NEUROMIELITE ÓPTICA: os desafios para o diagnóstico e tratamento de uma doença grave e incapacitante

Hospital Universitário Clementino Fraga Filho/UFRJ
CENTRO DE REFERÊNCIA EM ESCLEROSE MÚLTIPLA E OUTRAS DOENÇAS DESMIELINIZANTES INFLAMATÓRIAS IDIOPÁTICAS DO SNC

PROGRAMA DE PÓS GRADUAÇÃO EM NEUROLOGIA
UNIVERSIDADE FEDERAL DO ESTADO DO RIO DE JANEIRO (UNIRIO)

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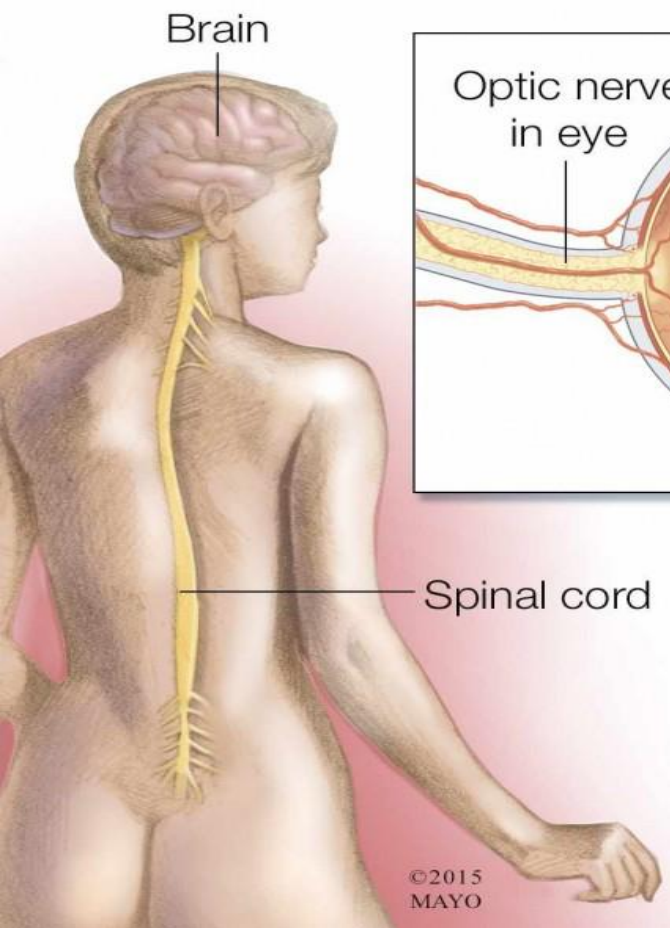
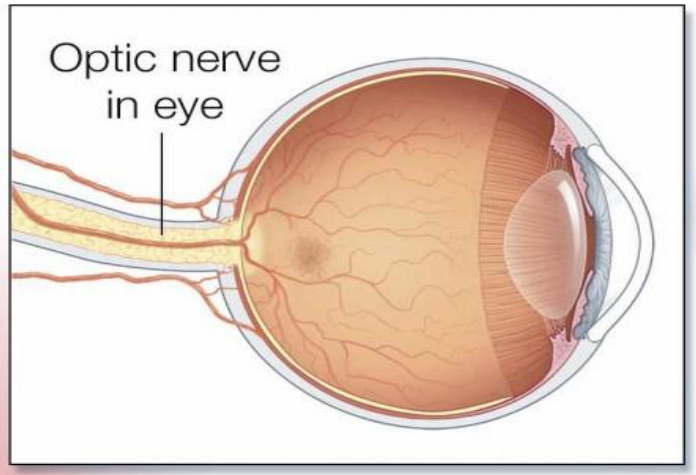
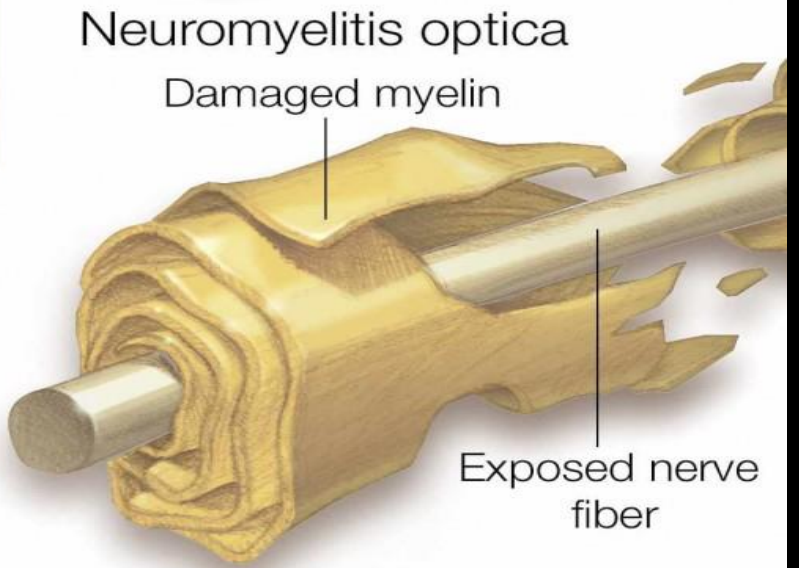
Neuromyelitis optica



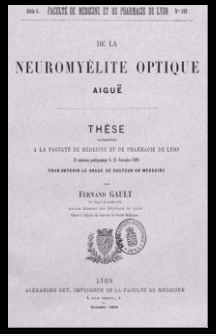




NEUROMIELITE ÓPTICA

Eugène Devic

Fernand Gault



M. E. Devic, de Lyon. — **Myélite aiguë dorso-lombaire avec névrite optique. — Autopsie.**

Femme de 45 ans, migraineuse et nerveuse, ayant eu plusieurs crises

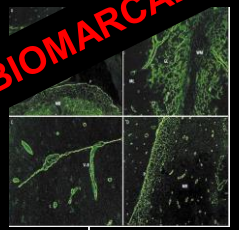
NEURITE ÓPTICA
MIELITE

travail peu rémunérateur, autant du moins que le lui permettait l'apparition de symptômes neurasthéniques bien caractérisés : insomnie, troubles digestifs, asthénie neuro-musculaire, palpitations et surtout céphalée. Ces symptômes augmentèrent peu à peu d'intensité et en septembre 1892 la malade dut cesser tout travail. En novembre 1892 la faiblesse générale et la céphalée subirent une recrudescence notable sous l'influence d'une vive frayeur.

- CONSIDERADA VARIANTE
- DA ESCLEROSE MÚLTIPLA (Brain WR, 193

MANIFESTAÇÃO ÚNICA SEM RECORRÊNCIA

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



BIOMARCADOR

Revised diagnostic criteria for neuromyelitis optica

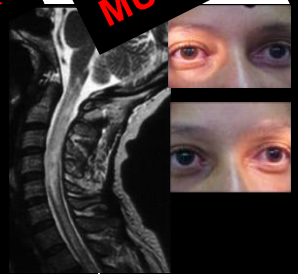
D.M. Wingerchuk, MD, FRCP(C); V.A. Lennon, MD, PhD; S.J. Pittock, MD; C.F. Lucchinetti, MD; and B.G. Weinshenker, MD, FRCP(C)

Table 3 Proposed diagnostic criteria for neuromyelitis optica (NMO)

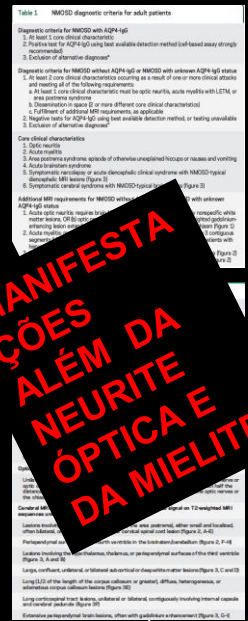
Definite NMO

Optic neuritis

NÃO MAIS UMA VARIANTE DA ESCLEROSE MÚLTIPLA



International consensus diagnostic criteria for neuromyelitis optica spectrum disorders



