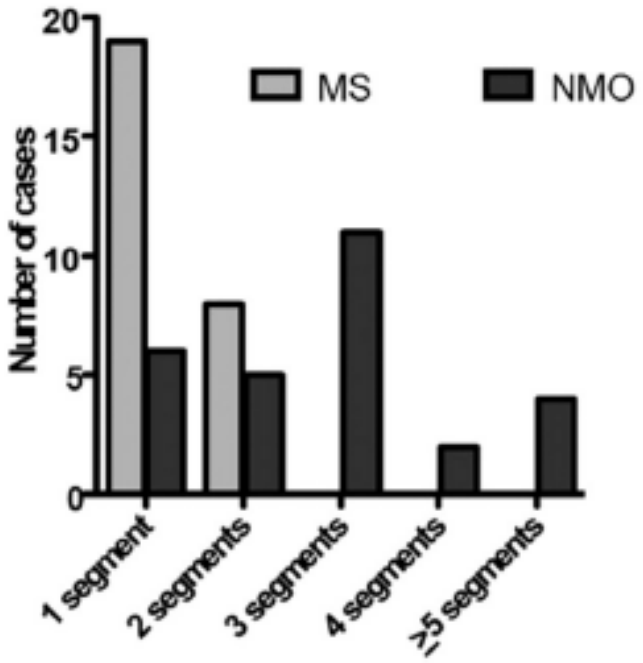
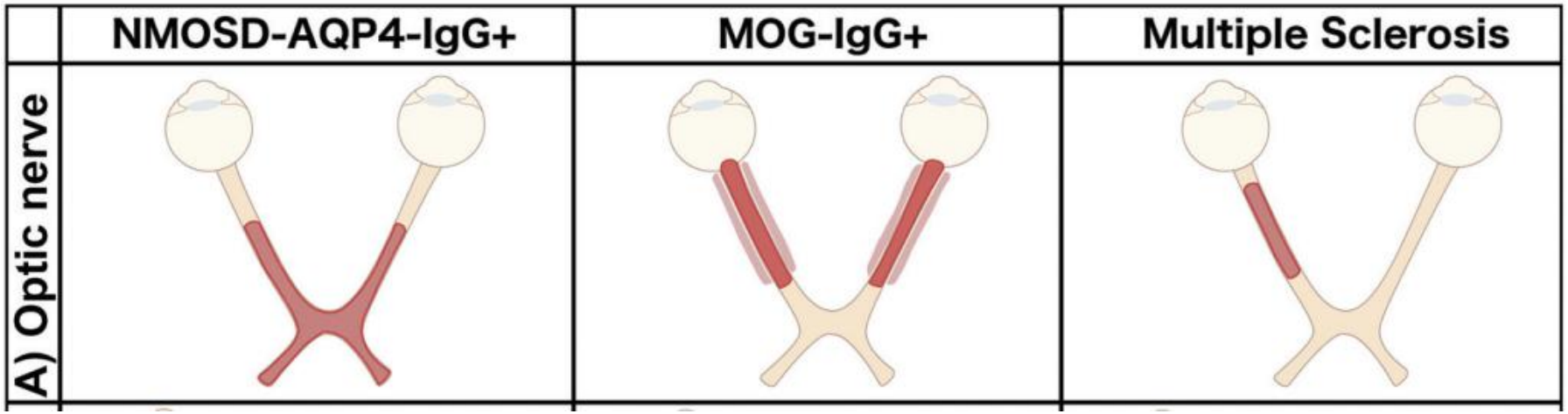


Table 2
NMO sensitivities and specificities by lesion length.

Lesion length (mm)	Sensitivity (%)	Specificity (%)	Likelihood ratio
≥5	100	4	1.06
≥10	100	46	1.81
≥15	85	73	3.16
≥17.6	**80.8**	**76.9**	**3.50**
≥20	77	77	3.33
≥25	62	81	3.20
≥30	46	92	5.83
≥35	35	100	
≥40	19	100	
≥45	12	100	
≥50	10	100	

The bold data represent the optimal cut point on the ROC curve.

Neurite Óptica



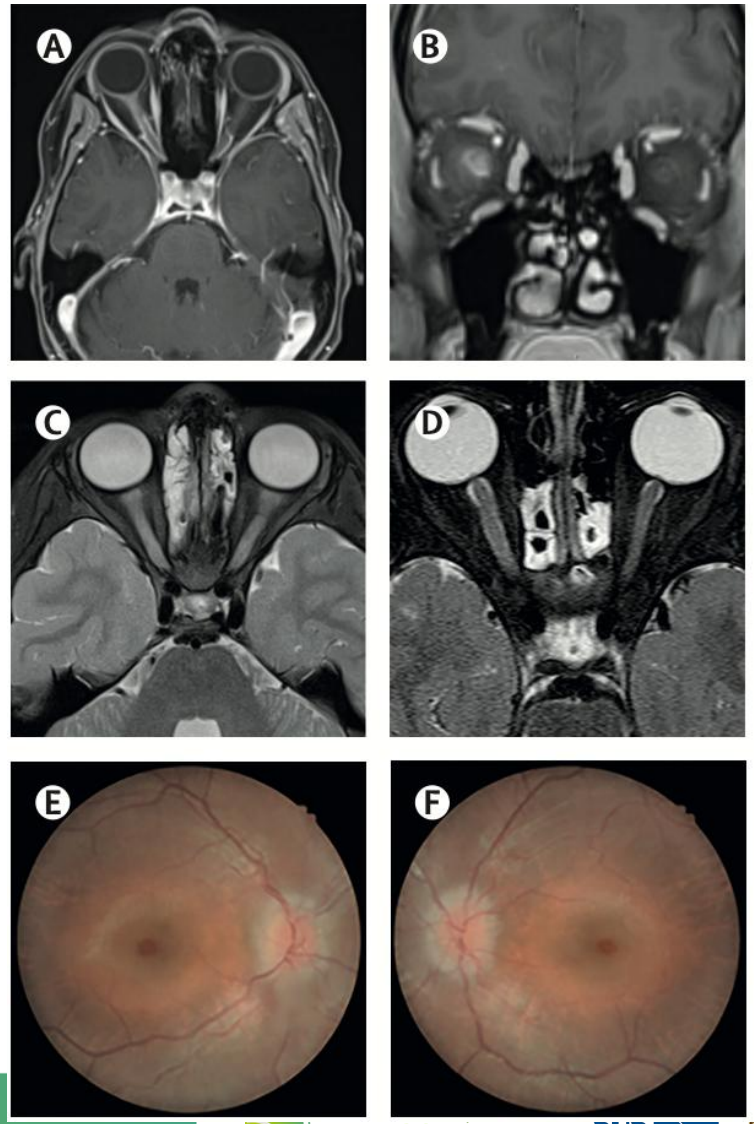
Neuromyelitis Optica Spectrum Disorders: Spectrum of MR Imaging Findings and Their Differential DiagnosisB
Hoffmann Nunes, and Antônio Carlos Martins Maia JúniorRadioGraphics 2018 38:1, 169-193

Neurite Óptica — Características que podem sugerir MOGAD

Perineurite e intenso edema de NO

Acometimento bilateral com edema em disco ópico

Edema importante a fundoscopia



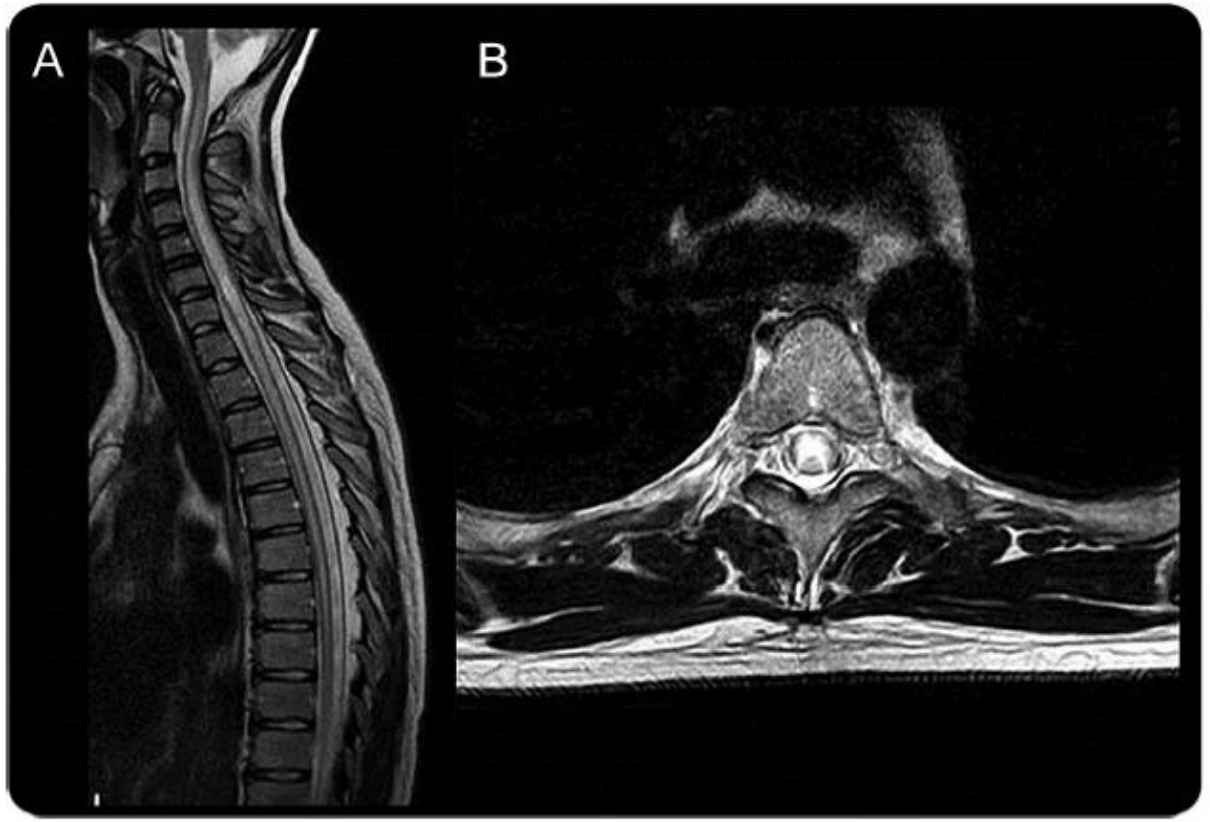
Banwell B, Bennett JL, Marignier R, Kim HJ, Brilot F, Flanagan EP, Ramanathan S, Waters P, Tenembaum S, Graves JS, Chitnis T, Brandt AU, Hemingway C, Neuteboom R, Pandit L, Reindl M, Saiz A, Sato DK, Rostasy K, Paul F, Pittock SJ, Fujihara K, Palace J. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. Lancet Neurol. 2023 Mar;22(3):268-282.

