Arq. Neuro-Psiquiatr. 2024;82(Suppl 1):S1–S52.

DOI: 10.1055/s-0044-1789317

Autoimmune limbic encephalitis presenting with fasciobrachial dystonic seizures: a case report

Alana Bacelar Limeira Sales[1], Samia Talise El Horr de Moraes[1], Caio César Diniz Disserol[1], Claudia Suemi Kamoi Kay[1], Cesar Minoru Toita Koga[1]
[1]*Universidade Federal do Paraná, Hospital de Clínicas, Curitiba PR, Brazil.*

Address for correspondence: Alana Bacelar Limeira Sales (email: alanabls@hotmail.com).

Abstract
Case Presentation: We present the case of a 64-year-old woman, with essential hypertension, referred to our hospital for investigation of refractory epilepsy. She had a history of prolonged inpatient treatment in another hospital due to several complications of her state: bronchoaspiration, pneumonia, and hyponatremia of hard control. The patient had already received a loading dose of phenobarbital followed by phenytoin due to long-duration seizures. Upon admission, the patient exhibited decreased mental status, diurnal excessive somnolence, episodes of hyponatremia, and seizures characterized by fasciobrachial dystonias.
Discussion: While the seizures were initially controlled, the patient progressed to a non-convulsive status epilepticus, necessitating a loading dose of levetiracetam for management. Suspecting autoimmune encephalitis, we conducted thorough laboratory investigations and a lumbar puncture, initially yielding no remarkable results. Consequently, the patient received pulse therapy with methylprednisolone (1 g daily for 5 days), followed by maintenance treatment with prednisone (50 mg daily). Subsequent improvement in the patient's condition was observed, with resolution of seizures and hyponatremia, and gradual improvement in mental status. Analysis of the autoimmune panel of the cerebrospinal fluid revealed positivity for anti-LGI1 antibodies, confirming the diagnosis of autoimmune limbic encephalitis. Autoimmune encephalitis, particularly the anti-LGI1 subtype, is often underdiagnosed despite its significant clinical manifestations, including seizures, hyponatremia, and fasciobrachial dystonic seizures. The treatment primarily involves pulsed corticosteroid therapy followed by maintenance with prednisone. Our patient exhibited an excellent response to corticosteroids, allowing for gradual tapering of prednisone dosage.
Final Comments: This case underscores the importance of considering autoimmune encephalitis in patients presenting with refractory seizures and associated clinical features. Prompt diagnosis and initiation of appropriate treatment are essential for favorable outcomes in these patients.

DOI: 10.1055/s-0044-1789318

Concomitant MOG-related optic neuritis and conus medullaris involvement: a case report

Amanda Freitas Alves[1], Herval Ribeiro Soares Neto[1], Isadora Cunha Leão Figueredo[1], Tainá Gonçalves[1], Giovanni Simões[1], Pedro Pontes[1]
[1]*Hospital do Servidor Público Estadual de São Paulo, São Paulo SP, Brazil.*

Address for correspondence: Amanda Freitas Alves (email: amandafreitasa11@gmail.com).

Abstract
Case Presentation: A 39-year-old man presented with blurred vision in the right eye along with painful eye movements. After 3 days, he began to experience lower back pain with irradiation down the legs and tingling sensation in both soles of the feet. He denied fever, recent infections or vaccination. A month earlier, he had had a similar visual condition with complete recovery after intravenous corticosteroid therapy, which was still under investigation. Upon examination, the visual acuities were 20/25 OD and 20/20 OS, with red desaturation and central scotoma at OD. There was no RAPD, and the fundoscopy examination showed bilateral normal optic disc. The rest of his neurological examination was normal. Orbits and spine MRI captured a high T2 signal involving the intraorbital segment of the right optic nerve and the conus medullaris, with no contrast enhancement on fat-suppressed T1 images. Lumbar puncture revealed an elevated white blood cell count (15 cells/μL, lymphocytes: 90%), with normal protein and glucose level. AQP4-IgG was tested seronegative, while the MOG-IgG was positive. He was treated with 5 days of 1 g of intravenous methylprednisolone followed by intravenous immunoglobulin 0,4 g/kg once daily for 5 days and oral prednisone, with total improvement of visual acuity and pain complaints. Then, we decided to start maintenance therapy with tocilizumab to prevent relapses.
Discussion: In adults, myelin-oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD) commonly presents as optic neuritis and myelitis, with the conus medullaris frequently affected when compared with other demyelinating disorders of the CNS, like NMOSD and MS. The present is the first report of concomitant MOG-related optic neuritis and conus medullaris involvement.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Final Comments: Differentiation of the demyelinating disorders of the CNS can be challenging in practice and the involvement of the conus medullaris, especially if associated with optic neuritis, should raise the suspicion of MOGAD.

DOI: 10.1055/s-0044-1789319

Cervical spondylotic myelopathy in the differential diagnosis of autoimmune myelitis

Ana Carolina Dietrich[1], Lais Golendziner[1], Nicolly Vieira[1], Débora Bassotto[1], João Pedro Zolet[1], Lucas Locatelli Menegaz[1], Rafaela Sandri[1], Barbara Galbinski[1], Rafael Tomaszeski[2], Luiz Roberto Tomasi Ribeiro[2], André Cecchini[2]
[1]*Universidade Luterana do Brasil, Canoas RS, Brazil.*
[2]*Grupo Hospitalar Conceição, Porto Alegre RS, Brazil.*

Address for correspondence: Ana Carolina Dietrich (email: anadietrich@outlook.com).

Abstract

Case Presentation: A 36-year-old woman with hypoesthesia in the upper limbs for 30 days, progressing to weakness in the hands and lower limbs, experienced shocks going down her spine. She denied history of trauma. Upon examination, she had grade-4 bilateral tetraparesis, sign of pyramidal lesion, and hypoesthesia. The patient underwent cervical spine magnetic resonance imaging, which revealed spondylotic myelopathy at C4-C5. The patient underwent anterior C4-C5 cervical discectomy with fusion, without complications.
Discussion: Spondylotic myelopathy manifests as an aggravation of cervical spondylosis, causing stenosis of the vertebral canal. The manifestations are spinal cord ischemia and lesions in neurons related to the affected nerve roots. It is the main spinal neuropathy in the adult population, but its diagnosis is still discussed. Due to similar symptoms and less specific exams, it is a major differential diagnosis of autoimmune myelitis. Suspicion increases when there are gait changes with sensory or motor complaints in the upper limbs in individuals over 55 years of age. Autoimmune myelitis is an incapacitating neurological syndrome characterized by weakness, sensibility alterations, and autonomic dysfunction. The symptoms present with a sudden onset, with lower back pain, sensation of a tight belt around the affected area, headaches, and cervical dorsalgia. Cervical magnetic resonance is the primary method of diagnosis, followed by testing of the spinal fluid, serological tests, and antibody tests. It generally occurs in an isolated form, or as a secondary complication, in which case secondary infections and infiltration of leukocytes in wounded parts of the spinal cord are the main etiological factors.
Final Comments: Cervical Spondylotic Myelopathy presents a diagnostic challenge due to the lack of specific findings and the large number of differential diagnoses. It is important to be careful when interpreting symptoms and test results to guarantee an accurate diagnosis. Considering epidemiology, the case presented would have autoimmune myelitis as the main hypothesis.

DOI: 10.1055/s-0044-1789320

Chronic spontaneous urticaria during natalizumab therapy in a patient with multiple sclerosis: a case report

Ana Clara Rodrigues[1], Bianca Oliveira[1], Daniel Lima Júnior[1], Davi Guerra[1], Luiza Villarim[1], Jeanina Dionizio[1], Tania Albuquerque[1]
[1]*Centro de Referência em Esclerose Múltipla da Paraíba, João Pessoa PB, Brazil.*

Address for correspondence: Ana Clara Rodrigues (email: clariguilherme@gmail.com).

Abstract

Case Presentation: A 40-year-old female patient with a confirmed diagnosis of multiple sclerosis (MS) since 2016 was initially treated with interferon β-1a 44 mg. In 2022, natalizumab was initiated as part of her therapy regimen. In July 2023, she began to experience episodes of urticarial lesions accompanied by pruritus. By November 2023, she was diagnosed with chronic urticaria following the persistence of symptoms for more than 6 weeks. Differential diagnoses, including rheumatological conditions, were thoroughly investigated. Despite the administration of high-dose H1 and H2 antagonists as first- and second-line treatments, there was no improvement. Subsequently, omalizumab was introduced as a third-line therapeutic option.
Discussion: Chronic spontaneous urticaria (CSU) is characterized by the recurrent occurrence of pruritic wheals and/or angioedema lasting for over 6 weeks. Its etiology may involve autoantibodies or remain idiopathic, often devoid of identifiable external triggers. Previous literature has documented cases linking CSU with relapsing remitting multiple sclerosis, particularly in association with immunomodulatory agents such as interferons and alemtuzumab. Immunological dysregulation following medication administration appears to play a contributory role in this phenomenon. Standard therapeutic strategies involve the use of H1 and H2 antagonists, alongside leukotriene antagonists. In refractory cases, omalizumab, an anti-IgE monoclonal antibody, has emerged as a safe and efficacious option.
Final Comments: Omalizumab demonstrates a favorable response rate of ~ 84% in cases of chronic urticaria. Its consideration in refractory chronic urticaria subsequent to the treatment of MS with immunomodulatory agents and monoclonal antibodies is warranted.

DOI: 10.1055/s-0044-1789321

Cognitive progression independent of relapse activity in different multiple sclerosis phenotypes

Andre Augusto Lemos Vidal de Negreiros[1], Larissa Gois[1], Mariana de Sá[1], Gabriel Vieira[1], Alfredo Damasceno[1]
[1]*Universidade Estadual de Campinas, Campinas SP, Brazil.*

Address for correspondence: Andre Augusto Lemos Vidal de Negreiros (email: andrevidaldenegreiros@gmail.com).

Abstract

Background: It is unclear whether patients with progressive multiple sclerosis (PMS) present a distinct pattern of cognitive impairment (CI); whether the progression independent of relapse activity (PIRA) impacts CI; and how different is PIRA across relapsing-remitting MS (RRMS) and PMS.
Objective: To assess the trajectories of cognitive/clinical decline in RRMS/PMS patients, evaluating the association of neuroimaging parameters and reserve, and also characterizing according to PIRA.
Methods: Longitudinal four-year follow-up that was conducted in the MS center of a tertiary hospital. In total, 54 patients were enrolled (30 with PMS and 24 with RRMS) who underwent brain MRI, clinical and neuropsychological evaluations (BRB-N, Tower of London Test, and Boston Naming Test) at baseline (time 1) and after 4 years (time 2). The evaluations of cortical thickness and subcortical volumes were performed using Freesurfer. The Spinal Cord Toolbox was used to evaluate the area of spinal cord (SC) section at the C2 level.

Results: At time 1, 37.2% of the individuals presented CI and, at time 2, 52.4%. There were no major differences between the RRMS and PMS groups in the evolution of clinical, cognitive and radiological variables after 4 years of follow-up. For the worsening of clinical disability, the best predictive factors were the SC area and the striatum volume. For cognitive deterioration, striatum volume and cortical thickness were the best predictors. We observed PIRA in 65.11% of the patients: CI was observed in 46.5% at time 1, and, at time 2, in 59.2%, and there were no major differences between MS groups in terms of the clinical, cognitive or neuroimaging variables.
Conclusion: There were no major differences between MS groups in the trajectories of clinical, cognitive and neuroimaging variables, pointing to a uniformity in the clinical courses of the disease. The similar trajectories across the RRMS and PMS groups with PIRA may suggest a common mechanism driving progression.

DOI: 10.1055/s-0044-1789322

Assessment of cognitive function and fatigue in multiple sclerosis

Caio Góes[1], Diego Olympio Peixoto Lopes[2], Maria Tereza Martinez[3], Luis Eduardo d'Almeida Manfrinati[3], Guilherme Ferreira Custódio[3], Fernanda Herculano[4], Diogo Haddad Santos[4]
[1]*Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.*
[2]*Universidade Santo Amaro, São Paulo SP, Brazil.*
[3]*CPQuali Pesquisa Clínica, São Paulo SP, Brazil.*
[4]*Hospital Alemão Oswaldo Cruz, São Paulo SP, Brazil.*

Address for correspondence: Caio Góes (email: caio.goes@aluno.fcmsantacasasp.edu.br).

Abstract
Multiple sclerosis is an inflammatory, chronic demyelinating disease that affects the central nervous system. Its resulting lesions can incur in progressive fatigue and cognitive function impairment, severely impacting quality of life and the economic burden of disease, regardless of the physical disability. Almost half of the patients defined as NEDA-3 had deterioration in at least 2 cognitive domains in a 2-year follow-up. The study's aim was to compare the Symbol Digit Modalities Test (SDMT) and the Modified Fatigue Impact Scale (MFIS) results when applied to patients with multiple sclerosis, and to determine if a higher level of fatigue impacted the performance in cognitive function evaluation. The SDMT is a neuropsychological tool to assess sustained attention and information processing speed, two cognitive domains commonly impaired in multiple sclerosis, with a lower score indicating worse performance and more impairment. Conversely, the MFIS is an instrument to measure the subjective experience of fatigue, such that a higher score indicates larger impact, and it was used in place of the 40-item-long Fatigue Impact Scale to avoid unnecessary patient fatigue without skewing the results. Participants with a previous diagnosis of multiple sclerosis were chosen from the general population of the city of São Paulo, Brazil. They were instructed on how to adequately fill the MFIS and, upon finishing, the SDMT was applied by a trained researcher. The results were then compiled in a spreadsheet and compared through the Pearson r of each test result's z-score. The test results were Pearson r = -0.273 when correlating the SDMT and MFIS z-scores, with $p = 0.007$, indicating a statistically significant negative correlation between the SDMT and MFIS. The results enable us to infer that, indeed, patients with multiple sclerosis suffering from fatigue perform worse in cognitive demanding tasks.

DOI: 10.1055/s-0044-1789323

Description of symptoms in the latest multiple sclerosis relapse in the elderly population

Camila Figueiredo[1], Marcelle Prado[1], Eliana Tomomi Shimabukuro da Cunha[1], Amanda Selvatici dos Santos Dias[1]
[1]*Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.*

Address for correspondence: Camila Figueiredo (email: camila04_lopes@hotmail.com).

Abstract
Background: Historically, multiple sclerosis (MS) has been recognized as a young person's disease, with the typical onset occurring between 20 and 40 years of age. However, with increasing life expectancy, patients over 60 years of age have been increasingly represented among those with this disease.
Objective: To analyze the symptoms of the last relapse in patients over 60 years of age compared with those under 60 years of age.
Methods: The medical records of 42 patients diagnosed with MS who were being followed up at a reference center in São Paulo, Brazil, were analyzed. The patients were divided into the < 60 years of age group and the ≥ 60 years of age group. The time of diagnosis, symptoms and sequelae of MS, and the Expanded Disability Status Scale (EDSS) score were evaluated. The Fisher and Pearson Chi-squared tests were applied for the statistical analysis.
Results: A total of 42 patients were evaluated, of whom 9 were male and 33 were female; 66.6% ($n = 28$) of the patients were over 60 years of age. A trend was found towards visual changes in the last relapse in patients under 60 years of age (42.9%) compared with the population over 60 years of age (17.9%) ($p = 0.082$), as well as paresthesia in the lower limbs in patients under 60 years of age (28.6% versus 7.1%) ($p = 0.061$). Regarding pulse therapy in the last relapse, patients over 60 years of age underwent this procedure only in 35.7% of the cases compared with those under 60 years of age, who underwent pulse therapy in 78.6% of the cases ($p = 0.011$).
Conclusion: A trend was found towards visual and sensory changes in the last relapse of MS in patients under 60 years of age, with a higher rate of pulse therapy in this population compared with those over 60 years of age.

DOI: 10.1055/s-0044-1789324

Challenges in diagnosing multiple sclerosis: case report of pseudotumor lesion presentation

Diego Olympio Peixoto Lopes[1], Caio Góes[2], Maria Tereza Martinez[3], Guilherme Ferreira Custódio[3], Luis Eduardo d'Almeida Manfrinati[3], Carina Tellaroli Spedo[4], Fernanda Herculano[5], Diogo Haddad Santos[5]
[1]*Universidade Santo Amaro, São Paulo SP, Brazil.*
[2]*Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.*
[3]*CPQuali Pesquisa Clínica, São Paulo SP, Brazil.*
[4]*Universidade de São Paulo, São Paulo SP, Brazil.*
[5]*Hospital Alemão Oswaldo Cruz, São Paulo SP, Brazil.*

Address for correspondence: Diego Olympio Peixoto Lopes (email: diego_olympio@hotmail.com).

Abstract
The diagnosis of multiple sclerosis (MS) can be challenging, especially when patients present with atypical clinical features or imaging findings, such as pseudotumor lesions. We present the case of a 28-year-old male Youtuber, previously healthy, who complained of tingling in his right leg. Over the course of six days, he developed progressive numbness and tingling affecting the entire right side, along with reduced sensation on the left side of his face and binocular diplopia. Blood tests for infection and autoimmune disease were negative, as well as anti-MOG and anti-AQP4. Skull magnetic resonance imaging (MRI) revealed a nodular lesion at the base and peduncle of the pons on the left, with pseudotumor characteristics. It was asked whether there was contrast uptake in the periphery of the lesion. Pulse therapy was performed for 5 days without improvement in symptoms. A subsequent cranial MRI scan showed typical MS lesions perpendicular to the corpus callosum. Then, an analysis of the cerebrospinal fluid (CSF) showed positive oligoclonal bands. The diagnosis of multiple sclerosis was confirmed. The patient underwent another 5 days of pulse therapy, totaling 10 days, with practically complete improvement in symptoms. We then decided to start therapy with natalizumab. Pseudotumor lesions in MS can mimic the appearance of neoplastic tumors on imaging studies, leading to diagnostic uncertainty and delays in starting treatment. In this case, the initial presentation and imaging findings raised concerns of a pseudotumor lesion, highlighting the importance of considering MS in the differential diagnosis of such lesions. The diagnosis of MS can be challenging, especially when patients present with pseudotumor lesions. Clinicians must maintain a high index of suspicion for MS, especially in young individuals presenting with neurological symptoms, to ensure timely diagnosis and initiation of the appropriate treatment. More research is needed to better understand the pathophysiology and clinical implications of pseudotumor lesions in MS.

DOI: 10.1055/s-0044-1789325

Beyond conventional scales: a critical reflection on the diagnosis of depression and fatigue in multiple sclerosis

Diego Olympio Peixoto Lopes[1], Caio Góes[2], Maria Tereza Martinez[3], Guilherme Ferreira Custódio[4], Luis Eduardo d'Almeida Manfrinati[3], Carina Tellaroli Spedo[4], Fernanda Herculano[5], Diogo Haddad Santos[5]
[1]Universidade Santo Amaro, São Paulo SP, Brazil.
[2]Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.
[3]CPQuali Pesquisa Clínica, São Paulo SP, Brazil.
[4]Universidade de São Paulo, São Paulo SP, Brazil.
[5]Hospital Alemão Oswaldo Cruz, São Paulo SP, Brazil.

Address for correspondence: Diego Olympio Peixoto Lopes (email: diego_olympio@hotmail.com).

Abstract
The present work aims to identify quick and effective methods to assess mood and fatigue changes in patients with multiple sclerosis (MS). Initially, patients were assessed through three specific questions during routine consultation for a quick evaluation of mood and fatigue. Subsequently, no more than 30 days after the first assessment, the same patients were evaluated using the MFIS and the BDI and BAI scales. This quick assessment method was developed based on responses from an interview with 20 experienced neuroimmunologists, who identified the following questions as the most effective for a preliminary assessment of mood and fatigue: 1) "Have you been feeling sad in the past few weeks?"; 2) "Have you been feeling tired or without energy to do your daily activities?"; and 3) "Have you noticed changes in your sleep or appetite in the past few weeks?". Of the 105 patients, only 21 (20%) responded positively to some of the questions when asked informally. After 30 days from the first assessment, the same patients were evaluated using the MFIS and the BDI and BAI scales. In the BDI, most patients were classified as not depressed (53.3%), followed by mild/moderate depression (30.4%), moderate/severe depression (14.28%), and severe depression (1.9%). In the BAI, 44.7% of patients had minimal anxiety, 30.4%, mild anxiety, 17.1%, moderate anxiety, and 7.69%, severe anxiety. The MFIS found that 30.4% exhibited fatigue. Only 20% of the patients indicated symptoms of depression, anxiety, or fatigue when questioned informally, while structured assessments revealed that a significantly larger proportion of patients exhibited signs of mild to moderate depression, mild anxiety, and fatigue. This difference underscores the technical importance of using validated scales in the clinical practice, as they provide a more systematic and sensitive approach to identifying symptoms that may be underestimated or undetected in less structured assessments.

DOI: 10.1055/s-0044-1789326

Neurological presentation of sarcoidosis

Elisangela Ferraz Pazinato[1], Alex Eduardo Silva[1], Ana Luisa Rufino de Sousa[1], Giovani Zago Borges[1], Amanda Soares Pimenta[1], Daniela Aparecida Lima Viana[1], João Henrique da Matta Clementino[1]
[1]Universidade Federal do Triângulo Mineiro, Uberaba MG, Brazil.

Address for correspondence: Elisangela Ferraz Pazinato (email: elisangelapazinato@gmail.com).

Abstract
Case Presentation: We herein present the case of a 49-year-old woman with complaints of vertigo, diplopia, nausea, headache, global paresis, inappetence, and intermittent febrile peaks in the afternoon. She had a history of hospitalization for evaluation and complementary propedeutics and underwent pulse therapy with corticosteroids for inflammatory disease of the unspecified central nervous system, with good response to corticosteroids. After four months, it evolved with worsening of gait, imbalance, mental confusion, bilateral facial paresis, speech disorders, progressive dysphagia for liquids and solids, consumption syndrome, and persistence of intermittent fever. The patient was hospitalized again and diagnosed with pan-hypopituitarism. Inguinal lymph node biopsy was performed, with findings of non-caseous epithelioid granulomas, configuring sarcoidosis with neurological presentation. Immunosuppressive treatment was instituted with adjustments according to therapeutic response, and treatment with rituximab and corticosteroids was maintained.
Discussion: Sarcoidosis consists of a systemic inflammatory disease that is characterized by the development of granulomas in any organ; however, neurosarcoidosis is a rare and difficult manifestation to diagnose. Although the most common manifestations in the central nervous system are cranial neuropathies, leptomeningeal disease, intraparenchymal lesions, and myelitis, the disease can manifest as stroke, seizure, hypopituitary, neuropsychiatric symptoms, and encephalopathy. We reported the case of a patient whose diagnostic investigation was challenging due to the multiple systemic and neurological manifestations.
Final Comments: The diagnosis of neurosarcoidosis is challenging because it is a chronic granulomatous disorder with

no identified pathogen. The nerve injury most commonly involved is Bell paralysis. Isolated lumbar and thoracic root lesions have also been described, but sensorimotor neuropathy is rarely observed.

DOI: 10.1055/s-0044-1789327

Systemic autoimmunity in a multiple sclerosis patient: thyroid and liver overlap

Giuseppe Dick Bonato[1], Marcieli Gerhardt[1], Jefferson Becker[1]
[1]*Pontifícia Universidade Católica do Rio Grande do Sul, Hospital São Lucas, Porto Alegre RS, Brazil.*

Address for correspondence: Giuseppe Dick Bonato (email: g.d.bonato@hotmail.com).

Abstract

Case Presentation: We present the case of a 62-year-old female patient with multiple sclerosis (MS) and systemic autoimmunity syndrome. She was an outpatient in a tertiary neuroimmunology clinic and was also followed by rheumatology, dermatology, hepatology and endocrinology specialists. She presented trouble walking at age 53, developing sensory and weakness in her lower limbs in the following 4 years. There was no marked clinical attack. Cervical-thoracic MRI scans showed multiple short thoracic demyelinating lesions in the lateral and dorsal funiculi and corresponding volume reduction. Brain MRI scans showed periventricular, deep white matter, pons, medulla oblongata, cerebellar peduncles and cerebellar hemispheres lesions. She was diagnosed with primary progressive MS (PPMS) and is currently under treatment with ocrelizumab. At age 38, she was diagnosed with hypothyroidism, and a positive anti-TPO antibody enabled the establishment of the diagnosis of Hashimoto thyroiditis. Persistently high transaminases and biliary tract inflammation led to the diagnosis of autoimmune sclerosing cholangitis. Rheumatologic workup showed anti-mitochondria cytoplasmatic ANA 1:320, p-ANCA 1:80, and anti-mitochondria 1:160. She had type-3 oligoclonal banding. At her last clinical visit, the EDSS score was of 3.5 and the T25FW time was of 12 and 13 seconds. She presented trouble walking, urinary urge incontinence, lower limb sensory and motor deficits and multiple pyramidal signs.

Discussion: Autoimmunity markers are often seen in MS patients, as well as a strong correlation to other autoimmunity diseases. Some cases present a particularly complex challenge in differentiating between comorbidity and neurological manifestation of a systemic disease. Clinical features and radiological findings can help establish the diagnosis.

Final Comments: We presented an uncommon case of PPMS with systemic autoimmunity features. The complexity and frequency of other autoimmunity disorders make a high level of suspicion necessary. This case illustrates the importance of continuous multidisciplinary evaluation and follow-up.

DOI: 10.1055/s-0044-1789328

Bilateral MOG-related optic neuritis after Varicella Zoster reactivation: a case report

Ingrid Lorena da Silva Gomes[1], Amanda Freitas Alves[1], Herval Ribeiro Soares Neto[1]
[1]*Hospital do Servidor Público Estadual de São Paulo, São Paulo SP, Brazil.*

Address for correspondence: Ingrid Lorena da Silva Gomes (email: ilsgomes@yahoo.com).

Abstract

Case Presentation: A 67-year-old Japanese woman presented with a 14-day history of bilateral and painful vision loss. The symptom was first noted in the left eye, with right-eye involvement within 7 days. Her medical history was unremarkable, except for an episode of non-complicated lower thoracic herpes zoster infection four weeks prior to the visual disturbance, for which she received adequate treatment with oral acyclovir for 7 days, with full recovery. She had no other neurological symptoms. At our first evaluation, visual acuities were of 20/100 OD and 20/200 OS, with red desaturation at OD. There was no RAPD. Fundoscopy revealed bilateral papillary edema. An MRI scan of the brain and orbits revealed right anterior and left posterior optic nerve enhancement on T1 fat-suppressed postcontrast sequence, suggestive of bilateral optic neuritis. Lumbar puncture showed slightly increased white blood cells, with normal glucose and protein levels. After negative infectious/inflammatory and metabolic laboratory testing, she was treated with 5 days of 1 g intravenous methylprednisolone followed by 60 mg of oral prednisone. Progressive improvement of visual acuity was observed after 2 days of treatment, and full recovery was established by the 5th day. Later, the serum MOG antibodies were found positive.

Discussion: Similar to other neuroimmunological disorders, a few reports regarding anti-MOG optic neuritis after infections have been published. Even though cases associated to the Herpesviridae family are available, the present is the first report of bilateral anti-MOG ON following a VZV reactivation.

Final Comments: Anti-MOG must be considered as a differential diagnosis for patients with bilateral optic neuritis, including elderly patients and those of oriental descent. To date, there is no causality relationship between VZV infection and the clinical manifestations of MOGAD; however, it should be on the radar of clinicians who face individuals with post-infectious neurological symptoms associated with inflammatory demyelinating diseases.

DOI: 10.1055/s-0044-1789329

The importance and challenges of the late diagnosis of optic neuropathies

Johnatan Felipe Ferreira da Conceição[1], Luiza de Aguiar Lima[1], Nathane Braga[1], Viviane Carvalho[2], Gutemberg Augusto Cruz dos Santos[1]
[1]*Universidade Federal Fluminense, Niterói RJ, Brazil.*
[2]*Hospital São Francisco na Providência de Deus, Rio de Janeiro RJ, Brazil.*

Address for correspondence: Johnatan Felipe Ferreira da Conceição (email: johnatanfelipe@id.uff.br).

Abstract

Case Presentation: A 17-year-old male patient presented with 12 months of progressive painless loss of vision in the right eye. After 2 years from the first symptom, he presented to our service with finger count in and a central scotoma in left eye, worsening in the last 2 weeks. He had had a previous diagnosis of autism with important restricted eating. An MRI from neuroaxis showed atrophy of the optic nerves, with a high-intensity signal in the left nerve on the T2-weighted imaging, with no other lesion. He had a bilateral pale disc, with no retinal involvement. MOG and AQP4-IgG (CBA) were negative. A trial of high-dose intravenous methylprednisolone was attempted, with no improvement. The most important hypotheses were nutritional and hereditary neuropathy, with inconclusive tests: 4 mitochondrial mutations were tested, with no positive results; however, the FGF-21 was high. Complex B vitamins were: B12 – 148; and folic

acid – 5.4; vitamin A was of 0.2. Both nutritional replacement and antioxidant therapy were implemented.
Discussion: Leber hereditary optic neuropathy (LHON) is an inherited mitochondrial disease that leads to decreased vision in both eyes. The loss of vision usually consists in bilateral central scotoma, but the entire visual field can be lost. Nutritional optic neuropathy, especially complex B and vitamin A, also presents a painless bilateral progressive visual loss, with a central scotoma, and time-dependent treatment response. Unfortunately, in this case, the time it took from the first symptom to first assistance may have inflicted poorer prognosis.
Final Comments: The differential diagnosis for optic neuropathies is challenging, especially in a public service with limited tools available. Besides demyelinating diseases, infections and systemic autoimmune diseases, and genetic and nutritional etiologies should always be remembered.