MANIFESTAÇÕES ALÉM DA NEURITE ÓPTICA E DA MIELITE

1894 // 1895 1930 2004 2006 2015

Published Ahead of Print on June 19, 2015 as 10.1212/WNL.0000000000001729

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

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;85:1–13

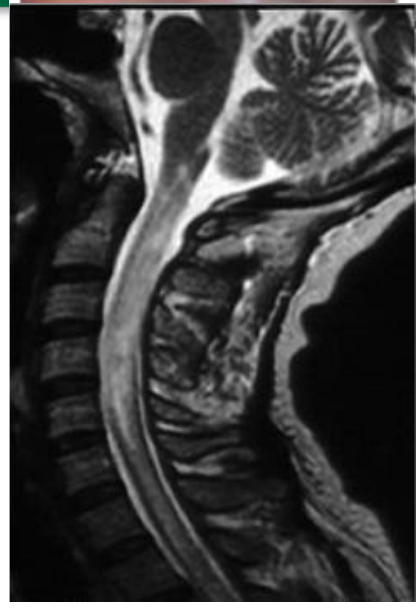


Table 1 NMOSD diagnostic criteria for adult patients

Diagnostic criteria for NMOSD with AQP4-IgG
1. At least 1 core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses[a]

Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status
1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
   a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome
   b. Dissemination in space (2 or more different core clinical characteristics)
   c. Fulfillment of additional MRI requirements, as applicable
2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses[a]

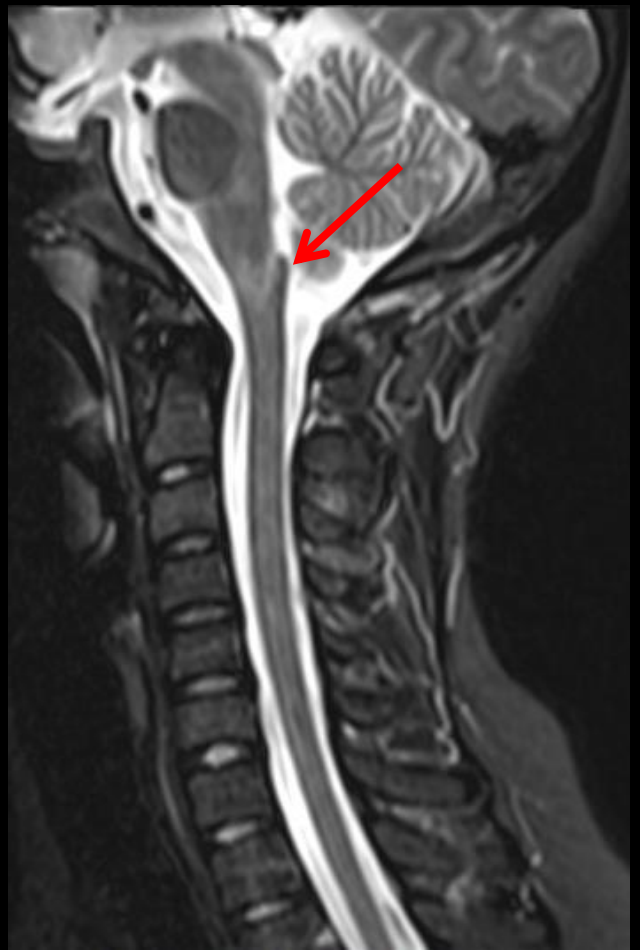
Core clinical characteristics
1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions (figure 3)
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions (figure 3)

Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with unknown AQP4-IgG status
1. Acute optic neuritis: requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm (figure 1)
2. Acute myelitis: requires associated intramedullary MRI lesion extending over ≥3 contiguous segments (LETM) OR ≥3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis (figure 1)
3. Area postrema syndrome: requires associated dorsal medulla/area postrema lesions (figure 2)
4. Acute brainstem syndrome: requires associated periependymal brainstem lesions (figure 2)

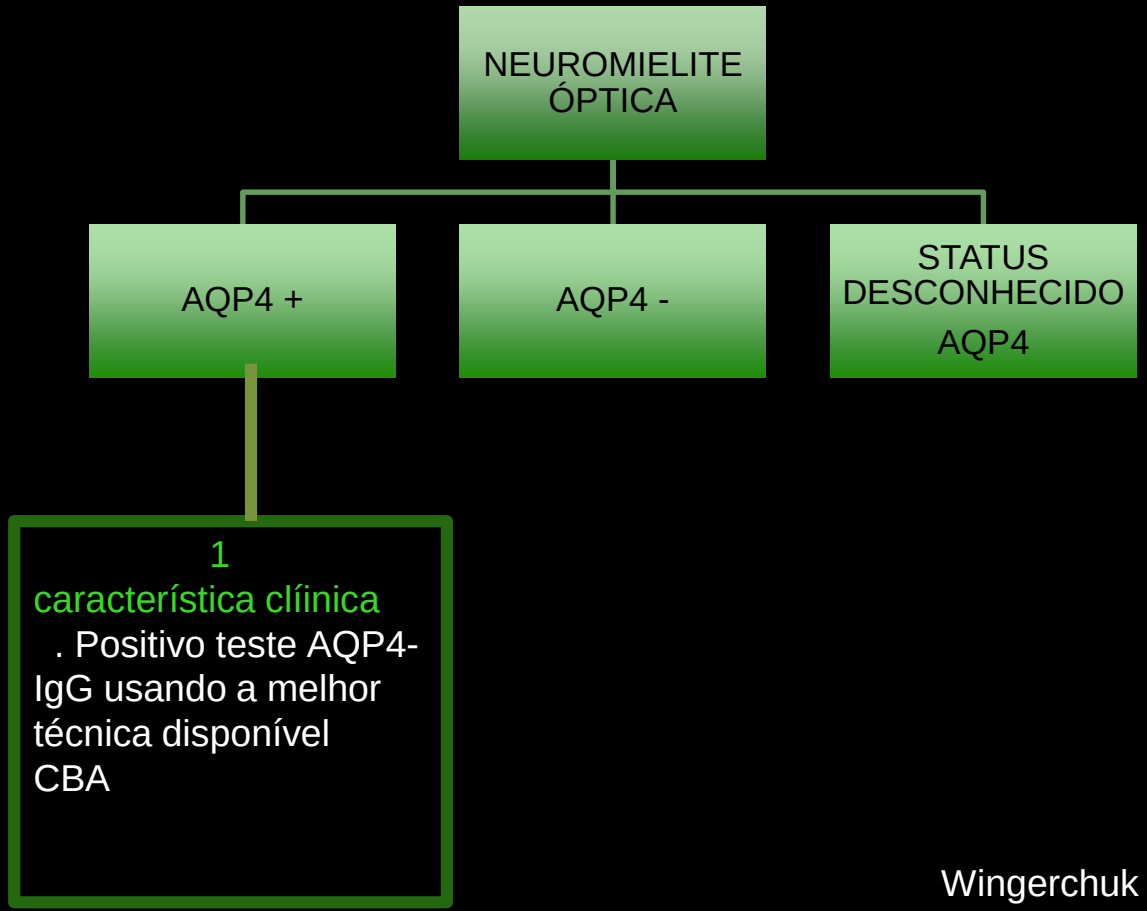
✓NEURITE ÓPTICA (PERDA DA VISÃO)
✓LESÃO MEDULAR (PARALISIA)
✓LESÃO ÁREA PÓS TREMA (SOLUÇOS E VÔMITOS INCOERCÍVEIS)

OUTROS SINTOMAS ASSOCIADOS COM NMO

- ✓SOLUÇOS CONSTANTES (MIOCLONIA PALATINA)
- ✓NÁUSEAS E VÔMITOS INCOERCÍVEIS
- ✓PARALISIA DE NERVOS CRANIANOS
- ✓DISTÚRBIOS DO SONO
- ✓OUTROS…