Mielite Aguda

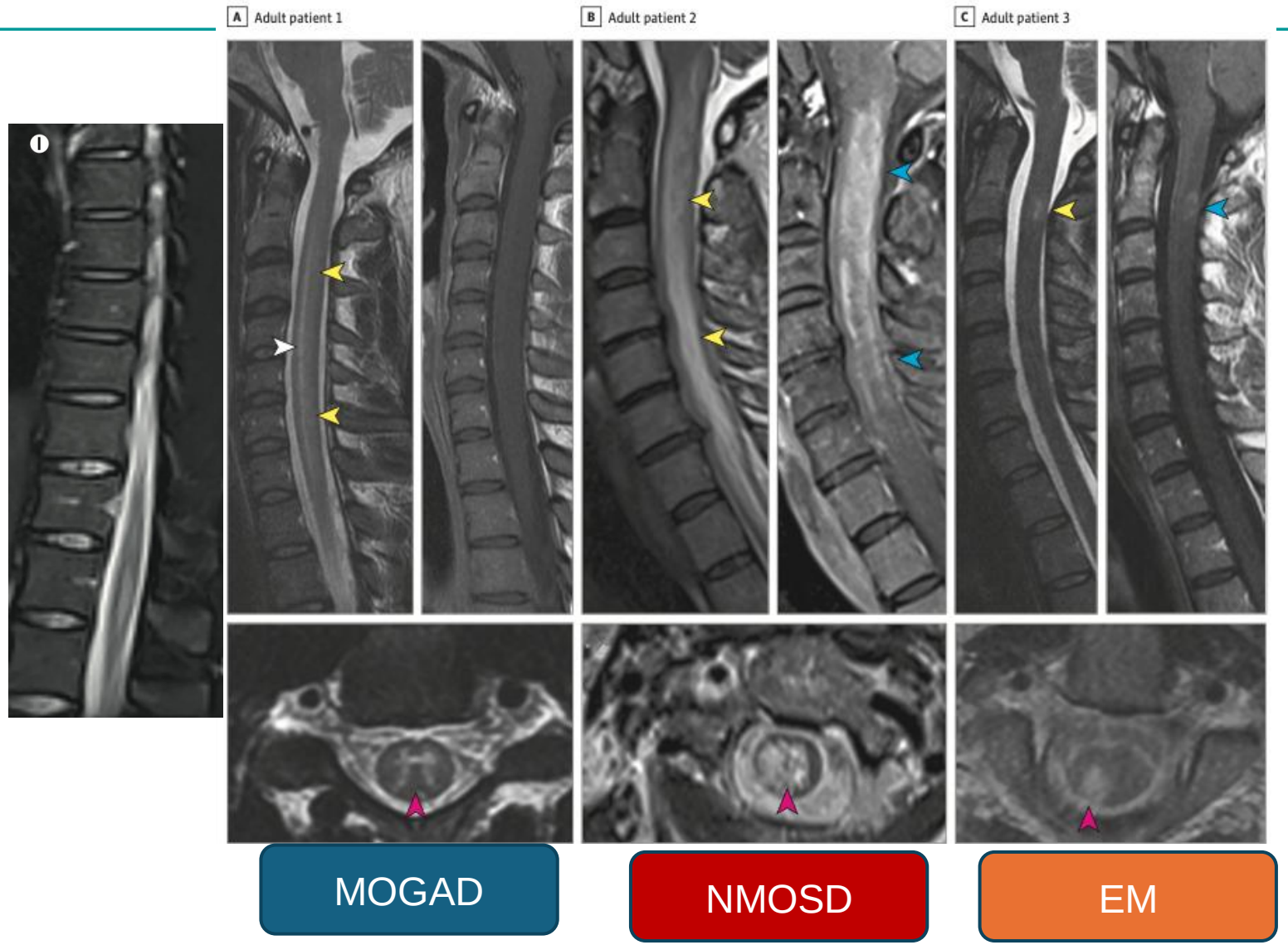
Mielite Transversa Aguda Grave

Extensa longitudinalmente (>3 corpos vertebrais)

Acometimento predominante central da medula

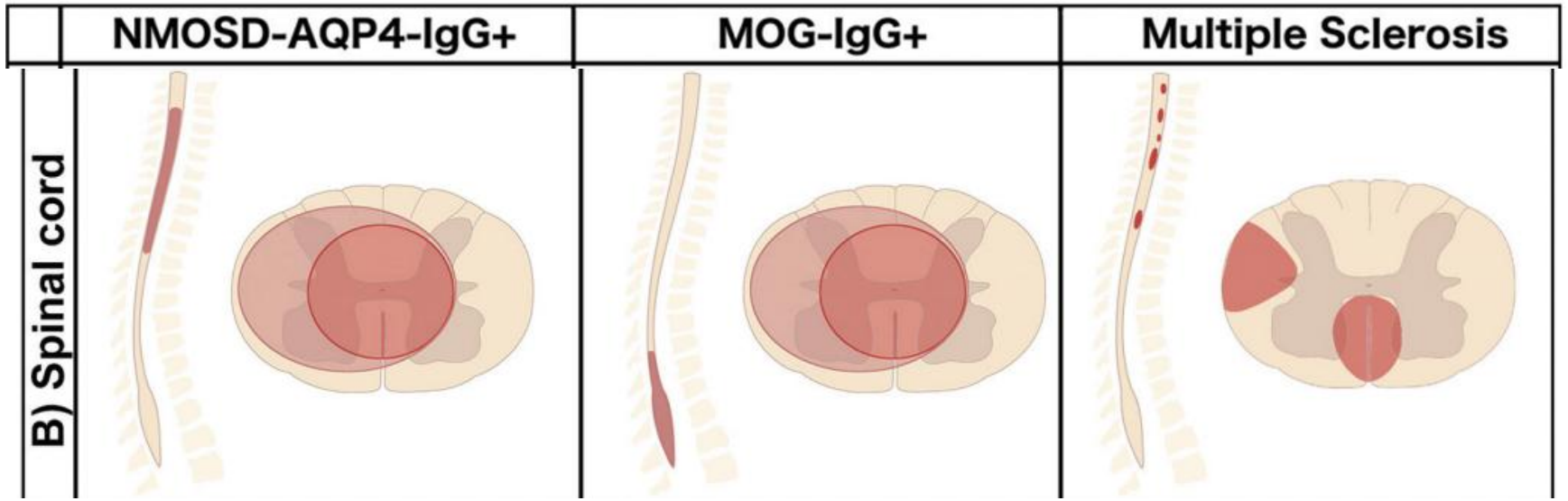


Mielite Aguda



Dubey, Divyanshu et al. "Clinical, Radiologic, and Prognostic Features of Myelitis Associated With Myelin Oligodendrocyte Glycoprotein Autoantibody." *JAMA neurology*vol. 76,3 (2019): 301-309. doi:10.1001/jamaneurol.2018.4053

Mielite Aguda



Neuromyelitis Optica Spectrum Disorders: Spectrum of MR Imaging Findings and Their Differential Diagnosis
Rocha, Renato Hoffmann Nunes, and Antônio Carlos Martins Maia JúniorRadioGraphics 2018 38:1, 169-193

Mielite Aguda

MULTIPLE SCLEROSIS JOURNAL | MSJ

Topical Review

Bright spotty lesions as an imaging marker for neuromyelitis optica spectrum disorder