DOI: 10.1055/s-0044-1789330

Longitudinally-extensive myelitis as a first presentation of neurosarcoidosis

Johnatan Felipe Ferreira da Conceição[1], Nathane Braga[1], Viviane Carvalho[2], Gutemberg Augusto Cruz dos Santos[1], Flávia de Aguiar Machado[1], Luiza de Aguiar Lima[1]
[1]*Universidade Federal Fluminense, Niterói RJ, Brazil.*
[2]*Hospital São Francisco na Providência de Deus, Rio de Janeiro RJ, Brazil.*

Address for correspondence: Johnatan Felipe Ferreira da Conceição (email: johnatanfelipe@id.uff.br).

Abstract
Case Presentation: A male patient, aged 64 years, presented an acute condition of paresthesia in the right lower limb and paresis in the left lower limb, impairing ambulation. He denied associated systemic symptoms, as well as urinary or bowel changes, or painful symptoms. During hospitalization, he underwent a neuroaxis magnetic resonance imaging scan, which showed T2 hypersignal in the central portion of the spinal cord, extending from the D6-D7 level to the D10-D11 level, with elongated left paramedian enhancement between D8 and D10, defined as longitudinally-extensive myelitis. Laboratory tests did not show significant alterations, and cerebrospinal fluid analysis showed only an increase in proteins (76 mg/dL). The search for acid-alcohol resistant bacillus, fungi, and bacteria was negative. Thoracoabdominal computed tomography revealed random pulmonary nodules and hilar adenopathy, as well as inguinal lymphadenopathy and splenic nodular lesions. A biopsy of the inguinal lymph node was performed, showing chronic granulomatous inflammation with typical sarcoid granulomas, leading to the diagnosis of sarcoidosis. The patient received an initial pulse therapy regimen with 1 g of methylprednisolone for 5 days and maintenance of oral corticosteroid therapy, resulting in complete improvement of the clinical symptoms.
Discussion: Sarcoidosis is a chronic granulomatous inflammatory disease, with different clinical spectra involving both pulmonary and extrapulmonary manifestations. Neurosarcoidosis is one of its presentations, either isolated or involving other systems, affecting both the central and peripheral nervous systems. In the context of myelitis, it typically occurs subacutely or even chronically, resulting in variable deficits and with topography more associated with long tracts of white matter. It generally shows a significant clinical response to corticosteroids, with good recovery of the neurological deficits.
Final Comments: Longitudinally-extensive transverse myelitis presents numerous differential diagnoses, with clinical reasoning being essential for etiological determination. Seeking clinical characteristics and findings from complementary exams can guide accurate diagnosis and subsequent therapeutic success.

DOI: 10.1055/s-0044-1789331

Silent bilateral optic papillitis after COVID-19: a case report

Juliana Santiago-Amaral[1], Lucas Alexandre Santos Marzano[1], Vinicius Rezende Avelar[1], Jéssica Resende Vaz de Melo[1], Izabela Cristina de Faria Martins[1], Rodrigo Kleinpaul[1]
[1]*Instituto de Previdência dos Servidores de Minas Gerais, Belo Horizonte MG, Brazil.*

Address for correspondence: Juliana Santiago-Amaral (email: julimss@gmail.com).

Abstract
Case Presentation: A 23-year-old female patient presented bilateral optic papilla edema in a routine ophthalmological consultation, without related complaints or neurological deficits. She had bilateral eyelid edema and redness, had been diagnosed with COVID-19, confirmed by the PCR method, and shown spontaneous improvements two months before. She was previously myopic, without other comorbidities or use of medications. A neurological evaluation showed normal visual acuity, no color vision deficiencies or marked visual field defects, and other neurological deficits were absent. Cerebral and orbital magnetic resonance imaging scans were normal, even as cerebrospinal fluid analysis. Optical coherence tomography (OCT) and ultrasonography excluded optic nerve drusen. Differential diagnosis investigation showed non-reactive anti-aquaporin 4 antibody and myelin oligodendrocyte glycoprotein antibodies, and the metabolic, rheumatological, and infectious screenings were also normal. The patient was diagnosed with bilateral papillitis, possibly triggered by SARS-CoV-2 infection. No acute or prophylactic treatment was started. Two years after the diagnosis, the fundus remained stable.
Discussion: The present case report aims to demonstrate an atypical manifestation of neurological alteration after SARS-CoV-2 infection. There are no similar reports in the Brazilian literature. Among the few cases described, the diagnosis was confirmed through clinical history and extensive complementary work-up, and the patients presented significant loss of visual function after infection or vaccination for SARS-CoV-2, requiring corticosteroid therapy as a therapeutic approach, with a good response and almost complete recovery of the deficits in most cases.
Final Comments: The present case report demonstrates an uncommon occurrence of silent bilateral optic papillitis after SARS-CoV-2 infection, highlighting parainfectious causes as differential diagnosis of multiple diseases that affect the optic nerve, such as multiple sclerosis, neuromyelitis optica spectrum disorders, and myelin oligodendrocyte glycoprotein antibody-associated disease.

DOI: 10.1055/s-0044-1789332

Atopic myelitis as a differential diagnosis of demyelinating diseases: a case report

Juliana Santiago-Amaral[1], Gabriel Lage Neves[1], Ana Júlia Resende Rocha[1]
[1]*Faculdade de Ciências Médicas de Minas Gerais, Belo Horizonte MG, Brazil.*

Address for correspondence: Juliana Santiago-Amaral (email: julimss@gmail.com).

Abstract
Background: Atopic myelitis (AM) is a rare syndrome in which patients with persistent hyperimmunoglobulin E and eosinophilia present with an episode of myelopathy. The disease typically affects the posterior funiculus of the cervical or thoracic spinal cord, and symptoms are predominantly sensory. There have been ~ 100 reported cases of AM in Japan. In Brazil, no cases of AM have been reported.
Objective: To report a case of suspected AM and emphasize the importance of this syndrome as a differential diagnosis of demyelinating diseases.
Methods: Case report following the CARE criteria.
Results: A 37-year-old man, previously healthy, started paresthesia in his left foot, which, within a few days, became bilateral and ascended to the level of T6, without associated motor or sphincter symptoms. Brain and spinal cord magnetic resonance imaging (MRI) scans revealed a hyperintense T2 image at the T4-T6 vertebrae level, centrally located within the spinal cord, with nodular contrast enhancement in the T1 sequence. Cerebrospinal fluid analysis showed absence of oligoclonal bands or other abnormalities. Pulse therapy was administered, with partial improvement. After oral corticosteroid maintenance therapy with gradual tapering, complete improvement was observed. Laboratory screening for rheumatological, endocrinological, metabolic, and infectious diseases was negative. Anti-aquaporin 4 and anti-MOG antibodies were also negative. The patient presented with persistent eosinophilia and hyperimmunoglobulin E without a defined cause, and he did not improve after empirical treatment with secnidazole and albendazole prescribed by a gastroenterologist. Considering these findings and the exclusion of other more common causes, a probable diagnosis of AM was considered. Currently under outpatient follow-up, the patient is asymptomatic and without new lesions on MRI.
Conclusion: The present case report highlights the importance of considering AM, an etiology that had not been previously described in Brazil in the literature, as a possible differential diagnosis of myelopathies of infectious, metabolic, and demyelinating diseases.

DOI: 10.1055/s-0044-1789333

Beyond neurology: dermatological manifestations in the prodromal phase of multiple sclerosis

Juliana Santiago-Amaral[1], Gabriel Lage Neves[1], Gabriel Freitas Fraga[1], Amaro Lança Neto[1], Ana Júlia Resende Rocha[1]
[1]*Faculdade de Ciências Médicas de Minas Gerais, Belo Horizonte MG, Brazil.*

Address for correspondence: Juliana Santiago-Amaral (email: julimss@gmail.com).

Abstract
Background: Prodromal signs (PSs) of multiple sclerosis (MS) are nonspecific symptoms that precede the first neurological symptoms by an average of 5 years. Recent studies have focused on identifying early indicators of the disease, with musculoskeletal and genitourinary symptoms being well-documented, while cutaneous lesions (CLs) have received less attention.
Objective: To present a case series of patients with dermatological changes as potential PSs of MS.
Methods: A descriptive retrospective study was conducted using medical records of MS patients.
Results: The characterization of 5 patients diagnosed with relapsing-remitting MS was evaluated, showing the emergence of cutaneous lesions before the diagnosis of the disease (in 40%, CLs started in childhood, in 40%, they started 1 year before the diagnosis, and, in 20%, they started 9 years before the diagnosis). Among the patients, 80% were female, with a mean age at MS diagnosis of 33.6 years. In all patients, CLs were characterized as erythematous hyperchromic plaques, with 20% diagnosed with lichen planus, 20%, with nummular eczema, 20%, with discoid lupus – histopathological report: moderate nonspecific chronic vulvitis with lichenification –, and the remaining 40%, without a definitive diagnosis of the lesions. Regarding associated symptoms, 40% had intense itching in the CLs and 20% had hypoesthesia in the CLs. The CLs were in different areas in each patient (abdomen, pelvis, legs, vulva, tongue, upper eyelids, and above the upper lip). All patients had differential diagnoses excluded (rheumatological, endocrinological, metabolic, or infectious diseases). As for treatment, 60% of patients showed improvement of the CLs with the use of topical, oral, or intravenous corticosteroids (pulse therapy).
Conclusion: The results of the present study highlight a possible association between the presence of dermatological lesions and the prodromal phase of MS. This is the first report in the literature.

DOI: 10.1055/s-0044-1789334

Impact of comorbidities on cognition in multiple sclerosis patients: a multivariable analysis

Marco Caneda[1], Camila B. Oliveira Silva[1], Marjana Reis Lima[1], Maria Cecília Vecino[1]
[1]*Hospital Moinhos de Vento, Porto Alegre RS, Brazil.*

Address for correspondence: Marco Caneda (email: mcaneda@terra.com.br).

Abstract
Background: Cognitive impairment (CI) is common in multiple sclerosis (MS); it can have disabling consequences on quality of life, and it is often prioritized among MS patients. Its causes are multifactorial. An association between cortical injury and CI has been consistently demonstrated. Furthermore, clinical factors, such as comorbidities, seem to contribute to CI onset; however, few studies have examined their impact on MS cognition.
Objective: To evaluate the association between comorbidities and CI in MS.
Methods: Patients with MS underwent brain MRI scans, a neuropsychological (NP) assessment, and were screened for the presence of comorbidities. Cortical lesions (CLs) were identified by phase-sensitive inversion recovery (PSIR) MRI sequences. The NP assessment was performed using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS), with z-scores calculated based on Brazilian normative values. The clinical data and results of the patients without comorbidities (C-) and of those with comorbidities (C+) were compared. The association between CLs, comorbidities, and CI was assessed by a multivariable logistic regression (MLR) analysis.

Results: We included 48 individuals: 45.8% were C- and 54.2%, C+. The C+ group was older (48.5 versus 41 years; $p = 0.02$) and contained more individuals with CI ($p = 0.009$). The C- group had a higher number of CLs (5±5 versus 2.5±3.2; $p = 0.04$), but not a higher number of individuals with CL ($p = 0.31$), and scored better than the C+ group in the SDMT (55.1±16 versus 45.6±21; $p = 0.04$) and BVMT (24.4±5.9 versus 21.1±7.4; $p = 0.05$). The MLR analysis identified only comorbidities as significant ($p = 0.018$) for CI (B = 2.06; OR = 7.85; 95%CI: 1.41–43.4; $p = 0.02$).
Conclusion: Comorbidities increase the chances of developing 0CI. The association of the CL load with CI seems to depend on its interaction with cofactors. Strategies to optimize comorbidities management in MS are warranted.

DOI: 10.1055/s-0044-1789335

Lyme disease as a differential diagnosis for multiple sclerosis

Mariana Carvalho[1], Joyce Gomes[1], Sanny Yoshida[1]
[1]*Universidade Federal de Ouro Preto, Ouro Preto MG, Brazil.*

Address for correspondence: Mariana Carvalho (email: mariana.dgtc@gmail.com).

Abstract
Background: Multiple sclerosis (MS) is a chronic, autoimmune, demyelinating disease that affects the central nervous system. This disorder leads to symptoms such as ataxia, fatigue, and impaired cognitive abilities. Lyme disease (LD), on the other hand, is caused by infection by the bacterium *Borrelia burgdorferi* and is transmitted by tick bites. Although its etiology is distinct from that of MS, LD can manifest with symptoms similar to those of MS in the human body when it comes to neurological impairments. Therefore, it is of utmost importance that LD be considered as a diagnostic hypothesis when MS is suspected, given that the treatment and diagnostic approaches for these diseases are significantly different.
Objective: To compare the pathophysiology and symptoms of LD and MS, emphasizing the importance of clinical findings for early diagnosis.
Methods: The present is a systematic review in which ten articles were selected from three databases (SciELO, PubMed, and LILACS), using the keywords *multiple sclerosis*, *Lyme disease*, *symptoms*, *demyelinating*, *neurological disorder*, and *clinical progression*. Only original studies published from 2010 onwards were considered eligible.
Results: There is significant symptomatic similarity between MS and LD, particularly in the late stage of LD (when cognitive deficits, paresis, and polyneuropathies can occur). For a case of MS to be correctly diagnosed, it is essential to consider the possibility of LD, especially in the presence of a clinical history of pathogen exposure and residence in an endemic area.
Conclusion: Since early diagnosis of MS is challenging due to the nonspecific symptoms accompanying the initial disease presentation, considering other diseases such as LD is crucial. Therefore, efforts are being made to improve timely diagnoses and treatments for each condition, aiming for a better quality of life for patients.

DOI: 10.1055/s-0044-1789336

Early high-efficacy disease-modifying therapy in multiple sclerosis: a 4-year real-world study

Mario Emilio Dourado[1], Bárbara Cristina Vieira Aquino[1], Felipe Toscano Lins Menezes[1], Maria Weryca de Souza Belo Silva[1], Alcileia Rodrigues Marques[1], Glauciane Costa Santana[1], Maíra Melo do Vale Lira[1]
[1]*Universidade Federal do Rio Grande do Norte, Hospital Universitário Onofre Lopes, EBSERH, Natal RN, Brazil.*

Address for correspondence: Mario Emilio Dourado (email: medourado03@gmail.com).

Abstract
Background: The treatment strategy for multiple sclerosis (MS) is a highly controversial debate. Disease-modifying therapies for MS are divided into escalation therapies and early high-efficacy therapies. Observational studies suggest that the early use of high-efficacy therapy the improves long-term outcomes.
Objective: To evaluate clinical disability in relapsing-remitting MS (RRMS) patients treated with early high-efficacy disease-modifying therapies (heDMTs).
Methods: Patients with RRMS with ≥ 4 years of follow-up and ≥ 3 visits after the beginning of the disease-modifying therapy (DMT) were selected from the HUOL/UFRN MS Registry. These patients had been followed since 2006, with visits every 3 to 6 months. We included naive individuals treated with heDTM and patients in whom heDMTs was started within the first 2 years of therapy. The drugs considered as heDMTs were: fingolimod, natalizumab, ocrelizumab, rituximab, alemtuzumab, cladribine, and mitoxantrone. The effect of heDMTs was measured by the 4-year change in the score on the Expanded Disability Status Scale (EDSS) and 10-m walk test (10MWT). We also assessed outcomes in groups of patients who started heDMTs before 5 years of the disease and after more than 5 years of the disease.
Results: A total of 38 patients were included in the study. At baseline, the median EDSS score was of 1.5 (IQR: 0–3) and the median 10MWT was of 9.7 (IQR: 8.2–18). After 4 years of treatment onset, the median EDSS score was of 1.7 (IQR: 0–4.5), and the median 10MWT was of 10 (IQR: 8.4–37). When we evaluated the outcomes of the groups based on the delay in starting treatment, after 4 years of treatment onset, the median EDSS score in the $<$ 5-year delay group was of 1.5, versus 2 in the $>$ 5year delay group ($p = 0.0440$).
Conclusion: Our results are similar to those of studies on the early use of heDMTs, with a mean EDSS score ranging from 1.5 to 2. Early treatment with heDMTs may improve the long-term outcomes by minimizing the accumulation of disability early in the disease course.

DOI: 10.1055/s-0044-1789337

Anxiety and depression in multiple sclerosis: prevalence and associated factors

Clayton Zoccoli[1], Isabella Avolio[1], Olivia Pires[1], Mateus Boaventura de Oliveira[1,2]
[1]*Hospital São Camilo, São Paulo SP, Brazil.*
[2]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br).

Abstract
Background: Multiple sclerosis (MS) is an inflammatory, autoimmune, and demyelinating disease. Comorbidities such as anxiety and depression, by themselves, can lead to cognitive deficits, and their presence associated with MS can have impacts on the patient's quality of life and their symptoms.
Objective: To evaluate the prevalence of anxiety and depression in patients diagnosed with MS, and to investigate the

impact of these comorbidities on physical disability and cognitive scales.
Methods: The present is an observational, cross-sectional, retrospective, and single-center study. The Hospital Anxiety and Depression Scale (HADS) was applied to determine the prevalence of the aforementioned comorbidities. Scores ≥ 8 on each of the HADS subscales were used to define a clinically-meaningful anxiety or depression disorder. Statistical associations were performed with the Expanded Disability Status Scale (EDSS), the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS), the Modified Fatigue Impact Scale (MFIS), and the Multiple Sclerosis Impact Scale (MSIS-29).
Results: A total of 99 subjects were included in the study (77.8% of female individuals, with a mean age of 39.8±10.6 years, and a mean disease duration of 9.5±7.3 years). Anxiety and depression were identified in 51 (51.5%) and 39 (39.4%) patients respectively. The median and interquartile range scores for anxiety and depression were of 8 (4–12) and 6 (3–10) respectively. Patients with anxiety and depression had a higher MFIS score ($p < 0.001$) and a higher MSIS-29 score ($p < 0.001$). There were no differences between patients with and without anxiety or depression regarding other scales, such as the EDSS, and all BICAMS tests.
Conclusion: Multiple sclerosis patients with anxiety and depression demonstrated higher fatigue and global impact disease scores. Although the data do not demonstrate a causal relationship, the treatment of the comorbidities is relevant to determine the improvement of the most impaired functions.

DOI: 10.1055/s-0044-1789338

IgG index versus oligoclonal bands in a Brazilian multiple sclerosis center

Mateus Boaventura de Oliveira[1,2], Murilo Pinoti[2], Letícia Cavaglieri[2], Sandro Matas[3]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Centro Universitário São Camilo, São Paulo SP, Brazil.*

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br).

Abstract
Background: Multiple sclerosis (MS) diagnostic criteria have evolved over time and continue to apply a combination of clinical, imaging, and laboratory findings. Although biomarkers of intrathecal cerebrospinal fluid (CSF) synthesis have been less emphasized in successive iterations to the McDonald criteria, it remains a valuable diagnostic test, especially in developing countries and specific populations (patients with atypical findings, children, older patients, and those with overlapping cerebrovascular disease). The last recommendation allows the positive CSF oligoclonal bands (OCBs) as an alternative to dissemination in time. The same last panel suggests that elevated immunoglobulin G (IgG) index should be interpreted with caution when testing for OCBs is negative or not performed.
Objective: To investigate whether the IgG index can reliably predict OCB findings in a Brazilian setting.
Methods: In the present cross-sectional study, we analyzed persons with MS (PwMS) who fulfilled the 2017 McDonald criteria, with available OCB and IgG index results. The IgG index was considered elevated if ≥ 0.700. We calculated the positive predictive value (PPV), negative predictive value (NPV), and the area under the receiver operating characteristic (ROC) curve with 95% confidence intervals (95%CIs).
Results: A total of 108 PwMS were analyzed, 81.5% of whom were OCB positive, and 72.5% showed an elevated IgG index. The IgG index value ≥ 0.7 showed a PPV of 94.9% (95%CI: 87.4–98.6%) when OCBs were positive. The NPV of a normal IgG index was of 44.8% (95%CI: 26.4–64.3%) when OCBs were negative. The area under the ROC curve was of 0.817 (95%CI: 0.693–0.940; $p < 0.001$).
Conclusion: The high PPV for the presence of OCBs can facilitate the MS diagnostic process in typical clinical and imaging situations, especially in developing countries with difficulty or delay in determining the presence of OCBs (given the low cost and easy accessibility of the IgG index). However, a normal IgG index has a low capacity to predict a negative OCB result.

DOI: 10.1055/s-0044-1789339

Lower prevalence of cognitive impairment in a specific MS population: associated factors and probable reasons

Isabella Avolio[1], Olivia Pires[1], Clayton Zoccoli[2], Murilo Pinoti[2], Mateus Boaventura de Oliveira[1,3]
[1]*Hospital São Camilo, São Paulo SP, Brazil.*
[2]*Centro Universitário São Camilo, São Paulo SP, Brazil.*
[3]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br).

Abstract
Background: Multiple sclerosis (MS) symptoms vary according to the affected brain topography and can result in cognitive dysfunction, a common cause of limitations in everyday life that is highly associated with the risk of ongoing disability.
Objective: To assess the frequency of cognitive impairment (CI) in MS patients and its association with other variables of interest.
Methods: In the present cross-sectional study, we applied the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) as a cognitive measurement. Cognitive impairment was considered when the test performance of an individual fell by 1.5 standard deviation (SD) in relation to the normative values. Statistical associations were performed with: age, sex, years of schooling, disease duration, previous relapse number, brain lesional load, the Expanded Disability Status Scale (EDSS), the Modified Fatigue Impact Scale (MFIS), the Multiple Sclerosis Impact Scale (MSIS-29), and the Hospital Anxiety and Depression Scale (HADS).
Results: In total, 98 subjects were included in the study (78.9% of female individuals, with a mean age of 39.0±9.8 years, a median disease duration of 7.6 years [IQR = 4.3–11.0], and a median EDSS score of 2.0 [IQR = 2.0–3.0]). The mean processing speed z-core was of -0.18, with 4.1% < 1.5 SD; the mean verbal memory z-score was of -0.60, with 17.3% < 1.5 SD; and the mean visual memory z-score was of -0,16, with 9.2% < 1.5 SD. Worse processing speed scores were found in progressive phenotypes. Significant correlations between visual memory and the EDSS score ($r = -0.324$; $p = 0.002$) and processing speed and the EDSS score ($r = -0.298$; $p = 0.004$) were identified. No significant associations of the BICAMS z-score tests were observed with age, sex, schooling, disease duration, previous relapse number, lesional load, and the MFIS, MSIS-29, and HADS scores.
Conclusion: The findings pointed to a lower frequency of CI (of up to 17.3%) in the present study, as compared with classical cohorts previously described. This result may be related to early treatment in the current era, access to health resources,

shorter duration of the disease, and a higher cognitive reserve in our sample.

DOI: 10.1055/s-0044-1789340

Patient-reported outcomes (SymptoMScreen) in a Brazilian scenario: most common symptoms and their correlations with conventional scales

Mateus Boaventura de Oliveira[1,2], Larissa Cruz Gatti[2], Murilo Pinoti[2], Olivia Pires[3], Clayton Zoccoli[2], Isabella Avolio[3]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Centro Universitário São Camilo, São Paulo SP, Brazil.*

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br.

Abstract
Background: Multiple sclerosis (MS) is an autoimmune and polysymptomatic disease with a relevant need for recording and monitoring symptoms. In this scenario, patient-reported outcomes (PROs) are important to measure the impact of the disease and to monitor issues such as silent progression. The SymptoMScreen was developed in 2017 and is designed to evaluate the impact of MS symptoms through 12 neurological domains. It is a quick user-friendly scale with high reproducibility, easy access, previous use in clinical trials, and potential association with well-known scales.
Objective: To describe the most common debilitating symptoms in MS patients by using the SymptoMScreen and its correlations in a Brazilian setting.
Methods: The present is an observational, cross-sectional study, conducted in an MS Outpatient Clinic where this PRO is routinely applied. The median of the global SymptoMScreen score was calculated and correlated with: the Expanded Disability Status Scale (EDSS), the Timed 25-Foot Walk (T25FW), the Nine-Hole Peg Test (9HPT), the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test (CVLT), the Brief Visuospatial Memory Test – Revised (BVMT-R), the Multiple Sclerosis Impact Scale (MSIS-29), and the Modified Fatigue Impact Scale (MFIS).
Results: The study included 123 MS patients (with a mean age of 38.3±10.5 years, 76.4% of female subjects; a mean disease duration of 9.5±7.5 years, and a median baseline EDSS score of 2.0). The three most affected domains were fatigue, cognition, and anxiety. The global SymptoMScreen score was significantly associated with the scores on the EDSS ($r = 0.561$; $p < 0.001$), T25FW ($r = 0.370$; $p < 0.001$), 9HPT ($r = 0.352$; $p = 0.007$), MSIS-29 ($r = 0.556$; $p < 0.001$), and MFIS ($r = 0.448$, $p < 0.001$). Concerning correlations with the SDMT, CVLT and BVMT-R, only trends were observed.
Conclusion: The SymptoMScreen is a high-quality valuable tool for documenting and addressing patient symptoms in clinical settings, and it may support remote monitoring. The global score was significantly correlated with conventional scales in the present study.

DOI: 10.1055/s-0044-1789341

Disability functional profile of patients with progressive multiple sclerosis and its association with disease-modifying therapy in a hospital in Northeastern Brazil

Matheus Rolim Mendes de Alencar[1], Ivna Lacerda Pereira Nóbrega[1], Igor Bessa[2], Paulo Sérgio Lisboa[2], Keyla Rejane[1], Rodrigo da Ponte Barbosa[1], Lucas Silvestre[2], Patrícia Chagas Rocha D'Almeida[1], Gabriela Martins[2], José Artur Costa D'Almeida[2], Milena Sales Pitombeira[2]
[1]*Hospital Geral de Fortaleza, Fortaleza CE, Brazil.*
[2]*Hospital Geral de Fortaleza, Departamento de Neuroimunologia, Fortaleza CE, Brazil.*

Address for correspondence: Matheus Rolim Mendes de Alencar (email: matheus_alencar_1@hotmail.com).

Abstract
Background: Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system associated with neurodegeneration. Regarding treatment and epidemiological data about MS, there is a lack of scientific studies in Brazil and Latin America, mainly regarding the development of treatment protocols, as well as better strategies for clinical and diagnostic evaluations mainly in cases of the progressive forms of the disease.
Objective: To evaluate the disability profile of patients with progressive MS followed up at a hospital in Northeastern Brazil.
Methods: The present was a retrospective cohort study, which evaluated the disability profile of patients with progressive MS and the associations with treatment, between t 2020 and 2024. The disability profile was assessed by the Expanded Disability Status Scale from the analysis of medical records, along with available clinico-epidemiological data, using the BRANDO platform, a database developed by the Brazilian and the Latin American committee for studies in MS, for data collection, along with available clinico-epidemiological data. We also analyzed the association involving disability, clinical, and disease-modifying therapy (DMT).
Results: We included 42 patients with a PMS diagnosis, 26 (61.9%) of whom were female. The median EDSS score was of 6.5 (range: 1.5–9.5), which is in line with the impairment in labor activities observed in this cohort, as 34 (80.9%) patients were reported as retired or unemployed due to MS. Age was correlated with greater disability, while no significant difference was observed between the samples as to the disease progression and DMT use.
Conclusion: Significant disability and high work impairment were observed in the population with PMS analyzed. Older age was the only factor correlated with higher EDSS scores in our sample. New studies will be necessary to better evaluate the patients disability profile, including a complete approach and more broad functional tests in a systematic way to better monitor the patient and evaluate therapeutic response.

DOI: 10.1055/s-0044-1789342

Longitudinally-extensive transverse myelitis: impact on functional prognosis and mortality in a 10-year follow-up cohort

Paula Baleeiro Rodrigues Silva[1], Samira Luisa Apóstolos-Pereira[1], Graziella Aguiar Santos Faria[1], Sara Terrim[1], Flávio Vieira Marques Filho[1], Mariana Gondim Peixoto Spricigo[1], Mateus Boaventura de Oliveira[1,2], Guilherme Diogo Silva[1], Douglas Kazutoshi Sato[3], Tarso Adoni[1]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil.*

Address for correspondence: Paula Baleeiro Rodrigues Silva (email: paula.baleeiro1@gmail.com).

Abstract
Background: Neuromyelitis optica spectrum disorder (NMOSD) is a leading cause of longitudinally-extensive transverse myelitis (LETM). Due to advancements in early

diagnosis and treatment, NMOSD mortality has declined. However, mortality data for patients with first-episode LETM are scarce.
Objective: To assess the final diagnosis and long-term prognosis of patients with first-episode LETM.
Methods: The present is an observational retrospective study involving all consecutive patients diagnosed with LETM who were sequentially referred to the Clinical Neurology Department of a Brazilian tertiary hospital between January 2005 and December 2011. Only patients meeting the criteria for the first episode of idiopathic LETM were included. Data were retrieved from electronic medical records from October 2023 to January 2024. The statistical analysis used the Mann-Whitney and Fisher exact tests in the R Studio software.
Results: In total, 39 patients met the inclusion criteria. After a median 12-year follow-up, the final diagnoses were as follows: 51% of isolated monophasic seronegative LETM, 28% of AQP4-IgG positive NMOSD, 7.7% of AQP4-IgG negative NMOSD, 5% of myelin oligodendrocyte glycoprotein antibody associated disease, 5% of recurrent seronegative LETM, and 2.6% of multiple sclerosis. The mortality rate was of 10% at the end of the follow-up, with a median (m) time to death of 3 years, and the deceased patients had a higher age at the onset of LETM (m = 56; IQR = 42–69; OR = 1.09; 95%CI = 1.01–1.21; $p = 0.043$). Among the survivors, 17% had an Expanded Disability Status Scale (EDSS) score ≥ 7 at the last clinical follow-up. The predictors of severe sequelae included higher EDSS score at nadir (m = 8.5; IQR = 8.5–8.88; OR = 5.29; 95% CI = 1.38–39; $p = 0.011$), pain as an initial myelitis symptom (83%; OR = 11.1; 95%CI = 1.51–230; $p = 0.028$), and spinal shock during the first myelitis (100%; $p < 0.001$).
Conclusion: In the cohort of the present study, half of the patients remained as isolated monophasic seronegative LETM, mortality reached 10%, and 83% of the survivors were ambulatory after a median 12-year follow. The prognostic factors included age, pain, and initial severity.