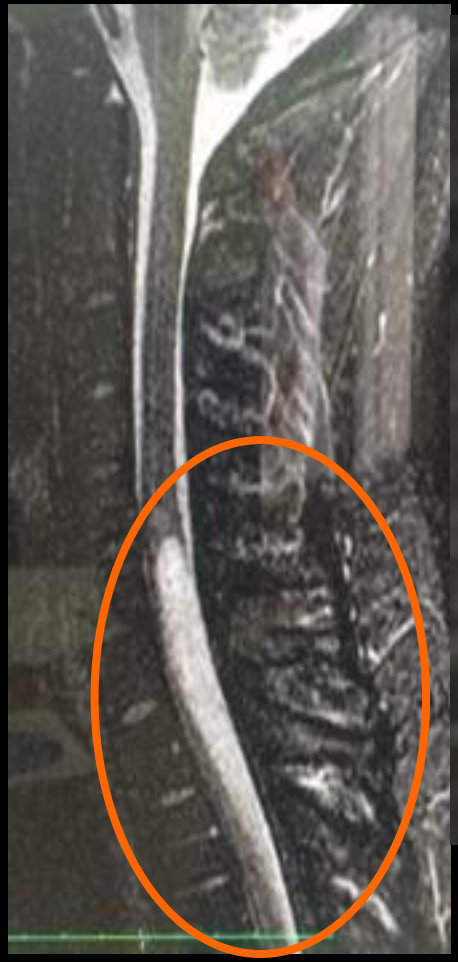


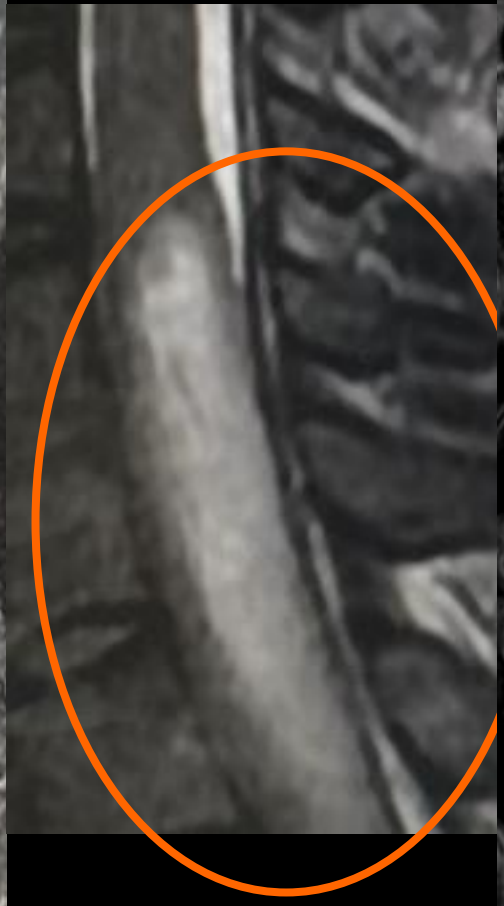
NEUROMIELITE ÓPTICA E SEU SPECTRUM

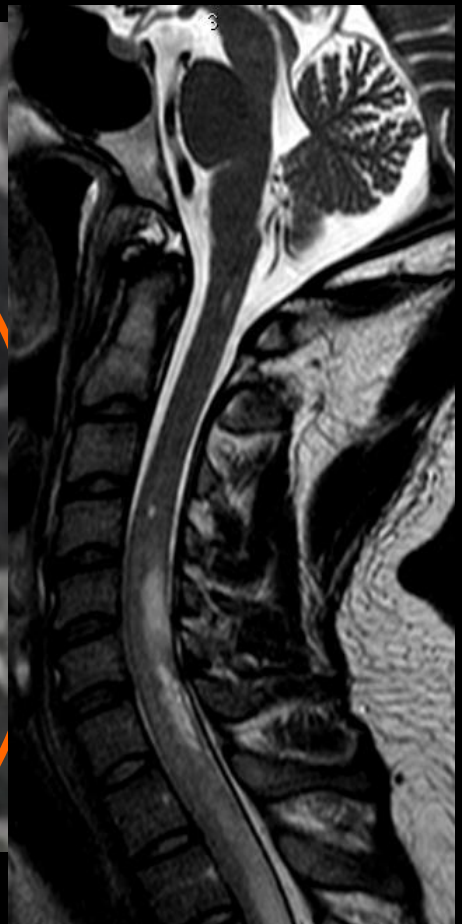


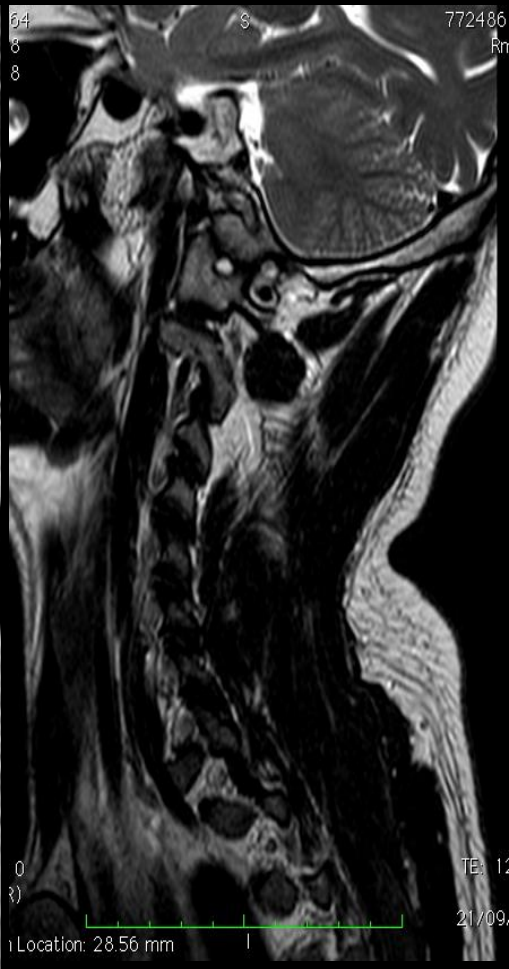
Wingerchuk et al, Neurology, 2015

J, GOLEIRO, 19 ANOS. APRESENTOU HÁ 1 ANO EPISÓDIO DE SOLUÇOS E NÁUSEAS QUE O LEVARAM A EMERGÊNCIA, SEM DIAGNÓSTICO. SEIS MESES DEPOIS PARALISIA DE MEMBROS INFERIORES