Sara Salama and Michael Levy

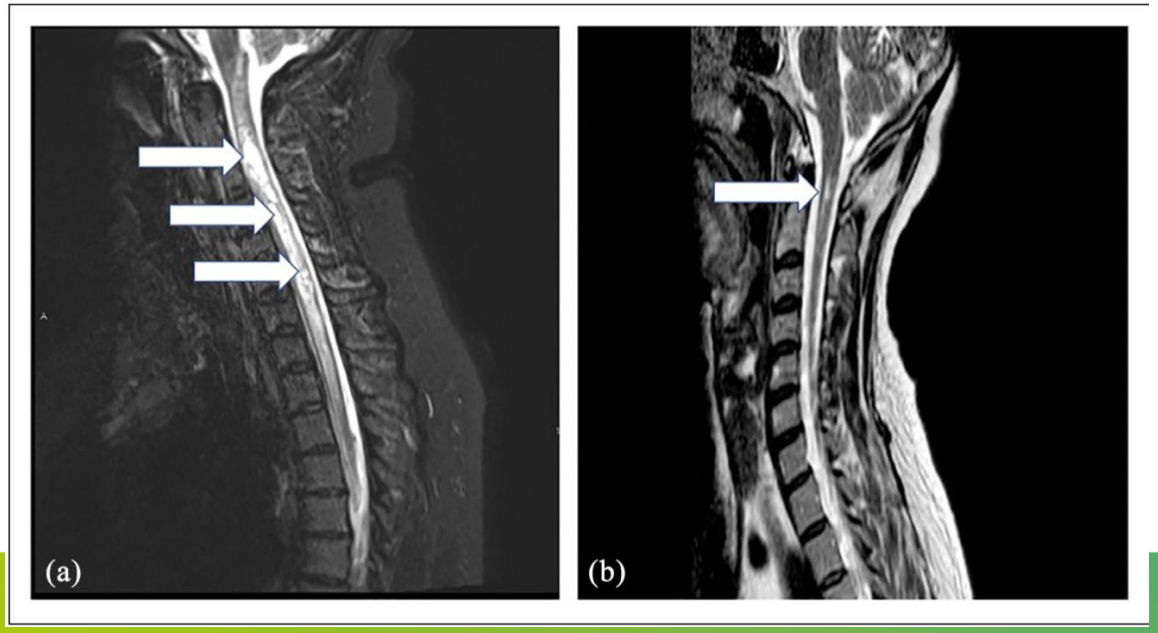
Multiple Sclerosis Journal

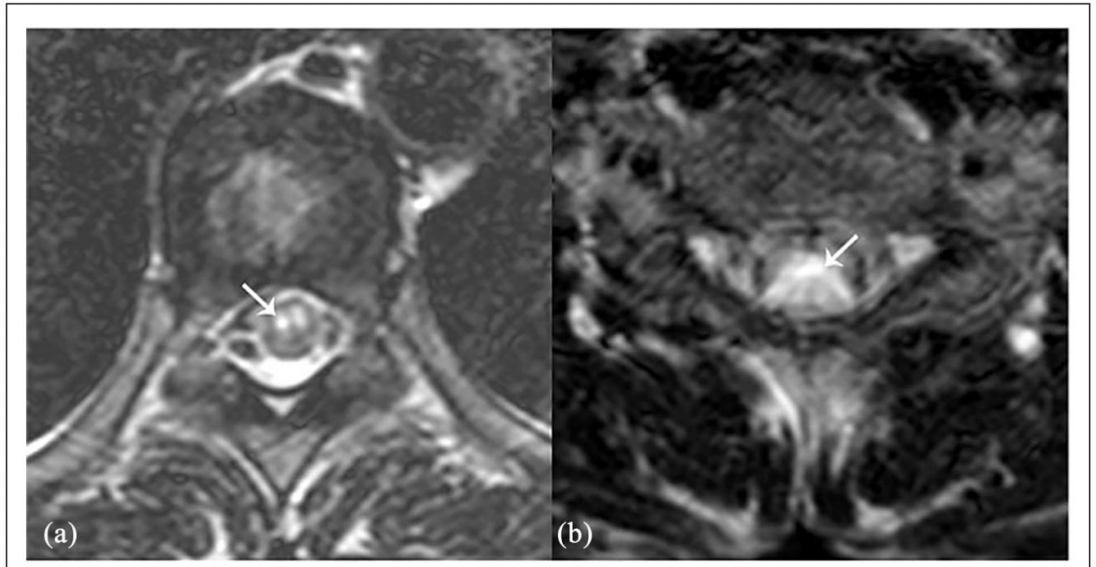
1–4

DOI: 10.1177/1352458521994259

Table 1. Summary of the studies that reported specificity and sensitivity of BSLs in diagnosing NMOSD.

Study	Specificity	Sensitivity
Yonezu et al.[6]	97%	54%
Hyun et al.[5]	100%	27.4%
Pekcevik et al.[8]	89.1%	64.6%
Chee et al.[9]	93%	69%
Rabasté et al. (axial BSLs)[7]	94%	40%
Rabasté et al. (sagittal BSLs)[7]	98.5%	26.7%

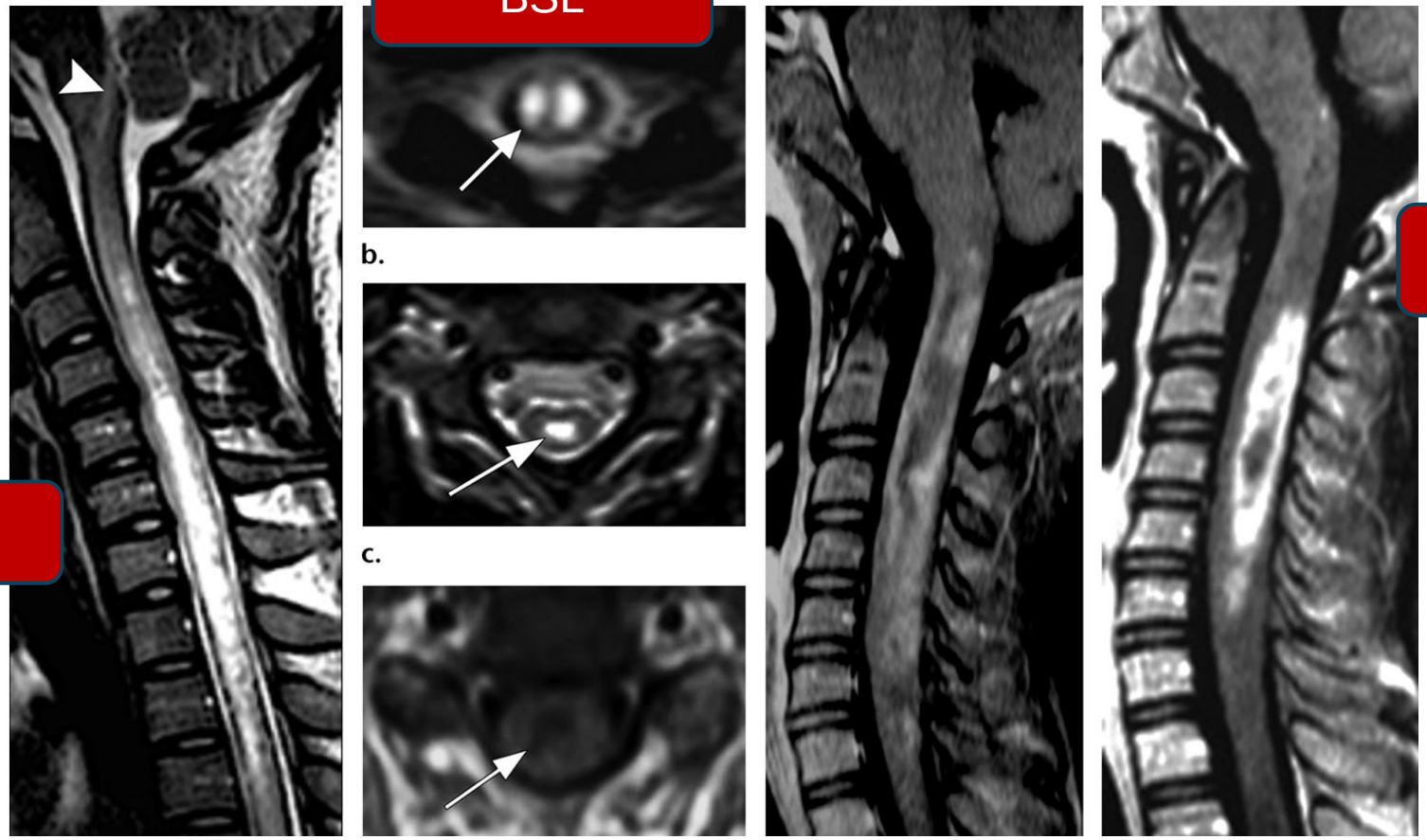




Mielite Aguda

BSL

Extensa



Realce periférico em lente

Neuromyelitis Optica Spectrum Disorders: Spectrum of MR Imaging Findings and Their Differential Diagnosis Bruna Hoffmann Nunes, and Antônio Carlos Martins Maia JúniorRadioGraphics 2018 38:1, 169-193

Mielite Transversa

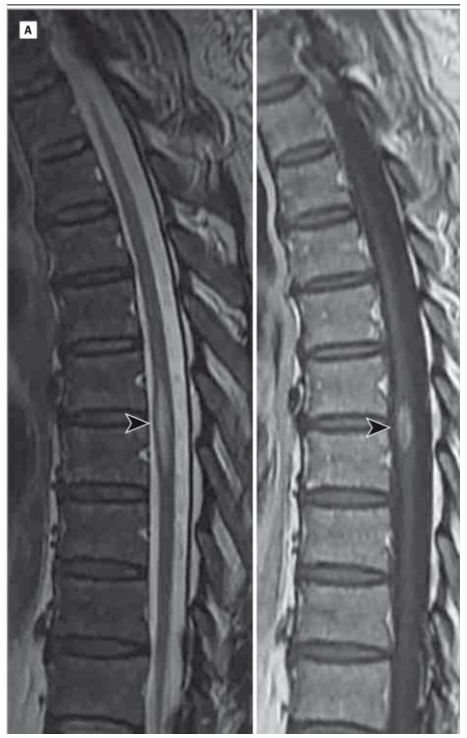
JAMA Neurol. 2015;72(1):81-87. doi:10.1001/jamaneurol.2014.2137
Published online November 10, 2014.