DOI: 10.1055/s-0044-1789343

Fatigue and sleep disturbances predict depressive symptoms in people with multiple sclerosis

Paulo Matheus Casal de Souza[1], Carlos Bernardo Tauil[2], Cintia Ramari[3], Renata Lameira Oliveira[1]
[1]*Escola Superior de Ciências da Saúde, Brasília DF, Brazil.*
[2]*Universidade de Brasília, Brasília DF, Brazil.*
[3]*Hasselt University, Brazilian Committee for Treatment and Research in Multiple Sclerosis, Hasselt, Belgium.*

Address for correspondence: Paulo Matheus Casal de Souza (email: paulomatheus928@hotmail.com).

Abstract
Background: Depressive symptoms are common in multiple sclerosis (MS), with a rate of ~ 50% of risk of development. Depression exacerbates MS symptoms, and sleep disturbances, fatigue, and MS-related disabilities intensify depressive symptoms. This interaction is further complicated by social factors as well as impaired cognitive and motor functions.
Objective: To investigate potential predictors of anxiety and depression symptoms in people with MS.
Methods: Data from 241 persons diagnosed with MS, inserted into the BRANDO database from Sinapse Clinic, were analyzed. Depressive symptoms were assessed using the Beck Depression and Anxiety Inventory (BDI and BAI) and the Hospital Anxiety and Depression Scale (HADS-A and HADS-D). The predictive factors were: Expanded Disability Status Scale (EDSS) score, sleep disturbances, sphincter control, sexual dysfunction, manual dexterity (Nine Hole Peg Test – NHPT), short walking capacity (Timed 25-Foot Walk Test – T25FWT), processing speed (Symbol Digit Modality Test – SDMT) and fatigue (Modified Fatigue Impact Scale – MFIS). Both correlation and stepwise multiple regression analyses were conducted.
Results: Significant yet weak correlations were found between depressive symptoms (across all scales) and sleep disturbances (R = 0.23–0.32; $N = 78$), sphincter control (R = 0.25–0.33; $N = 78$), NHPT (R = 0.17–0.21; $N = 228$), and SDMT (R = -0.20 to -0.26, $N = 209$). Moderate correlations were observed with the EDSS (R = 0.33–0.42; $N = 231$), and MFIS (R = 0.54–0.69; $N = 218$). Multiple regression identified fatigue (MFIS) as the main predictor for the BAI (R-squared = 0.51), and fatigue and sleep changes as main predictors for the BDI (R-squared = 0.49), HADS-A (R-squared = 0.36), and HADS-D (R-squared = 0.58).
Conclusion: While depressive symptoms in MS are associated with a range of symptoms that affect from motor to cognitive functions, the main predictors in the sample of the present study were fatigue and sleep disturbances. Future studies should assess how depressive symptoms may change in response to interventions targeting fatigue management, such as behavioral interventions and physical exercise.

DOI: 10.1055/s-0044-1789344

COVID-19 and vaccination in children and adolescents with neuroimmunological disorders

Renata Paolilo[1], Ingrid Pessoa[1], Roberta Diniz[1], Ana Leão[1], Juliana Gaigher[1], João Santana[1]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*

Address for correspondence: Renata Paolilo (email: renatabpaolilo@gmail.com).

Abstract
Background: The understanding of how COVID-19 impacts children with neuroimmunological diseases and those receiving immunosuppressant treatment remains limited. Moreover, despite the progress in vaccinating the pediatric population, the safety and efficacy of immunization agents in this specific group of children need to be more extensively investigated.
Objective: To analyze the clinical manifestations and impact of COVID-19 disease and vaccination in the pediatric population with neuroimmunological disorders followed up in a Brazilian specialized center.
Methods: The present is a cross-sectional and retrospective evaluation of pediatric patients with neuroimmunological disorders followed from January 2019 until March 2022. Demographics, clinical and therapeutic features, COVID-19 pandemic aspects, suspected/confirmed cases of COVID-19, laboratory and radiological findings, vaccination details, and disease exacerbations were recorded.
Results: We identified 93 patients; 63 (67.7%) were female, and 31 (44.9%), of white ethnicity. The mean age at disease onset was of 6.65 (±4.1) years. At the last follow-up, the final diagnoses were: multiple sclerosis (19.4%), myasthenia gravis (11.8%), opsoclonus myoclonus ataxia (23.7%), neuromyelitis spectrum disorders (6.5%), MOG-IgG-associated disorder (5.4%), ADEM (5.4%), CIS (7.6%), autoimmune encephalitis (5.4%), CIDP (2.2%), and other (13%). A total of 38 (42.2%) patients presented with a relapsing-remitting disease course, and 28.1% had a relapse during the pandemic. Overall, 17 patients were diagnosed with COVID19: fever, cough, asthenia, and dyspnea were the most common clinical features, and 16.7% of the patients required hospitalization. No patient

required ICU or died. Four (23.5%) patients reported worsening of the neurological symptoms during COVID-19. Two patients disclosed new brain MRI lesions, and 57.6% (34/59) of the parents reported hesitation to vaccinate their children. Two (4%) out of 50 vaccinated children reported worsening of neurological symptoms after vaccination.
Conclusion: Neurological complications of the COVID-19 infection and vaccination in patients diagnosed with neuroimmunological disorders were rare. Most parents hesitated to vaccinate their children. Telephone interviews were a feasible instrument in our population.

DOI: 10.1055/s-0044-1789345

Kappa index in the diagnosis of multiple sclerosis

Rodrigo Pereira[1], Maria Lucia Vellutini Pimentel[1], Carlos Brandão[2], Vanessa Miranda[2], Leticia Mansur[1], Carlos Pinho[2], Celina Oliveira[2], Cristiane Casanova[2], Dalton Ferreira[2], Francisjane Lopes[2], Léo Correira[2], Felipe Nascimento[1], Danilo Almeida[1], Thiago Araújo[1], Raquel Costa[1], Barbara Dias[1], Gabriel Amaral[1], Kathleen Monteiro[1], Pedro Chamma[1], Marianela Rios[1]
[1]*Santa Casa da Misericórdia do Rio de Janeiro, Rio de Janeiro RJ, Brazil.*
[2]*Neurolife Laboratórios Ltda, Rio de Janeiro RJ, Brazil.*

Address for correspondence: Rodrigo Pereira (email: rodrigopereira@hotmail.co.uk).

Abstract
Background: Investigations into biomarkers aim to aid in the early diagnosis of multiple sclerosis (MS). Kappa free light chain (KFLC) in the cerebrospinal fluid (CSF) and blood is one such biomarker linked to neuroinflammatory disorders.
Objective: To investigate KFLC's usefulness in MS diagnosis, particularly in patients with negative CSF oligoclonal bands (OCBs).
Methods: A quantitative study was performed, searching for the relationship between high levels of the Kappa index and the diagnosis of MS. Medical records, the results of the CSF OCBs and the Kappa index were analyzed from 55 patients treated at our service from 2018 to 2023. The cutoff value for the Kappa index was of 2.9. The Chi-squared test was used to perform the statistical analysis. Patients with MS who had records of a CSF test with OCBs and Kappa index analysis were included.
Results: In total, 22 patients (40%) had relapsing-remitting MS (RRMS). One patient had a negative Kappa index, and three had negative OCBs. The Chi-squared value for the Kappa index was of 13.5561 ($p = 0.000232$), and for the OCBs, it was of 15.3954 ($p = 0.000087$). All three patients with negative OCBs had a positive Kappa index.
Conclusion: The 2017 McDonald criteria enabled the diagnosis of MS in patients with a typical clinically-isolated syndrome, along with clinical or MRI evidence of dissemination in space and the presence of OCBs in the CSF. In the present study, both OCBs and the Kappa index effectively distinguished MS from non-MS patients using the Chi-squared analysis. The Kappa index could help confirm the diagnosis when OCBs are negative.

DOI: 10.1055/s-0044-1789346

Development of a clinical score to estimate the probability of neuromyelitis optica in patients presenting with optic neuritis

Sara Terrim[1], Guilherme Diogo Silva[1], Fernando Falcão[1], Flavio Marques Filho[1], Paula Baleeiro Rodrigues Silva[1], Graziella Faria[1], Mateus Boaventura de Oliveira[1,2], Ana Claudia Piccolo[3], Carolina Rimkus[1], Luiz Roberto Comerlatti[1], Ida Fortini[1], Marcia Rubia Rodrigues Gonçalves[1], Luiz Henrique Martins Castro[1], Tarso Adoni[1], Samira Luisa Apóstolos-Pereira[1], Dagoberto Callegaro[4]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Faculdade de Medicina do ABC, São Paulo SP, Brazil.*
[4]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Sara Terrim (email: sterrim.sara@gmail.com).

Abstract
Background: Neuromyelitis optica spectrum disorder (MMOSD) represents an important cause of optic neuritis (ON), with a high risk of sequelae and recurrence. Early diagnosis is crucial, but the recognition of ON in the acute phase may be difficult. Anti-aquaporin-4 antibody (anti-AQP4) testing is not easily available in limited-resource scenarios, and different methods offer variable sensitivity profiles. These limitations represent a challenge for the early diagnosis of NMOSD and emphasize the important prognostic role of clinical aspects in acute phase ON for suspicion of the disease.
Objective: To develop an easily-appliable prognostic model for suspicion of NMOSD in patients with ON.
Methods: Patients admitted to our Emergency Department between 2015 and 2020 with a diagnosis of ON were enrolled in the present study. We performed univariable analysis to identify variables associated with a final diagnosis of NMOSD. Based on our findings and on previous literature, we selected four variables to develop a prognostic model to predict the risk of a diagnosis of NMOSD regardless of the anti-AQP4 status.
Results: We enrolled 63 participants with ON (45 women [71%]; median age: 34 [interquartile: range 29–47] years), 18 of whom were diagnosed with NMOSD (12 anti-AQP4-positive; and 6 anti-AQP4-negative) and 45 with other demyelinating diseases. Our prognostic model included four variables and one point attributed to each of them: female gender, bilateral ON, painless, and chiasmal involvement in MRI. The application of our score in the sample of the present study provided the following distribution of NMOSD patients: 0 – 0/7 (0%); 1 –5/23 (22%); 2 –6/23 (26%); 3 –6/9 (67%); and 4 – 1/1 (100%).
Conclusion: An easily-accessible score with clinical and radiological information may predict the risk of NMOSD early to help in diagnostic and therapeutic decisions.

DOI: 10.1055/s-0044-1789347

Description of suspected autoimmune encephalitis cases in two neurological reference hospitals in Curitiba, Brazil

Alana Bacelar Limeira Sales[1], Samia Talise El Horr de Moraes[1], Caio César Diniz Disserol[1], Claudia Suemi Kamoi Kay[1]
[1]*Universidade Federal do Paraná, Hospital de Clínicas, Curitiba PR, Brazil.*

Address for correspondence: Alana Bacelar Limeira Sales (email: alanabls@hotmail.com).

Abstract
A description of suspected cases of autoimmune encephalitis (AIE) was conducted among patients admitted to two neurological reference hospitals in the city of Curitiba, state of Paraná, Brazil. The objective was to assess the frequency of possible AIE and the positivity of known antibodies in these

patients. Samples of suspected AIE were collected for an autoimmune panel to determine how many of them had relevant antibodies and met the criteria for possible AIE. Out of 56 patients with suspected AIE, 28 met the criteria for possible AIE, 7 tested positive for antibodies (of these, all met the criteria for possible AIE, except 1 case with positive anti-GAD, diagnosed with Rasmussen encephalitis, with etiological factors not yet defined in the literature and uncertain relationship with the antibody in question); 7 patients are still waiting for the antibody results (all meeting criteria for possible AIE). Among the patients with positive antibodies, 3 had positive anti-GAD65, 2 had positive anti-NMDA, 1 had positive anti-Yo, and 1 had positive anti-AMPA. Possible AIE is defined by subacute onset with progression in fewer than 3 months of deficits in working memory, alteration in mental status, or psychiatric symptoms. Furthermore, the patients should present at least one of the following: new focal neurological findings, epileptic seizures unexplained by a known previous disease, pleocytosis in the cerebrospinal fluid, and/or MRI findings suggestive of encephalitis. However, it is essential to exclude alternative diagnoses. These findings highlight the importance of considering AIE in patients presenting with specific clinical criteria. Prompt diagnosis and appropriate management are crucial to improve patient outcomes.

DOI: 10.1055/s-0044-1789348

Association of myelin content and neuropsychological tests with the risk of brain atrophy in multiple sclerosis

Alessandra Gallo[1], Giordani Rodrigues Dos Passos[1], Rafael Canani Sommer[1], Pedro Rodrigues Neves[1], Ana Djulia Tesche[1], Augusto Cesar Bressanim[1], Francisco Zuanazzi[1], Ana Paula Reginatto Tubiana[1], Luciana Schermann Azambuja[1], Gisele Hansel[1], Douglas Kaz[1]

[1]*Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil.*

Address for correspondence: Alessandra Gallo (email: alegallo.ajg@gmail.com).

Abstract

Background: Multiple sclerosis (MS) is characterized by demyelination and focal neurological deficits that can be reversed with the recovery of the damaged myelin sheath – remyelination. Cladribine is an MS disease-modifying drug that leads to B and T lymphocyte apoptosis, reducing disease activity. However, there are few studies which have evaluated the effects of cladribine treatment with advanced quantitative imaging. We tested patients using the q-Space Myelin Map and calculating the normalized leptokurtic diffusion (NLD) values, as a proxy for myelin content.

Objective: To evaluate the association of baseline NLD values with clinical and brain volume changes in MS patients treated with cladribine.

Methods: Twelve patients with highly-active MS were followed for 12 months. Clinical and neuroimaging variables were collected. Myelin microstructure was analyzed using the baseline NLD values for T2 lesions and normal-appearing white matter (NAWM).

Results: Lower mean lesional NLD and NAWM at baseline were associated with a positive total brain and thalamic volume changes after 1 year (NAWM x thalamic volume: $R^2 = 0.58$; $p < 0.01$; NAWM x brain volume: $r = 0.76$; $p < 0.01$; lesional NLD x thalamic volume: $R^2 = 0.21$; $p = 0.08$; lesional NLD x cerebral volume: $r = 0.73$; $p < 0.01$). Furthermore, baseline corrected gray and white matter volumes were associated with better performance in the 9-hole peg test (GM: $r = 0.52$; $p = 0.08$; WM: $r = 0.59$; $p = 0.08$), and NAWM NLD at baseline demonstrated a trend toward a positive association with the Paced Auditory Serial Addition Test score ($r = 0.54$; $p = 0.06$).

Conclusion: Myelin content both in lesions and NAWM correlated with brain atrophy after 1 year, as well as some clinical scales, suggesting NLD may be used as a biomarker for atrophy risk and, therefore, disease progression.

DOI: 10.1055/s-0044-1789349

Quantitative evaluation of remyelination in patients with multiple sclerosis and its correlation with quality of life and functionality

Ana Djulia Tesche[1], Daissy Liliana Mora Cuervo[1], Rafael Canani Sommer[1], Alessandra Jahn Gallo[1], Pedro Rodrigues Neves[1], Vitoria Pimentel[1], Douglas Kazutoshi Sato[2]

[1]*Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil.*

[2]*Pontifícia Universidade Católica do Rio Grande do Sul, Hospital São Lucas, Porto Alegre RS, Brazil.*

Address for correspondence: Ana Djulia Tesche (email: anadjuliatesche@gmail.com).

Abstract

Background: The treatment for multiple sclerosis (MS) aims to reduce the demyelinating action with the use of immunomodulators (DMDs). However, few available treatments had their remyelinating performance examined, having in mind that the conventional neuroimaging methods fail to detect the remyelination.

Objective: q-Space Myelin Map (qMM), to comparatively measure the remyelinating activity in patients treated for MS, and we aim to correlate remyelination with clinical improvement.

Methods: An observational study to analyze neuroimaging biomarkers in 27 patients using DMDs, with a mean age of 31.88 ± 7.18 years, 68.6% of female subjects, and 81.3% of patients of white ethnicity. In this preliminary analysis 27 patients cam for 2 visits (months 0 and 6) and underwent a neurological evaluation. Remyelination was evaluated through magnetic resonance imaging by qMM through the result of normalized leptokurtic diffusion (NLD) as a proxy for myelin content.

Results: We evaluated the ΔNLD at 6 months and its association with clinical scales in the period. The lesional ΔNLD correlated positively with the change in the Multiple Sclerosis Quality of Life-54 (MSQOL-54) questionnaire ($r = 0.23$; $p = 0.03$ in the mental health component; and $r = 0.44$; $p = 0.04$ in the physical health component) and in the Timed 25-foot walked (T25W; $r = 0.55$; $p < 0.01$). We also evaluated the variation of NLD in normal-appearing white matter (ΔNAWM), which was associated with favorable evolution in the T25W ($r = 55.2$; $p = 0.01$). The present was the first study with qMM that evaluated the quantitative evolution of lesional NLD changes and clinical improvement of MS.

Conclusion: According to our hypothesis, an increase in NLD at 6 months (reflecting remyelinating activity) was associated with clinical improvement, especially with subjective quality of life and function of the lower limbs.

DOI: 10.1055/s-0044-1789350

Cognitive-behavioral syndrome, a diagnostic challenge in NMOSD: the arch bridge pattern can help

Arthur Dias[1], Victor Costa[2], Camila Nepomuceno[1], Felipe Juliatti[1], Maria Fernanda Hamamoto Leati[1], Gabriel Vieira[3], Flávio Vieira Marques Filho[4]

[1]*Hospital Santa Marcelina, São Paulo SP, Brazil.*
[2]*Universidade Federal de Juiz de Fora, Hospital Universitário, Juiz de Fora MG, Brazil.*
[3]*Universidade Estadual de Campinas, Departamento de Neurologia, Campinas SP, Brazil.*
[4]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*

Address for correspondence: Arthur Dias (email: arthurdemedeirosdias@gmail.com).

Abstract

Case Presentation: In July 2022, a 59-year-old female patient started a vertiginous syndrome with asymmetric and bilateral involvement. Six months later, she had a bitemporal painless visual disability that developed a few days after taking the fourth dose of the COVID-19 vaccine. In August 2023, she developed rapidly-progressive dementia with impairment of memory, praxis, and visuospatial orientation, without hallucinations or behavioral changes. On MRI, T2/FLAIR revealed hypersignal surrounding the posterior horns of the lateral ventricles, affecting the splenium of the corpus callosum (arch bridge pattern). Indirect immunofluorescence showed the patient was aquaporin-4 antibody positive (1:80) by the TBA method.

Discussion: Neuromyelitis optica spectrum disorder (NMOSD) is a disease that was better elucidated with the discovery of the anti-aquaporin-4 antibody due to its high sensitivity (around 80%) and even higher specificity (99%). The diagnostic delay due non-hospitalization or investigation of a pons syndrome (rare presentation in NMO) and, consequently, non-treatment, enabled the occurrence of an even rarer syndrome, a cognitive condition associated with corpus callosum injury (the arch bridge pattern). This sign (described in our patient) is typically involved in its ependymal surface, often affecting most of its length; in acute phases, edematous and heterogeneous hyperintensity on FLAIR/T2-weighted images are usually observed, assuming a typical marbled. Corpus callosum injuries are present in 18% of all patients, but the arch sign is much rare.

Final Comments: This clinical case leads us to reflect upon the urgency for neuroimmunology patients to reach reference hospitals, to promptly receive adequate diagnosis and treatment, as well as to explain rare presentations in patients with (NMO: pons and corpus callosum), and finally leads us to increasingly testing anti-aquaporin-4 in cases that have not yet been elucidated.

DOI: 10.1055/s-0044-1789351

Mortality and causes of death in patients with neuromyelitis optica spectrum disorder and multiple sclerosis at a reference center

Bianca Oliveira[1], Daniel Lima Junior[2], Arthur Felipe Barbosa Vasconcelos[1], Jeanina Dionizio[1], Adriana Silva[1], Tania Albuquerque[1], Ana Cicília Araujo[1], Beatriz Barbosa[1], Daniele Maia[1], Ana Clara Rodrigues[1]

[1]*Centro de Referência em Esclerose Múltipla da Paraíba, João Pessoa PB, Brazil.*
[2]*University of California San Diego, San Diego CA, United States.*

Address for correspondence: Bianca Oliveira (email: oliveira_bes@hotmail.com).

Abstract

Background: Neuromyelitis optica spectrum disorder (NMOSD) and multiple sclerosis (MS) are neurological conditions associated with significant morbidity and mortality. While NMOSD is known for its rapid disability progression, MS is rarely fatal by itself, with mortality often attributed to complications.

Objective: To examine mortality rates and causes of death among NMOSD and MS patients evaluated and followed up at a reference center in the state of Paraíba, Brazil.

Methods: A retrospective study encompassing a 10-year follow-up of NMOSD and MS patients evaluated at a neuroimmunology reference center. Data were collected from April 2014 to April 2024.

Results: Over the 10-year period, 25 deaths were recorded, comprising 5 NMOSD patients (1 male, 4 female) and 20 MS patients (7 male, 13 female). The causes of death among the NMOSD patients included sepsis (1), pulmonary thromboembolism (1), COVID-19 (1), and cases of unknown etiology (2). In the MS cohort, the causes of death varied, and included sepsis (6), aspiration pneumonia (4), stroke (1), acute heart attack (2), dengue virus infection (1), high digestive bleeding (1), COVID-19 (1), acute respiratory insufficiency (1), and 1 case certified as MS.

Conclusion: Mortality in NMOSD and MS patients is often attributed to infections, particularly respiratory infections, and conditions associated with advanced disability and immobility. The NMOSD relapses can be severe and directly contribute to mortality. These findings underscore the importance of clinical interventions, professional education, and advancements in disease-modifying therapies to mitigate the frequency and severity of complications, potentially improving survival outcomes for patients with NMOSD and MS.

DOI: 10.1055/s-0044-1789352

Epidemiological study on multiple sclerosis in Brazil: demographic and clinical characteristics according to geographic distribution – a BRANDO study

Alfredo Damasceno[1], Carlos Bernardo Tauil[2], Henry Koiti Sato[3], Dagoberto Callegaro[3], Maria Fernanda Mendes[4], José Artur Costa D'Almeida[5], Denise Sisterolli Diniz[6], Osvaldo J. M. Nascimento[3], Laura Fiuza Parolin[7], Thiago Goncalves Fukuda[3], Paulo Diniz da Gama[8], Herval Neto[3], Marco Lana-Peixoto[9], Giordani Rodrigues dos Passos[10], Rayllene da Silva Caetano[10], Kleber Cavalcante dos Santos[11], Caio César Diniz Disserol[12], Gabriel Vieira[1], Eliana Tomomi Shimabukuro da Cunha[13], Guilherme Diogo Silva[13], Natália Cirino Talim[9], Cintia Ramari[14], Jefferson Becker[10]

[1]*Universidade Estadual de Campinas, Campinas SP, Brazil.*
[2]*Universidade de Brasília, Brasília DF, Brazil.*
[3]*Universidade de São Paulo, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*
[4]*Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.*
[5]*Hospital Geral de Fortaleza, Departamento de Neuroimunologia, Fortaleza CE, Brazil.*
[6]*Universidade Federal de Goiás, Goiânia GO, Brazil.*
[7]*Neurovie, Departamento de Neurologia, Joinville SC, Brazil.*
[8]*Pontifícia Universidade Católica de São Paulo, Sorocaba SP, Brazil.*
[9]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*
[10]*Pontifícia Universidade Católica do Rio Grande do Sul, Hospital São Lucas, Porto Alegre RS, Brazil.*

[11]Secretaria de Saúde do Distrito Federal, Brasília DF, Brazil.
[12]Universidade Federal do Paraná, Hospital de Clínicas, Curitiba PR, Brazil.
[13]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.
[14]University of Hasselt, Brazilian Committee for Treatment and Research in Multiple Sclerosis, Hasselt, Belgium.

Address for correspondence: Cintia Ramari (email: cintiaramarif@gmail.com).

Abstract
Background: Multiple sclerosis (MS) is an inflammatory and neurodegenerative disorder whose prevalence varies across Brazil (15 to 18 per 100 thousand people on average; Southern region: 27 per 100 thousand people), and the absence of an extensive national study limits the epidemiological understanding of MS in a nation as diverse as Brazil.
Objective: To describe the epidemiological differences among people with MS across four Brazilian regions.
Methods: Data from 2,974 MS patients in the Collaborative Latin American Database for Multiple Sclerosis (BRANDO) were analyzed. We assessed demographics (sex, ethnicity) and clinical outcomes (age at onset, disability status, relapse frequency and topography, MS phenotype, and initial treatment) to elucidate regional differences.
Results: The cohort was predominantly female (72.5%) with age at MS onset of 30.6 years. Ethnicity: Caucasian (75.8%), Mixed – Brown/Mulato (18.5%), African descent (5.3%), and Asian (0.4%). Relapse topography involved the optic nerve (48.8%), brain (51.4%), posterior fossa (37.6%), and spinal cord (53.6%). Relapsing-remitting (RR) was the most common phenotype (81.0%). Natalizumab (18%) and beta-interferon 1A (10.4%) were the most prevalent initial treatments. Regional differences: lower predominance of female patients (68.7%; $p = 0.003$) in the Southeastern region; higher mixed ethnicity ($p = 0.000$), of 40.3% and 63.7%, in the Midwestern and Northeastern regions respectively; Differences ($p = 0.000$) in the number of relapses (Southeast [1.6] = Northeast [1.5] > South [0.98] > Midwest [0.51]); higher EDSS score in the Northeast (4.0; $p = 0.000$) compared with all other regions (mean range: 2.6–3.2); Higher prevalence of RR in the Southeast and Midwest (87%; $p < 0.001$), while the Northeast presented ($p < 0.001$) the highest rates of primary progressive (15.8%) and secondary progressive MS (18%). Glatiramer acetate (19.7%) was the prevalent initial treatment in the Northeast, compared with natalizumab (15%–21%) in the other regions.
Conclusion: Marking Brazil's first extensive MS cohort study, our findings underscore regional epidemiological variations, and we advocate for tailored approaches in MS management and research.

DOI: 10.1055/s-0044-1789353

Antibody-mediated demyelinating disease: a voxel-based morphology analysis

Diego Fragoso[1], Carolina Rimkus[2], Isabella Avolio[3], Samira Luisa Apóstolos-Pereira[2], Dagoberto Callegaro[3], Mateus Boaventura de Oliveira[1,4], Eduardo Tieppo[2], Guilherme Diogo Silva[2]
[1]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Instituto de Radiologia, São Paulo SP, Brazil.
[2]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.
[3]Universidade de São Paulo, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.
[4]Hospital São Camilo, São Paulo SP, Brazil.

Address for correspondence: Diego Fragoso (email: dcfragoso@hotmail.com).

Abstract
Background: Identifying magnetic resonance imaging (MRI) markers in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and aquaporin-4-positive neuromyelitis optica spectrum disorder (NMOSD-AQP4) is essential to establish objective outcome measures.
Objective: The primary aim was to explore differences within the brain morphology changes through voxel-based morphology (VBM) between MOGAD and NMOSD-AQP4 patients during the remission stage and compare them with healthy controls (HCs).
Methods: In the present cross-sectional study, 27 patients with MOGAD, 27 with NMOSD-AQP4, and 30 HCs were recruited from 2018 to 2020. All 84 participants were scanned with the same standardized MRI protocol on a 3-T MRI scanner. Structural T1-weighted images were processed and analyzed using the Computational Anatomy Toolbox (CAT12, Gaser, C. Structural Brain Mapping, Group, Jena University Hospital, Jena, Germany; https://www.neuro.uni-jena.de/cat/) implemented in Statistical Parametric Mapping (SPM12, Wellcome Trust Centre for Neuroimaging, London, UK; https://www.fil.ion.ucl.ac.uk/spm/software/ spm12/). Processing and analysis steps were followed according to the preset parameters with the standard protocol described in the manual (https://www.neuro.uni-jena.de/cat12/CAT12-Manual.pdf).
Results: Compared with the HCs, MOGAD patients demonstrated gray matter volume reduction in the left ventral superior frontal gyrus and left superior temporo-occipital ($p < 0.001$). The NMOSD-AQP4 patients showed a greater extension of cerebral volume reduction, more significantly in the subependymal areas (adjacent to the third ventricle and bilateral periatrial) and the left lingual cortex ($p < 0.001$).
Conclusion: During the remission stage, the MOGAD and NMOSD-AQP4 patients exhibited distinct patterns of brain volume reduction. Our findings could be explained, at least in part, by the differences in pathophysiology between these diseases. Although we conducted a group analysis, these results can support the transition of future studies analyzing the potential use of VBM analysis as a surrogate tool at the individual level.

DOI: 10.1055/s-0044-1789354

The value of iron imaging and central vein sign in the diagnostic and follow-up of multiple sclerosis

Douglas Mendes Nunes[1,2], Carolina Rimkus[3]
[1]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Instituto de Radiologia, São Paulo SP, Brazil.
[2]Grupo Fleury, São Paulo SP, Brazil.
[3]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.

Address for correspondence: Douglas Mendes Nunes (email: douglasmendesnunes@gmail.com).

Abstract
Background: Updates in the diagnostic criteria and the correct therapeutic management have provided a better quality of life and prognosis for the patients.
Objective: To review and illustrate the imaging patterns of typical and atypical multiple sclerosis lesions and to describe the importance of imaging findings based on pathophysiology in the accurate diagnosis and monitoring of multiple sclerosis.