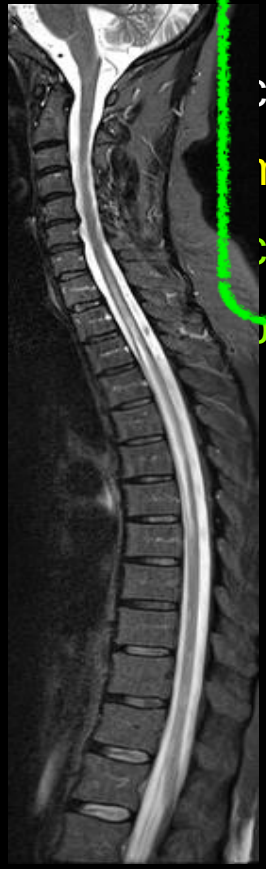






CARACTERÍSTICAS DA RM NEUROMIELITE ÓPTICA

- MIELITE TRANSVERSA LONGITUDINAL EXTENSA



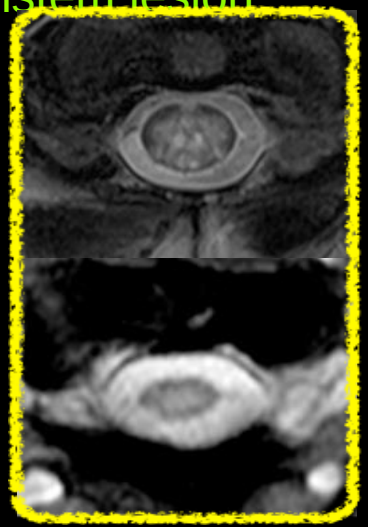
>3 vertebral segments

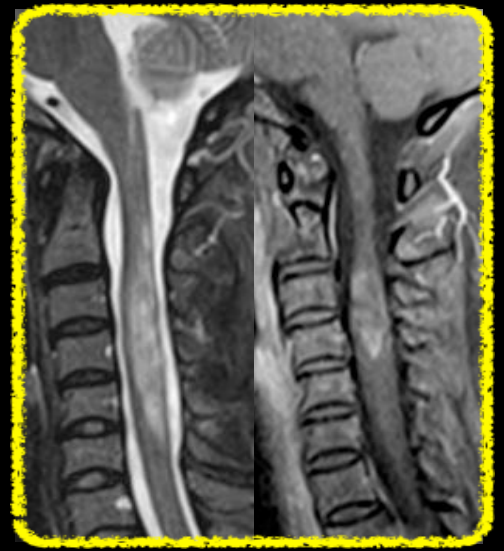
cervical toracic segment

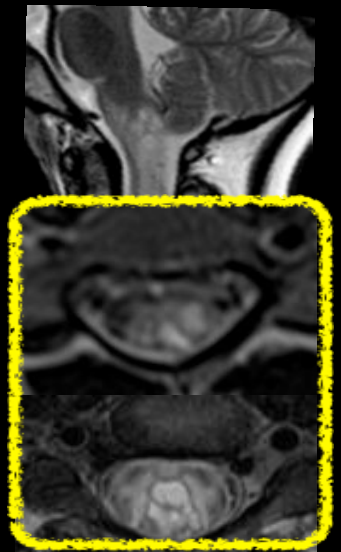
mass efect and GD enhancement

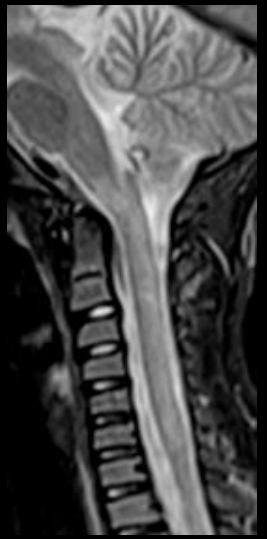
cystic lesion

brainstem lesion

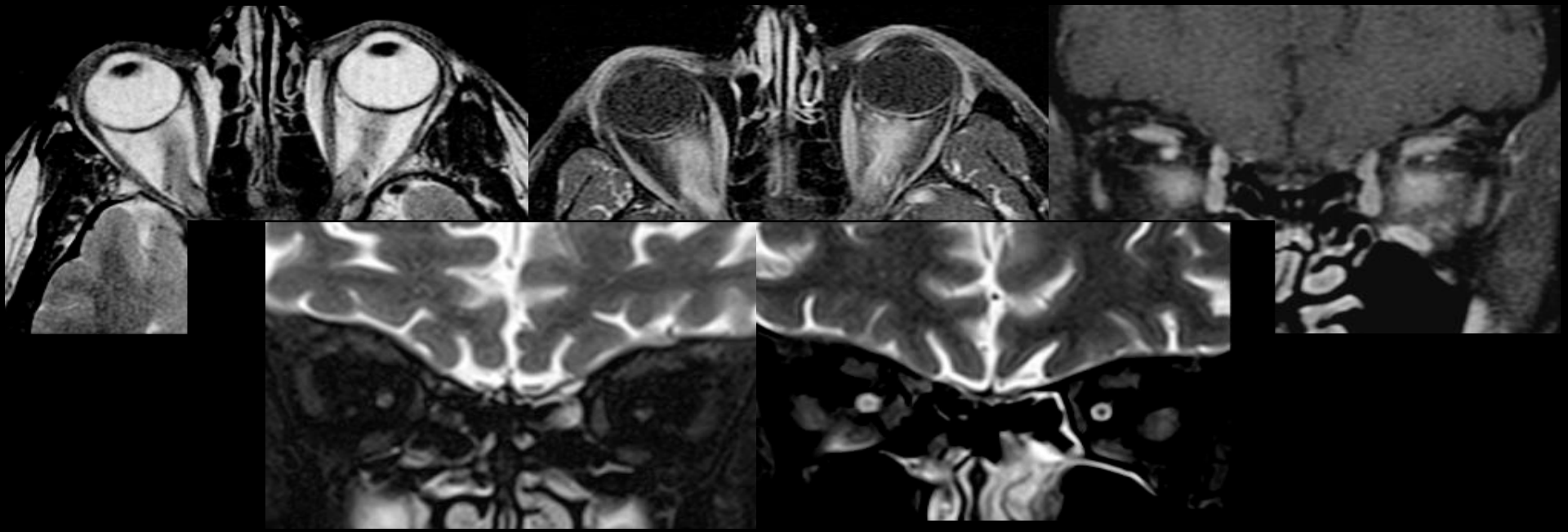








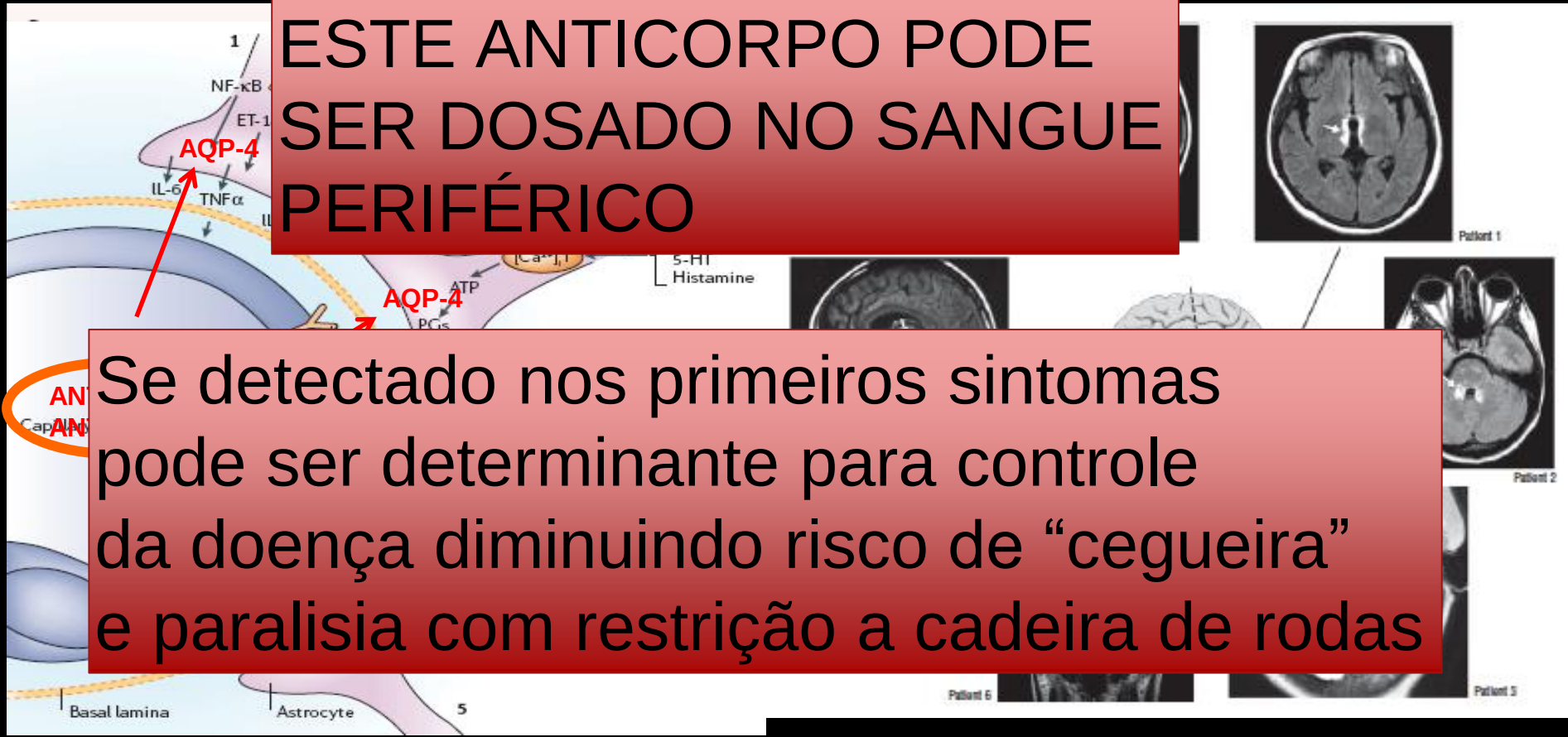
NEUROMIELITE OPTICA



Pau D et al. Optic neuritis. Eye (London) 2011; Apr 29.

PORQUE ISSO ACONTECE ?