Original Investigation

Short Myelitis Lesions in Aquaporin-4-IgG–Positive Neuromyelitis Optica Spectrum Disorders

Eoin P. Flanagan, MBBCh; Brian G. Weinshenker, MD; Karl N. Krecke, MD; Vanda A. Lennon, MD, PhD; Claudia F. Lucchinetti, MD; Andrew McKeon, MBBCh; Dean M. Wingerchuk, MD; Elizabeth A. Shuster, MD; Yujuan Jiao, MD; Erika S. Horta, MD; Sean J. Pittock, MD

"Uma lesão curta (<3 segmentos vertebrais) foi o primeiro evento de mielite transversa em 25 de 176 pacientes (14%)"



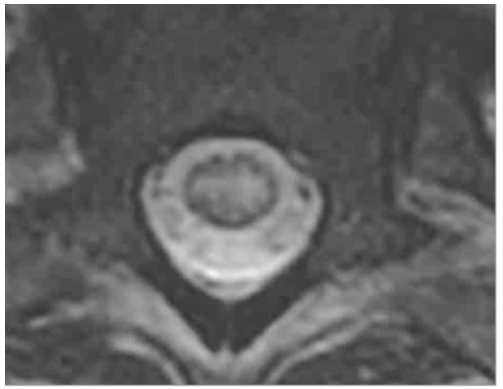


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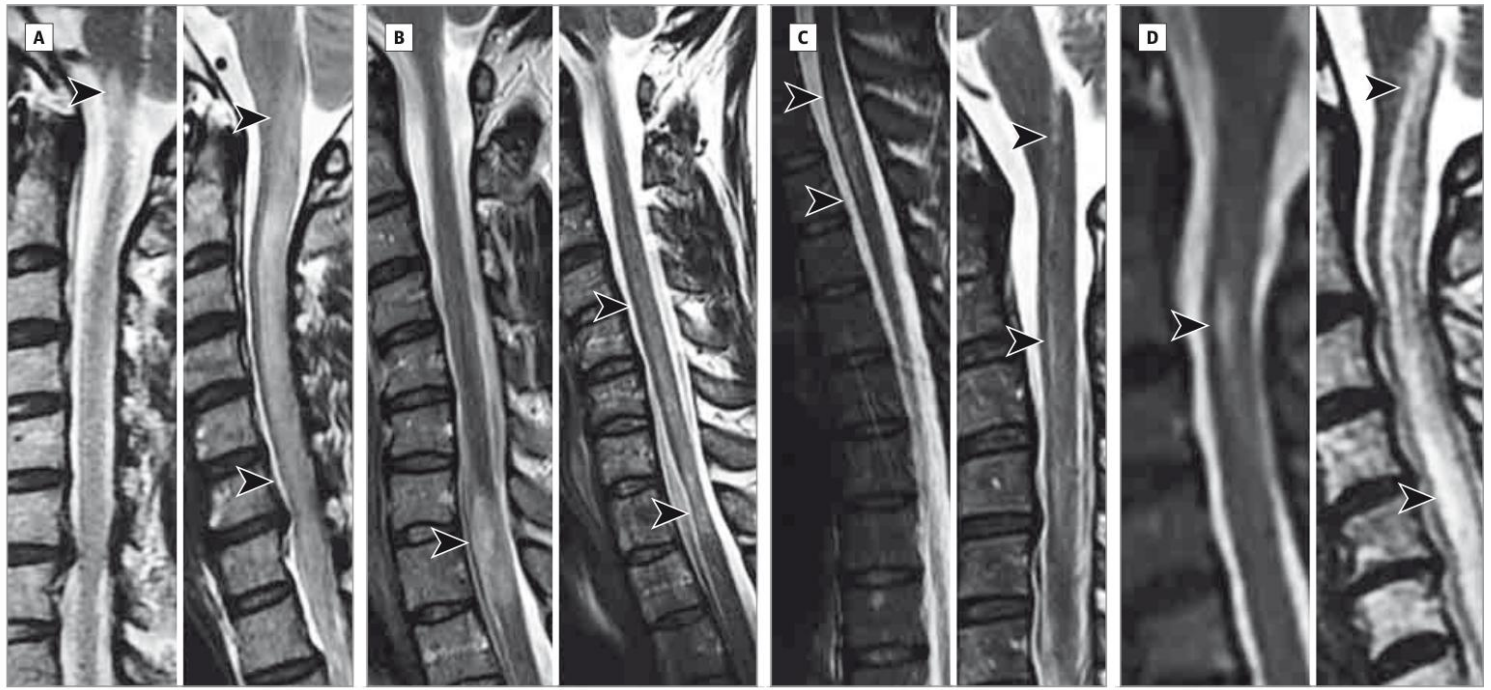
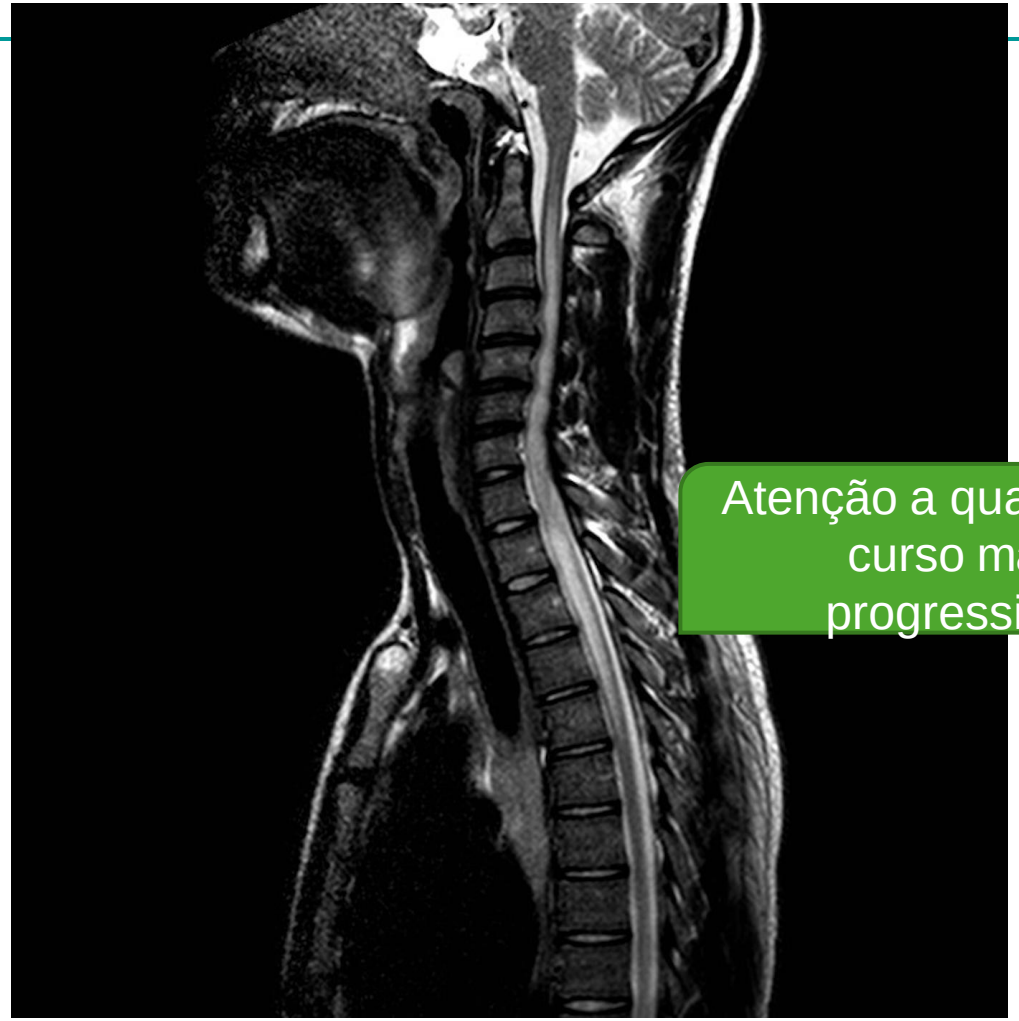
Figure 2. Magnetic Resonance Imaging in 4 Patients With an Initial Short Transverse Myelitis Followed by a Subsequent Longitudinally Extensive Myelitis