Methods: The 2017 McDonald diagnostic imaging criteria for multiple sclerosis were applied. Then, the analysis of image findings based on pathophysiology was added.
Results: The analysis of diagnostic imaging criteria and imaging findings based on pathophysiology have increased the diagnostic accuracy, early diagnosis, monitoring of disease activity and therapeutic response, and it evaluates disease progression and establishes prognosis.
Conclusion: The integration of imaging findings based on pathophysiology in the 2017 McDonald diagnostic imaging criteria reduces errors of diagnostic interpretation and increases monitoring of disease activity and therapeutic response, especially of atypical lesions.

DOI: 10.1055/s-0044-1789355

Preliminary data on the importance of susceptibility imaging in the diagnosis of multiple sclerosis

Douglas Mendes Nunes[1,2], Bruno Casola Olivetti[1,2], Carolina Rimkus[1]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Instituto de Radiologia, São Paulo SP, Brazil.*
[2]*Grupo Fleury, São Paulo SP, Brazil.*

Address for correspondence: Douglas Mendes Nunes (email: douglasmendesnunes@gmail.com).

Abstract
Background: The MRI is the most important paraclinical tool to support the diagnosis of multiple sclerosis (MS) and identify disease mimics. Applying current diagnostic criteria (McDonald, 2017) increases the number of cases diagnosed but has demonstrated a reduction in specificity. People with MS also have risk factors for cerebral small vessel disease (CSVD), compromising correct allocation of new lesions to their cause, and such uncertainty may directly impact on treatment decisions. The inclusion of signals from conventional MRI sequences, such as the "central vein signal (CVS)" and the "paramagnetic rim lesion (PRL)" extracted from magnetic susceptibility (SWI) sequences, can contribute to increased specificity.
Objective: To explore the potential of the WSI sequence to distinguish lesions caused by MS from disease mimics, particularly CSVD, in a clinical setting, according to the current 2017 McDonald imaging criteria.
Methods: In a retrospective analysis, we reviewed 3T brain MRI scans of patients ($n = 668$) from January 2016 to0 December 2020 with white-matter focal lesions (MS: $n = 63$; and CSVD: $n = 606$). White-matter lesions (WMLs) detected using fluid-attenuated inversion recovery (FLAIR), SWI, phase-sensitive, and T1-weighted images were analyzed by two experienced neuroradiologists, who identified and characterized WMLs, including the presence of the CVS and PRL.
Results: The identification of ≥ 1 PRL was the optimal cut-off and had high specificity (99.9%; confidence interval [CI] = 98.20–99.99%) when distinguishing MS from CSVD. All patients with a PRL showing a CVS in the same lesion ($n = 48$) had MS, yielding a specificity of 100% (CI =98.8–100.0%).
Conclusion: The integration of imaging findings based on pathophysiology in the 2017 McDonald diagnostic imaging criteria reduces errors of diagnostic interpretation in MS.

DOI: 10.1055/s-0044-1789356

Unveiling the silent threat: exploring latent tuberculosis in multiple sclerosis patients undergoing novel therapies

Flávio Vieira Marques Filho[1], Sara Terrim[2], Paula Baleeiro Rodrigues Silva[1], Graziella Faria[2], Tarso Adoni[2], Samira Luisa Apóstolos-Pereira[3], Guilherme Diogo Silva[2], Rafael Paternò Castello Dias Carneiro[3], Mateus Boaventura de Oliveira[1,4], Dagoberto Callegaro[1]
[1]*Universidade de São Paulo, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*
[2]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[3]*Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.*
[4]*Hospital São Camilo, São Paulo SP, Brazil.*

Address for correspondence: Flávio Vieira Marques Filho (email: flaviovmf@icloud.com).

Abstract
Background: Latent tuberculosis, defined as positive IGRA or positive PPD (< 5 mm) in the absence of clinical or radiological signs of active TB or other confounding factors, prevails in a quarter of the world's population. About 10% of latent TB carriers may develop active TB, especially in the context of immunosuppression. Such context is constantly experienced by multiple sclerosis (MS) patients using disease-modifying drugs, raising concerns about their impact on the increased incidence of latent TB and conversion to active TB. Screening for latent TB is not always recommended and/or performed in MS patients, so data from this subgroup, especially in endemic countries, is scarce.
Objective: To define the prevalence of latent TB in MS patients screened for the prescription of alemtuzumab, rituximab, and oral cladribine at a reference center in an endemic country for tuberculosis, to evaluate the risk factors for latent TB (such as smoking, diabetes) in the screened population, as well as characteristics of MS (such as gender, age, disease duration) in the latent-TB subgroup compared with the TB-negative subgroup.
Methods: Subgroups with and without latent TB were defined and compared in a sample of 60 MS patients screened for the prescription of alemtuzumab, rituximab, and oral cladribine. The Fisher exact test was used to compare the qualitative variables, while the Mann-Whitney test (non-parametric) was employed for the quantitative variables. Statistical significance was established at $p < 0.05$.
Results: The frequency of latent TB in the sample was of ~ 24%. Smoking was the only factor that correlated with a higher chance of latent TB.
Conclusion: The frequency of latent TB was significantly higher, as expected, than in similar studies conducted in North America and Europe, but similar to the prevalence of the general population in endemic countries. Larger sampling is necessary to adequately correlate prevalence, risk factors for latent TB, and MS characteristics.

DOI: 10.1055/s-0044-1789357

Diffusion-tensor imaging findings related to disability and quality of life in multiple sclerosis: a 12-year follow-up

Gabriel Vieira[1], Mariana de Sá[1], Andre Augusto Lemos Vidal de Negreiros[1], Ana Carolina Andrade[1], Alfredo Damasceno[1]
[1]*Universidade Estadual de Campinas, Campinas SP, Brazil.*

Address for correspondence: Gabriel Vieira (email: gabrieldedeusvieira@gmail.com).

Abstract
Background: Diffusion-tensor imaging (DTI) is an advanced magnetic resonance imaging (MRI) technique that provides information on microscopic structural damage in white-matter tracts, related to demyelinating and axonal damage.
Objective: To evaluate 12-year longitudinal metrics in functional tests and DTI parameters.
Methods: We selected 30 patients from a previous cohort, and a new assessment was performed 12 years after (time point 2, tp2) the baseline assessment. The clinical variables evaluated were the EDSS, 9HPT, T25FW, and SDMT. The Brief Repeatable Battery of Neuropsychological Tests (BRB-N) was applied to all patients. We also evaluated the quality-of-life parameters. The DTI images were acquired on a 3-T device and analyzed using MRtrix3 (https://www.mrtrix.org). We selected the following tracts and fascicles: uncinate (UnF), cingulate (CgF), inferior fronto-occipital (IFOF), corpus callosum (CC), corticospinal tract (CST), and the fornix (FxF). Group comparisons were performed with the paired *t*-test. A multivariable linear regression was also performed.
Results: Regarding the functional and cognitive tests, those that showed a significant variation between baseline and tp2 were the EDSS ($t(29) = -2.715$; $p < 0.01$), 9HPT ($t(40) = -2.202$; $p < 0.05$), and PASAT z-score ($t(40) = -2.829$; $p < 0.01$). During baseline, no clinical variables were entered into the equation for DTI analyses. During tp2, the IFOF-FA delta was related to the T25FW ($R2 = 0.701$; $\beta = -0.992$; $p < 0.001$), the MCC-FA delta was related to fatigue ($R2 = 0.289$; $\beta = -0.699$; $p = 0.02$), and the UnF-FA delta ($R2 = 0.171$; $\beta = -0{,}423$; $p = 0.009$) and the UnF-RD delta ($R2 = 0.218$; $\beta = -0.466$; $p = 0.006$) were related to depression.
Conclusion: In the 12 years of follow-up, damage to the IFOF-FA was a predictor of changes in the T25FWT, in addition to UnF-FA being related to depression.

DOI: 10.1055/s-0044-1789358

Prevalence of trigeminal neuralgia in a tertiary multiple sclerosis reference center in Northeastern Brazil

Carla Welch da Silva[1], Patrícia Chagas Rocha D'Almeida[1], José Artur Costa D'Almeida[2]
[1]*Hospital Geral de Fortaleza, Fortaleza CE, Brazil.*
[2]*Hospital Geral de Fortaleza, Departamento de Neuroimunologia, Fortaleza CE, Brazil.*

Address for correspondence: José Artur Costa D'Almeida (email: arturdalmeida@gmail.com).

Abstract
Background: Trigeminal neuralgia (TN) is a condition that causes intense facial pain. Patients diagnosed with multiple sclerosis (MS) may experience TN as a result of lesions related to MS. The prevalence of TN in MS patients varies from 0.1 to 9.7% and remains poorly understood. A recent systematic review of 19 studies comprising 30,348 patients found a TN prevalence of 3.4% (Houshi et al, 2022).
Objective: To determine the prevalence and clinical characteristics of trigeminal neuralgia at a specialized multiple sclerosis center in the city of Fortaleza, Northeastern Brazil.
Methods: In the present cross-sectional study, we analyzed the registries of 564 MS patients looking for those that present symptoms of TN according to the definition of The International Classification of Headache Disorders (TICHD), 3rd edition.
Results: We identified 9 patients who met the TICHD criteria for TN; among them, the clinical phenotype was categorized as EMPP (1), EMSP (3), and EMRR (5). The median age of these patients was of 42 years, and 66% of them were female. Out of the 9 patients, 5 had BOC present in their cerebrospinal fluid (CSF), while we currently do not have this data for the remaining 4 patients. The EDSS ranged from 0.0 to 8.0, with a median score of 2.0. At our MS center, the prevalence of TN was found to be of 1.6%.
Conclusion: The prevalence of TN in MS patients at our center was within the range of the lowest and highest prevalences published in the medical literature. Moreover, it is very similar the prevalence rate published in a recent systematic review.

DOI: 10.1055/s-0044-1789359

Evaluation of parameters and prognosis factors associated with benign evolution of multiple sclerosis patients

Josué de Almeida David[1], Thomas Vieira de Paula[1], Alfredo Damasceno[1]
[1]*Universidade Estadual de Campinas, Campinas SP, Brazil.*

Address for correspondence: Josué de Almeida David (email: j219131@dac.unicamp.br).

Abstract
Background: The present study aims to analyze the cognitive and clinical aspects of benign MS (BMS) patients, to understand more about this entity in general, as well as its development in the Brazilian reality.
Methods: We included 60 patients followed up at a tertiary MS service, 30 with EDSS scores below 3.0 and at least 10 years of disease onset. They underwent a cognitive evaluation, and an assessment of mood and fatigue disorders, as well motor disorders.
Results: We found that most BMS patients in the present cohort were female, with low mean EDSS scores (1.9) and good performance on the T25FW and 9HPT motor tests. The prevalence of cognitive deficits was higher in traditional MS than in BMS. The frequency of depression was similar in both groups. Furthermore, the use of more stringent criteria did not show better clinical performance, or better cognitive performance.
Conclusion: The present work corroborates previous epidemiological findings in other countries, as well as in Brazil. In addition, it shows the high prevalence of non-motor symptoms and cognitive impairment both in classical MS patients and in the ones classified as "benign," which suggest the need for a different analysis approach in this patient group. However, the use of more stringent criteria (EDSS < 3.0 and more than 10 years of disease onset), did not show patients with better performance.

DOI: 10.1055/s-0044-1789360

Evaluation of MRI findings associated with worse prognosis in benign multiple sclerosis patients

Josué de Almeida David[1], Thomas Vieira de Paula[1], Alfredo Damasceno[1]
[1]*Universidade Estadual de Campinas, Campinas SP, Brazil.*

Address for correspondence: Josué de Almeida David (email: j219131@dac.unicamp.br).

Abstract
Objective: The present study aims to analyze neuroimaging aspects of benign MS (BMS) and traditional MS patients, to understand more about this entity in general, as well as its development in the Brazilian reality.
Methods: We included 60 patients followed up at a tertiary MS service, 30 with EDSS scores below 3.0 and at least 10

years of disease onset. They underwent a clinical evaluation and analysis of the number of cerebral, infratentorial, and medullary lesions.
Results: We found that patients with worse prognosis presented higher numbers of infratentorial and medullary lesions. We also found that the use of more stringent criteria for BMS definition did not show better neuroimage aspects.
Conclusion: The present work corroborates previous works in literature that shows a worse prognosis on patients with a greater number of infratentorial and medullary lesions.

DOI: 10.1055/s-0044-1789361

Time between the first symptom, diagnosis, and treatment of multiple sclerosis in a Brazilian cohort: the impact of early diagnosis

Juliana Santiago-Amaral[1], Jéssica Resende Vaz de Melo[1], Lucas Alexandre Santos Marzano[1], Rodrigo Kleinpaul[1]
[1]*Instituto de Previdência dos Servidores de Minas Gerais, Belo Horizonte MG, Brazil.*

Address for correspondence: Juliana Santiago-Amaral (email: julimss@gmail.com).

Abstract

The diagnosis of multiple sclerosis (MS) can be challenging, especially in populations in which the disease is rare. Delayed diagnosis and access to disease-modifying drugs (DMDs) can have a negative impact on the course of MS. The main aim of the present study was to estimate the mean time between the first relapse, the diagnosis of MS, and the initiation of treatment in a cohort of Brazilian MS patients, and to estimate the impact of these variables in the morbidity. The present is an observational study based on clinical records of patients followed up in a Neurology Clinic at Hospital Governador Israel Pinheiro (HGIP), in the city of Belo Horizonte, state of Minas Gerais, Brazil. The data of 61 patients were analyzed. Approximately 73,8% (45) of the subjects were women. The mean ages at the onset of the first symptom, the diagnosis and DMT initiation were of 30.93 ($\pm$11.94), 32 (25–43), and 36.17 ($\pm$14.2) years respectively. Approximately 50.82% (31) of the patients had an early diagnosis, within the first year of the disease, in 26.23% (16), the diagnosis was established in 1 to 5 years, and 22.95% (14) had a delay of more than 5 years. Once the diagnosis was established, 50% had access to DMDs within 6 months, and 77,05%, in the first year. Patients with early diagnosis had their first symptom at a younger age, with a median of 27 years compared with 32.5 years among those with late diagnoses ($p = 0.63$). In the follow-up, the median EDSS score was of 2.5 among those with late diagnoses, while among patients with early diagnoses, the median EDSS score was of 1.5 ($p < 0.05$). The diagnosis of MS can be challenging, especially in developing countries, where the suspicion can be lower and there are fewer resources widely available for the investigation. It is important to establish a correct diagnosis in these poorly-studied populations, especially because patients with delayed diagnosis and DMT initiation appear to present more disability.

DOI: 10.1055/s-0044-1789362

Evolution of the EDSS score in patients with progressive multiple sclerosis

Marcelle Prado[1], Maria Fernanda Mendes[1], Camila Figueiredo[1], Amanda Selvatici dos Santos Dias[1], Guilherme Olival[1]
[1]*Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.*

Address for correspondence: Marcelle Prado (email: marcellesanjuan@gmail.com).

Abstract

Background: Progressive multiple sclerosis (PMS) is a type of MS; secondary PMS (SPMS) typically follows a relapsing course before progressing steadily, while primary PMS (PPMS) involves a gradual disability build-up from the start.
Objective: To describe the duration of illness in PMS patients.
Methods: A retrospective observational study involving 33 patients diagnosed with PMS, 10 with PPMS and 23 with SPMS, treated at tertiary hospital in the city of São Paulo, Brazil. The medical records were analyzed between December 2023 and March 2024. The Pearson Chi-squared test was used for the statistical analysis.
Results: Out of the 33 PMS patients evaluated, in the group with EDSS scores $\leq$ 6.5, 85% were women, and, in the group with EDSS scores $>$ 7, the percentage of women reduced to 53.8% ($p = 0.05$). The mean age at the onset of symptoms was of 32.79 years. The time between the onset of symptoms and the diagnosis of the disease was of 5.25 years, both for the PPMS and SPMS patients. The initial EDSS score was of 2.0, and the final, of 6.5, with a difference of 4.5 points approximately 16 years after the disease onset. Furthermore, we observed that 100% of the patients with current EDSS score $\geq$ 7 showed partial regression of the symptoms during outbreaks, while 70% of those with current EDSS score $\leq$ to 6.5 showed incomplete regression.
Conclusion: The evolutionary description of EDSS scores in patients with PMS can help us better understand the history of the disease. A homogeneity in the prevalence of gender was noticed with an increase in the EDSS score, with the onset of symptoms in this population occurring around the age of 32 years.

DOI: 10.1055/s-0044-1789363

Impacts of environmental tobacco smoke on the onset and progression of multiple sclerosis: a systematic review

Marco Antônio Machado Schlindwein[1], Marcelo de Moura Campos[1], Leticia Breis[1], Beatriz Sordi Chara[1], Clara Sasse Scherer[1], Vitória Augusta Piva Caminski[1], Arthur Stedile Ribeiro Pacheco[1], Gabriel Erzinger[1], Ruan Carlos da Silva[1], Mayra Emi Guinoza Inushi[1], Murilo Luis Geremias[1], Andre Matta[2], Marcus Vinicius Magno Gonçalves[3]
[1]*Universidade da Região de Joinville, Joinville SC, Brazil.*
[2]*Sem afiliação.*
[3]*Neurovie, Departamento de Neurologia, Joinville SC, Brazil.*

Address for correspondence: Marcelo de Moura Campos (email: marcelo.campos88@hotmail.com).

Abstract

Background: Multiple sclerosis (MS) is a chronic inflammatory, demyelinating, autoimmune disorder of the central nervous system (CNS) with a prevalence of ~ 140/100 thousand inhabitants in North America and of 108/100 thousand in Europe. The etiology of MS remains unclear, but environmental and lifestyle components, accompanied by genetic susceptibility, have been associated with an increased risk of

developing MS. Tobacco smoking has been consistently reported as an MS environmental risk, increasing the propensity of developing such a disorder. Moreover, smoking is additionally mentioned as a risk factor for a more aggressive disease progression. Unlike cigarette smoking, environmental tobacco smoke (ETS) has not been well described as an environmental risk for the development of MS, nor as a risk factor for disease progression.
Methods: We reviewed the association between ETS and the risk of onset and/or progression of multiple sclerosis through a systematic screening of the PubMed/MEDLINE, Science Direct, LILACS, and SciELO databases in search of articles published between January 1st, 2010, and July 5th, 2021, with the following keywords: *multiple sclerosis and smoking*; *multiple sclerosis and passive smoking*; and *multiple sclerosis and secondhand smoking*.
Results: We included 15 articles in the review, comprising 2 meta-analyses, 2 systematic reviews, and 11 observational studies. The meta-analyses reported an impact of passive smoking on the onset of MS among passive smokers. Both systematic reviews mostly reported associations between smoking and the development of MS. Seven observational studies reported higher odds of MS onset when associated with passive smoking. And four observational studies did not show a relationship between passive smoking and MS development or progression.
Conclusion: Most articles showed a positive association between environmental tobacco smoke exposure and the risk of developing multiple sclerosis. On the other hand, an association between ETS and a higher risk for MS progression could not be established.

DOI: 10.1055/s-0044-1789364

Lost time, lost function? Unraveling the impact of diagnosis delay on disability progression in multiple sclerosis

Maria Fernanda Hamamoto Leati[1], Victor Costa[2], Camila Nepomuceno[1], Nayara Guerreiro[1], Arthur Dias[1], Maria Sheila Rocha[1], Flávio Vieira Marques Filho[1]
[1]*Hospital Santa Marcelina, São Paulo SP, Brazil.*
[2]*Universidade Federal de Juiz de Fora, Hospital Universitário, Juiz de Fora MG, Brazil.*

Address for correspondence: Maria Fernanda Hamamoto Leati (email: mfleati@gmail.com).

Abstract
Background: Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system (CNS) with inflammatory and neurodegenerative components, and it is the most common nontraumatic disabling neurologic condition in young adults. The prevalence of MS has increased in recent decades, with greater life expectancy and functionality being attributed to a better understanding of the disease and its early diagnosis.
Objective: To correlate the delay in diagnosis and the onset of the first symptom with the Expanded Disability Status Scale (EDSS).
Methods: An observational study was performed, with 199 patients analyzed through chart reviews from the Demyelinating Outpatient Clinic from July to December 2023. Using data from the table, two groups were separated: time from the first symptom to diagnosis and time from the first symptom to the start of follow-up. In this sense, a comparison was made with the EDSS score and the number of years that patients took to start follow-up or receive the diagnosis. After tabulation, inferential and exploratory data analyses were performed. All analyses were performed using the IBM SPSS Statistics for Windows software, version 20.0. Statistical significance was established at $p < 0.05$.
Results: Using the Spearman rank correlation coefficient, we found that the group of time from the first symptom to diagnosis presented a coefficient of $+0.277$ ($p < 0.05$), while the group of time from the first symptom to the start of follow-up presented a coefficient of $+0.337$ ($p < 0.05$).
Conclusion: Although the correlation is intuitive, the data analyzed in the present study evidenced a weak relationship between these variables, and this result might be attributed to two important limitations of the study: the intervals were counted in years, not in months, and the EDSS was applied by different examiners using different methodologies. Therefore, it is necessary to broaden the scope of the present study, aiming for better correction of variables and potential biases.

DOI: 10.1055/s-0044-1789365

Migraine in multiple sclerosis patients

Murilo Pinoti[1], Letícia Cavaglieri[1], Clayton Zoccoli[1], Olivia Pires[2], Isabella Avolio[1], Mateus Boaventura de Oliveira[2,3]
[1]*Centro Universitário São Camilo, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br).

Abstract
Background: Multiple sclerosis (MS) is a chronic demyelinating, autoimmune disease with a significant impact on patients' functionality. Apart from the accumulation of demyelinating lesions, MS is also associated with several comorbidities, among which migraine, the focus of the present study, deserves attention due to its high prevalence and impact on quality of life.
Objective: To determine the prevalence of migraine in persons with MS (PwMS) and its associations with variables of interest among patients with and without migraine.
Methods: The present cross-sectional study included PwMS prospectively evaluated in clinical routine for the presence of comorbidities, including migraine. After identifying migraine diagnosis, we made statistical associations with demographic variables, the Expanded Disability Status Scale (EDSS), the SymptoMScreen, and the impact in daily routine through the Multiple Sclerosis Impact Scale (MSIS-29) and the Fatigue Severity Scale (FSS).
Results: A total of 204 PwMS were included (78.4% of female subjects, with a mean age of 38.8 ± 10.7 years, and a median EDSS score of 2.0). The prevalence of migraine was of 27.9% ($n = 57$). By comparing PwMS with and without migraine, we identified: age – 38.8 versus 38.8 years ($p = 0.273$); female patients – 91.2% versus 73.5% ($p = 0.006$); median EDSS score – 2.0 versus 2.0 ($p = 0.966$); median SymptoMScreen score – 16 versus 12 ($p = 0.503$); median Hospital Anxiety and Depression Scale (HADS) score – 8 versus 7 ($p = 0.351$) and 7 versus 5 ($p = 0.587$) respectively; median FSS score – 47 versus 40 ($p = 0.543$); and median MSIS-29 score – 67 versus 65 ($p = 0.897$) respectively.
Conclusion: Overall, the clinical features of patients with and without migraine did not vary significantly in the present study. Higher sample sizes, longitudinal designs, and more detailed variables (such as the moment of headache onset, need for medical leave, prophylaxis or intravenous analgesia, and migraine frequency and intensity) could yield different findings.

DOI: 10.1055/s-0044-1789366

Delayed diagnosis in multiple sclerosis: Unraveling risk factors in a Brazilian setting

Letícia Cavaglieri[1], Murilo Freire Pinoti Bernardo[1], Olivia Pires[2], Clayton Zoccoli[1], Isabella Avolio[2], Mateus Boaventura de Oliveira[2,3]

[1]Centro Universitário São Camilo, São Paulo SP, Brazil.
[2]Hospital São Camilo, São Paulo SP, Brazil.
[3]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br).

Abstract

Background: Several multiple sclerosis (MS) diagnostic criteria have been updated over the last decades, aiming to improve accuracy and early diagnosis. However, other factors may continue to contribute to a delayed diagnosis, potentially resulting in a faster progression rate of the disease.
Objective: To expand the perspective on factors contributing to delayed diagnosis despite the evolution of diagnostic criteria.
Methods: A multicenter cross-sectional study was conducted. Multivariable logistic regression examined whether age, sex, race, level of schooling, functional system affected, health insurance availability at disease onset, and autoimmune familial history were associated with delayed diagnosis. The time gap between disease onset and the official diagnosis was considered delayed when surpassing 12 months.
Results: We included 208 patients (78.4% of female subjects; mean age at diagnosis of 32.1 years; mean disease duration of 9.1 years; and median EDSS score of 2.0). Older age was significantly associated with delayed diagnosis ($p = 0.008$). Women had early diagnosis in 60.1% of the cases, contrasting with 40% among men, but with no statistical significance in the adjusted analysis. Access to private insurance significantly reduced the likelihood of delay by 75%. Patients with an autoimmune family history were diagnosed early in 68.3% of the cases, compared with 49.2% of those without such history ($p = 0.013$). Sensory symptoms were significantly associated with early diagnosis ($p = 0.027$). The independent factors for delayed diagnosis after multivariable logistic regression were: older age, no access to private healthcare at the onset of the first symptom, absence of family history, and first symptom not involving the sensory functional system. Lower level of schooling and race (non-white) only showed a trend towards an association with delayed diagnosis.
Conclusion: The factors associated with delayed diagnosis include age, type of healthcare access, autoimmune family history, and functional system affected. Our findings reinforce the importance of carrying out a correct diagnostic workup in addition to expanding and improving public health care.

DOI: 10.1055/s-0044-1789367

Family history of multiple sclerosis and other autoimmune diseases in multiple sclerosis

Lucas Silva[1], Murilo Freire Pinoti Bernardo[2], Mateus Boaventura de Oliveira[1,3]

[1]Hospital São Camilo, São Paulo SP, Brazil.
[2]Centro Universitário São Camilo, São Paulo SP, Brazil.
[3]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br).

Abstract

Background: Multiple sclerosis (MS) is a multifactorial and disabling autoimmune disease. The association between MS and genetic risk factors has been widely studied, through population-based studies, studies of family clusters, specific genetic works, and associations with other autoimmune diseases (ADs).
Objective: To evaluate the prevalence of MS and other ADs in relatives of MS patients, and to determine whether the family history (FH) is associated with a different clinical course of disease.
Methods: The present is an observational, cross-sectional, multicenter study, in which FH of MS and other ADs was analyzed in MS patients. Associations of positive FH of ADs/MS with the score on the Expanded Disability Status Scale (EDSS), previous disease activity (number of previous relapses), and the score on the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) scale were investigated.
Results: A total of 198 patients were evaluated (mean age: 38.9±10.8 years; 78.8% of female subjects; mean disease duration: 8.8±7.2 years). Positive FH for any AD (including MS) was identified in 67 (33.8%) subjects. We identified 23 (11.6%) MS patients who had relatives with MS. After MS, the three other main familial ADs observed were: Hashimoto thyroiditis, systemic lupus erythematosus and vitiligo. There were no statistically significant associations involving positive FH of MS or ADs with the EDSS score, disease activity, and the BICAMS tests.
Conclusion: Multiple sclerosis, Hashimoto thyroiditis, systemic lupus erythematosus, and vitiligo were the autoimmune diseases most often identified in relatives of MS patients. The presence of FH was not associated with worse physical and cognitive outcomes.

DOI: 10.1055/s-0044-1789368

Tissue integrity outside of lesions in NMOSD: new evidence with multiparametric brain MRI

Mateus Boaventura de Oliveira[1,2], Diego Cardoso Fragoso[3], Isabella Avolio[4], Samira Luisa Apóstolos-Pereira[4], Dagoberto Callegaro[4], Claudia da Costa Leite[3], Alex Rovira[5], Jaume Sastre-Garriga[6], Deborah Pareto[5], Carolina Rimkus[3]

[1]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.
[2]Hospital São Camilo, São Paulo SP, Brazil.
[3]Instituto de Radiologia, São Paulo SP, Brazil.
[4]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.
[5]Hospital Universitari Vall d'Hebron, Unitat de Radiologia, Secció de Neurorradiologia, Barcelona Spain.
[6]Centre d'Esclerosi Múltiple de Catalunya (Cemcat), Servei de Neurologia-Neuroimmunologia, Barcelona, Spain.

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br).

Abstract

Background: Neuromyelitis optica spectrum disorder (NMOSD) is characterized by acute destructive lesions in the spinal cord, optic nerve, and periependymal brain regions. Besides the macroscopic visible lesions, it is still a matter of debate whether there is diffuse damage in normal-appearing white matter (NAWM) and gray matter (NAGM).
Objective: To investigate the presence of diffuse brain parenchymal damage in NMOSD patients by using a

multiparametric MRI approach: T1-weighted/T2-weighted ratio (T1-w/T2-w), magnetization-transfer ratio (MTR) and diffusion-tensor imaging (DTI). Also, to explore whether there is an association between MRI metrics and clinical variables.
Methods: In the present cross-sectional study, we prospectively evaluated anti-aquaporin-4-positive NMOSD patients and healthy controls (HCs) matched for age and sex. The mean values of T1-w/T2-w, MTR, fractional anisotropy (FA), axial diffusivity (AD), mean diffusivity (MD), and radial diffusivity (RD) were obtained in NAWM, NAGM, and lesion masks.
Results: A total of 105 participants (59 NMOSD patients and 46 HCs) were included in the study. The T1-w/T2-w was lower in the NAWM of NMOSD patients versus HCs ($p = 0.029$), while no significant differences were found in the NAWM or NAGM across the following metrics: MTR, FA, AD, MD, and RD. In addition, the T1-w/T2-w in the NAWM was inversely correlated with time to start immunosuppressive therapy ($r = -0.278$; $p = 0.036$) and with MD ($r = -0.325$; $p = 0.014$). Cavitated lesions showed lower mean values of T1-w/T2-w, MTR, and FA, and higher diffusivity metrics as compared with non-cavitated lesions ($p < 0.001$).
Conclusion: Diffuse brain damage seems unlikely in NMOSD, according to MTR or DTI metrics, with loss of microstructural integrity restricted to lesional tissue. In this setting, decreased T1-w/T2-w ratio in the NAWM may reflect blood-brain barrier dysfunction (subclinical water accumulation) possibly linked to astrocyte pathology. The NMOSD cavitated lesions have shown a severe degree of microstructural damage.