Anticorpo no sangue periférico, destrói os canais de Aquaporina (AQP4) que ficam no final dos neurônios provocando morte neuronal



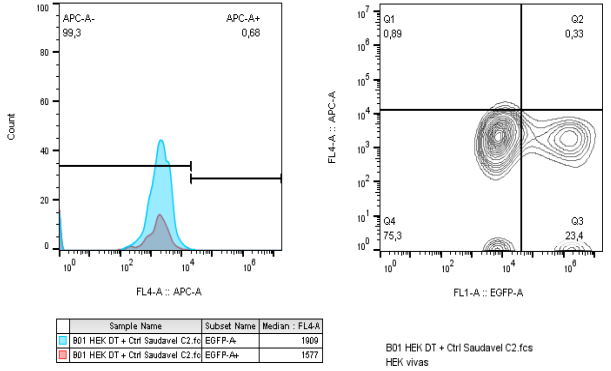
Técnica CBA

AQP4 and MOG

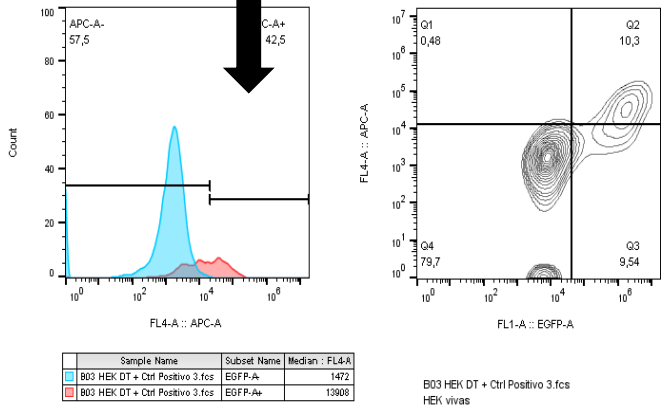
CBA thecnic -(cell-based assay (strongly recommended)

(células frescas transfectadas por plasmídio que codifica proteínas e verificando por citometria de fluxo)

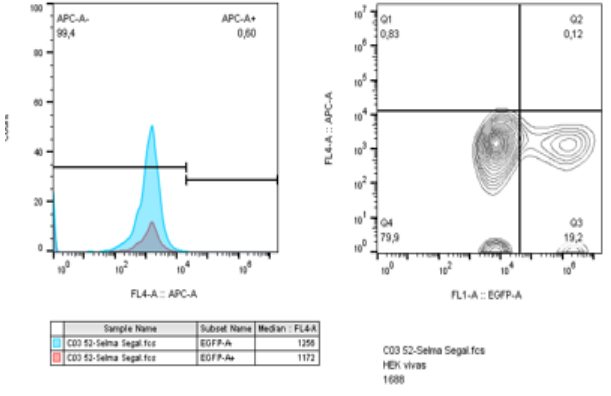
Anti-AQP4 (-)



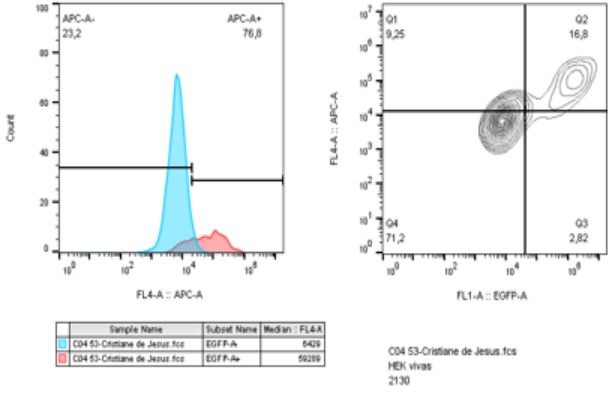
Anti-AQP4 (+)



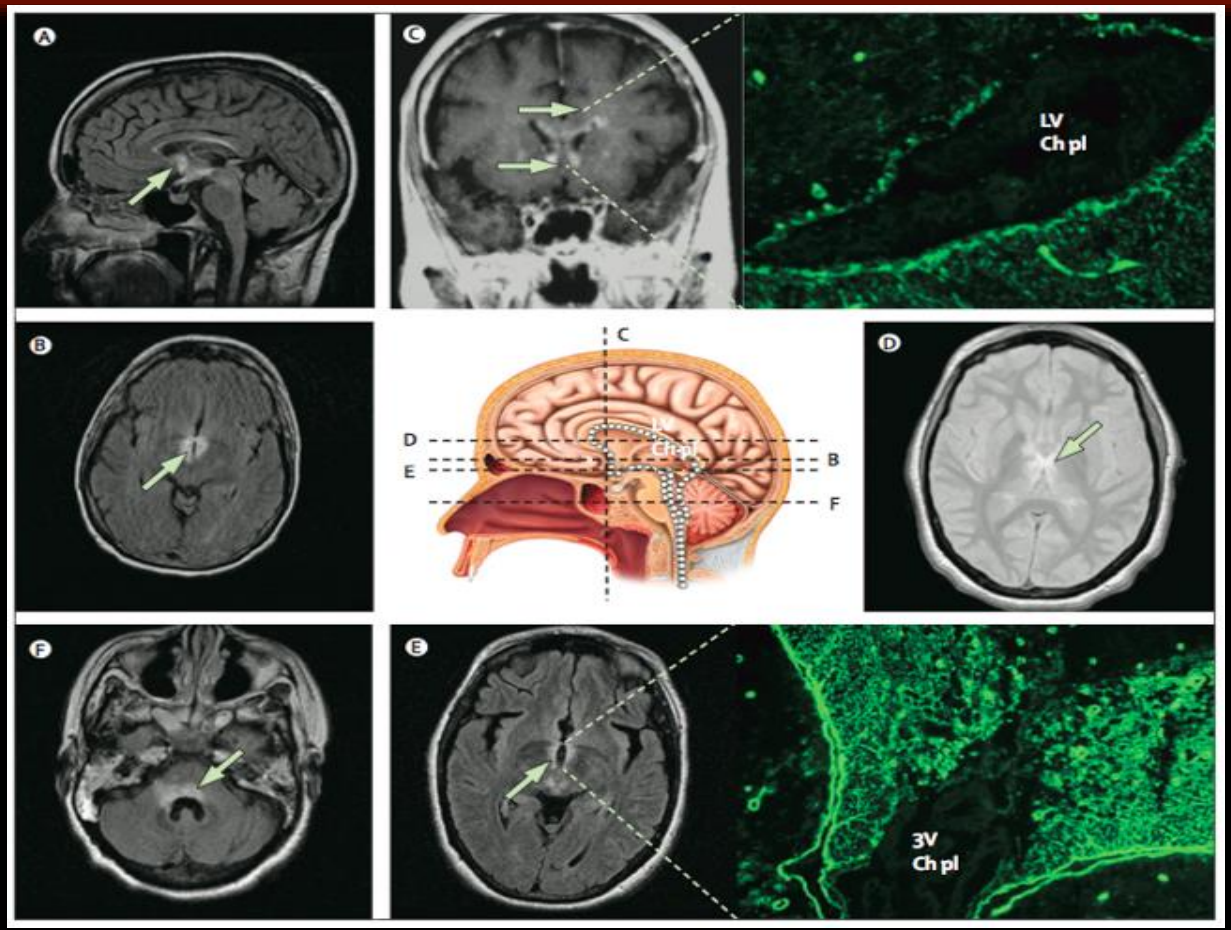
Anti-MOG (-)



Anti-MOG (+)



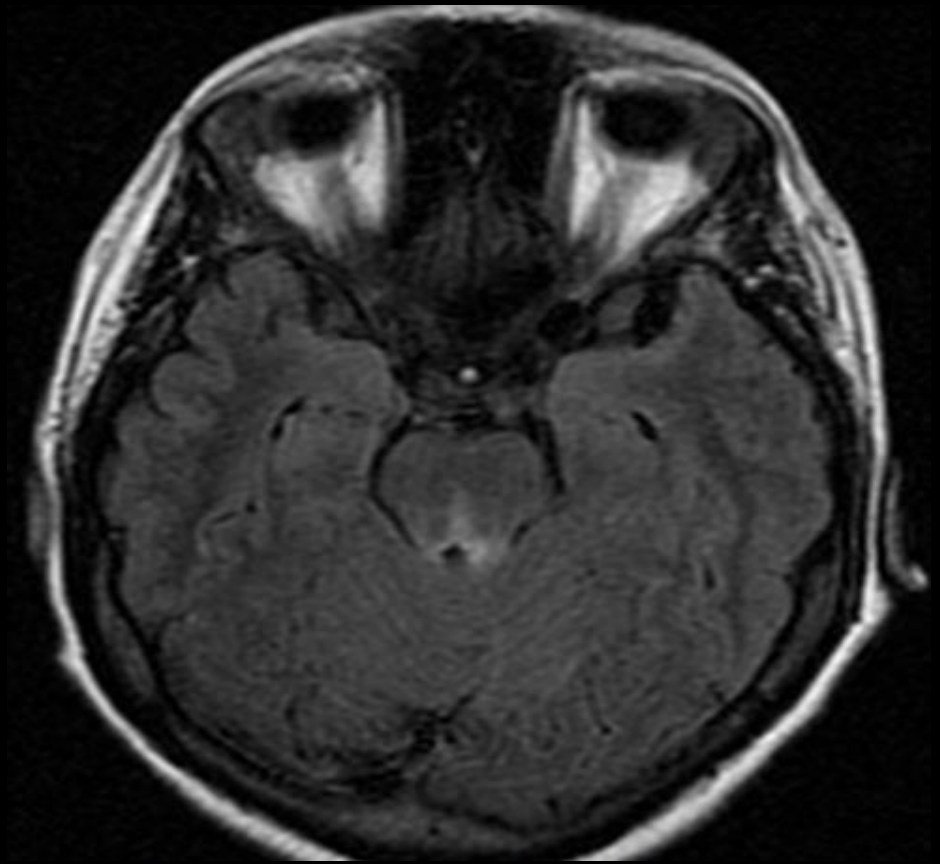
AQP 4
IgG NMO
Sens: 73%
Spec: 91%



Wingerchuck DM et al. The spectrum of neuromyelitis optica. Lancet Neurology

PODEMOS FAZER DIAGNÓSTICO PRECOCE DA NEUROMIELITE ÓPTICA ?