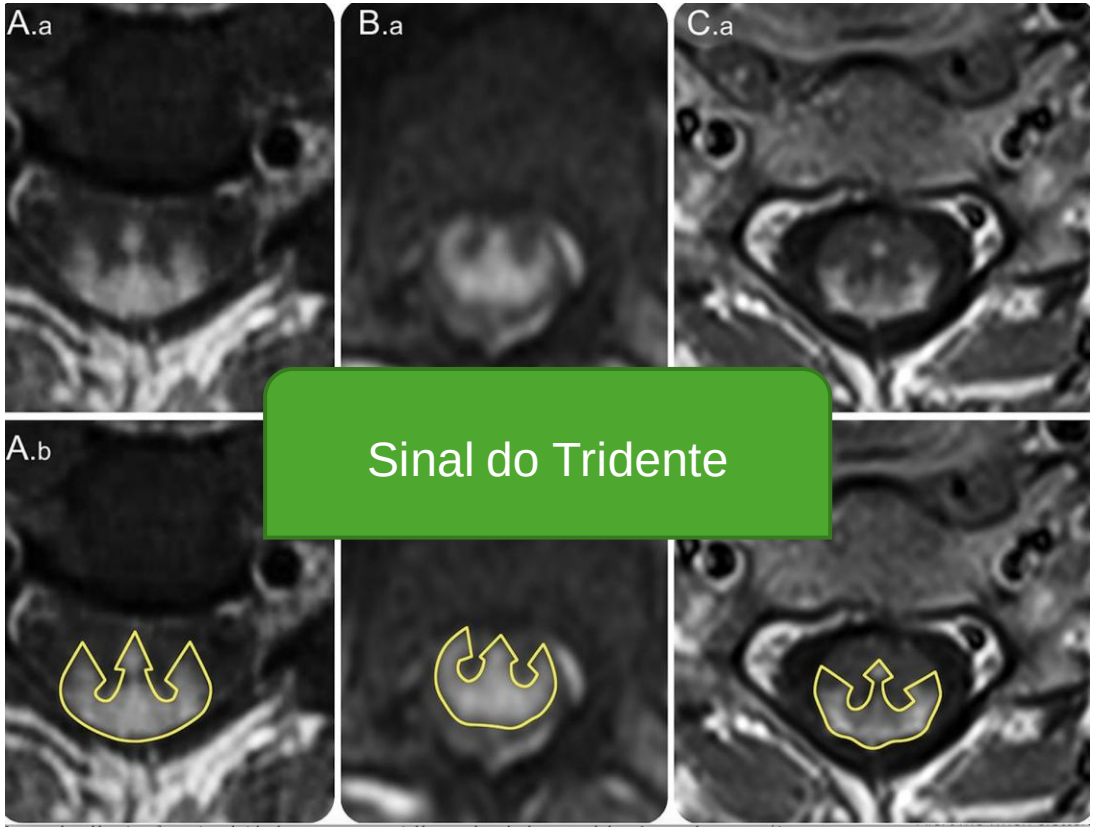


Outros Diagnósticos Diferencias

Sarcoidose



Atenção a quadros de curso mais progressivos



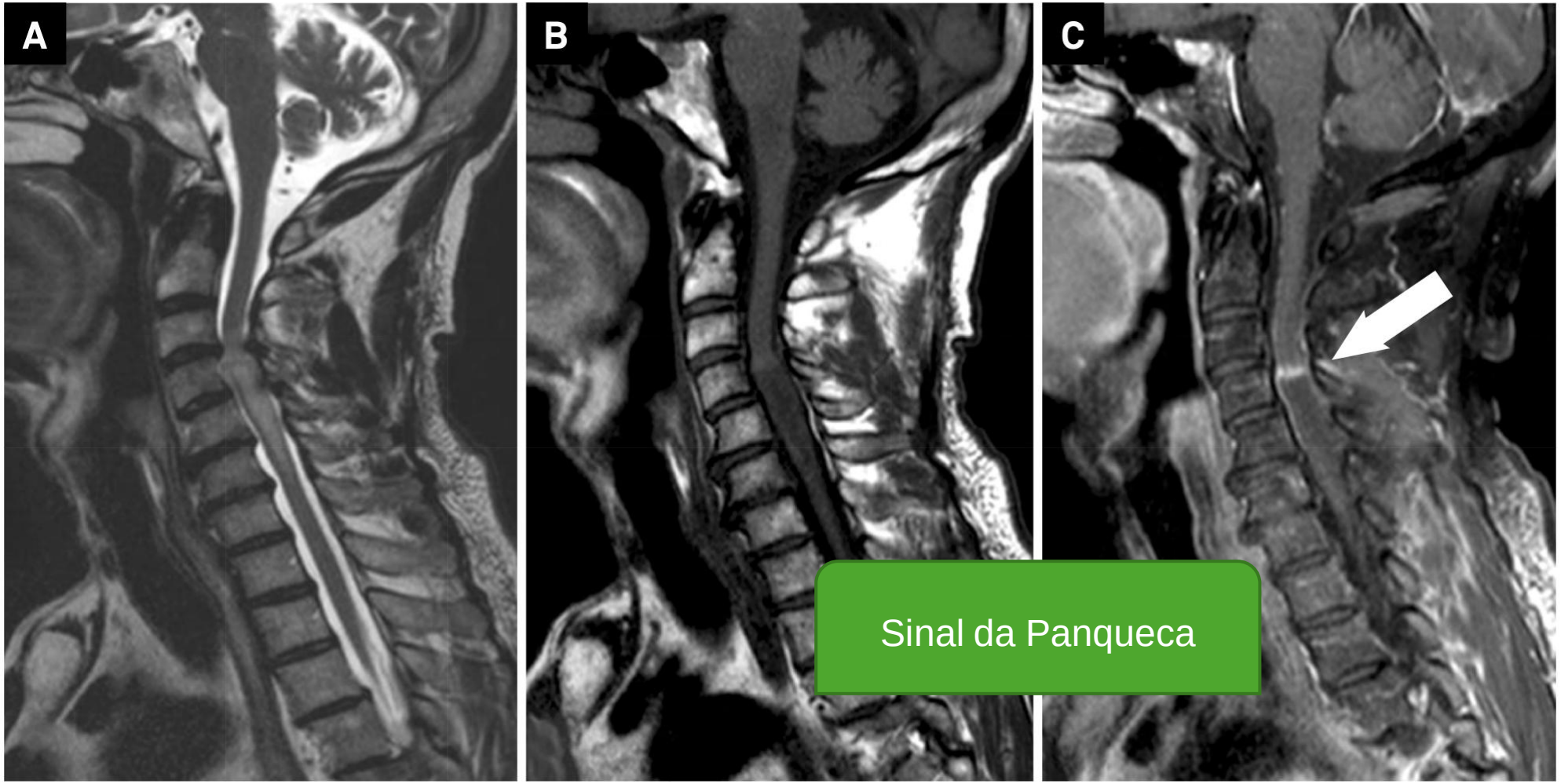
Sinal do Tridente

Case courtesy of Yune Kwong, Radiopaedia.org, rID: 21946

L. Conway, Andrew McKeo
Neurology Aug 2016, 87 (7
43-7

Outros Diagnósticos Diferencias

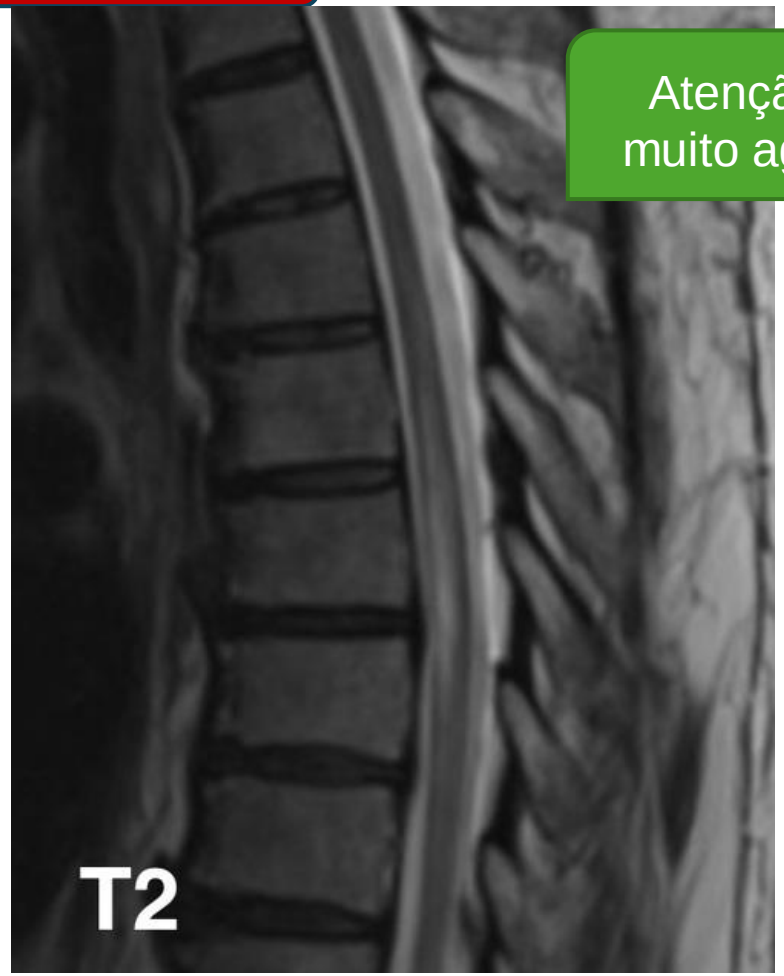
Mielopatia espondilótica



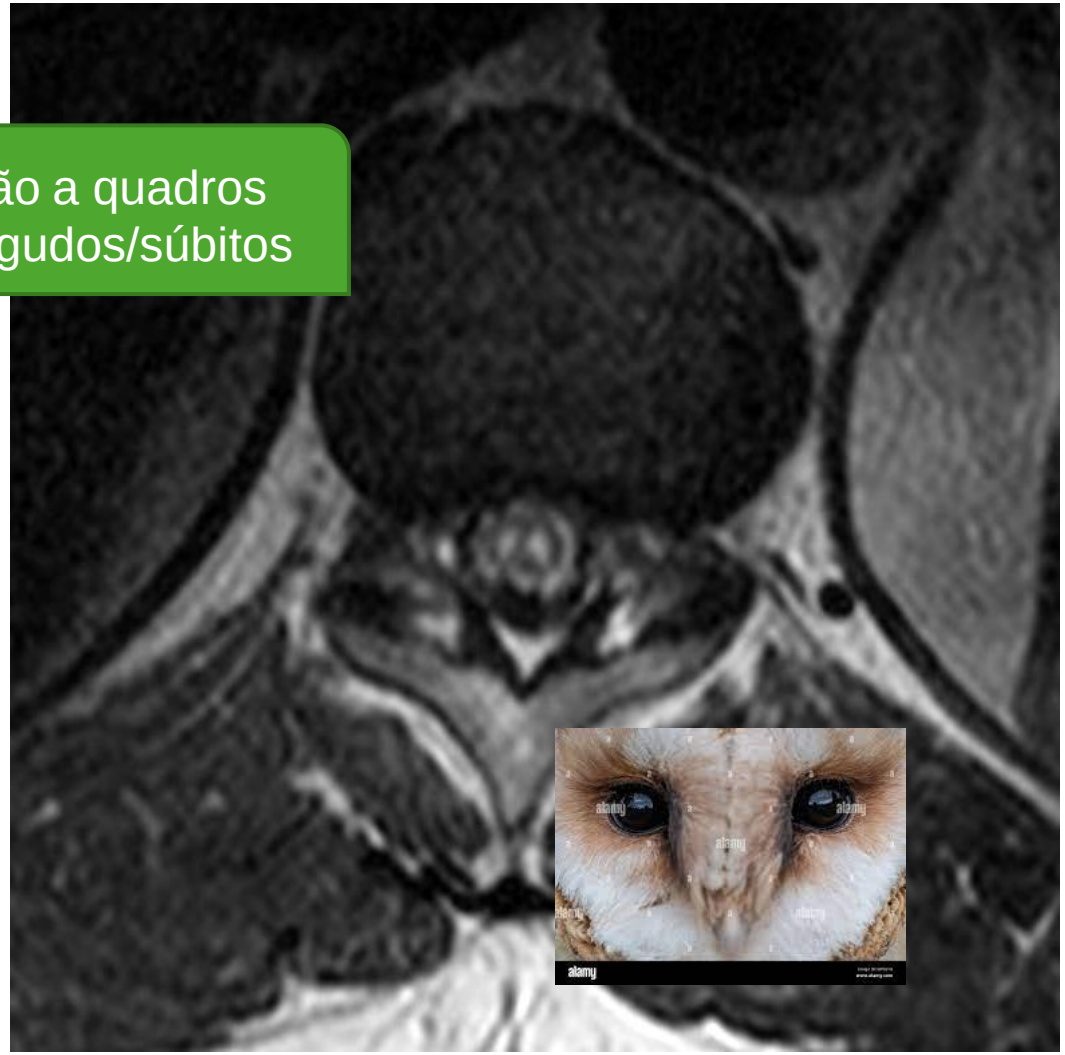
Contarato GC, Rosa Júnior M. Pancake-like gadolinium enhancement in the spinal cord: an image pattern that suggests spondylotic myelopathy. Arq Neuropsiquiatr. 2018 Jun;76(6):424-425. doi: 10.1590/0004-282X20180042. PMID: 29972426.