DOI: 10.1055/s-0044-1789369

Exploring very late-onset NMOSD: frequency and clinical features in Latin America

Marco A. Lana-Peixoto[1], Natália Cirino Talim[1], Paulo Pereira Christo[1], Thiago Gonçalves Fukuda[2], José Artur Costa D'Almeida[3], Milena Sales Pitombeira[3], Sheila Castro-Suarez[4], Claudia Pestchanker[5], Juan Rojas[6], Verónica Tkachuk[7], Pablo Lopez[8], Edgar Carnero Contentti[8], Maria Lucia Brito Ferreira[9], Vanessa Daccach[10], Maria Fernanda Mendes[11], Alfredo Damasceno[12], Edgar Patricio Correa-Diaz[13], Irene Treviño-Frenk[14], Carlos Navas[15], Jefferson Becker[16], Lorna Galleguillos[17], Carlos Oehninger[18], Paulo Diniz da Gama[19], Ethel Ciampi[20], Sidney Gomes[21], Marcus Vinicius Magno Gonçalves[22], Adriana Carra[23], Ibis Soto DeCastillo[24], Henry Koiti Sato[25], Gustavo Figueira[26], Carlos Bernardo Tauil[27], Samira Luisa Apóstolos-Pereira[28], Vinicius Andreoli Schoeps[28], Bruno Pedreira[2], Lara de Menezes Andrade[9], Katharina Messias[10], Rafael Paternò Castello Dias Carneiro[29], Dagoberto Callegaro[28]
[1]Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla (CIEM), Belo Horizonte MG, Brazil.
[2]Universidade Federal da Bahia (UFBA), Faculdade de Medicina da Bahia, Complexo Hospitalar Universitário Professor Edgard Santos, Salvador BA, Brazil.
[3]Hospital Geral de Fortaleza, Neuroimunologia, Fortaleza CE, Brazil.
[4]Centro Básico de Investigación en Demencia y Enfermedades Desmielinizantes del Sistema Nervioso, Lima, Peru.
[5]Hospital Central "Dr. Ramón Carrillo", Departamento de Neurología, San Luis, Argentina.
[6]Centro de Esclerosis Múltiple de Buenos Aires (CEMBA), Buenos Aires, Argentina.
[7]Universidad de Buenos Aires, Hospital de Clínicas "José de San Martín", Servicio de Neurología, Sección de Neuroinmunología y Enfermedades Desmielinizantes, Buenos Aires, Argentina.
[8]Hospital Alemán, Departamento de Neurociencias, Unidad de Neuroinmunología, Buenos Aires, Argentina.
[9]Hospital da Restauração, Recife PE, Brazil.
[10]Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Hospital das Clínicas, Ribeirão Preto SP, Brazil.
[11]Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.
[12]Universidade Estadual de Campinas (Unicamp), Campinas SP, Brazil.
[13]Pontificia Universidad Católica del Ecuador (PUCE), Hospital Carlos Andrade Marín, Quito, Ecuador.
[14]Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán," Ciudad de México, Mexico.
[15]Clínica Universitaria Colombia, Bogotá, Colombia.
[16]Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre RS, Brazil.
[17]Clínica Alemana y Universidad del Desarrollo, Santiago, Chile.
[18]Universidad de la República Uruguay (UDELAR), Facultad de Medicina, Montevideo, Uruguay.
[19]Pontifícia Universidade Católica de São Paulo, Sorocaba SP, Brazil.
[20]Pontificia Universidad Católica de Chile, Facultad de Medicina, Complejo Asistencial Dr. Sótero del Río, Santiago, Chile.
[21]BP – A Beneficência Portuguesa de São Paulo, São Paulo SP, Brazil.
[22]Neurovie, Departamento de Neurologia - Joinville SC, Brazil.
[23]Hospital Británico de Buenos Aires, Buenos Aires, Argentina.
[24]Hospital Clínico, Maracaibo, Venezuela.
[25]Instituto de Neurologia de Curitiba, Curitiba PR, Brazil.
[26]Hospital São Francisco na Providência de Deus, Rio de Janeiro RJ, Brazil.
[27]Universidade de Brasília, Brasília DF, Brazil.
[28]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.
[29]Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract
Background: Age-related changes in the immune system can affect the occurrence and clinical expression of autoimmune disorders. While some studies have explored neuromyelitis optica spectrum disorder (NMOSD) in older adults, analysis of very late-onset NMOSD (VLO-NMOSD), with onset at 70 years or older, remains limited to individual cases.
Objective: To assess the frequency, clinical characteristics, and outcomes of VLO-NMOSD patients in a large Latin American (LATAM) NMOSD cohort.
Methods: The study included NMOSD patients from 9 LATAM countries who met the 2015 IPND criteria. The patients were categorized into the VLO-NMOSD (≥ 70 years) and non-VLO-NMOSD (onset at < 70 years) groups, and we assessed their demographic and clinical features.
Results: Out of 1,185 NMOSD patients, data on age at onset were available for 1,179, with 14 (1.2%) in the VLO-NMOSD group. Among these 14 patients, the median age was of 73 (71–83) years, 12 (85.7%) were female subjects, the most common presenting symptoms were myelitis and optic neuritis (10 and 7 cases respectively), and the median disease duration was of 40.9 (9.0–149.0). The median ARR was of 0.37, and the median EDSS score was of 6.0 (5.0–7.5). Compared with the non-VLO-NMOSD group, the VLO-NMOSD group contained a higher proportion of females and patients of mixed race/ethnicity, fewer Caucasians, and more cases of myelitis and optic neuritis (71.4% versus 48.1% and 50% versus 48.1% respectively). None of the cases of VLO-NMOSD presented with area postrema, cerebral, or diencephalic syndromes. The VLO-NMOSD group presented lower ARR (0.37) and higher EDSS scores ($p = 0.004$). Differences in other characteristics between the groups did not reach statistical significance.

Conclusion: Very late-onset NMOSD is rare and demonstrates unique clinical characteristics, with more severe outcomes. Notably, VLO-NMOSD in LATAM presents with optic neuritis more frequently at onset compared with other population series.

DOI: 10.1055/s-0044-1789370

Synthetic MRI in progressive MS: associations with disability

Nathane Braga[1], Xavier Aymerich[2], Julio Alonso[2], Neus Mongay-Ochoa[2], Deborah Pareto[2], Xavier Montalban[2], Angela Vidal-Jordana[2], Jaume Sastre-Garriga[2], Alex Rovira[2]
[1]*Universidade Federal Fluminense, Niterói RJ, Brazil.*
[2]*Hospital Universitari Vall D'Hebron, Barcelona, Spain.*

Address for correspondence: Nathane Braga (email: nathanebsr@gmail.com).

Abstract
Background: Synthetic MRI (SyMRI) is a short-time acquisition sequence that generates different contrast-weighted images based on the measurement of tissue properties, and it provides quantitative volumetric, relaxation, and myelin maps. It has been used as an alternative to conventional MRI sequences in relapsing-remitting MS for the detection of focal lesions and volumetric analysis.
Objective: To find a SyMRI variable that would predict EDSS scores ≥ 6 in progressive patients.
Methods: A total of 24 patients with progressive MS underwent SyMRI using a 2D axial QRAPMASTER pulse sequence. We analyzed the segmentation map for volumetric parameters, global myelin fraction (MyCF), and quantitative values derived from maps of PD, R1, R2, and myelin for the following masks: normal-appearing white and gray matters, lesion, and corpus callosum. A *t*-test compared SyMRI variables between the groups, followed by univariate binary logistic regression for significant ($p < 0.05$) or trending results ($p < 0.09$).
Results: The patients were categorized into two groups (EDSS < 6 and EDSS ≥ 6). The variables with significant differences between the groups were: BPF ($p = 0.05$), WMF ($p = 0.05$), MyCF ($p = 0.04$), and corpus callosum volume ($p = 0.04$). In the binary logistic regression analysis, the best predictor was MyCF, the *p*-value of 0.08, and an odds ratio of 0.59.
Conclusion: Our results corroborate the differences in volumetric parameters according to the EDSS using a single MRI acquisition. Besides, our findings suggest that higher MyCF values were associated with lower odds of having an EDSS score ≥ 6.

DOI: 10.1055/s-0044-1789371

Association between myelin content variation and clinico-radiological activity in multiple sclerosis

Pedro Rodrigues Neves[1], Daissy Liliana Mora Cuervo[1], Rafael Canani Sommer[1], Alessandra Jahn Gallo[1], Ana Djulia Tesche[1], Douglas Kazutoshi Sato[1], Vitoria Pimentel[1]
[1]*Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil.*

Address for correspondence: Pedro Rodrigues Neves (email: pedro.neves@edu.pucrs.br).

Abstract
Background: Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system, characterized by focal demyelinating lesions and neurodegeneration, resulting in a variety of neurological impairments, which leads remyelination to play a key role in patient recovery and in the prevention of disease progression.
Objective: The REMIT-MS is an ongoing observational study that aims to evaluate the relationship between clinical factors and remyelination activity in MS patients treated with disease-modifying drugs (DMDs), including natalizumab (NTZ).
Methods: The present study included 27 patients (18 in the NTZ group) who underwent 2 evaluations over 6 months, during which clinical and magnetic resonance imaging assessments were performed using advanced sequences, including myelin evaluation through the q-space myelin map sequence, using the calculation of normalized leptokurtic diffusion (NLD). Treatment group, clinical changes, conventional neuroimaging radiological activity, and NLD variation in lesions and in normal appearing white matter (NAWM) over 6 months were tested for correlations.
Results: Regarding treatment, there was a trend in the NTZ group towards a lower risk of developing new T2 lesions (OR: 0.11; $p = 0.07$) and negative association between new T2 or enhancing lesions and the Timed 25-foot Walk Test ($p < 0.01$ and $p = 0.01$ respectively). Variation in NLD lesions was negatively associated with the occurrence of new T2 lesions ($p < 0.01$) and new Gd+ enhancing lesions ($p = 0.05$). Moreover, patients with an average NLD variation < 5 a.u. over 6 months (lower quartile of the sample) had a significantly increased risk for occurrence of new T2 lesions (OR: 25.7 [2.2–698.5]; $p < 0.01$).
Conclusion: The present was the first study to evaluate the association of NLD lesion variation with conventional metrics used in the radiological monitoring OF MS activity. We conclude that patients with increased NLD, thus higher remyelinating activity, presented a lower incidence of new T2 and Gd+ lesions.

DOI: 10.1055/s-0044-1789372

Do demographic and clinical outcomes differ between antidepressant users and non-users in MS?

Renata Lameira Oliveira[1], Carlos Bernardo Tauil[2], Cintia Ramari[3], Paulo Matheus Casal de Souza[1]
[1]*Escola Superior de Ciências da Saúde, Brasília DF, Brazil.*
[2]*Universidade de Brasília, Brasília DF, Brazil.*
[3]*University of Hasselt, Brazilian Committee for Treatment and Research in Multiple Sclerosis, Hasselt, Belgium.*

Address for correspondence: Renata Lameira Oliveira (email: renata.lameira@escs.edu.br).

Abstract
Background: Multiple sclerosis (MS) is a chronic neurodegenerative condition prevalent in young adults. Depression, a frequent comorbidity in MS, poses a 50% development risk. Antidepressants are pivotal in managing depressive symptoms in MS patients, enhancing mood, improving social interactions, and increasing the management of physical health challenges. However, it is crucial to note that, while benefits prevail, certain antidepressants might exacerbate MS symptoms, such as fatigue, a prevalent issue in MS.
Objective: To investigate the demographic and clinical differences between MS patients who use antidepressants and those who do not.
Methods: We analyzed data from 241 individuals diagnosed with MS, collected in the Sinapse Clinic and inserted into the BRANDO database. The outcomes included marital and employment status, sleep disturbances, sphincter control, sexual dysfunction, score on the Expanded Disability Status Scale (EDSS), Nine Hole Peg Test – NHPT, walking capacity (Timed 25-Foot Walk Test – T25FWT), cognitive processing speed

(Symbol Digit Modality Test – SDMT), and fatigue (Modified Fatigue Impact Scale – MFIS). Depression and anxiety were assessed by the Beck Depression and Anxiety Inventory (BDI and BAI) and Hospital Anxiety and Depression Scale (HADS-A and HADS-D). The Chi-Squared and independent *t*-tests compared users and non-users of antidepressants.
Results: The differences between the groups revealed that antidepressant users presented significantly higher EDSS scores ($p = 0.03$), more prevalent sleep disturbances ($p = 0.013$), and higher fatigue levels (MFIS) ($p < 0.001$) compared with non-users. No significant differences were found in demographic outcomes or motor and cognitive functions. Depressive symptoms were significantly higher in the antidepressant user group.
Conclusion: The higher depressive symptoms in the group of antidepressant users suggest the correct screening for medication use. Given that sleep changes and fatigue are associated with depressive symptoms, it is challenging to determine whether these are adverse effects of antidepressants or if they are characteristic of the population using them. Future studies should longitudinally assess the effects of antidepressant treatment in MS-related symptoms.

DOI: 10.1055/s-0044-1789373

Antibody awareness and diagnosis recognition in neuromyelitis optica spectrum disorder and MOG-associated disease: a cross-sectional study

Samira Luisa Apóstolos-Pereira[1], Sara Terrim[1], Roger Araujo[1], Eduardo Tieppo[1], Graziella Faria[1], Paula Baleeiro Rodrigues Silva[1], Flávio Vieira Marques Filho[1], Mateus Boaventura de Oliveira[1,2], Guilherme Diogo Silva[1], Tarso Adoni[1], Dagoberto Callegaro[3]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Sara Terrim (email: sterrim.sara@gmail.com).

Abstract
Background: Neuromyelitis optica spectrum disorder (NMOSD) and MOG-associated disease (MOGAD) present a high risk of disability. Testing for anti-aquaporin-4 (anti-AQP4) antibodies and anti-myelin oligodendrocyte (anti-MOG) antibodies is essential for early diagnosis, which is associated with a better prognosis. However, awareness regarding these antibodies remains limited, and there is inadequate information about the understanding of the condition on the part of the patients.
Objective: To report the frequency of antibody serostatus and diagnosis awareness among patients with NMOSD/MOGAD in an outpatient tertiary clinic.
Methods: The present cross-sectional study was conducted between March and July 2023. We administered questionnaires to patients diagnosed with anti-AQP4-positive NMOSD, MOGAD, and those with seronegative optic neuritis or longitudinally-extensive transverse myelitis to assess their comprehension of their condition. Data were recorded by clinical chart. Descriptive analyses were performed.
Results: We interviewed 69 patients; 54 (78%) were female, and the median age was of 44 (IQR: 37–54) years. Self-reported racial backgrounds were: black or brown in 45 patients (65%), white in 22 (32%), and yellow in 2 (3%). The median years of schooling was of 12 (IQR: 8–14) years. In total, 31/35 patients with AQP4-positive NMOSD (88%) recognized their diagnosis, but only 19 (54%) were aware of their AQP4-antibody positivity, 4 (11%) were unaware of their antibody result, while 12 (34%) were unaware of the antibody. A total of 11/14 patients with MOGAD (78%) correctly reported their diagnosis, and 9 (64%) were aware of antibody positivity. Among 20 seronegative patients, only 6 (30%) were aware of being negative for both antibodies.
Conclusion: The knowledge about antibody serostatus was missing in almost half of the patients. Also, awareness about NMOSD and MOGAD diagnoses is insufficient among patients with these conditions, even in a tertiary center care. Questions about how determinants social of health may impact on the aptitude to seek proper and early diagnosis and treatment need to be better evaluated in the NMOSD/MOGAD scenario.

DOI: 10.1055/s-0044-1789374

From water pores to aquaporins: a history of human discoveries... and controversies

Fernando Faria Andrade Figueira[1], Gustavo Figueira[2], Raquel Silveira[1], Viviane Carvalho[1], Alexandra Seide Cardoso Vidal[1], Matheus Castro[1], Paula Soares[1]
[1]*Hospital São Francisco na Providência de Deus, Rio de Janeiro RJ, Brazil.*
[2]*Hospital São Francisco de Assis, Rio de Janeiro RJ, Brazil.*

Address for correspondence: Fernando Faria Andrade Figueira (email: fernando@ffigueira.net).

Abstract
Water movement across cell membranes has been the object of research since the 1950s. The initial steps involved indirect biophysical models of erythrocytes in saline solutions, and, despite their simplicity, these studies enabled the development of models and concepts closely aligned with our present knowledge. Modern physiology has been able to clarify both the structure and functioning of water channels, as well as the pathophysiological correlates for a group of disorders known as *water channelopathies*. We describe the evolution of knowledge and controversies regarding water channels, since their discovery, first descriptions, and their pathological correlates. We herein provide a retrospective and critical view on published data regarding the history of water channels. Pioneer studies come from Sidel in 1950s, using a model of saline solution bath described as *the pore-radius concept*. In the late 1970s Parisi took this concept to a new level, showing that water moves in membrane pores in a single file of nine molecules. Peter Agre (1993) described the archetypal molecular water channel, aquaporin CHIP, stated possible therapeutic benefits on modulation of these structures on treatment of some human diseases, and also provided a better insight into biological phenomenon of osmotic water movement. Despite the controversies regarding its originality, Agre was laureated with the Nobel in 2003. In 2001, Vanda Lennon described the presence of aquaporin 4 antibodies in patients with neuromyelitis optica, providing a biological marker of this autoimmune disease. Water channel disorders are a developing field of research encompassing autoimmune, toxic and vascular etiopathogenesis. A rational approach to these diseases, including their diagnostic criteria and modern treatment strategies, requires expertise. It must be based on the proper understanding of their pathophysiology, and studying the history of their discovery and evolution can be a valuable way to enhance our familiarity with this fascinating and dramatic group of diseases.

DOI: 10.1055/s-0044-1789375

FCGR2A rs1801274 polymorphism is associated with response to natalizumab in multiple sclerosis patients

Matheus D. de Matos[1], Rafaella C. Cardoso[2], Larissa A. Duarte[3], Barbara D. Guimenez[1], Giovanni K. Pavani[1], Kamilla A. Fernandez[4], João Gabriel Dib Farinhas[5], Felipe da R. Schmidt[4], Guillherme C. Montes[1], Soniza V. Alves-Leon[3], Fabricia L. Fontes-Dantas[1]

[1]*Universidade do Estado do Rio de Janeiro, Departamento de Farmacologia e Psicobiologia, Laboratório de Neurobiologia do Desenvolvimento, Rio de Janeiro RJ, Brazil.*
[2]*Universidade do Estado do Rio de Janeiro, Rio de Janeiro RJ, Brazil.*
[3]*Universidade Federal do Estado do Rio de Janeiro, Laboratório de Neurociência Translacional, Rio de Janeiro RJ, Brazil.*
[4]*Universidade do Estado do Rio de Janeiro, Hospital Universitário Pedro Ernesto, Serviço de Neurologia, Rio de Janeiro RJ, Brazil.*
[5]*Instituto de Ensino e Pesquisa Americas, Rio de Janeiro RJ, Brazil.*

Address for correspondence: João Gabriel Dib Farinhas (email: jgabrieldib@gmail.com).

Abstract

Multiple sclerosis (MS) is recognized as the most prevalent autoimmune disorder affecting the central nervous system (CNS). Natalizumab (NTZ) is among the commonly-used high-efficacy treatments, showing efficacy in reducing MS activity and progression in most patients. It acts by targeting α-4 integrin subunits on lymphocytes, which is crucial to facilitate leukocyte trafficking to sites of inflammation. Several environmental or genetic factors can influence MS treatment success. Currently, there are few established pharmacogenetic predictors of response to treatment in MS patients. One genetic variant associated with therapeutic response to the monoclonal antibodies used in the treatment is the single nucleotide polymorphism (SNP) rs1801274 in the *FCGR2A* gene. Therefore, the objective of the present study is to assess whether this genetic variant can serve as a potential predictor of therapeutic failure in NTZ treatment for MS. A total of 104 blood samples were collected from patients admitted to 2 university hospitals in Rio de Janeiro, with approval from the Ethics Committee (CAAE:5,782,087). Genomic DNA was extracted from leukocytes for subsequent use in real-time PCR genotyping. Among the patients, nine exhibited confirmed therapeutic failure to NTZ treatment. Following statistical analysis, a significant association was identified between the GG genotype of *FCGR2A* ($p = 0.0004$; OR = 0.3530) and therapeutic failure. Additionally, a higher frequency of the AG genotype was observed in patients who did not experience therapeutic failure ($p = 0.0002$; OR = 3.144). Previous research has posited that FCgRs may also impact the efficacy and tolerability of human monoclonal antibody strategies targeting anti-α-4 integrin. Given the genetic diversity of the Brazilian population due to miscegenation, our preliminary findings suggest the necessity to investigate the role of *FCGR2A* rs1801274 as a potential pharmacogenetic predictor for MS patients' response to NTZ.

DOI: 10.1055/s-0044-1789376

Strongyloidiasis prophylaxis: ivermectin in neurological patients undergoing immunosuppressive treatment

Marcelo de Moura Campos[1], Ariel José Gomes Marques Neto[1], Murilo Luis Geremias[1], Mayra Emi Guinoza Inushi[1], Carolina Helena Haveroth[1], Gabriel Erzinger[1], Rodrigo Kleinpaul[2], Marcus Vinicius Magno Gonçalves[3]

[1]*Universidade da Região de Joinville, Joinville SC, Brazil.*
[2]*Instituto de Previdência dos Servidores de Minas Gerais, Belo Horizonte MG, Brazil.*
[3]*Neurovie, Departamento de Neurologia, Joinville SC, Brazil.*

Address for correspondence: Marcelo de Moura Campos (email: marcelo.campos88@hotmail.com).

Abstract

Background: Strogyloides stercolaris is a nematode that, after infection, can remain in asymptomatic form for decades. Autoimmune neurological disorders with impairment of Th2 cell-mediated immunity or involving the use of immunosuppressive and immunomodulatory drugs might predispose patients to the hyperinfection syndrome and disseminated disease called *strongyloidiasis*, which is associated with a high mortality rate. Therefore, a prophylactic treatment with ivermectin has been suggested for patients from endemic regions undergoing immunosuppressive treatment.
Objective: To analyze if ivermectin should be recommended in patients with autoimmune neurological disorders undergoing immunosuppressive treatment.
Methods: The present is a non-systematic review. All articles used were searched in PubMed and Google Scholar. We selected the most relevant articles available in English or Portuguese. The terms used in the search were related to neuroimmunological patients, strongyloidiasis, immunosuppressive drugs, and ivermectin.
Results: Ivermectin as a prophylactic treatment did not demonstrate evidence of efficacy in neurological patients with deficient cellular immunity or under an immunosuppressive therapeutic regimen. A study exposes the hypothesis that anti-parasitic medication might cause depletion of intestinal microbes that contribute to immune tolerance, which could result in a greater predisposition to neurological inflammatory disorders, such as multiple sclerosis. Current evidence indicates that ivermectin's effectiveness is mainly limited to confirmed cases of strongyloidiasis or suspected infections, rather than as a prophylactic measure.
Conclusion: Currently, there are neither studies nor evidence to assess the effectiveness and side effects of the use of ivermectin as a prophylactic treatment for strongyloidiasis in immunosuppressed neurological patients. More studies, such as clinical trials, are necessary to estimate its real effectiveness and the possible associated unwanted effects.

DOI: 10.1055/s-0044-1789377

Mast cells: a key component in the pathogenesis of neuromyelitis optica spectrum disorder?

Washigton Luiz Gomes de Medeiros Junior[1], Isabelle Pastor Bandeira[1], André Eduardo de Almeida Franzoi[1], Mário Natalício de Gasperi[1], Radassa Vieira[1], Carolina Helena Haveroth[1], Thomas Cubas Baggio[1], Marcelo de Moura Campos[1], Wesley Nogueira Brandão[1], Ana Carolina Cardoso dos Santos Durão[2], Marcus Vinicius Magno Gonçalves[3]

[1]*Universidade da Região de Joinville, Joinville SC, Brazil.*
[2]*Universidade de São Paulo, São Paulo SP, Brazil.*
[3]*Neurovie, Departamento de Neurologia, Joinville SC, Brazil.*

Address for correspondence: Marcelo de Moura Campos (email: marcelo.campos88@hotmail.com).

Abstract

Background: The involvement of mast cells (MCs) in the pathogenesis of neuromyelitis optica spectrum disorders (NMOSD) is diverse and significant. Mast cells are sentinel cells that recognize different antigens and signal cytokines and mediators that induce inflammation.

Objective: To highlight the role of MCs in the pathogenesis of neuromyelitis optica (NMO), pointing out their interactions with various cells of the immune system and the respective damage to the central nervous system (CNS), as well as to emphasize their influence on determining pathological variations within NMOSD.
Methods: The present is a literature review study based on studies published from 1999 to 2019 that address diagnostic, pathophysiological and immunological criteria for unilateral and bilateral NMO, acute myelitis, and CNS symptoms.
Results: Mast cells are granular cells residing mainly in the abluminal region of blood vessels that can cross the blood-brain barrier and communicate with neurons, glial cells, endothelial cells, and the extracellular matrix. Activated MCs can present the antigens aquaporin 4 (AQP4) and myelin oligodendrocyte glycoprotein (MOG) to T lymphocytes, promoting the emergence of autoreactive clones in the periphery or reactivating them within the CNS. Mast cells can activate B lymphocytes, inducing blast proliferation and increased release of AQP4 and MOG antibodies. Consequently, the death of astrocytes and oligodendrocytes increases. Moreover, MCs increase cell recruitment, adhesion, and permeability, and they can direct neutrophils to the cornea to assist in the inflammatory process after local injury. The increased expression of cytokines in microglial cells reflects the increase in the neuroinflammatory response and cellular damage.
Conclusion: Mast cells represent a regulator of innate and adaptive immune responses. These are cells that can present antigens that activate T lymphocytes, as well as release cytokines that activate B lymphocytes, astrocytes and microglia, contributing to the different pathways of the neuroinflammation cascade present in NMOSD.

DOI: 10.1055/s-0044-1789378

COVID-19 vaccine in multiple sclerosis patients treated with disease-modifying therapies: a systematic review

Vitória Alagia Ripari[1], Maria Constancio Miranda[1], Aline Cristina da Silva Duarte[1], Déborah Schulthais Ramos[2]
[1]*Pontifícia Universidade Católica de Minas Gerais, Belo Horizonte MG, Brazil.*
[2]*Hospital Madre Teresa, Belo Horizonte MG, Brazil.*

Address for correspondence: Vitória Alagia Ripari (email: vitoriaalagia@gmail.com).

Abstract
Background: Multiple sclerosis is a neurological disease defined by the accumulation of immune-mediated damage in the central nervous system, and most of the patients are immunocompromised. After the COVID-19 pandemic outburst in 2020, it became extremely important to understand the effects of disease-modifying therapies on the immunological responses to the COVID-19 vaccination.
Objective: To analyze studies on the impact of disease-modifying drugs on the immunological responses to COVID-19 vaccines in multiple sclerosis patients.
Methods: The present systematic review was conducted through searches on the PubMed and Virtual Health Library databases, using the following subject headings: *multiple sclerosis*, *drug therapy*, *COVID-19*, and *vaccine*. Studies were retrieved following the PRISMA methodology, and results are as follows: 390 articles were found, 208 of which were excluded after applying the filters (publication year – articles published in the past 5 years; language – full articles written in English); 144 were excluded after reading the titles; and 13 were excluded after reading the abstracts. Lastly, 25 articles were fully read, and 19 were included in the present review.
Results: Most articles presented results showing that the majority of disease-modifying drugs enabled a satisfactory immune response to COVID-19 vaccination in multiple sclerosis patients. Nonetheless, some studies have shown that anti-CD20 therapies cause an increased risk of insufficient vaccination response, while the interference of fingolimod had variable results. In these cases, it seems to be beneficial to use a booster dose, and serological monitoring could be required to assess the immune response.
Conclusion: Despite the fact that it has been shown that some disease-modifying drugs interfere in the immune response to the COVID-19 vaccine, it is not recommended to discontinue or modify the treatment to improve vaccine efficacy, as the risk of disease reactivation and progression outweighs the potential benefits. Additionally, it is accepted that a reduced response is better than no response. Further studies are needed to clarify the situation.

DOI: 10.1055/s-0044-1789379

Nonalcoholic steatohepatitis as an important differential diagnosis for drug-induced liver injury in patients using fingolimod: a case report

Ana Beatriz Simon Nogueira[1], Paula Baleeiro Rodrigues Silva[1], Arthur Cesário de Holanda[1], Thiago Santillan[1], Rafael Augusto Rosalem[1], Débora Terrabuio[1], Aline Chagas[1], Mariana Spricigo[1], Mateus Boaventura de Oliveira[1,2], Tarso Adoni[1], Guilherme Diogo Silva[1], Samira Luisa Apóstolos-Pereira[1], Dagoberto Callegaro[3]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Ana Beatriz Simon Nogueira (email: anabnogueira@outlook.com).