Cristina, 34 anos, visão dupla por paralisia do nervo oculomotor
2006



EVOLUÇÃO

- ✓ 2007 – Perda da Visão Esquerda!
- ✓ Ac Anti-AQP4 (+)
- ✓ Há 10 anos usando AZATIOPRINA (não autorizado no CID-10 para NMO)
- ✓ Nunca sofreu lesão medular

ESCALA DE INCAPACIDADE EXPANDIDA – EDSS

QUAL A FREQUÊNCIA DA NEUROMIELITE ÓPTICA NO BRASIL e IMPACTO NA INCAPACIDADE E MORTE?

Research Paper

MULTIPLE SCLEROSIS JOURNAL | MSJ

The impact of diagnostic criteria for neuromyelitis optica in patients with MS: a 10-year follow-up of the South Atlantic Project

Regina M Papais-Alvarenga[1,2], Claudia CF Vasconcelos[2], Soniza V Alves- Leon[2,3], Elizabeth Batista[1], Claudia MM Santos[2], Solange MGG Camargo[1], Mauricio Godoy[4], Maria C Lacativa[2,5], Mariangela Lorenti[4], Benito Damasceno[7], Alfredo Damasceno[7], Doralina Brum[8], Amilton A Barreira[9], Maria S Guimarães Rocha[10], Helcio Alvarenga[2] and Charles P Tilbery[11]

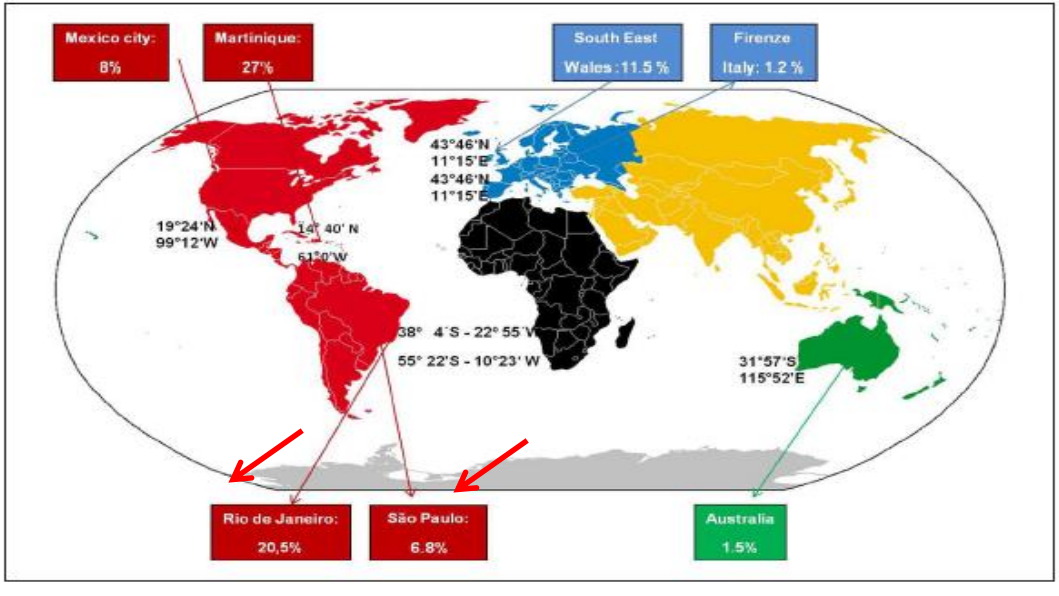


Figure 2. Relative frequency of NMO cases among total cases (MS + NMO).
MS: Multiple sclerosis; NMO: neuromyelitis optica.

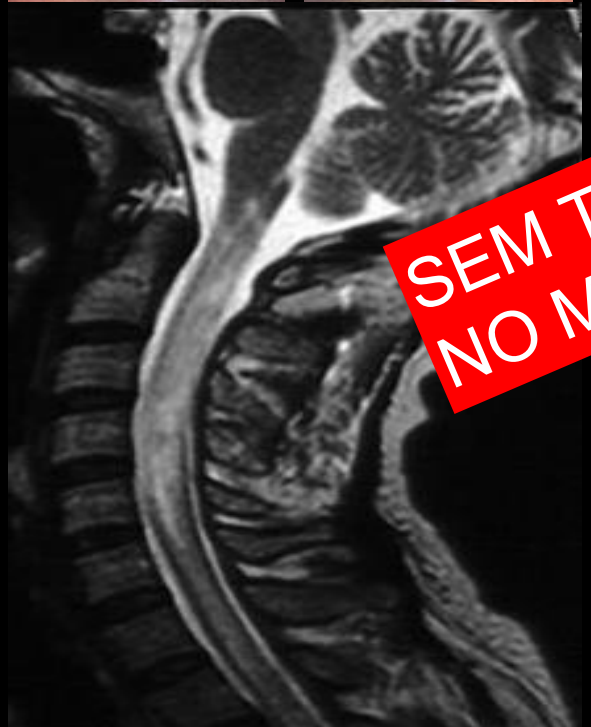
Table 2. Comparison between NMO and RRMS characteristics of the population sample from the Southeast region of Brazil.

Variable	NMO (n = 49)	RRMS (n = 221)	p value
Sex (%)			
Female	77.6%	80.1%	$p = 0.690$
Male	22.4%	19.9%	
Ethnicity (%)			
African	55.1%	27.6%	$p = 0.000$
White	44.9%	72.4%	
Time			
Age at onset, mean ± SD (range)	30.57 ± 11.27 (7–55)	29.19 ± 9.50 (8–54)	$p = 0.406$
Disease duration, Mean ± SD (range)	14.89 ± 7.71 (1–32)	18.46 ± 8.16 (10–53)	$p = 0.005$
Last EDSS			
Median (range)	6.0 (1–10)	4.0 (0–10)	$p = 0.001$
Mild disability (%)	16.3%	39.4%	$p = 0.002$
Moderate disability (%)	28.6%	17.2%	$p = 0.07$
Severe disability (%)	55.1%	43.4%	$p = 0.14$
Deaths (%)	30.6%	5.9%	$p = 0.000$

EDSS: Expanded Disability Status Score; MS: multiple sclerosis; NMO: neuromyelitis optica; RRMS: relapsing–remitting MS at onset.