Outros Diagnósticos Diferencias

Mielite Isquemica



Atenção a quadros muito agudos/súbitos

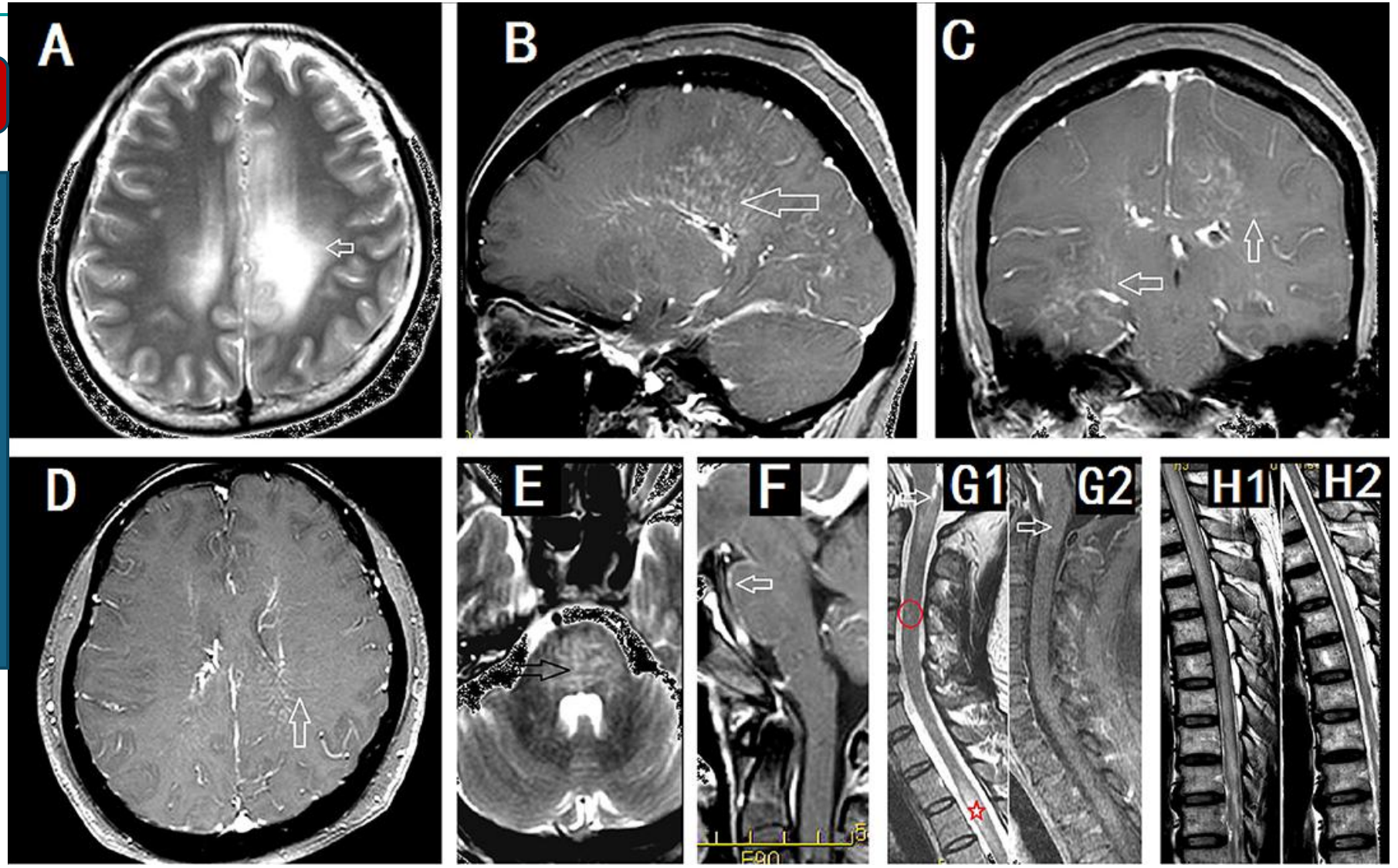


Mudgal, P., Gaillard, F. Ventral cord syndrome. Reference article, Radiopaedia.org. (accessed on 11 Nov 2022) https://doi.org/10.53347/rID-31244

Outros Diagnósticos Diferencias

Astrocitopatia GFAP

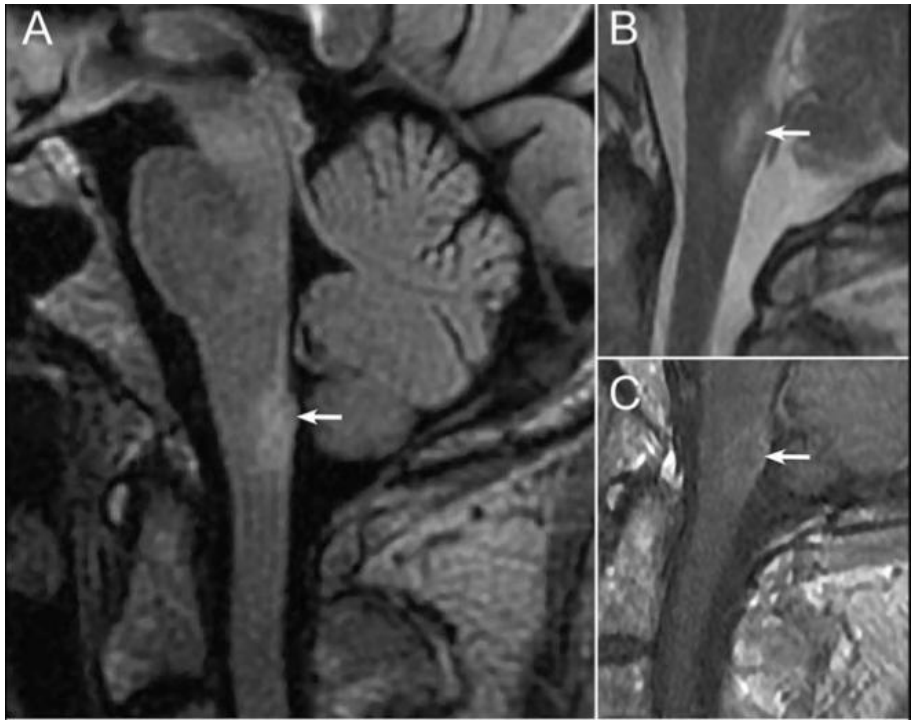
Descrita em 2016
Agudo/recorrente ou progressivo
Meningoencefalite
Ataxia
Mielite
Alterações visuais
Dist. Movimento



Síndrome da área postrema

- Duração superior a 48 horas
  - Náuseas;
  - Vômitos;
  - Soluços Incoercíveis ;

- A depender da série pode ocorrer em até 15 - 30 % dos pacientes.



Quando ocorre como primeira manifestação pode ser confundida com patologias gastrointestinais ou vestibulares

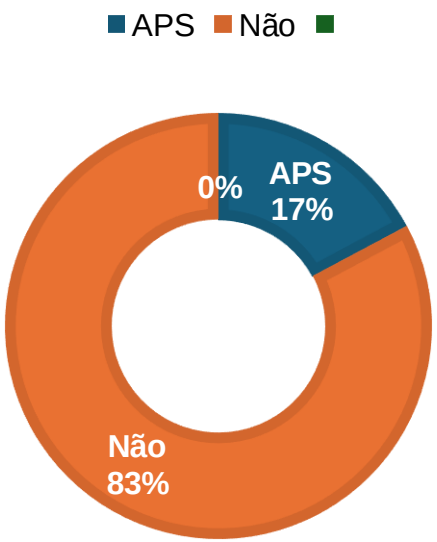
Manifestações Clínicas

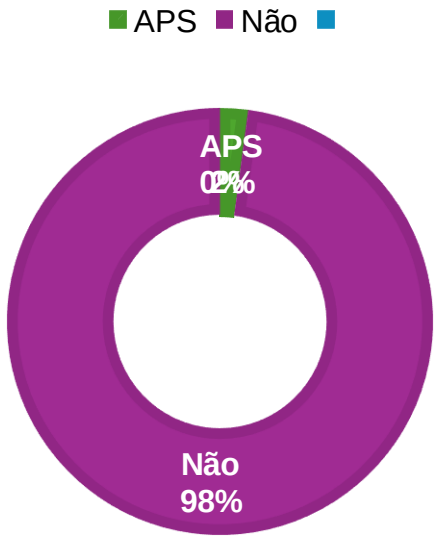
frontiers in Neurology

BRIEF RESEARCH REPORT
published: 04 June 2020
doi: 10.3389/fneur.2020.00396

Value of Area Postrema Syndrome in Differentiating Adults With AQP4 vs. MOG Antibodies

*Jae-Won Hyun[1], Young Nam Kwon[2,3], Sung-Min Kim[2], Hye Lim Lee[4], Woo Kyo Jeong[5,6], Hye Jung Lee[5,6], Byoung Joon Kim[5,6], Seung Woo Kim[7], Ha Young Shin[7], Hyun-June Shin[8], Sun-Young Oh[8], So-Young Huh[9], Woojun Kim[10], Min Su Park[11], Jeeyoung Oh[12], Hyunmin Jang[1], Na Young Park[1], Min Young Lee[1], Su-Hyun Kim[1] and Ho Jin Kim[1]**