Abstract
Case Presentation: We herein report the case of a 28-year-old woman living with obesity and relapsing-remitting multiple sclerosis (MS) with a high lesion load, who discontinued natalizumab due to JCV seropositivity and started fingolimod. Previously, she had mildly-elevated transaminase levels that increased progressively within 3 months into the new therapy. Abdominal ultrasonography suggested nonalcoholic steatohepatitis (NASH), and the laboratory findings improved significantly with weight loss, while the patient was still using fingolimod. Posteriorly, after weight gain and a rise in cholesterol levels, new worsening of the canalicular and hepatic enzymes of over five times the upper limits of normal (ULN) prompted a change in disease-modifying therapy.
Discussion: Fingolimod discontinuation may be associated with rebound in MS patients. One of the main causes of fingolimod discontinuation is elevated liver enzymes. While this medication is associated with hypertransaminasemia, it is usually mild, asymptomatic, and regresses after therapy discontinuation. Severe hepatotoxicity ($>$ 5 times the ULN) occurs in ~ 2% of patients, and those with preexisting liver conditions are more at risk. Conversely, the prevalence of nonalcoholic steatohepatitis (NASH) is estimated to be of approximately 3 to 6% among the adult population, and it is the main cause of chronic liver disease in Latin America. The therapeutic approach to NASH includes diet, exercise, and weight loss. Early identification of this condition and proper management may prevent progression to cirrhosis, which happens in ~ 20% of this population. Obesity is a risk factor for both MS and NASH. Adequate differential diagnosis and

treatment through lifestyle intervention may prevent unnecessary changes in immunotherapy.
Final Comments: The case herein presented illustrates the need for differential diagnosis between drug-induced hepatic aggression and other treatable causes of hypertransaminasemia in MS patients, preventing unnecessary changes in immunotherapy. Nonalcoholic steatohepatitis is especially important, and it can be treated through lifestyle changes.

DOI: 10.1055/s-0044-1789380

Profile of infusion-associated reactions with alemtuzumab in a Brazilian reference center

Ana Beatriz Simon Nogueira[1], Arthur Cesário de Holanda[1], Rafael Augusto Rosalem[1], Thiago Santillan[1], Sara Terrim[1], Paula Baleeiro[1], Graziella Aguiar[1], Flávio Vieira[1], Guilherme Diogo Silva[1], Mateus Boaventura[1], Mariana Gondim Peixoto Spricigo[1], Tânia Húngaro[1], Maristela Barros de Sousa[1], Erik Magnus Lindh[1], Luiz Henrique Martins Castro[1], Ida Fortini[1], Márcia Rúbia Gonçalves[1], Eduardo Genaro Mutarelli[1], Adalberto Studart[1], Tarso Adoni[1], Samira Luísa Apostolos Pereira[1], Dagoberto Callegaro[1]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*

Address for correspondence: Ana Beatriz Simon Nogueira (email: anabnogueira@outlook.com).

Abstract
Background: High efficacy therapies (HET) are crucial in treating multiple sclerosis (pwMS), often administered via infusion. Alemtuzumab is commonly linked with Infusion-associated reactions (IAR), occurring within 24 hours post-administration, usually mild to moderate. However, their frequency and specific management protocols are unclear. This observational study aims to describe common IARs to inform precautionary measures.
Objectives: The study aims to describe IAR profiles during the initial Alemtuzumab treatment cycle for pwMS at a São Paulo tertiary center.
Methods: Retrospective review of 40 consecutive pwMS undergoing their first Alemtuzumab cycle between February 2023 and February 2024. Sociodemographic, disease-related, and IAR data were extracted from clinical charts. All received routine premedication per protocol. Descriptive statistics were used for analysis.
Results: Among 40 patients, 52.5% were male, 17.5% had black ancestry, median age 34.5 years. 87.5% reported side effects during the 5-day infusion; women had a higher IAR rate. Common IARs included skin rash (47.5%), pruritus (32.5%), and headache (27.5%). Less common were fever (5%), hypotension (2.5%), and insomnia (2.5%). 7.5% experienced worsening neurologic deficits, 5% interrupted infusion for stroke-like symptoms. Thrombocytopenia occurred in 4 patients, and hypertransaminasemia in 3, transiently. All completed infusion without life-threatening events.
Conclusion: This study underscores the prevalence of IARs associated with Alemtuzumab therapy in pwMS. While mostly mild and responsive to symptomatic treatment, vigilance is crucial for managing severe reactions, like stroke-like symptoms, if they occur.

DOI: 10.1055/s-0044-1789381

Hyperkeratotic lesions associated to natalizumab treatment for multiple sclerosis: case report and literature review

Arthur Cesário de Holanda[1], Sara Terrim[1], Ana Beatriz Simon Nogueira[1], Rafael Augusto Rosalem[1], Thiago Santillan[1], Vinicius da Silva Moreira[1], José Antônio Sanches Júnior[1], Mariana Gondim Peixoto Spricigo[1], Guilherme Diogo Silva[1], Mateus Boaventura de Oliveira[1,2], Samira Luisa Apóstolos-Pereira[1], Tarso Adoni[1], Dagoberto Callegaro[3]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Arthur Cesário de Holanda (email: arthur.c.holanda@gmail.com).

Abstract
Case Presentation: A 29-year-old female patient was referred to our service after 3 recurrent episodes of partial transverse myelitis during 1 year. Multiple sclerosis (MS) was diagnosed based on compatible clinical, MRI, and CSF data (Figure 1). She had no personal or family history of dermatologic or autoimmune diseases. Treatment with natalizumab was indicated, and shed had only a minor reaction (cervical pruritus) after the first infusion. A few days after the second infusion, however, she developed painful crusted erythematous plaques and vesicles in both hands (Figure 2A). A biopsy revealed spongiotic dermatitis with acanthosis and perivascular infiltrates (Figure 2B). The patient improved completely after oral and topical corticosteroids. The lesions recurred on the fifth day after the third dose, this time involving all limbs and the trunk. After a review of the case with Dermatology, she started a course of prednisone 20 mg per day from 2 days before until 3 days after each infusion. The subsequent infusions, three so far, were carried out without lesion recurrence (Figure 2C).
Discussion: Natalizumab has one of the safest profiles among high-efficacy disease-modifying therapies for MS. Although delayed allergic reactions are well recognized, other cutaneous abnormalities have been scarcely reported, as is the case of hyperkeratotic lesions (Table 1). Previous reports have suggested a relationship between natalizumab infusions and psoriasis development or worsening, and an increase in peripheral CD4+IL17+ lymphocytes has been postulated as a potential cause. Spongiotic dermatitis, in turn, has only been associated with natalizumab in one other case. Dysregulation of natural-killer cells by the drug has also been proposed as a mechanism.
Final Comments: The present report is the second to describe a possible relationship between natalizumab infusion and spongiotic dermatitis. Recognition of rare dermatologic complications of natalizumab and their adequate management are important, especially considering the role of natalizumab in MS treatment and the limitation to the prompt access to other high-efficacy options.

DOI: 10.1055/s-0044-1789382

Real-world experience with patient laboratory monitoring compliance during alemtuzumab treatment in a low-income country: a pilot descriptive study

Arthur Cesário de Holanda[1], Ana Beatriz Simon Nogueira[1], Rafael Augusto Rosalem[1], Thiago Santillan[1], Sara Terrim[1], Paula Baleeiro Rodrigues Silva[1], Flávio Vieira Marques Filho[1], Graziella

Aguiar[1], Mariana Gondim Peixoto Spricigo[1], Guilherme Diogo Silva[1], Mateus Boaventura de Oliveira[1,2], Samira Luisa Apóstolos-Pereira[1], Tarso Adoni[1], Dagoberto Callegaro[3]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Arthur Cesário de Holanda (email: arthur.c.holanda@gmail.com).

Abstract
Background: Compliance with multiple sclerosis treatment is highly variable across the literature, ranging from 41 to 93%. Due to its posology, alemtuzumab has been associated with better adherence. However, information regarding compliance to its monthly laboratory monitoring is scarce, and there is no data from low-income countries.
Objective: To describe the compliance to laboratory follow-up after initiation of treatment with alemtuzumab in patients from a tertiary center in the city of São Paulo, Brazil.
Methods: The present is a prospective descriptive study that included all consecutive patients who started treatment with alemtuzumab from February 2023 to February 2024. Sociodemographic and clinical data were retrieved though clinical chart review, and compliance rates and reasons for non-compliance with laboratory collection were acquired though patient enquiry.
Results: In total, 21/40 (52.5%) patients were male, 7/40 (17.5%) were non-white, and the mean age was of 34.5 (19–55) years. Overall, 11/40 (27.5%) properly performed all exams required each month; 12/40 (30%) had incomplete or delayed results in at least one month; and 17/40 (42.5%) missed all laboratory collections in at least one month. A total of 24/40 (61.6%) patients collected samples at our tertiary hospital, while only 2/40 (5.1%) used the drug's patient support program. The reasons for non-compliance were variable, but forgetfulness and other personal reasons were the most prevalent (46.7%). No exam was missed due to lack of request nor due to problems with scheduling at our center. Urinalysis was the most unperformed exam, while thyroid function periodicity varied considerably.
Conclusion: Compliance with laboratory follow-up was much lower in this sample than real-world data previously reported. There are several challenges to an adequate follow-up that need to be recognized to better select patients to treat with alemtuzumab. It is necessary to improve monitoring strategies, especially considering the impacts of the underdiagnosed adverse events of this therapy.

DOI: 10.1055/s-0044-1789383

Detection of latent tuberculosis infection in patients at a reference center for demyelinating diseases in the city of Recife, Brazil: initial sampling

Bruno Paulo Teles Chaves[1], Vanessa Cristina Fragoso Cassiano Alencar[1], Lara de Menezes Andrade[1], Lidiane Alves de Macedo Souza[1], Maria Iris de Morais Machado[1], Maria Lucia Brito Ferreira[1]
[1]*Hospital da Restauração, Recife PE, Brazil.*

Address for correspondence: Bruno Paulo Teles Chaves (email: brunopaulo.c@gmail.com).

Abstract
Background: Latent tuberculosis infection (LTBI) is a persistent immune response triggered by *Mycobacterium tuberculosis* antigens without evidence of clinical manifestations of active tuberculosis. In recent decades, it is estimated that approximately 5 to 10% of the patients develop the active form of the disease within the first 5 years after infection. Patients with multiple sclerosis (MS) and other neuroimmunological diseases who undergo treatments with immunosuppressants can develop active tuberculosis, making it necessary to carry out tests to detect LTBI before starting such treatments.
Objective: To establish the prevalence of LTBI in a group of patients with MS and other neuroimmunological diseases undergoing immunosuppressive therapy at the reference center for demyelinating diseases at Hospital da Restauração, in the city of Recife, Brazil.
Methods: We analyzed 49 medical records of patients who underwent a tuberculin skin test (PPD), defined as reactor when ≥ 5 mm and non-reactor when < 5 mm, and interferon-gamma release assay (IGRA), defined as positive or negative.
Results: Of the 49 patients, 30 were female (61%). The average age was of 42 (range: 17–67) years, and 32 had RRMS (65.3%), 11, SPMS (22.4%), 1, PPMS (2%), and 5, neuromyelitis optica spectrum disorder (10.2%). The PPD was performed in 44 patients (90%), and 5 underwent IGRA (10%). Of those who underwent PPD, 31 were classified as reactor (63.2%), and 12, as non-reactor (24.4%); of those who underwent IGRA, 2 were positive (4.2%), and 3, negative (6.2%). One patient had active tuberculosis.
Conclusion: We consider it essential to perform LTBI detection tests in groups of patients at a high risk of developing active tuberculosis. We could observe a high incidence of LTBI in the initial sampling of the present study, making it imperative to systematically carry out tests to detect LTBI to reduce morbidity and mortality in patients undergoing immunosuppressive therapies.

DOI: 10.1055/s-0044-1789384

Assessment of visual perception and impact of the use of high-efficacy medications on patients

Caio Góes[1], Diego Olympio Peixoto Lopes[2], Maria Tereza Martinez[3], Luis Eduardo D'Almeida Manfrinati[3], Guilherme Ferreira Custódio[3], Fernanda Herculano[4], Diogo Haddad Santos[4]
[1]*Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.*
[2]*Universidade Santo Amaro, São Paulo SP, Brazil.*
[3]*CPQuali Pesquisa Clínica, São Paulo SP, Brazil.*
[4]*Hospital Alemão Oswaldo Cruz, São Paulo SP, Brazil.*

Address for correspondence: Caio Góes (email: caio.goes@aluno.fcmsantacasasp.edu.br).

Abstract
Multiple sclerosis is a chronic demyelinating disease that affects the central nervous systems via inflammatory mechanisms. Its lesions may result in progressive and permanent disabilities affecting the visual pathways, which not only serve as common initial clinical event, but also serve as an important monitoring factor regarding the side effects of high-efficacy drugs and therapy response. The aim of the present study is to evaluate the patients' subjective perception of their vision through an objective assessment via the National Eye Institute Developed Visual Functioning Questionnaire (NEIVFQ-25), and to correlate the findings with the use of high-efficacy medications. The high-efficacy drugs investigated were natalizumab, fingolimod, siponimod, alemtuzumab, cladribine, rituximab, ofatumumab, and ocrelizumab, whereas the low-efficacy drugs were fumarate, teriflunomide, and glatiramer. The NEIVFQ-25 is a self-

administered questionnaire that assesses the impact of visual impairment on quality of life, and it has been shown to be a reliable instrument for evaluation of visual impairment in multiple sclerosis. The participants were elected from the general population of the city of São Paulo, Brazil, and had a previous diagnosis of multiple sclerosis. Data on medication use was extracted from patient medical records. The results were correlated though the *t*-test. While patients using high-efficacy drugs presented a median score of 71 on the NEIVFQ-25, and those in the group of low-efficacy drugs presented a median score of 68, this difference was not statistically significant ($p = 0.177$). This result enables us to infer that the impact of visual impairment is not solely related to the use of high-efficacy medication. It is possible that the patient, even when using high-efficacy medication, may have experienced their first relapse with visual alterations and subsequently developed sequelae, or that the diagnosis was delayed, resulting in a delay in starting the treatment with high-efficacy medication. We conclude, therefore, that even with the use of these medications, patients may experience visual complaints that negatively impact their quality of life.

DOI: 10.1055/s-0044-1789385

Exploring the impact of physical exercise on cognitive function in multiple sclerosis: a systematic review and meta-analysis

Carolina Moura[1], Nathane Braga[1], Ocilio Rocha[2], Ana Morgado[1], Clara Lemes[1], Viviane Carvalho[3], Victor Soares[4], Henrique Cal[5], Gutemberg Augusto Cruz dos Santos[1]
[1]*Universidade Federal Fluminense, Niterói RJ, Brazil.*
[2]*Universidade Federal de Pernambuco, Recife PE, Brazil.*
[3]*Hospital São Francisco na Providência de Deus, Rio de Janeiro RJ, Brazil.*
[4]*Universidade Federal dos Vales do Jequitinhonha e Mucuri, Diamantina MG, Brazil.*
[5]*Hospital Copa D'Or – Rede D'Or São Luiz, Rio de Janeiro RJ, Brazil.*

Address for correspondence: Carolina Moura (email: carolinabraga28@gmail.com).

Abstract
Background: Cognitive impairment is a common and disabling symptom in individuals with multiple sclerosis (MS), prompting interest in interventions such as exercise training to improve cognitive function. Despite growing research in this area, the overall impact of exercise on cognitive performance in MS patients remains unclear.
Objective: The present literature review aims to investigate the effects of physical activity and exercise on cognitive function in individuals with MS.
Methods: A systematic review and meta-analysis were conducted by searching the PubMed, Embase, and Cochrane databases up to April 2024. The study focused on aerobic exercise interventions and their impact on the Symbol Digit Modalities Test (SDMT) score in MS patients. The inclusion criterion was randomized controlled trials (RCTs) examining cognitive outcomes in MS. Two independent reviewers extracted relevant data, including patient characteristics and intervention details. Data synthesis used random- or fixed-effects models among the included studies.
Results: The meta-analysis comprised 5 RCTs involving 608 patients, with the SDMT score as the primary outcome measure. Patient subgroups were analyzed based on follow-up duration and Expanded Disability Status Scale (EDSS) score (≤ 4 points or > 4 points). Significant improvements in SDMT scores were observed among MS patients engaging in aerobic exercise for 24 weeks (mean difference $= 5.9$; 95%CI: 1.90–9.90; $p < 0.01$; $I^2 = 0\%$; Figure 1). When stratified by EDSS score, no statistically significant difference was found (mean difference $= 1.7$; 95%CI -1.40–4.80; $p = 0.16$; $I^2 = 43\%$; Figure 2), although patients with an EDSS score ≤ 4 points showed higher SDMT scores.
Conclusion: The findings support aerobic exercise as a promising intervention to manage cognitive impairment in individuals with MS, particularly with longer-term interventions. Further research is warranted to elucidate the optimal exercise parameters and long-term effects on cognitive function in this population.

DOI: 10.1055/s-0044-1789386

Modifying disease therapy in multiple sclerosis and breast cancer: case report

Felipe Nascimento[1], Rodrigo Pereira[1], Marianela Rios[1], Danilo Almeida[1], Thiago Araújo[1], Pedro Chamma[1], Leticia Mansur[1], Maria Lucia Vellutini Pimentel[1]
[1]*Santa Casa da Misericórdia do Rio de Janeiro, Rio de Janeiro RJ, Brazil.*

Address for correspondence: Felipe Nascimento (email: felipetdonascimento@gmail.com).

Abstract
Case Presentation: We herein report the cases of three female patients diagnosed with relapsing-remitting multiple sclerosis (RRMS) undergoing therapy with high-efficacy drugs, including natalizumab, ocrelizumab, and fingolimod. During treatment, they were diagnosed with breast nodules (BNs) and initially chose clinical monitoring. The first patient, aged 36 years, had been monitoring a BN with a specialist since 2018, starting ocrelizumab treatment. After three months, she was diagnosed with breast cancer. The second patient, aged 45 years, had been following a BN with a specialist since 2015, starting Fingolimod in 2018, and undergoing a breast biopsy that year, which revealed ductal hyperplasia. After partial breast resection in 2019, she relapsed, switching to natalizumab and experiencing cancer recurrence. The third patient, aged 38 years, rejected the conventional treatment, and opted for high-dose vitamin D therapy despite medical recommendations for disease-modifying drugs (DMD). Due to new relapses and increased lesion burden, she started natalizumab, and was later diagnosed with ductal carcinoma in situ, leading to bilateral mastectomy.
Discussion: Multiple sclerosis (MS) is an autoimmune inflammatory disease of the central nervous system that affects young women globally and is altered by disease-modifying therapy (DMT). Despite the proven efficacy, recent studies have suggested potential adverse effects, including neoplasms such as breast cancer. Many patients already have BNs before the DMT, due to lack of regular screening. Breast cancer is prevalent among women worldwide, and its diagnosis may result from disease progression or missed screening. Three patients with prior breast nodule follow-up, diagnosed with RRMS and on high-efficacy therapy, are herein presented, two with malignant breast neoplasia.
Final Comments: Although breast neoplasia occurred in the three patients, causality with disease-modifying drugs cannot be established. Further research is needed to understand their potential adverse effects. Implementing neoplasm screening protocols for patients on DMT is crucial.

DOI: 10.1055/s-0044-1789387

Breaking through the storm: combination therapy with ocrelizumab and cyclophosphamide in an unusual and severe case of multiple sclerosis

Flávio Vieira Marques Filho[1], Arthur Dias[2], Nayara Guerreiro[2], Maria Fernanda Hamamoto Leati[2], Victor Costa[3], Camila Nepomuceno[2], Guilherme Diogo Silva[1], Samira Luisa Apóstolos-Pereira[4], Tarso Adoni[1], Sonia Brucki[2], Maria Sheila Rocha[2], Dagoberto Callegaro[4]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital Santa Marcelina, São Paulo SP, Brazil.*
[3]*Universidade Federal de Juiz de Fora, Hospital Universitário, Juiz de Fora MG, Brazil.*
[4]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Flávio Vieira Marques Filho (email: flaviovmf@icloud.com).

Abstract
Case Presentation: A 27-year-old man, diagnosed with Multiple Sclerosis since 2019, with a history of 2 relapses and stable on fingolimod (first and only drug), was admitted in October 2023 with cognitive impairment (EDSS 2). An MRI showed a tumefactive lesion in the right parieto-occipital region, with diffusion restriction and no contrast enhancement, raising the hypothesis of progressive multifocal leukoencephalopathy (PML). Fingolimod was discontinued and JC virus levels were measured in the CSF (positive in blood). He received methylprednisolone EV, with significant clinical and radiological improvement. After 40 days without medication (considering the risk of PML) and waiting for anti-CD20, he presented with confusion, ataxia, and hemiparesis (EDSS 3), with an MRI showing multiple new tumefactive lesions supra- and infratentorially, again with diffusion restriction and no contrast enhancement, attributed to fingolimod rebound. The CSF JC virus was negative, and the patient underwent pulse therapy, plasmapheresis, and received the first dose of ocrelizumab, with slight improvement. Fourteen days after discharge, he returned to the emergency department, aphasic, paraparetic (wheelchair-bound), and confused (EDSS 8), with MMSE 9/30 and an MRI showing contrast-enhancing lesions. He received another course of pulse therapy, along with additional ocrelizumab and cycles of cyclophosphamide for 6 months. The patient returned after 3 months with EDSS 2, MMSE 27/30, and no new lesions on MRI.
Discussion: The initial MRI characteristics suggested PML, which limited therapy options. Furthermore, the patient experienced a severe rebound with atypical imaging shortly after the discontinuation of fingolimod, as well as clinical and radiological worsening after the first stage of treatment. This led us, after discussions with the family, to the addition of cyclophosphamide, aiming to control the severe inflammation.
Final Comments: Despite the inherent risks and the lack of descriptions in the literature, the combination of ocrelizumab and cyclophosphamide, in this context, seems to have contributed to a good outcome and control of the disease.

DOI: 10.1055/s-0044-1789388

Discontinuation of disease-modifying drugs in older multiple sclerosis patients with stable disease: a retrospective observational study

Graziella Aguiar Santos Faria[1], Paula Baleeiro Rodrigues Silva[1], Sara Terrim[1], Flávio Vieira Marques Filho[1], Mariana Spricigo[1], Mateus Boaventura de Oliveira[1,2], Guilherme Diogo Silva[1], Samira Luisa Apóstolos-Pereira[1], Dagoberto Callegaro[3], Tarso Adoni[1]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Graziella Aguiar Santos Faria (email: graziasf@hotmail.com).

Abstract
Background: Disease-modifying therapies (DMTs) effectively reduce multiple sclerosis (MS) relapses and improve survival; however, data on their efficacy and safety in older patients are limited. DISCOMS, the first trial of DMT discontinuation in MS, focused on patients aged over 55 years with stable disease, failed to demonstrate the non-inferiority of discontinuation versus continuation for relapse or new lesions.
Objective: To provide additional real-world evidence on the discontinuation of MS medication, particularly among older patients with stable disease, mirroring the inclusion criteria of the DISCOMS trial.
Methods: We conducted a retrospective observational study, reviewing records of MS patients aged 55 or older with no relapses in 5 years and no new MRI lesions in 3 years on DMT, consecutively seen between August 2023 and October 2023. The primary endpoints were time until first disease activity, defined as a new MS relapse or lesion on MRI. Suitable statistical tests compared the groups, and Kaplan-Meier curves depicted time-to-event outcomes, using the R software, version 4.2.0.
Results: Of the 436 patients assessed, 46 were included, with 18 (39.1%) discontinuing treatment. Most patients (N = 20; 47%) were treated with injectable therapies. More than one fifth of the patients were treated with unapproved therapies, reflecting treatment exposure prior to DMT availability (N = 9; 21.3%). A significant difference in baseline radiological stability duration favored discontinuation (median: 7.1 versus 5.1 years; $p = 0.042$), potentially impacting the decision to halt treatment. Following discontinuation, 8 patients (53%) experienced disease activity; however, no notable discrepancy in outcomes was observed between the assessed groups. Additionally, there was no significant variance in the time until disease activity (aHR=1.07; 95% CI: 0.84–1.37; $p = 0.584$).
Conclusion: Despite age-related expectations, the present study found higher disease activity compared to the DISCOMS trial. Yet, no significant differences between discontinuers and continuers were detected, suggesting that age might be the predominant factor influencing DMT cessation.

DOI: 10.1055/s-0044-1789389

Challenges in the differential diagnosis of leptomeningeal involvement in patients with multiple sclerosis: a case report of occipitotemporal leptomeningeal lesion

Gustavo Silva Schafascheck[1], Viviane Carvalho[2], Samuel Santos do Nascimento Junior[1], Ana Luísa Utrine Pimentel[1], Gutemberg Augusto Cruz dos Santos[1]
[1]*Universidade Federal Fluminense, Niterói RJ, Brazil.*
[2]*Hospital São Francisco na Providência de Deus, Rio de Janeiro RJ, Brazil.*

Address for correspondence: Gustavo Silva Schafascheck (email: gustavo.med2016@gmail.com).

Abstract
Leptomeningeal involvement in patients with multiple sclerosis (MS), although uncommon, poses a challenge due to its varied clinical symptoms and diverse and nonspecific radiological findings on neuroimaging. Differential diagnoses reported in the literature include inflammatory, infectious, neoplastic, and vascular causes. We herein present a case of occipitotemporal leptomeningeal lesion in a patient with MS, exploring the main associated differential diagnoses and the importance of systematic evaluation. A 60-year-old patient was diagnosed with MS in September 2022 and initiated treatment with copaxone. In January 2023, a new lesion was identified, followed by a positive test for latent tuberculosis in July of the same year, requiring additional treatment. In November 2023, a subsequent magnetic resonance imaging (MRI) scan revealed an occipitotemporal leptomeningeal lesion, a rare occurrence in MS. After extensive investigation for differential diagnoses, disease activity was confirmed. The medical team opted to initiate natalizumab, an immunomodulator, in November 2023. Two months after starting natalizumab therapy, a follow-up MRI scan showed substantial reduction of the leptomeningeal lesion, accompanied by significant clinical improvements, including fatigue reduction, improved vision, and increased walking stability. This case highlights the complexity of differential diagnosis of leptomeningeal involvement in patients with MS. A multidisciplinary approach and advanced diagnostic methods are essential for early and effective treatment, improving prognosis. Furthermore, careful consideration of differential diagnoses is crucial for the individualized and effective management of these patients.

DOI: 10.1055/s-0044-1789390

Exit strategies regarding natalizumab: the dilemma in limited-resource scenarios

Igor Bessa[1], Ivna Nóbrega[1], Lucas Silvestre[1], Milena Sales Pitombeira[1], José Artur Costa D'Almeida[1], Gabriela Martins[1]
[1]Hospital Geral de Fortaleza, Departamento de Neuroimunologia, Fortaleza CE, Brazil.

Address for correspondence: Igor Bessa (email: igor-bess@hotmail.com).

Abstract
Background: Natalizumab (NTZ) is a humanized monoclonal antibody indicated for people with multiple sclerosis (pwMS) with poor response to the first-line treatment or naive patients with highly-active disease. Exposure to NTZ in patients seropositive for the JC virus (JCV) increases the risk of developing a severe opportunistic infection called *progressive multifocal leukoencephalopathy* (PML). By searching for an exit strategy for NTZ cessation we can undermine PML risk in such patients.
Objective: To evaluate NTZ exit strategies in a Northeastern Brazilian MS center.
Methods: We collected observational data from patients under NTZ treatment between July 2010 and April 2024.
Results: A total of 21 patients were enrolled, with a median follow-up of 7 (IQR: 5–11) years; 86% were female, with a median age of 39 (IQR: 32–44) years and median disease duration of 15 (IQR: 7–23) years. The median EDSS score during NTZ follow-up was of 2 (IQR: 1.5–5), and the average for infusion was of 29 (±20). Although 90% of the patients had disease activity 2 years prior NTZ, only 1 had relapse during treatment. Eighteen patients interrupted NTZ due JCV index higher than 1.5, and 3, between 0.9 and 1.5. out of 21 patients undergoing cessation, 1 switched to fingolimod, 1, to ofatumumab, 5, to rituximab, and 14, to ocrelizumab. There were no relapses after interruption; 2 patients presented signs of radiologic activity, and the median EDSS score remained 2 (IQR: 1.5-5). After cessation, 5 patients under ocrelizumab had infusion delays due availability issues, and the one under fingolimod switched to rituximab due side effects.
Conclusion: The risk of developing PML remains a major concern, and there is a lack of solid strategies for patients under NTZ for more than 24 months and positive JCV. Ocrelizumab has a high patient-per-year cost, and it is not currently available in public health care system in Brazil, which may increase the risk of disease activity due erratic use. Rituximab is an available option in limited-resource scenarios.

DOI: 10.1055/s-0044-1789391

Rituximab as a treatment for multiple sclerosis: a literature review

Juliana Santiago-Amaral[1], Ana Júlia Resende Rocha[1], Gabriel Lage Neves[1], Izabela Cristina de Faria Martins[2]
[1]Faculdade de Ciências Médicas de Minas Gerais, Belo Horizonte MG, Brazil.
[2]Instituto de Previdência dos Servidores de Minas Gerais, Belo Horizonte MG, Brazil.

Address for correspondence: Juliana Santiago-Amaral (e-mail: julimss@gmail.com).

Abstract
Background: The evidence of the role of B cells in the pathogenesis of multiple sclerosis (MS) has increased the interest in the development of anti-CD20 drugs, such as ocrelizumab and ofatumumab, medications already approved by the FDA for the treatment of MS. Rituximab (RTX), a monoclonal anti-CD20 antibody used for the treatment of certain neoplasms and autoimmune diseases, has been studied as a therapeutic option for MS.
Objective: To analyze the use of RTX as a therapeutic option for MS.
Methods: A search was conducted on PubMed using the descriptors *multiple sclerosis*, *rituximab*, and *comparative effectiveness research*. Filters were applied for study type (*clinical trial* and *randomized controlled trial*). No filters were applied for the publication date. In the initial search, 31 articles were found, 14 of which were excluded based on the eligibility criteria (10 were excluded based on title, 3, based on abstract, and 1 was excluded because the full article could not be found).
Results: Preliminary clinical trials and randomized controlled trials have shown that RTX in patients with MS resulted in depletion of B cells, reduction in self-reactive T cells, decrease in the number of active demyelinating lesions, and relapses of MS over a treatment period of 24 to 48-weeks. Intravenously-administered RTX was well tolerated in the analyzed studies, with no significant reported side effects. When compared to other disease-modifying drugs, RTX showed superior efficacy to dimethyl fumarate and glatiramer acetate, and greater tolerability and efficacy than fingolimod as a switch from natalizumab. Rituximab was not able to modify the EDSS score of patients with secondary progressive MS.
Conclusion: Rituximab acts by depleting the pool of B cells, and it may represent an alternative for MS treatment. Although its use is still off-label, according to the present review, it demonstrates good safety and efficacy for MS treatment.