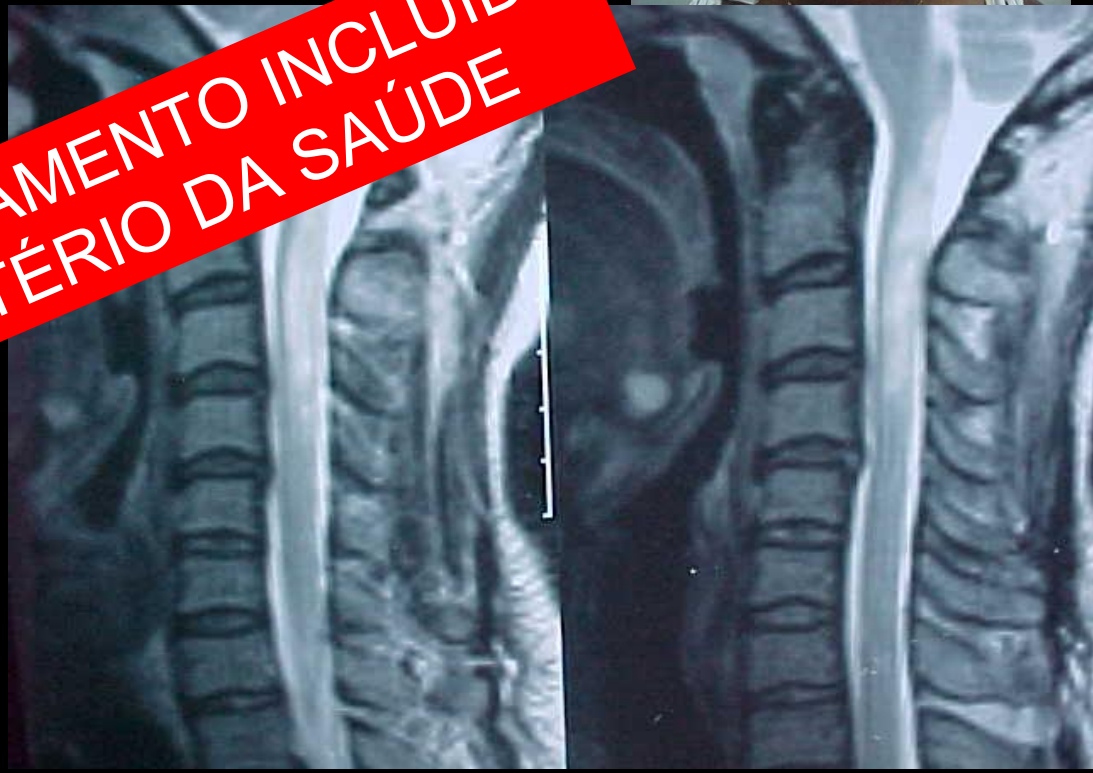
NMO

28 ANOS, BRANCO,
2001 - NEURITE ÓPTICA BILATERAL
2002 – MIELITE CERVICAL



NMO

39 ANOS, AFRO DESCENDENTE
1998 - NEURITE ÓPTICA
1999 – MIELITE (EDSS 8.0)



SEM TRATAMENTO INCLUÍDO NO MINISTÉRIO DA SAÚDE

A LESÃO MEDULAR É SEMPRE EXTENSA? NÃO...

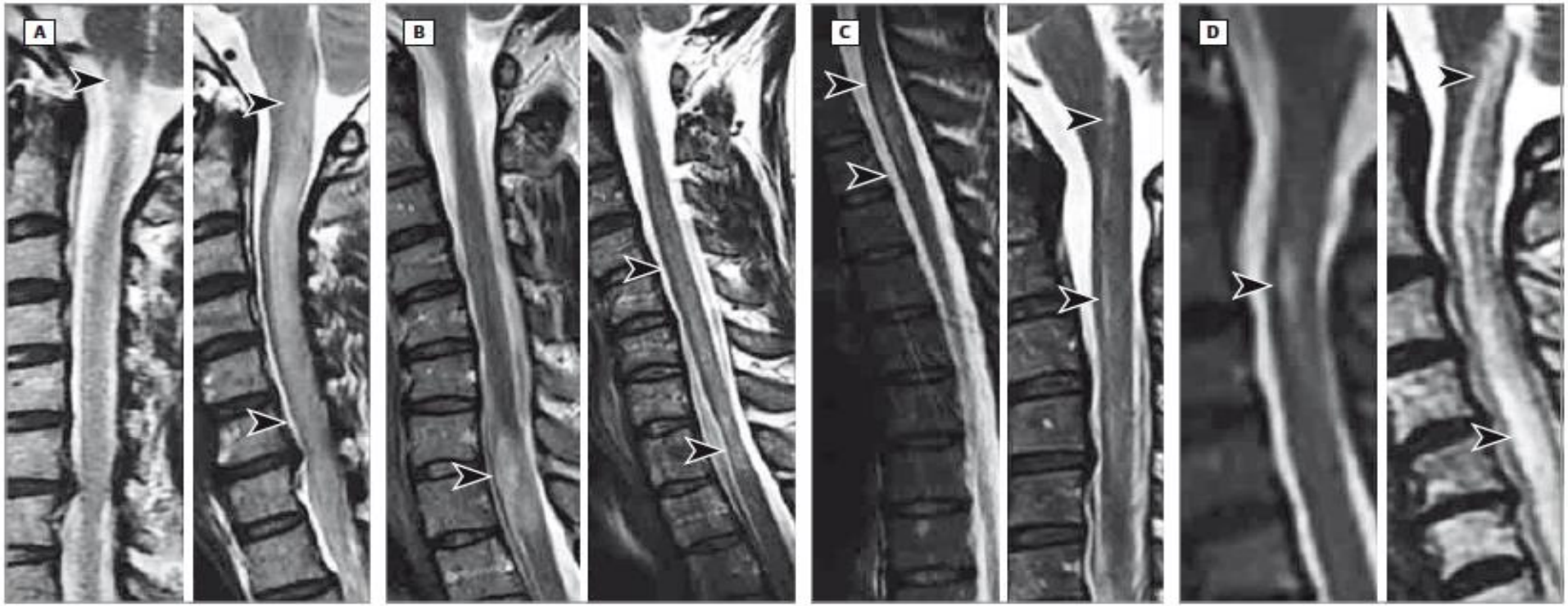
Original Investigation

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

JAMA Neurology Published online November 10, 2014

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



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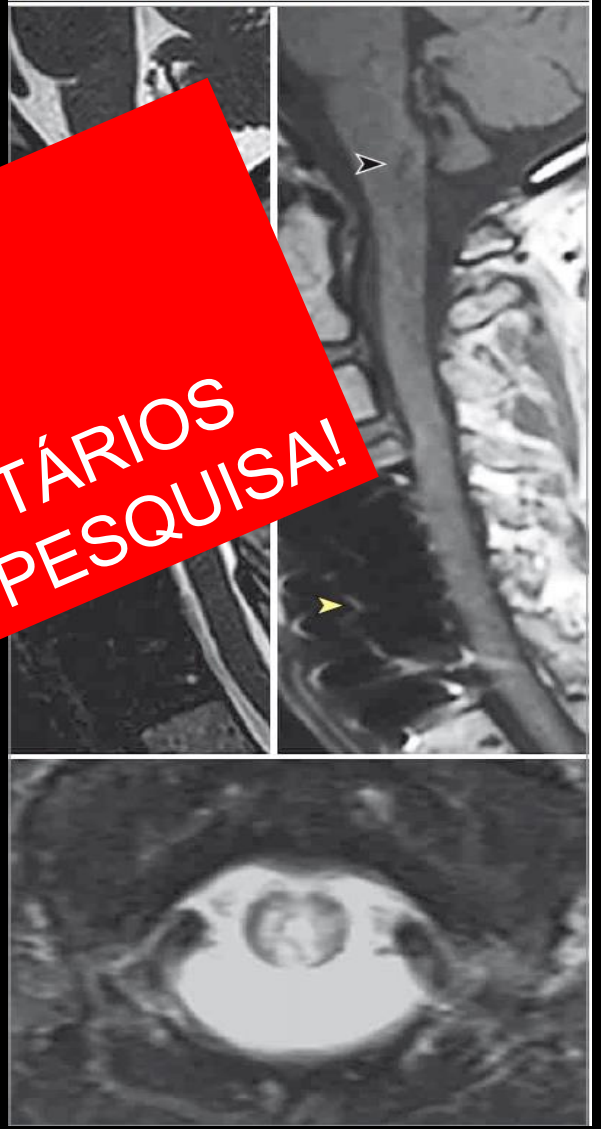
CONCLUSIONS AND RELEVANCE Short transverse myelitis is not
when it is present, delays diagnosis and treatment. Clini
identified in this study may help select patients wit
NMOSD. Short transverse myelitis does not
NMOSD diagnosis.