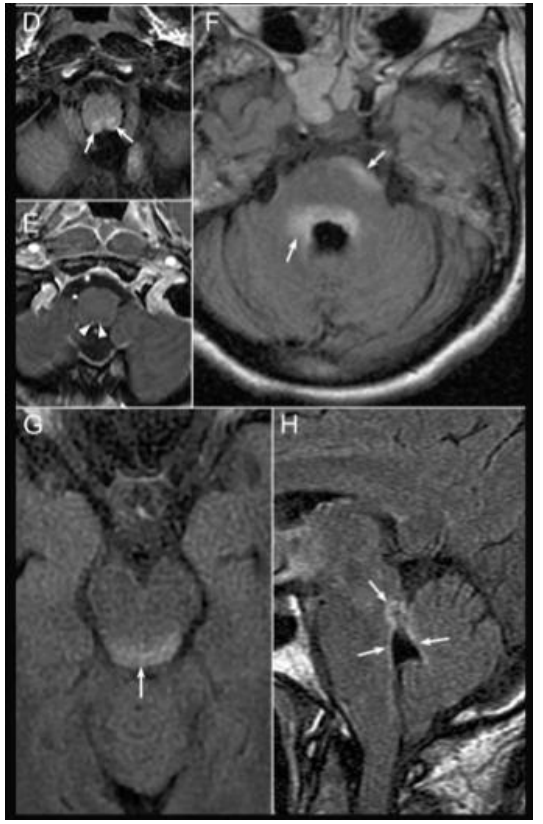




Síndrome aguda de tronco encefálico

Sintomas Agudos de Tronco

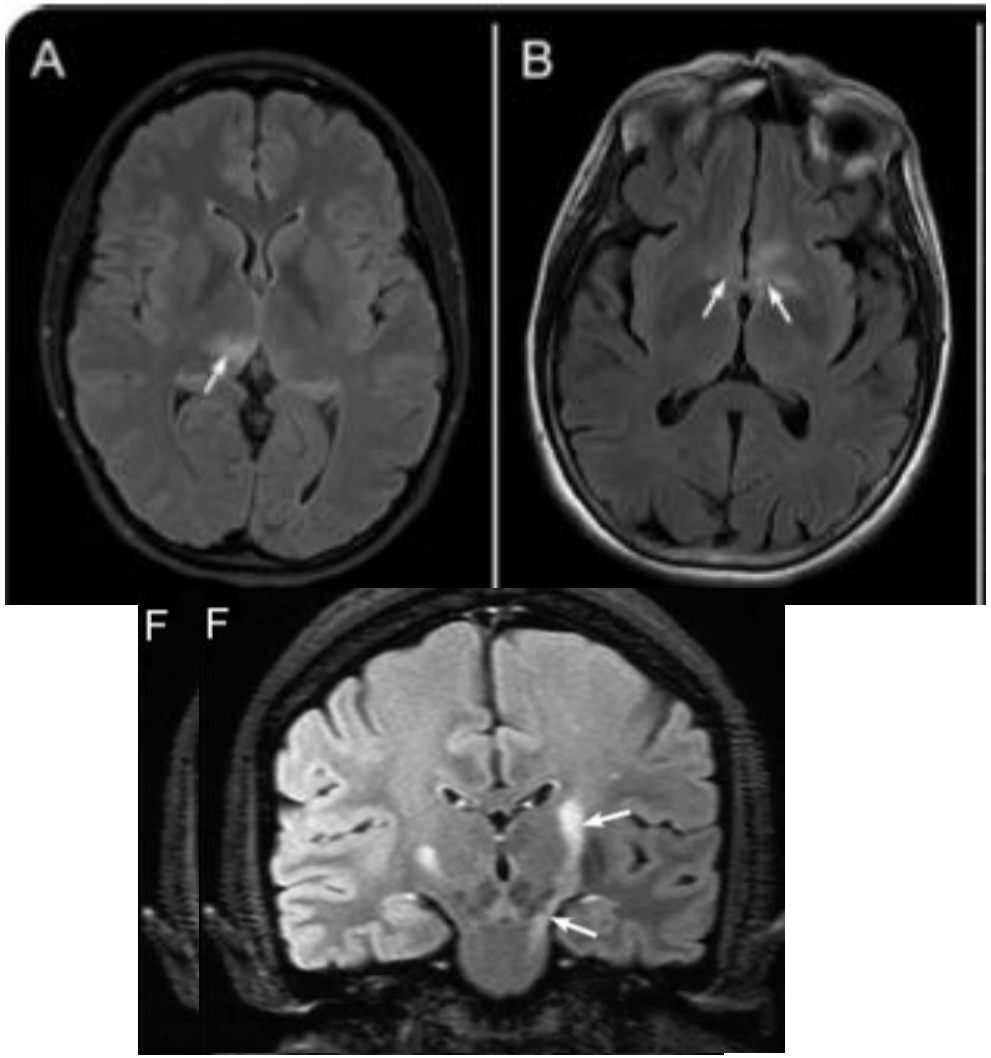
- Diplopia
- Tontura
- Paresia facial
- Disartria
- Hipoestesia facial
- Disfagia
- Paresia facial
- Alteração de consciência e respiratória



Manifestações Clínicas

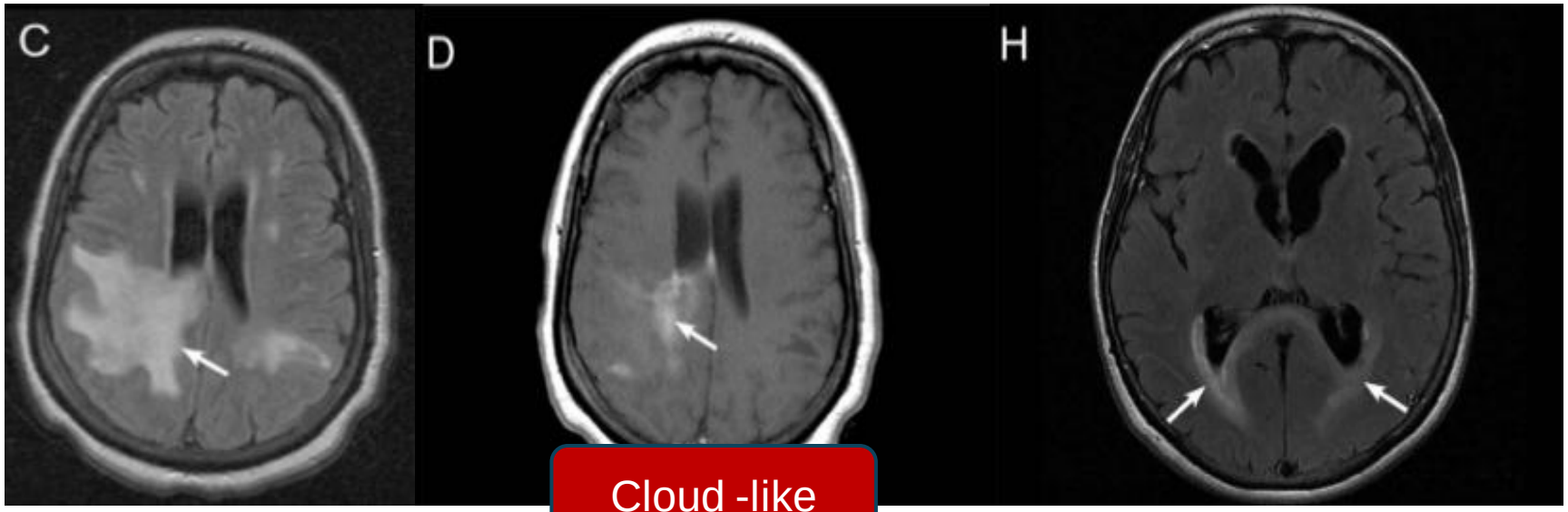
Síndrome Diencefálica

- **Narcolepsia sintomática**
- **Sonolência diurna**
- **Alterações autonômicas**
- **Amenorréia**
- **Síndrome da secreção inapropriada de ADH**



Etemadifar, M., Nouri, H., Khorvash, R. *et al.* Frequency of diencephalic syndrome in NMOSD. *Acta Neurol Belg* **122**, 961–967 (2022). https://doi.org/10.1007/s13760-021-01792-1

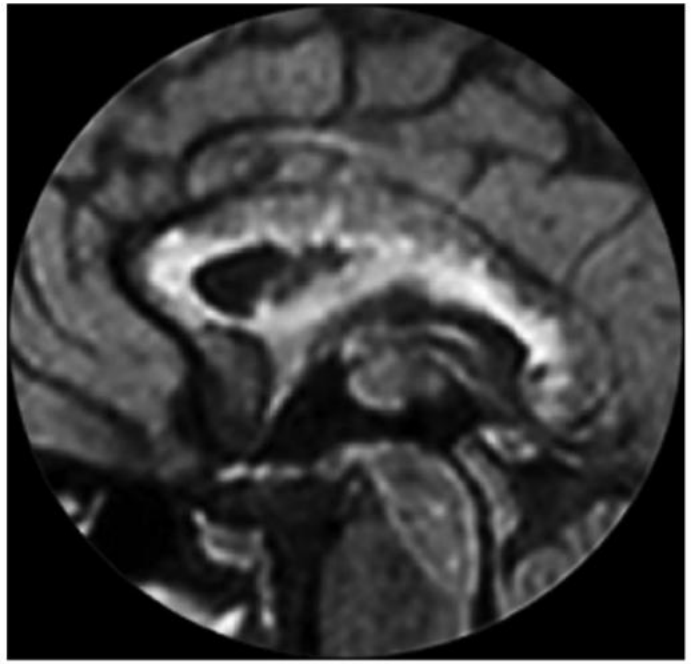
Síndrome Cerebral Sintomática



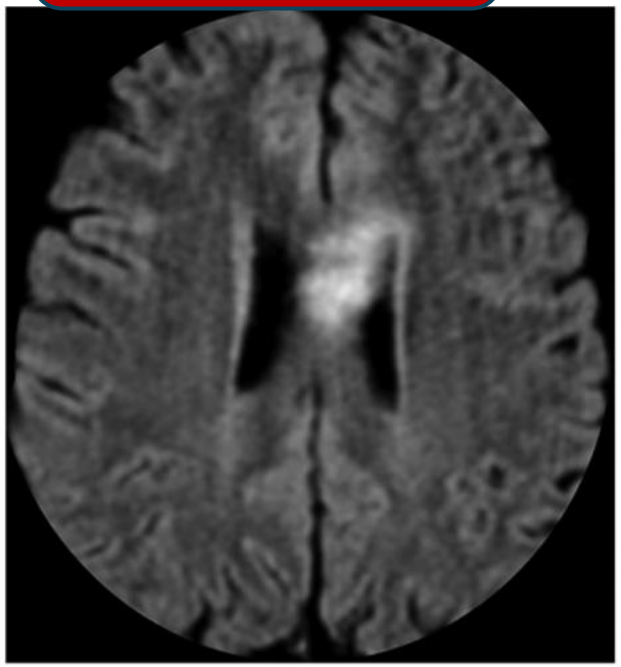
Encefalopatia
Casos de edema cerebral difuso
Hemiparesia