DOI: 10.1055/s-0044-1789392

Fourteen years of experience in natalizumab infusion at a neuroimmunology service in the city of Pernambuco, Brazil

Lidiane Alves de Macedo Souza[1], Vanessa Cristina Fragoso Cassiano Alencar[1], Bruno Paulo Teles Chaves[1], Lara de Menezes Andrade[1], Maria Lucia Brito Ferreira[1], Maria Iris de Morais Machado[1]
[1]*Hospital da Restauração, Recife PE, Brazil.*

Address for correspondence: Lidiane Alves de Macedo Souza (email: lidianemacedohr@gmail.com).

Abstract
Background: Natalizumab (NTZ) is an effective therapy for the treatment of relapsing-remitting multiple sclerosis (RRMS), consisting of a recombinant humanized monoclonal antibody directed to the α4 subunit of integrins, launched in the market in 2005. Hospital da Restauração (HR), in the city of Recife, state of Pernambuco, Brazil, is a reference in the treatment of MS, and NTZ infusions began in 2009.
Objective: To retrospectively evaluate the 14-year experience in NTZ infusion in HR, in terms of demographic aspects, time until diagnosis, disease classification, time of medication use, previous use of immunosuppressants, and John Cunningham virus (JCV) status.
Methods: In total, 146 patients were exposed to the medication from 2009 to December 2023, 44 of whom were excluded due to loss to follow-up, resulting in a sample of 102 patients. The research was carried out through the evaluation of medical records and face-to-face interviews.
Results: The medication was being used by 71.5% of the affected patients. Treatment was discontinued in 28.43%; 0.98% developed progressive multifocal leukoencephalopathy, 3.92% died, 4.90% abandoned the treatment, 5.88 had a change of address, and in 11.76% the medication was suspended: in 9.98%, due to therapeutic failure, and 1.96%, per irregular use. Of the sample, 72.6% were female, 51.96% were of mixed race, 90.1% were classified as having RRMS, 6.86% had secondarily progressive MS, and 3.92% had primarily progressive MS with activity. The time until diagnosis was shorter than 6 months in 22.54%, from 6 to 12 months in 23.52%, from 12 to 24 months in 12.74%, longer than 24 months in 17.64%, and, for 23.52% there was no information. In total, 3.92% of the patients had previously used immunosuppressants. Of the sample, 38.3% had been using the medication for fewer than 2 years, 16.43%, between 2 and 4 years, and 45.5%, for more than 4 years. The rate of JCV positivity was of 34.24%.
Conclusion: Natalizumab is frequently used in HR, mainly in female patients and in those with RRMS. During treatment, surveillance is important for the early detection of complications.

DOI: 10.1055/s-0044-1789393

Treatment for multiple sclerosis and reactivation of latent tuberculosis: is there a relationship?

Luiza Andraus Dantas[1], Marina Steingraber Pereira[1], Amanda de Miranda Gauza[1], Maria Eduarda Bonetti Schulz[1], Gustavo Figueiredo da Silva[1], Maria Eduarda Marchi Martin[1], Washigton Luiz Gomes de Medeiros Junior[1], Ruan Carlos da Silva[1], Arthur Stedile Ribeiro Pacheco[1], Radassa Vieira[1], Mário Natalício de Gasperi[1], Thomas Cubas Baggio[1], Marcelo de Moura Campos[1], Marcus Vinícius Magno Gonçalves[2]
[1]*Universidade da Região de Joinville, Joinville SC, Brazil.*
[2]*Neurovie, Departamento de Neurologia, Joinville SC, Brazil.*

Address for correspondence: Marcelo de Moura Campos (email: marcelo.campos88@hotmail.com).

Abstract
Background: Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, transmitted through the air. According to the World Health Organization, it has a global prevalence of 10 million people. Multiple sclerosis (MS) is a chronic inflammatory neurological disease characterized by demyelination and neuronal loss. According to the MS Atlas, in 2020, 2.8 million people suffered from this disorder. In its treatment, medications with immunosuppressive effects on the body are widely used, so patients undergoing MS treatment could be more susceptible to latent tuberculosis infection (LTBI).
Objective: To elucidate the relationship between MS and LTBI through a systematic review.
Methods: The PubMed/MEDLINE, Cochrane, ScienceDirect, LILACS and SciELO databases were systematically reviewed from 2010 to 2020, and Google Scholar, from 2015 to 2020, to detect articles eligible for the study.
Results: We included 14 studies on the relationship between MS and LTBI: 2 case reports, 2 prevalence studies, 4 non-systematic reviews, 2 expert consensuses, and 4 case-control studies. Most of the articles stated that screening for LTBI should be performed before the start of the MS treatment. Screening is highly recommended in patients before starting alemtuzumab, cladribine, teriflunomide, corticosteroids, azathioprine, cyclophosphamide, and methotrexate.
Conclusion: Few articles addressed the association between the contagious disease and the treatment for MS. articles selected were observational studies, which offer limited data and differ in several aspects. These divergences make it difficult to compare the results of the articles, making it impossible to accurately state whether there is a relationship between the treatment for MS and LTBI. However, most studies recommend screening for LTBI before starting MS treatment, especially in countries with high tuberculosis rates.

DOI: 10.1055/s-0044-1789394

Combination of secukinumab and natalizumab in the treatment of a patient with psoriatic arthritis and multiple sclerosis

Marciéli Gerhardt[1], Giuseppe Dick Bonato[1], Giordani Rodrigues dos Passos[1], Jefferson Becker[1]
[1]*Pontifícia Universidade Católica do Rio Grande do Sul, Hospital São Lucas, Porto Alegre RS, Brazil.*

Address for correspondence: Marciéli Gerhardt (email: marcieligerhardt@yahoo.com.br).

Abstract
Case Presentation: A woman with recurrent episodes of uveitis, polyarthritis, and enthesitis, as well as a history of sacroiliitis, a skin biopsy with psoriasiform chronic dermatitis, and a family history of a son with psoriasis, was diagnosed with psoriatic arthritis. After receiving methotrexate and azathioprine without a satisfactory response, she began treatment with adalimumab. She had a demyelinating episode while receiving this treatment, leading to the diagnosis of very active multiple sclerosis. Adalimumab was discontinued, and treatment with secukinumab, natalizumab, and sulfasalazine was started. Since then, she had an improvement in arthralgias and low back pain, without any major adverse events described to date. Neither did she have any new attacks during this period. Currently, she has been

receiving natalizumab for a year and a half, and secukinumab, for half a year.
Discussion: The association of psoriatic arthritis with multiple sclerosis is rare. In this case, the use of anti-TNF may have been a trigger for the manifestation of a demyelinating disease. Because of the risk of having new demyelinating episodes, this medication is contraindicated for this patient. The absence of a single drug that could appropriately treat both conditions brings up the need for a combined therapy, increasing the risk of adverse effects, and testing the efficacy of these drugs when used together. To date, the combination of secukinumab and natalizumab has been shown to be safe and effective.
Final Comments: Considering that finding patients in these same circumstances as those of the case herein reported is infrequent, conducting controlled randomized trials may be extremely difficult. Therefore, case reports like the present can be helpful for the clinical practice. Monitoring this patient for a longer time might help establish with greater accuracy the safety and effectiveness of this combined therapy, which may also be useful in other clinical contexts.

DOI: 10.1055/s-0044-1789395

Time until treatment and prognosis of multiple sclerosis beyond physical disability

Letícia Cavaglieri[1,2], Murilo Pinoti[1,2], Olivia Pires[1], Clayton Zoccoli[1,2], Isabella Avolio[1], Mateus Boaventura de Oliveira[1,3]
[1]*Hospital São Camilo, São Paulo SP, Brazil.*
[2]*Centro Universitário São Camilo, São Paulo SP, Brazil.*
[3]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br).

Abstract
Background: Multiple sclerosis (MS) is the most common non-traumatic debilitating condition affecting young adults, with a global incidence on the rise. This trend contributes to its significant socioeconomic impact, which is related to physical disability and cognitive dysfunction. Investing in early diagnosis and treatment may reduce the daily limitations faced by the affected individuals.
Objective: To statistically elucidate the true long-term impact that the time gap between the initial onset of symptoms and treatment has on prognosis.
Methods: The present is a multicenter study, in which MS patients from three outpatient clinics were ambispectively analyzed. The time gap from disease onset to the first disease-modifying treatment (TFDT) and the time between disease onset and the first high-efficacy therapy (TFET) were calculated. Sociodemographic and clinical data were collected through the local database, and the course of the disease was evaluated through classic physical/cognitive disability scales and burden symptoms questionnaire (SymtoMScreen).
Results: A total of 184 MS patients were included in the baseline analysis (77.7% of female subjects; mean age at analysis of 39.1(±10.8) years; mean at disease onset of 29.8 (±9.4) years; mean disease duration of 9.3(±7.6) years; and median baseline EDSS score of 2.0). Significant correlations were observed between: TFDT and EDSS ($r = 0.374$; $p < 0.001$); TFET and EDSS ($r = 0.442$; $p < 0.001$); TFDT and processing speed ($r = -0.207$; $p = 0.042$); TFDT and visual memory ($r = -0.271$; $p = 0.008$); and TFET and SypmtoMScreen ($r = 0.203$; $p = 0.049$). No significant correlations were observed between both time intervals and the Modified Fatigue Impact Scale (MFIS) or the Multiple Sclerosis Impact Scale (MSIS-29).
Conclusion: A longer time to start treatment is associated with worse physical disability, cognitive dysfunction, and symptom severity. These findings may support decisions regarding the need for early MS therapy in the Brazilian setting, beyond just the classic physical outcomes.

DOI: 10.1055/s-0044-1789396

Real-world study of oral cladribine for Brazilian patients with multiple sclerosis: results from the BRANDO registry

Mateus Boaventura de Oliveira[1,2], Jefferson Becker[3], Carlos Bernardo Tauil[4], Laura Fiuza Parolin[5], Samira Luisa Apóstolos-Pereira[1], Alfredo Damasceno[6], Thiago Gonçalves Fukuda[7], Maria Fernanda Mendes[8], Gabriela Martins[9], Denise Sisterolli Diniz[10], Henry Koiti[11], Herval Neto[12], Paulo Diniz da Gama[13], Giordani Rodrigues dos Passos[14], Kleber Cavalcante dos Santos[5], Marcus Vinicius Magno Gonçalves[6], Mariana de Sá[6], Dagoberto Callegaro[15]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Pontifícia Universidade Católica do Rio Grande do Sul, Hospital São Lucas, Porto Alegre RS, Brazil.*
[4]*Universidade de Brasília, Brasília DF, Brazil.*
[5]*Neurovie, Departamento de Neurologia, Joinville SC, Brazil.*
[6]*Universidade Estadual de Campinas, Campinas SP, Brazil.*
[7]*Universidade Federal da Bahia, Hospital Universitário Professor Edgar Santos, Salvador BA, Brazil.*
[8]*Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.*
[9]*Hospital Geral de Fortaleza, Departamento de Neuroimunologia, Fortaleza CE, Brazil.*
[10]*Universidade Federal de Goiás, Goiânia GO, Brazil.*
[11]*Instituto Neurológico de Curitiba, Curitiba PR, Brazil.*
[12]*Hospital do Servidor Público Estadual de São Paulo, São Paulo SP, Brazil.*
[13]*Pontifícia Universidade Católica de São Paulo, Sorocaba SP, Brazil.*
[14]*Secretaria de Saúde do Distrito Federal, Brasília DF, Brazil.*
[15]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Mateus Boaventura de Oliveira (email: mateusboaventura@yahoo.com.br).

Abstract
Background: Treatment with oral cladribine was approved in Brazil in 2019; since then, it has been prescribed to different multiple sclerosis (MS) patient profiles, with no local real-world experience data.
Objective: To report the main reasons to initiate cladribine treatment in Brazil. To report the efficacy and persistence among Brazilian MS patients under cladribine treatment.
Methods: The present is an observational, retrospective, longitudinal study of cladribine-treated MS patients reported by neurologists in the Collaborative Latin American Database for Multiple Sclerosis (BRANDO) registry. The inclusion criteria were: age over 18 years, diagnosis of relapsing-onset MS according to current criteria, and initiation of oral cladribine at least 6 months before analysis. The core clinical data included disease activity (relapses and follow-up MRI) and worsening of the score on the Expanded Disability Status Scale (EDSS).
Results: We included 39 cladribine-treated patients in the baseline analysis, 29 (74.4%) of them female subjects. The median age at disease onset was of 24.9 (19.9–47.8) years, and at the start of the cladribine treatment, it was of 28.9 (19–

49.5) years. The median baseline EDSS score was of 2.5 (0–6.0). The main reasons to prescribe cladribine were: previous treatment failure (8/25; 32%); naive patients (6/25; 24%); risk of development of progressive multifocal leukoencephalopathy (PML; 6/25; 24%); adverse event (1/25; 4%); and other reasons (4/25; 16%). After a median follow-up of 24.7 (6.0–43.4) months, 25/39 (64.1%) patients remained relapse-free, 25/27 (92.6%) were EDSS progression-free, 18/35 (51.4%) patients did not present MRI activity, and 8/26 (30.8%) patients were on NEDA-3. Concerning discontinuation, 7 (17.9%) patients switched to another treatment after cladribine. Lymphopenia of grades 3 or 4 occurred in 4/28 (14.3%) MS patients.
Conclusion: Our real-world observational data discloses a heterogenous profile of cladribine indication. We observed higher failure of treatment measures compared with pivotal trials, which may be related to the fewer naive patients in our sample. Larger sample sizes are needed to confirm our results, as well as to provide statistical power regarding which patient subgroups are at greatest risk of therapeutic failure.

DOI: 10.1055/s-0044-1789397

Understanding Hodgkin lymphoma occurrence after fingolimod withdrawal

Thales Ponsá Pinto[1], Natália Cirino Talim[1], Paulo Pereira Christo[1], Carolina Reis Araújo Abrantes[1], Ana Cristina Cotta-Queiroz[1], Anna Christina Higino Rocha[1], Grazielle Fialho[1], Felipe B. Brunheroto[1], Marco Lana-Peixoto[1]
[1]Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract
Fingolimod, an oral immunomodulator commonly prescribed for the treatment of relapsing-remitting multiple sclerosis (MS), has been associated with lymphoma cases. While it effectively manages MS symptoms, concerns have been raised regarding its association with lymphoma development. Interestingly, some research suggests that fingolimod might exert anticancer effects by reducing the number of tumor-infiltrating lymphocytes. The aim of the present article is to describe a patient with MS who developed symptoms of Hodgkin lymphoma 11 months after discontinuing fingolimod.
Case Presentation: A 46-year-old female patient with relapsing-remitting MS since 2007, which evolved to secondary progressive MS by 2016. Treated with fingolimod from 2017 to 2022, she discontinued the medication due to persistent lymphopenia. Eleven months after the discontinuation, she presented with cough and dyspnea. A chest CT scan revealed a mediastinal mass, diagnosed as Hodgkin lymphoma upon biopsy.
Discussion: Fingolimod modulates the sphingosine-1-phosphate (S1P) receptor, sequestering lymphocytes in lymphoid tissue. This mechanism underpins its efficacy in MS treatment, but also raises concerns about its potential oncogenicity. Chronic fingolimod use has been associated with an increased risk of neoplasms. Although some studies have reported cases of non-Hodgkin lymphoma linked to fingolimod in humans, its relationship with Hodgkin lymphoma is not so clear. Notably, Reed-Sternberg cells, the hallmark neoplastic cells in Hodgkin lymphoma, may express the S1P receptor on their surface. Exposure to fingolimod could inhibit the migration and proliferation of these cells, inducing apoptosis and possibly enhancing the efficacy of chemotherapy.
Final Comments: The 11-month interval between drug discontinuation and symptom onset, along with the diagnosis of Hodgkin lymphoma, suggests fingolimod may not have a pro-oncogenic effect on Hodgkin lymphoma. Instead, it might suppress Reed-Sternberg cell migration and growth through the mediastinal lymph node chain during treatment.

DOI: 10.1055/s-0044-1789398

Early relapse after alemtuzumab treatment: a case report of highly active multiple sclerosis

Rafael Augusto Rosalem[1], Ana Beatriz Simon Nogueira[1], Arthur Cesário de Holanda[1], Thiago Santillan[1], Sara Terrim[1], Mariana Gondim Peixoto Spricigo[1], Guilherme Diogo Silva[1], Mateus Boaventura de Oliveira[1,2], Samira Luisa Apóstolos-Pereira[1], Tarso Adoni[1], Dagoberto Callegaro[3]
[1]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.
[2]Hospital São Camilo, São Paulo SP, Brazil.
[3]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.

Address for correspondence: Rafael Augusto Rosalem (e-mail: rafael.rosalem@hc.fm.usp.br).

Abstract
Case Presentation: A 26-year-old male patient with an RRMS diagnosis since the age of 19 had his DMT switched to alemtuzumab after experiencing a relapse during regular treatment with standard interval dosing natalizumab for 9 infusions. His EDSS score was of 3.0 due to double hemiparesis. Seven months after completing the first cycle, he developed upper limb paresthesias. A brain MRI scan showed a new enhancing lesion. As symptoms had improved spontaneously, steroid treatment was not prescribed. Two months later, the patient sought the outpatient clinic with a new complaint of vertigo and visual fixation impairment that had started one month earlier. A neurological examination revealed a new body lateropulsion to the left. He was admitted as an in-patient, and a brain MRI showed six new T2/FLAIR hyperintense lesions, four of which displayed gadolinium enhancement. Lymphocyte immunophenotyping showed reconstitution of CD19, CD4 and CD8 lymphocytes. The patient received a 5-day course of methylprednisolone, with symptom improvement, and a proposition to expedite the second alemtuzumab cycle before the 12-month interval.
Discussion: Alemtuzumab is an anti-CD52 monoclonal antibody approved for RRMS and SPMS that was included in the Brazilian public health system in 2021 and is reserved for highly-active MS with failure or contraindication to natalizumab. The definitions of such cases vary and may include poor recovery from the first two relapses, high relapse frequency, and signs of breakthrough disease within two years of treatment with high-efficacy DMT. Therapeutic approach in such cases is controversial.
Final Comments: Alemtuzumab is regarded as a higher-efficacy treatment for MS patients with failure of other DMTs in the Brazilian public health system. Due to its recent incorporation, we are still gathering real-world experience in its use. Currently, the best approach to cases that exhibit relapses during the first year of therapy has not been established.

DOI: 10.1055/s-0044-1789399

Cytokine storms during alemtuzumab infusion: a case series

Thiago Santillan[1], Herval Neto[2], Sara Terrim[1], Flávio Vieira Marques Filho[1], Ana Beatriz Simon Nogueira[1], Arthur Cesário de Holanda[1], Rafael Augusto Rosalem[1], Pedro Pontes[2], Mariana Gondim Peixoto Spricigo[1], Guilherme Diogo Silva[1], Mateus Boaventura de Oliveira[1,3], Samira Luisa Apóstolos-Pereira[1], Tarso Adoni[1], Dagoberto Callegaro[4]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital do Servidor Público Estadual de São Paulo, São Paulo SP, Brazil.*
[3]*Hospital São Camilo, São Paulo SP, Brazil.*
[4]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Thiago Santillan (email: thiago.santillan@hc.fm.usp.br).

Abstract

Case Presentation: Alemtuzumab, a high efficacy therapy (HET) for multiple sclerosis (MS) patients in Brazil's public healthcare system, is reserved for cases where natalizumab has failed or is contraindicated due to its effectiveness. Despite being relatively common, infusion-associated reactions (IAR) with alemtuzumab are mostly mild and manageable with pre-infusion protocols involving corticosteroids, antihistamines, and analgesics. However, severe IARs can occur, posing risks to patients, yet data on clinical presentation and management remain limited. The objective of this study is to report three cases of serious adverse reactions linked to alemtuzumab infusion in MS patients. These patients were treated at two neuroimmunology clinics in São Paulo. Inclusion criteria encompassed MS patients treated with alemtuzumab infusion without contraindications. All received 12 mg of intravenous alemtuzumab, premedicated with methylprednisolone, diphenhydramine, and acetaminophen. Nursing and medical staff were trained to manage adverse effects promptly. Case 1 involved a 45-year-old female experiencing acute generalized pain, somnolence, dyspnea, and hypertensive crisis during her second infusion. Treatment was paused, and a new cycle of steroids and symptomatic drugs was initiated. Case 2, a 35-year-old male, developed acute ataxia, hypertension, and fever within two hours of infusion on the third day. The infusion was paused, and a stroke protocol was enacted to rule out vascular complications. Case 3, a 44-year-old female, presented with bilateral leg weakness and fever within two hours of infusion. Similar symptoms d during previous MS relapses were reported, yet both patients underwent a stroke protocol due to acute onset. Symptoms resolved with antipyretics.
Discussion: Suggests these IARs correspond to cytokine storm syndrome, involving release of TNF-alpha, IFN-Gamma, and IL-6, leading to fever, rash, dyspnea, and blood pressure fluctuations.
Final Comments: Infusion-associated reactions, exceeding 90%, highlight the importance of healthcare providers being vigilant regarding potential side effects associated with alemtuzumab infusion in MS treatment.

DOI: 10.1055/s-0044-1789400

The long Journey to achieve high-efficacy therapy: Alemtuzumab in Brazilian public scenario

Thiago Santillan[1], Arthur Cesário de Holanda[1], Sara Terrim[1], Flávio Vieira Marques Filho[1], Ana Beatriz Simon Nogueira[1], Rafael Augusto Rosalem[1], Mariana Gondim Peixoto Spricigo[1], Guilherme Diogo Silva[1], Mateus Boaventura de Oliveira[1,2], Samira Luisa Apóstolos-Pereira[1], Tarso Adoni[1], Dagoberto Callegaro[3]
[1]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[2]*Hospital São Camilo, São Paulo SP, Brazil.*
[3]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Thiago Santillan (email: thiago.santillan@hc.fm.usp.br).

Abstract

Background: Early initiation of High Efficacy Therapy (HET) improves prognosis in Multiple Sclerosis (MS) patients. In Brazil's public healthcare, only three HET options (fingolimod, natalizumab, and alemtuzumab) are available for around 70% of the population. Alemtuzumab (ALT) was added in 2021 for highly active MS cases after natalizumab failure or contraindication. However, switching therapies is complex due to individual and disease factors.
Objective: To assess the impact of delayed ALT access on maintaining its indication in MS patients.
Methods: A cross-sectional study at São Paulo University's Neuroimmunology Clinic in 2023 included MS patients meeting alemtuzumab criteria set by the Brazilian Ministry of Health in 2021. Data collected during the indication phase included demographics, disease details, and reasons for switching to ALT. Despite being ordered in October 2021, alemtuzumab wasn't available until February 2023. Reassessment was done post-availability.
Results: Initially, 47 patients qualified for alemtuzumab infusion. Three were excluded due to new contraindications (autoimmune diseases, chronic kidney disease). Five had latent tuberculosis requiring treatment first. Seven developed higher disability while awaiting treatment, and two had social risk factors. One had an active autoimmune disease during the latest assessment.
Conclusion: A two-year delay in access leads to missed treatment opportunities for MS patients needing HET. This underscores the importance of patient circumstances and access challenges in treatment selection. Neurologists should consider delayed access in MS treatment decisions, sometimes necessitating alternative offers due to infusion delays impacting outcomes.

DOI: 10.1055/s-0044-1789401

Acute non-autoimmune hepatitis induced by alemtuzumab: a case report

Vanessa Lauanna Lima Silva[1], João Marcus Alves[1], Bárbara Loiola Santos[1], João Pedro Gomes[1], Camila Aquino Cruz[1], Katharina Messias[2], Charles Mantovani[1], Vanessa Daccach[2]
[1]*Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Ribeirão Preto SP, Brazil.*
[2]*Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Hospital das Clínicas, Ribeirão Preto SP, Brazil.*

Address for correspondence: Vanessa Lauanna Lima Silva (email: vanessalauanna@gmail.com).

Abstract

Case Presentation: A 37-year-old female patient with highly-active relapsing-remitting multiple sclerosis (RRMS) was admitted for alemtuzumab treatment. The formal protocol of 12 mg for 5 days with 1 g of methylprednisolone daily for the first 3 days plus concomitantly acyclovir, diphenhydramine, and acetaminophen (< 4 g a day) was performed. On

the third day of infusion, an unexpected rise in her liver function tests was detected. The basal ALT raised from 20 U/L to 1441 U/L on day 3, with an AST of 522 U/L, ALP of 119 U/L, GGT of 433 U/L, and bilirubin of 0.5 mg/dL. There were no signs of acute liver failure, such as encephalopathy, coagulopathy, hepatomegaly or hepatorenal syndrome. Serologies were negative (hepatitis A, B, and C antibodies, cytomegalovirus, and Ebstein-Barr virus IgM). Antinuclear, antimitochondrial, anti-LKM1, and anti-smooth muscle antibodies were negative. The Gastroenterology team was consulted, and a drug-induced liver injury (DILI) associated with alemtuzumab was suspected. The Roussel Uclaf Causality Assessment Method (RUCAM) score was of 6, making DILI "probable". Alemtuzumab was definitely interrupted on the fourth day of treatment, coinciding with a drop in ALT from 440 U/L on day 8. Nowadays, the patient is under regular treatment with rituximab.
Discussion: Alemtuzumab is a monoclonal antibody to human CD52 on lymphocytes. It is a highly-effective therapy for RRMS treatment. Alemtuzumab is related with some adverse events, including opportunistic infections and autoimmunity. Thyroid disorders, immune thrombocytopenic purpura, nephropathies, and autoimmune hepatitis have been described. Despite previously-reported autoimmune hepatitis, DILI is an unexpected adverse effect of this medication.
Final Comments: We herein report a case of acute non-autoimmune hepatitis induced by alemtuzumab in a patient with RRMS during the first round of treatment. To our knowledge, the present is the second published report on DILI associated with alemtuzumab, which highlights the scientific relevance of the present case report.

DOI: 10.1055/s-0044-1789402

Seronegative de novo myasthenia gravis induced by alemtuzumab: a case report

Vanessa Lauanna Lima Silva[1], João Marcus Alves[1], João Pedro Gomes[1], Caroline Medeiros[1], Camila Aquino Cruz[1], Katharina Messias[1], Charles Mantovani[1], Vanessa Daccach[1]
[1]*Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Ribeirão Preto SP, Brazil.*

Address for correspondence: Vanessa Lauanna Lima Silva (email: vanessalauanna@gmail.com).

Abstract
Case Presentation: A 39-year-old female patient with relapsing-remitting multiple sclerosis (RRMS) was elected for alemtuzumab treatment. She had a medical history of diabetes, hypertension, obesity, and NASH. Alemtuzumab was indicated after treatment failure with natalizumab, evidenced by the presence of multiple new enhancing lesions. The formal protocol of 12 mg for 5 days with 1 g of methylprednisolone a day for the first 3 days, and, concomitantly acyclovir, diphenhydramine and acetaminophen, was performed. The first course was in May 2019 and the second course, in June 2020. Approximately one year after the last course, the patient presented with fluctuating muscle fatigue and ptosis, with worsening of the symptoms towards the end of the day. During the investigation for neuromuscular junction disease, anti-AChR and anti-MuSK were negative, and electromyography revealed single-fiber changes with pathological electro-decrement. A thoracic CT scan ruled out the presence of thymoma. Neoplastic screening with full body CT was unremarkable. After diagnosing myasthenia gravis (MG), treatment was started with pyridostigmine and prednisone, with improvement of the symptoms. The patient is currently undergoing treatment with rituximab to manage both autoimmune pathologies.
Discussion: Alemtuzumab, a monoclonal antibody that targets CD52 on lymphocytes, results in the depletion of B and T cells. While it is a highly-effective therapy approved for the treatment of RRMS, alemtuzumab is linked to adverse events, such as opportunistic infections and autoimmune reactions, with thyroid disorders being the most prevalent autoimmune adverse event observed. Notably, myasthenic syndromes represent an exceedingly rare and unexpected adverse effect of this medication, despite its autoimmune mechanism of action.
Final Comments: We herein report a case of a de novo seronegative MG induced by alemtuzumab in a patient with RRMS. To date, there is little data available on this topic. To our knowledge, the present is the second published report on MG following alemtuzumab therapy.

DOI: 10.1055/s-0044-1789403

Impact of multiple sclerosis treatments on the rate of cerebral remyelination assessed by advanced neuroimaging

Vitória Pimentel[1], Daissy Liliana Mora Cuervo[1], Rafael Canani Sommer[1], Alessandra Jahn Gallo[1], Pedro Rodrigues Neves[1], Ana Djulia Tesche[1], Douglas Kazutoshi Sato[1]
[1]*Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil.*

Address for correspondence: Vitória Pimentel (email: vitoriaps.silva@hotmail.com).