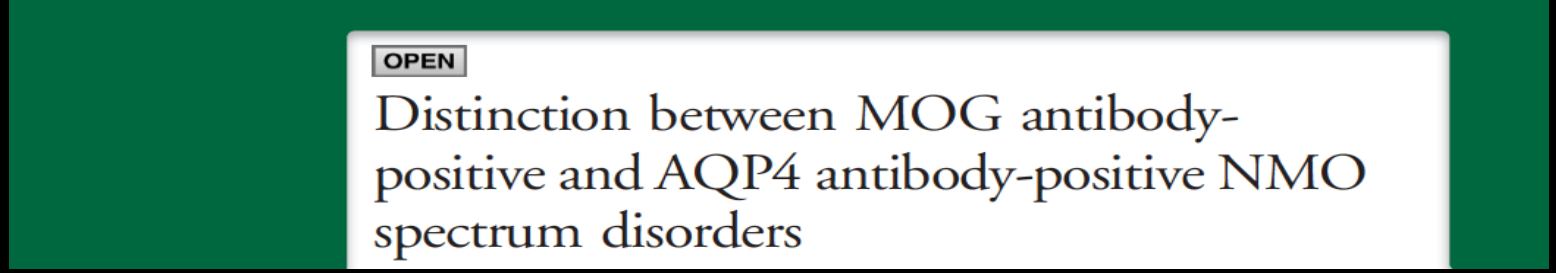
- ✓ O nã
  lesõ
  o trat
- ✓ Recor que todos devem testados para Ac Anti AQP-4

NENHUM SEVIÇO PÚBLICO DISPONIBILIZA ESSE EXAME,

POUCOS HOSPITAIS UNIVERSITÁRIOS REALIZAM COM INSUMOS DE PESQUISA!

Figure 3. Magnetic Resonance Imaging of Dorsal Medullary Lesion Extending to Upper Cervical Spinal Cord





- Características dos anti-MOG (+) comparados com AQP4 (+) e soronegativos

2015 – DESCOBERTA DE UM NOVO BIOMARCADOR – O ANT- MOG

TRATAMENTO

- FASE AGUDA

CORTICÓIDE

PLASMAFERE

IMU

- TRAT

PRESSORE

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MONOCLONAIS

DIFÍCIL ACESSO A TODOS OS TRATAMENTOS
- CID 10 DA NEUROMIELITE ÓPTICA NÃO ESTÁ LIGADO A NENHUM DELES

OUTROS DIAGNÓSTICOS DIFERENCIAIS...

Semin Reprod Med. 2016 Sep;34(5):273-279. Epub 2016 Sep 9.

Zika Virus-Associated Neurological Disease in the Adult: Guillain-Barré Syndrome, Encephalitis, and Myelitis.

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Abstract

Zika virus (ZIKV) has caused a major infection outbreak in the Americas since 2015. In parallel with the ZIKV epidemic, an increase in cases of neurological disorders which include Guillain-Barré syndrome (GBS), encephalitis, and myelitis have been linked to the infection. We reviewed the evidence suggesting a relationship between ZIKV and neurological disorders in adults. A search of the literature supporting such link included databases such as PubMed and the World Health Organization (WHO) surveillance system. Through June 1, 2016, 761 publications were available on PubMed using the search word "Zika." Among those publications as well as surveillance reports released by the WHO and other health organizations, 20 articles linked ZIKV with neurological complications other than microcephaly. They corresponded to population and surveillance studies ($n = 7$), case reports ($n = 9$), case series ($n = 3$), and case-control studies ($n = 1$). Articles were also included if they provided information related to possible mechanisms of ZIKV neuropathogenesis. Evidence based on epidemiological and virological information supports the hypothesis that ZIKV infection is associated with GBS. Although cases of encephalopathy and myelitis have also been linked to ZIKV infection, the evidence is scarce and there is a need for virological, epidemiological, and controlled studies to better characterize such relationship.

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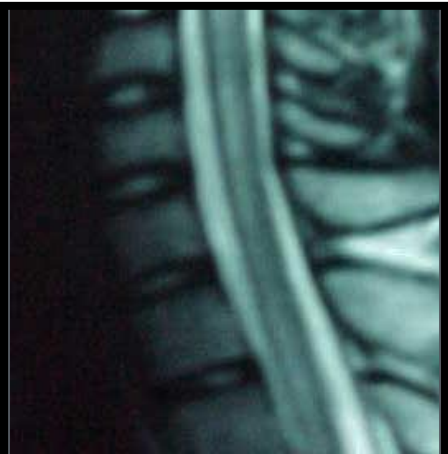
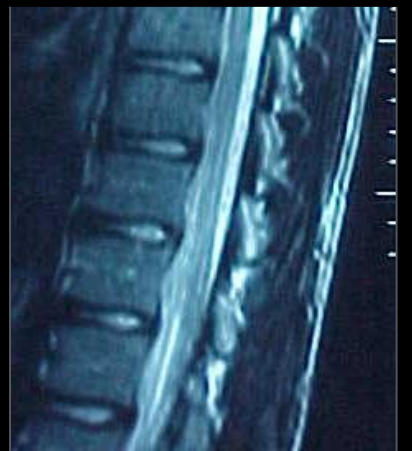
Rigidez de nuca terminal, paraparesia flacida, FM
grau II,
reflexos profundos presentes e simétricos,
cutâneo-plantar abolidos, cut. abdominais abolidos
hipoestesia superficial e profunda com nível em T4





Case Report

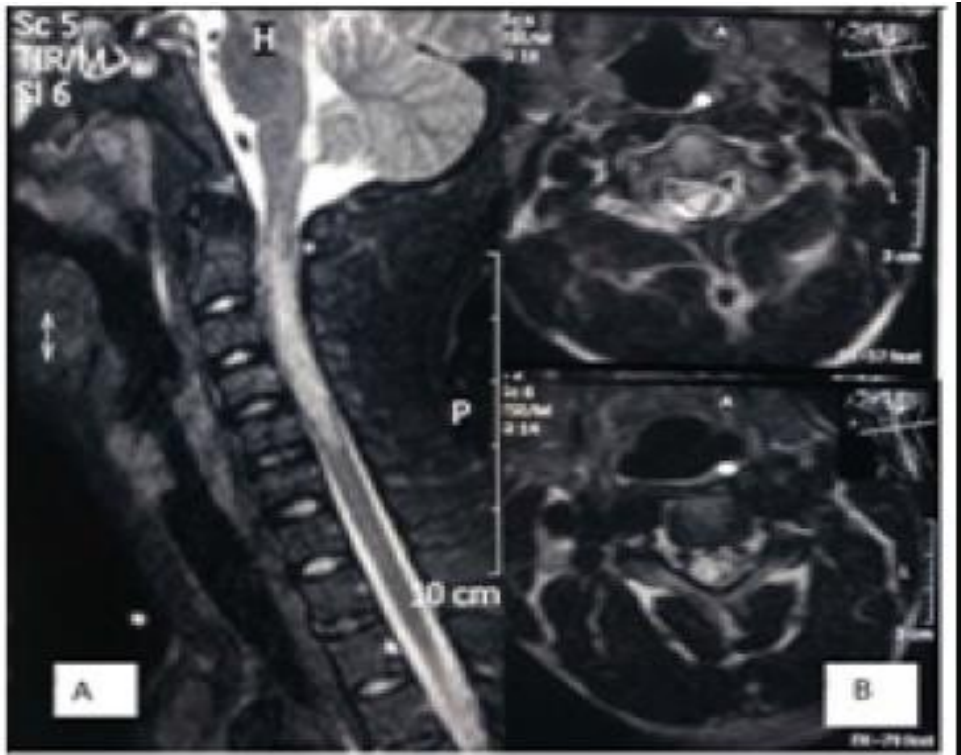
An Unusual Case of Myelitis with Myositis

NEERA CHOUDHARY[1], PRASHANT MAKHIJA[2], VINOD PURI[3], GEETA ANJUM KHWAJA[4], ASHISH DUGGAL[5]

ABSTRACT

The Chikungunya virus belonging to genus alphavirus and family togaviridae causes an arthropod-borne self-limiting febrile illness in humans. Neurological complications are rare with myelitis being even a rarer presentation. We report here a patient with Chikungunya fever who developed acute transverse myelitis with myositis during the convalescent period.

Keywords: Chikungunya, Myopathy, Spinal cord



CONSIDERAÇÕES FINAIS

- A suspeita de NEUROMIELITE ÓPTICA deve ser exaustivamen investigada e requer recursos de difícil ou impossível acesso
- O diagnóstico precoce de NMO pode impactar a evolução grav doença
- O spectrum da NMO inclui outras doenças autoimunes e até infecciosas como as mielites por Dengue, ZIKA e Chycungunya no diagnóstico diferencial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