Outros padrão de acometimento encefálico da NMOSD na RM

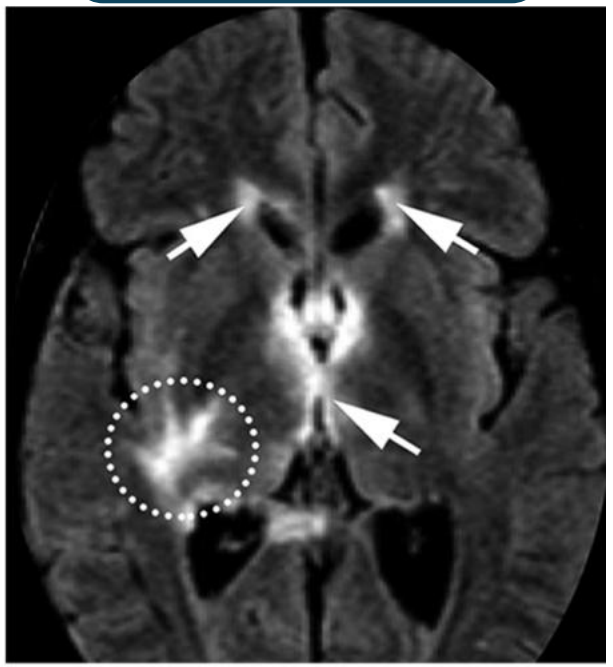
Mármore (epêndima do corpo caloso)



Arc Bridge (Ponte em arco)



Edema em tridente



Neuromyelitis Optica Spectrum Disorders: Spectrum of MR Imaging Findings and Their Differential Diagnosis Bruna Garbugio Dutra, Antônio José da Rocha, Renato Hoffmann Nunes, and Antônio Carlos Martins Maia JúniorRadioGraphics 2018 38:1, 169-193

Critérios de diagnóstico para NMOSD

2015 IPND (Painel Internacional para Diagnóstico NMOSD)

Critérios diagnósticos para NMOSD anti-AQP4(+)

1. Pelo menos 1 característica clínica central
2. Teste positivo para AQP4-IgG
3. Exclusão de diagnósticos alternativos

Principais características clínicas

1. NO
2. Mielite aguda
3. Síndrome póstrema da área : episódio de soluços inexplicáveis ou náuseas e vômitos
4. Síndrome aguda do tronco encefálico
5. Narcolepsia sintomática ou síndrome clínica diencefálica aguda com lesões de ressonância magnética (RM) diencefálicas típicas de NMO
6. Síndrome cerebral sintomática com lesões cerebrais NMO-típicas

Critérios diagnósticos para NMOSD sem AQP4-IgG e NMO com status desconhecido de AQP4-IgG

1. Pelo menos 2 características clínicas principais
   a. Pelo menos 1 característica clínica central deve ser ON, mielite aguda com LETM ou SAF
   b. Disseminação no espaço (≥2 características clínicas centrais diferentes)
   c. Cumprimento de requisitos adicionais de ressonância magnética, conforme aplicável
2. Teste negativo para AQP4-IgG usando o melhor método disponível ou teste indisponível
3. Exclusão de diagnósticos alternativos

Requisitos adicionais de ressonância magnética para NMOSD sem AQP4-IgG e NMOSD com status desconhecido de AQP4-IgG

1. ON aguda: requer ressonância nuclear magnética (RNM) cranioencefálica mostrando (a) achados normais ou apenas lesões inespecíficas da substância branca ou (b) ressonância nuclear magnética (RNM) do nervo óptico com lesão hiperintensa em T2 ou uma lesão com realce com gadolínio ponderada em T1 que se estende por >1/2 do comprimento do nervo óptico ou envolve o quiasma óptico
2. Mielite aguda: requer lesão de RNM intramedular associada que se estende por ≥3 segmentos contíguos (LETM) ou ≥3 segmentos contíguos de atrofia medular
3. SAF: requer lesões associadas de medula dorsal/área pós-rema
4. Síndrome do tronco encefálico agudo: requer lesões periependimárias associadas do tronco encefálico

A imagem não pode

DM Wingerchuk · 2015

Por que é importante fazer o diagnóstico de NMO?

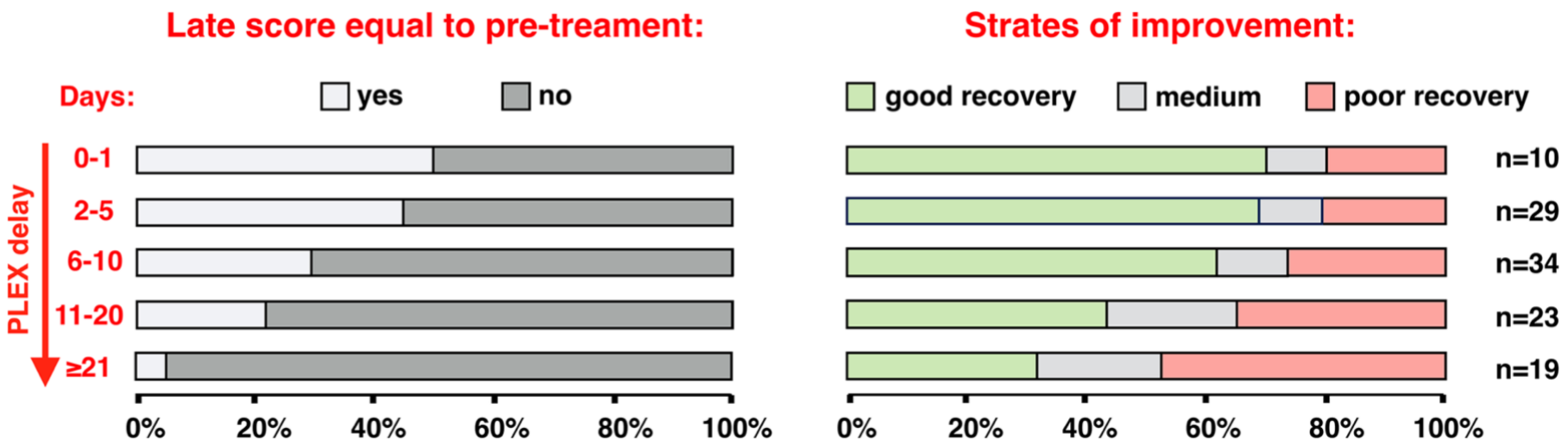
Temos tratamentos muito eficazes para tratar os surtos

Neuro-inflammation

RESEARCH PAPER

Short delay to initiate plasma exchange is the strongest predictor of outcome in severe attacks of NMO spectrum disorders

Mickael Bonnan,[1] Rudy Valentino,[2] Stéphane Debeugny,[3] Harold Merle,[4] Jean-Louis Fergé,[2] Hossein Mehdaoui,[2] Philippe Cabre[5]



Bonnan M, Valentino R, Debeugny s, *et al*. *J Neurol Neurosurg Psychiatry* 2018;**89**:346–351.

Por que é importante fazer o diagnóstico de NMO?

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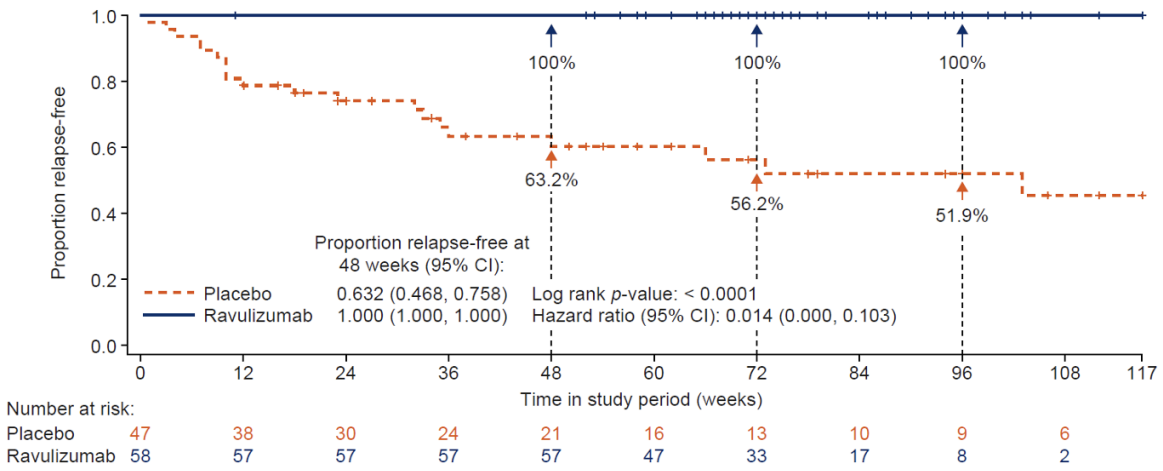

As novas terapias para Doença do Espectro da Neuromielite Óptica apresentam eficácia acima de 90%.

Pittock SJ, Barnett M, Bennett JL, Weinshenker BG, Fujihara K, Levy M, Traboulsee AL, Yamamura T, Zhang Y, Bar-Or A, et al. Ravulizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder. Ann Neurol. 2023;93(6):1053-1068. doi:10.1002/ana.26626.

Obrigado Pela Atenção!!

thiagofukuda@gmail.com

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