Abstract
Background: Multiple sclerosis (MS) is a chronic neurological condition caused by an autoimmune attack to the myelin sheath of the central nervous system axons. Several medications are capable of satisfactorily controlling neuroinflammation and preventing new outbreaks, but there is a lack of options that enhance endogenous remyelination and, thus, mitigate the neurodegeneration associated.
Objective: The present study aims to evaluate the brain remyelination capacity promoted by natalizumab (NTZ) treatment compared to other first-line MS therapies.
Methods: Patients aged 18 to 45 years with relapsing-remitting MS and EDSS scores < 5.5 who started NTZ, teriflunomide, dimethyl fumarate, beta-interferons or glatiramer acetate treatment up to 30 days before inclusion were recruited and then evaluated at baseline, 6 months, and 1 year. Clinical and quality of life parameters were assessed, as well as magnetic resonance imaging (MRI) brain scans and laboratory markers. Advanced quantitative MRI sequences include diffusion-tensor imaging, magnetization-transfer map and normalized leptokurtic-diffusion map (NLDm) calculated from q-Space diffusion. Quantitative changes in baseline chronic lesions and new lesions, with or without gadolinium enhancement, were assessed at 6 months. The values were normalized to a scale of 0 to 100 arbitrary units (a.u.), and the RD values were inverted to indicate a higher myelin content as the a.u. increased.
Results: We included 27 patients (18 NTZ and 9 controls). The preliminary results showed a tendency towards greater remyelination, measured by the change in lesional NLD over 6 months, in the NTZ group (mean-2.4; SD: 5.6; beta $= 7.51$; $p = 0.018$) compared to the control group (mean-5.6; SD: 7.9; beta $= 7.51$; $p = 0.018$) after correction for age, duration of the illness, ethnicity, and previous outbreaks characteristics.

Conclusion: This finding indicates an increased myelin content in the lesions of the NTZ patients compared to the controls, suggesting possible remyelination enhancement. Therefore, highly-effective treatments such as NTZ could improve the endogenous remyelination conditions, helping to stabilize neurological disability and reduce neurodegeneration.

DOI: 10.1055/s-0044-1789404

Use of mobile app to monitor patients with multiple sclerosis

Laisa Leite[1], Barbara Pereira Costa[2], Lays Villar da Silva[2], Ana Clara Morais Alves[2], Lígia Aparecida Machado[2], Carlos Bernardo Tauil[3]
[1]*Oncoclínicas, São Paulo SP, Brazil.*
[2]*Instituto Sinapse de Neurociências Clínicas, Campinas SP, Brazil.*
[3]*Universidade de Brasília, Brasília DF, Brazil.*

Address for correspondence: Carlos Bernardo Tauil (email: cbtauil@gmail.com).

Abstract
Advances and modernization of technology in healthcare have led to improvements in the treatment of serious, long-term illnesses such as multiple sclerosis (MS). Access to technological resources has facilitated the care and monitoring of patients undergoing treatment for MS and consequent adherence to the use of prescribed medications, in addition to controlling adverse reactions and monitoring relapses. Furthermore, it facilitates greater integration between the medical and multidisciplinary teams and the people with MS under monitoring. 1. Development of Clinical Protocols • MS Protocol • Development of Questionnaires (PHQ-9, GAD-7, AUDIT-C [alcohol use], NHANES [education], smoking [score], Epworth Sleepiness Scale, CSAT, Uhtlhoff phenomenon, sexual dysfunction, urinary and intestinal symptoms, sleep pattern, PDDS and MFIS) 2. Structuring dynamic forms • Data structuring of dynamic forms • Created dynamic historical record form for the patient's medical record • Created dynamic Infusion Record form 3. Coupled the dynamic historical record form until patient inclusion • The clinical information already recorded on patients was recorded from diagnosis until the moment the form was filled out (Form information; Date of MS diagnosis, Phenotype, Outbreaks, EDSS, 9HPT, T2SFW, DMD, MRI, and other results) • Added the event (scheduling the infusion with the medication the patient used) • Added the infusion protocol (When the protocol is added, the patient receives preinfusion exam requests) • Infusion record (it is a dynamic form that the nursing team needs to fill out at each patient's infusion with relevant data during the infusion, such as: date of current infusion, SVR, infusion cycle, medication, route of administration, complications during the infusion, among other information). The application proved to be useful for most people with multiple sclerosis who started using it regularly. The medical and multidisciplinary team also recognized benefits regarding patient monitoring.

DOI: 10.1055/s-0044-1789405

"The group's waiting room": a successful experience in the outpatient clinic for demyelinating diseases

Elisa Melo[1], Ivone Fernandes[1], Maria Fernanda Mendes[2]
[1]*Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo SP, Brazil.*
[2]*Santa Casa de São Paulo, Faculdade de Ciências Médicas, São Paulo SP, Brazil.*

Address for correspondence: Elisa Melo (email: elisamvmelo@gmail.com).

Abstract
Background: The presence of patients waiting for their medical appointments is a reality in the Brazilian public healthcare system. The National Humanization Policy of the Brazilian Ministry of Health advocates for welcoming and integrating care through the adoption of healthcare measures and communication among multiprofessional teams. One of the practices adopted by the healthcare team to share experiences, feelings, and knowledge is the "waiting room". In order to minimize this wait, the "The Group's Waiting Room" project was established in 2013, comprising patients, family members, caregivers, social workers, nurses, physiotherapists, neuropsychologists, among others, to provide a welcoming space to reduce anxiety and fears, provide guidance on rights, inform them about the disease, types of treatment, the importance of adherence, and adopting an exercise routine, offering patients, family members, and caregivers a welcoming space to develop a more active and participatory stance in their treatment. This project was interrupted during the pandemic and resumed in 2022, with approximately 250 participants since then.
Objective: To describe "The Group's Waiting Room" experience as part of humanized care for patients with MS, their families, and caregivers.
Methods: Welcoming, integration, and interaction are the keywords. Returning patients engage in conversations and share their experiences with recently-diagnosed patients, thus minimizing their anxiety and doubts. Health team professionals, including doctors, nurses, physiotherapists, social workers, and neuropsychologists, participate in the meetings, along with other invited professionals.
Results: Throughout the meetings, the questions raised by the participants are clarified, and these discussions foster topics for future meetings.
Conclusion: The project initiated in 2013 has been proven to be successful, with the participation of approximately 250 patients, family members, and caregivers.

DOI: 10.1055/s-0044-1789406

Infusional therapies in multiple sclerosis and neuromyelitis optica: long-term experience of a specialized neurological infusional therapy center at a university hospital in Rio de Janeiro

Patricia P. Magalhães Souto[1], Isadora P. Vanzeler[1], João Gabriel Dib Farinhas[1], Kamilla A. Fernandez[1], Fabiana S. Lima[1], Felipe da R. Schmidt[1], Cristiana P. Goes[1]
[1]*Universidade do Estado do Rio de Janeiro, Hospital Universitário Pedro Ernesto, Serviço de Neurologia, Rio de Janeiro RJ, Brazil.*

Address for correspondence: João Gabriel Dib Farinhas (email: jgabrieldib@gmail.com).

Abstract
Multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMOSD) are autoimmune disorders that affect the central nervous system (CNS). Infusional intravenous (IV) therapies have been used successfully in the treatment of relapses and as disease-modifying drugs for both conditions. Our aim is to demonstrate the experience in infusional therapies in MS and NMOSD of a specialized neurological infusional center at Hospital Universitário Pedro Ernesto (HUPE), in Rio de Janeiro. From June 2016 to April 2024,

4,510 infusions were registered in the medical electronic charts of 341 patients. Each patient consults with a physician and is evaluated by experienced nursing staff prior to each infusion. Out of the 341 patients, 109 (31.9%) were on natalizumab (NTZ), 35 (10.26%), on rituximab (RTX), 31 (9%), on the first doses of fingolimod (FTY), 16 (4.7%), on ocrelizumab (OCR), 2 (0.58%), on alemtuzumab, and 1 (0.29%), on eculizumab (ECU). Intravenous methylprednisolone (IVMP) and IV human immunoglobulin (IVIg), mostly used for the treatment of attacks, account for the remaining infusions. The most common adverse events reported, according to treatment, were: NTZ: 4/109 patients – headache (3.6%); 2/109 patients – pruritus (1.83%); RTX: 3 patients: pharyngeal pruritus, headache, nausea, vomiting, and agitation (1/33; 0.03%); sinus tachycardia (1/35; 0.03%); bronchospasm (1/35; 0.03%); FTY: asymptomatic prolonged bradycardia (1/31, 0.03%); OCR: allergic rash (2/16; 0.125%); alemtuzumab: allergic rash (2/2;100%); and ECU: none (0%). No deaths occurred during the observation period. Natalizumab was the most prevalent infusional therapy at our center. Long-term data from our center shows that most DMTs are safe when administered by trained and experienced medical and nursing staff. Most of the adverse events were mild and did not require interruption of treatment.

DOI: 10.1055/s-0044-1789407

MS unit – from concept to practice: analysis of depression, anxiety, fatigue, quality of life, and perception of disease in MS patients from a private MS unit in Rio de Janeiro: a nurse's perspective

Thaís Ribeiro T Miguel[1], João Gabriel Dib Farinhas[1], Felipe da R Schmidt[1]
[1]*Instituto de Ensino e Pesquisa Americas, Rio de Janeiro RJ, Brazil.*

Address for correspondence: João Gabriel Dib Farinhas (email: jgabrieldib@gmail.com).

Abstract
Multiple sclerosis (MS) is an autoimmune disorder that affects the central nervous system (CNS), and MS Units have been proposed to better address the needs of patients under multidisciplinary care. The present study aims to prospectively follow-up patients in a private MS Unit in Rio de Janeiro, focusing on the role of the nurse navigator in the care for MS patients. The nurse will be trained by an experienced neuroimmunologist and will be responsible for specialized nurse consulting exclusively with MS patients. During this consultation, the nurse will apply clinical tests for MS, such as the 25-foot-walk, 9-hole-peg test, as well as collect data from multiple validated medical scales evaluating: depression, anxiety, fatigue, and quality of life respectively. Moreover, the nurse will attest comprehension and educate patients about their diseases. The data will enable us to establish a registry of patients inside the RedCap database. The present is a prospective cross-sectional study with a duration of 24 months. All patients will undergo anamnesis, as well as physical and neurological examinations, performed by a specialist neurologist. Patients will also undergo MRI examinations of the brain, cervical and dorsal spines, routine blood tests, and cerebrospinal fluid examination for further evaluation. Clinical phenotypes and neurological manifestations are related to the scales under study. The present study aims to demonstrate the effectiveness and quality of the nurse navigator in the processes of application, data collection and maintenance of this service in a private MS Unit in Rio de Janeiro.

DOI: 10.1055/s-0044-1789408

Translation and validation of the multiple sclerosis knowledge assessment scale for use in Brazil

Denison Pedrosa[1], Natália Cirino Talim[2], Shirley Lacerda[1], Rodrigo Barbosa Thomaz[1], Rodolfo Francisco Marques[2], Henrique Sued Blanco Silva[2], Júlia Cristina Silva Rezende[2], Guilherme Santos Batista[2], Gabriel Eduardo Coelho Pinto Pinto[2], Lucas Bittar Sesso Freitas[2], Thales Ponsá Pinto[2], Carolina Reis Araújo Abrantes[2], Paulo Pereira Christo[2], Marco Lana-Peixoto[2]
[1]*Hospital Israelita Albert Einstein, São Paulo SP, Brazil.*
[2]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract
Background: Multiple sclerosis (MS) is a chronic condition of the central nervous system that significantly impacts the quality of life of patients. With the recent emergence of various medications for its treatment, the development of patient-reported outcome measures has become increasingly important to ensure adherence. The Multiple Sclerosis Knowledge Assessment Scale (MSKAS) is a tool validated in 2021 and designed to measure patient knowledge about the disease.
Objective: To translate and validate the original English-language MSKAS into Brazilian Portuguese and validate its cultural and linguistic equivalence for application in Brazil.
Methods: The MSKAS consists of 22 true/false statements assessing patient knowledge of MS pathogenesis, clinical manifestations, and treatment. The questionnaire underwent a rigorous translation and cross-cultural adaptation process following standardized guidelines. This involved initial translation by two independent bilingual translators, followed by back translation into English by a native English-speaking professional. Subsequently, a specialized committee, comprising professionals from various disciplines, reviewed and refined the translated version to ensure semantic and conceptual equivalence, adapting the content to the cultural context of the target population.
Results: The Brazilian Portuguese version of the MSKAS exhibited no significant conceptual discrepancies compared to the original English version. Following review and approval by the multiprofessional committee, the final version of the MSKAS in Brazilian Portuguese was deemed to be both linguistically accurate and culturally appropriate for use in Brazil.
Conclusion: The translation and validation of the MSKAS to Brazilian Portuguese is important, as this tool assesses patient understanding of the basic concepts of MS. Analyzing the comprehension of the disease across different regions of the country may aid in the development of educational strategies and enhance the active involvement of patients in their treatment.

DOI: 10.1055/s-0044-1789409

How much do Brazilian multiple sclerosis patients know about their disease? A MSKAS-based study

Denison Pedrosa[1], Shirley Lacerda[1], Rodrigo Barbosa Thomaz[1], Natália Cirino Talim[2], Rodolfo Francisco Marques[2], Henrique Sued Blanco Silva[2], Júlia Cristina Silva Rezende[2], Guilherme Santos Batista[2], Gabriel Eduardo Coelho Pinto Pinto[2], Lucas Bittar Sesso Freitas[2], Thales Ponsá Pinto[2], Carolina Reis Araújo

Abrantes[2], Paulo Pereira Christo[2], Marco Lana-Peixoto[2]
[1]Hospital Israelita Albert Einstein, São Paulo SP, Brazil.
[2]Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract
Background: Multiple sclerosis (MS) is a chronic immune-mediated disorder of the central nervous system, predominantly affecting young adults and leading to progressive disability. Treatment often requires long-term use of medications with potential side effects. Understanding the disease's nature, progression, and treatment options can help patients manage their condition more effectively and adhere to treatment.
Objective: To assess the knowledge level of MS patients about the disease's nature, clinical manifestations, and treatment using the Brazilian Portuguese version of the Multiple Sclerosis Knowledge Assessment Scale (MSKAS).
Methods: Patients diagnosed with MS according to the 2017 MacDonald criteria and cared for at the CIEM MS Research Center, in the city of Belo Horizonte, and Hospital Israelita Albert Einstein, in the city of São Paulo, were included. The participants filled out the MSKAS, which consists of 22 true/false questions on MS etiopathogenesis, course, clinical manifestations, and treatment. Data were analyzed based on age, gender, time since diagnosis, level of schooling, income, and disability severity measured by the Expanded Disability Status Scale (EDSS).
Results: The study included 65 patients, with 40 (61.5%) women and a median age of 40 (range: 17–78) years. Most had more than 8 years of schooling (92%). The majority had relapsing-remitting MS (77%), and 72.3% had an EDSS score $\leq$ 4.0. Regarding MS knowledge, 55.3% considered themselves highly knowledgeable, 37%, reasonably knowledgeable, and 7.7%, poorly knowledgeable. The median MSKAS score was of 19 (range: 13–22).
Conclusion: Most MS patients demonstrated a good understanding of their condition. The MSKAS proved to be a reliable and practical tool to assess patient knowledge about MS. Further studies involving larger patient cohorts across different regions of Brazil could offer valuable insights for the development of educational programs aimed at helping patients better manage their disease and treatment.

DOI: 10.1055/s-0044-1789410

Correlations between multiple sclerosis, cognition, human development index, and social vulnerability

Paulo Sérgio Lisboa[1], Keyla Rejane[2], Ivna Lacerda Pereira Nóbrega[2], Maria Luisa Pereira de Melo[1], José Artur Costa D'Almeida[1], Patrícia Chagas Rocha D'Almeida[2], Gabriela Martins[1], Igor Bessa[1], Lucas Silvestre[1], Carla Welch da Silva[2], Milena Sales Pitombeira[1]
[1]Hospital Geral de Fortaleza, Departamento de Neuroimunologia, Fortaleza CE, Brazil.
[2]Hospital Geral de Fortaleza, Fortaleza CE, Brazil.

Address for correspondence: Paulo Sérgio Lisboa (email: psneuropsi@gmail.com).

Abstract
Background: Multiple sclerosis (MS) is a chronic autoimmune, demyelinating, neurological disease. Cognitive disorders are common in people with MS, and they affect daily activities, professional outcomes, and quality of life.
Objective: To analyze the correlation between cognitive decline and social indices.
Methods: A quantitative, descriptive, and retrospective study aimed to identify the correlation of cognitive decline and social factors such as: longevity, schooling, income, urban infrastructure, human capital, and income/employment. Municipalities in the state of Ceará, Brazil, were adopted as units of analysis, with indicators calculated from demographic census variables. Psychometric data collection used the BICAMS battery.
Results: We evaluated 70 patients (49 with RRMS; 4 with PPMS; and 9 with SPMS): 48 female subjects and 21 male subjects, with a median age of 40.20 (range: 15–68) years. In total, 83% had more than twelve years of schooling (n = 58). The mean EDSS score was of 2.6. High-efficiency medication was used by 49 patients, platform drugs were used by 20 subjects, and 40 patients used psychotropic medication. Overall, 42 patients lived in the capital and 27, in rural areas. The municipalities where the patients resided had an average HDI of 0.71, which is considered medium (between 0.500 and 0.799). The final SVI was also medium (between 0.300 and 0.400), except in the work and income dimension, in which the capital's value is considered low, of 0.283 (n = 42). A total of 23 patients showed decline in visual memory (mean z-score = -3.35), 35 patients, in auditory verbal episodic memory (mean z-score = -1.4), and 18 patients, in information processing speed (mean z-score = -0.62).
Conclusion: No correlation was observed involving human development, urban infrastructure, human capital, and patients with cognitive decline in MS. However, factors such as economy, low income, and unemployment seem to be related to less favorable cognitive outcomes.

DOI: 10.1055/s-0044-1789411

The effect of total dietary antioxidant capacity (TDAC) in clinical and nutritional status in people with neuromyelitis optica spectrum disorder

Carine Costa dos Santos[1], Renan Souto Pereira[1], Alane de Sousa Nascimento Almeida[1], Pedro Henrique Aragão Gomes[1], Larissa Lara de Sousa Avelino[1], Ana Luísa Araújo Brito[1], Virna Luisa Nogueira Mesquita Braga[1], Lia Gomes Crisóstomo Sabóia[1], Ana Beatriz Soares Pontes[1], Ana Clara Sousa de Queiroz Campos[1], Rachel Elizabete Nascimento Serpa[1], Victor Vincent Morais de Lima[1], Gabriela Joca Martins[2], Lorena do Nascimento Rocha Mapurunga[2], Keyla Rejane Frutuoso de Morais[2], Carla Welch da Silva[2], Paulo Sérgio Lisboa[2], Paulo Filho Soares Marcelino[2], Patrícia Chagas Rocha D'Almeida[2], José Artur Costa D'Almeida[2], Maria Luisa Pereira de Melo[1]
[1]Universidade Estadual do Ceará, Fortaleza CE, Brazil.
[2]Hospital Geral de Fortaleza, Fortaleza CE, Brazil.

Address for correspondence: Renan Souto Pereira (email: renanpereira.ce@gmail.com).

Abstract
Background: The environmental risk factors of neuromyelitis optica spectrum disorder (NMOSD) are not fully understood. Some evidence suggests the possible protective effects of antioxidants on the progression of disease.
Objective: To analyze the total dietary antioxidant capacity (TDAC) and its relationship with the clinical and nutritional status of people with NMOSD.
Methods: The present cross-sectional study was approved by the Human Research Ethics Committee of Hospital Geral de Fortaleza (no. 365.222). We included 37 patients with a definite diagnosis of NMOSD, and collected data on demographic, clinical, and anthropometric characteristics. We

evaluated the Expanded Disability Status Scale (EDSS) score, body mass index (BMI) and percentage of body fat (BF%) that was calculated by bioelectrical impedance analysis (BIA). Two 24-hour dietary recalls were obtained, and the TDAC was estimated using the ferric reducing antioxidant potential (FRAP). The variables were expressed as simple frequencies, percentages, and mean, median, and standard deviation values. The normality of the data was verified by the Shapiro-Wilk test. To compare means, we used was the Mann-Whitney test ($p < 0.05$).
Results: The mean age was of 41.9±13.5 years, and there was a predominance of female patients (33 out of 37; 89.2%). Regarding family income, 74,3% of the patients reported receiving 1 to 3 minimum wages, while 75.7% had more than 8 years of schooling, and 78.4% had no professional occupation. According to the BMI, overweight/obesity was prevalent (59.5%), but the BF% was normal in 67.6%. The median EDSS score was of 3.0. The TDAC had a median of 3.7 mmol/1,000kcal, characterizing a diet low in antioxidant nutrients. There were no associations between the TDAC and the EDSS score ($p = 0.775$), the TDAC and the BMI ($p = 0.322$), or the TDAC and the BF% ($p = 0.231$).
Conclusion: Low consumption of antioxidant nutrients was not associated with clinical conditions or nutritional status.

DOI: 10.1055/s-0044-1789412

No correlation found regarding total dietary antioxidant capacity and multiple sclerosis phenotypes or EDSS score

Fernanda Nunes Maia[1], Renan Souto Pereira[1], Alane de Sousa Nascimento Almeida[1], Pedro Henrique Aragão Gomes[1], Larissa Lara de Sousa Avelino[1], Lia Gomes Crisóstomo Sabóia[1], Ana Luísa Araújo Brito[1], Virna Luisa Nogueira Mesquita Braga[1], Ana Beatriz Soares Pontes[1], Ana Clara Sousa de Queiroz Campos[1], Rachel Elizabete Nascimento Serpa[1], Victor Vincent Morais de Lima[1], Gabriela Joca Martins[2], Lorena do Nascimento Rocha Mapurunga[2], Keyla Rejane Frutuoso de Morais[2], Carla Welch da Silva[2], Paulo Sérgio Lisboa[2], Paulo Filho Soares Marcelino[2], Patrícia Chagas Rocha D'Almeida[2], José Artur Costa D'Almeida[2], Maria Luisa Pereira de Melo[1]
[1]*Universidade Estadual do Ceará, Fortaleza CE, Brazil.*
[2]*Hospital Geral de Fortaleza, Fortaleza CE, Brazil.*

Address for correspondence: Renan Souto Pereira (email: renanpereira.ce@gmail.com).

Abstract
Background: The environmental risk factors of multiple sclerosis (MS) are not fully understood. Some evidence suggest the possible protective effects of antioxidants on the etiology and progression of the disease.
Objective: To investigate the relationships involving total dietary antioxidant capacity (TDAC), multiple sclerosis phenotypes, and the score on the Expanded Disability Status Scale (EDSS) in people with MS (PwMS).
Methods: The present descriptive study was approved by the Human Research Ethics Committee of Hospital Geral de Fortaleza (no. 365.222). We included 127 patients with an MS diagnosis, and collected data on demographic, clinical (disease phenotype and– EDSS score), and anthropometric (body mass index, BMI, and body fat percentage, BF%) characteristics. Two 24-hour dietary recalls were obtained, and the TDAC was estimated using the ferric reducing antioxidant potential (FRAP). The variables were expressed as simple frequencies, percentages, and mean, median, and standard deviation values. The Mann-Whitney test and the Spearman correlation were performed regarding the variables and the TDAC.
Results: The mean age was of 35±8.4 years, with a predominance of female subjects (81.9%), and 45.7% of the patients had an income > 6 minimum wages. Regarding the clinical form of the disease, most patients (88.2%) had RRMS, with a mean time since diagnosis of 5.6±5.5 years. The median EDSS score was of 1.0, ranging from 0.0 to 9.0. According to the BMI, overweight/obesity was prevalent (59.5%), but the BF% was normal in 67.6% Of the sample. The median TDAC was of 8.5 mmol/1,000kcal. There were no associations involving the TDAC and the clinical form of the disease ($p = 0.999$) or the EDSS score ($p = 0.681$).
Conclusion: According to the findings, the TDAC does not show any correlation with either the clinical form of multiple sclerosis or the EDSS score. More studies with a larger number of patients are needed to confirm this result.

DOI: 10.1055/s-0044-1789413

Rehabilitation access profile of patients with progressive multiple sclerosis at reference center in Northeastern Brazil

Rodrigo da Ponte Barbosa[1], Keyla Rejane[1], Matheus Rolim Mendes de Alencar[1], Gabriela Martins[2], José Artur Costa D'Almeida[2], Milena Sales Pitombeira[2], Ivna Lacerda Pereira Nóbrega[1]
[1]*Hospital Geral de Fortaleza, Fortaleza CE, Brazil.*
[2]*Hospital Geral de Fortaleza, Departamento de Neuroimunologia, Fortaleza CE, Brazil.*

Address for correspondence: Rodrigo da Ponte Barbosa (email: rodrigodaponte.fisiatria@gmail.com).

Abstract
Background: Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system associated with neurodegeneration. It is a potentially disabling disease which may have impact on function and quality of life.
Objective: To describe the access to rehabilitation services among progressive MS (PMS) patients at a hospital in Northeastern Brazil.
Methods: Out of 42 PMS patients regularly followed up between 2020 and 2024, we included 32 patients from whom rehabilitation information was available. Clinical and epidemiological data were extracted from the platform of the Brazilian National Database for Multiple Sclerosis (BRANDO). Data regarding access to multidisciplinary rehabilitation was collected through a phone call survey as an institutional initiative after the inclusion of a physiatrist in our team.
Results: Out of 32 patients with a PMS diagnosis, 22 (68.7%) were female, and the median age was of 49 years (range: 23–76). The median EDSS score was of 6.0 (range: 3.0–9.0), and 9 (28%) patients reported being unemployed due to MS. In total, 16 (50%) used walking aids (walkers: 10; canes: 4, and crutches: 2), 10 (31%) used a wheelchair, 6 (18%) did not need assistive devices for ambulation. Moreover, 30 (94%) patients had undergone some type of rehabilitation treatment during the course of the disease, and 2 (6%) had never had access to rehabilitation therapy. Among the patients under rehabilitation, 17 (57%) had a mean time of uninterrupted treatment of 60 (range: 1–120) months, and 13 (43%) were not enrolled in a rehabilitation program, with a mean time until the discontinuation of therapies of 30 (range: 1–60) months.
Conclusion: Rehabilitation is essential for the treatment and maintenance of functionality among MS patients with disability. The present study showed that a high percentage of PMS patients had access to rehabilitation programs, but with premature discontinuation, even among patients with some

sort of assistive device for mobility, showing the need for rehabilitation services for our patients.

DOI: 10.1055/s-0044-1789414

Recognizing Weston-Hurst syndrome: a case report

Alana Bacelar Limeira Sales[1], Cesar Minoru Toita Koga[1], Samia Talise El Horr de Moraes[1], Caio César Diniz Disserol[1], Claudia Suemi Kamoi Kay[1]
[1]*Universidade Federal do Paraná, Hospital de Clínicas, Curitiba PR, Brazil.*

Address for correspondence: Alana Bacelar Limeira Sales (email: alanabls@hotmail.com).

Abstract

We herein report the case of a 27-year-old female patient with acute tetraparesis, diffuse paresthesias, and drowsiness 5 days after generalized myalgia, cough, and fatigue. Within a day, she became comatose and was transferred to the intensive care unit. Brain and spinal cord MRI scans revealed multifocal white-matter demyelinating lesions and longitudinally-extensive myelitis associated with hemorrhagic lesions in both the brainstem and spinal cord. An extensive investigation yielded negative results, including AQP4, MOG, and antineuronal antibodies panel. Treatment was administered with methylprednisolone, plasmapheresis, immunoglobulin, and cyclophosphamide, with partial recovery. After 118 days, the patient was discharged with quadriplegia, with discreet improvement in the upper limbs, and preserved consciousness. Not only the clinical presentation, with rapidly progressive and severe course, but also the MRI scans were compatible with hemorrhagic acute disseminated encephalomyelitis (ADEM), also known as Weston-Hurst syndrome. Hemorrhagic ADEM is considered a variant of ADEM, most commonly seen in adults, in contrast to its prototype disease. To date, the etiology is still not comprehended; however, it has been hypothesized to be an autoimmune process associated with viral or bacterial infection causing molecular mimicry. Considering the high mortality rate (of up to 70%), early diagnosis and referral to specialized centers are crucial for appropriate therapy, based on immunosupression.

DOI: 10.1055/s-0044-1789415

Functional disability of neuromyelitis optica spectrum disorder in Brazil

Bianca Oliveira[1], Bruna Rocha[2], Cleide Pires[2], Wedson Santos[2], Juliana Almeida[2], Dulcila Torres[2]
[1]*Centro de Referência em Esclerose Múltipla da Paraíba, João Pessoa PB, Brazil.*
[2]*Associação Brasileira de Neuromielite Óptica, Salvador BA, Brazil.*

Address for correspondence: Bianca Oliveira (email: oliveira_bes@hotmail.com).

Abstract

Background: Neuromyelitis optica spectrum disorder (NMOSD) is a central nervous system antibody-mediated disease which affects mainly the optic nerves and the spinal cord, but it may also present with acute brainstem syndrome, acute diencephalic syndrome, and cerebral syndrome with typical brain lesions. The disorder was identified as a distinct clinical entity with the discovery of aquaporin-4 immunoglobulin G antibodies (AQP4-IgG).
Objective: To assess aspects of functional disability found in 50 self-reported questionnaires.
Methods: The present is a cross-sectional observational study that used a self-reported questionnaire filled out by 50 individuals diagnosed with NMOSD. It was made available through an online platform after the individuals provided informed consent and distributed in online groups of NMOSD patients. This questionnaire was composed of questions on sociodemographic and functional aspects. General data were expressed through descriptive analysis, and count data were expressed through frequencies and percentages.
Results: In total, 41 valid questionnaires were obtained from the 50 individuals who filled it out throughout 2023, a process facilitated through a collaboration with the Brazilian Association of NMOSD (Associação Brasileira de Neuromielite Óptica, ABNMO, in Portuguese). The respondents were predominantly female (79%) and Caucasian (41%), with 49% in the age group between 20 and 39 years. Despite the fact that 57% of them had completed higher education, most (56%) were either unemployed or on leave. Approximately 42% relied on the public health system for medical care. Regarding treatment, 72% reported using off-label medications, while 25% relied solely on oral steroids. Visual and/or motor disability was reported by 49% of the patients, with 21% requiring a cane or walker for ambulation.
Conclusion: The present is the first collection of functional and social data through ABNMO data. These features are very important to know the functional impact on quality of life experienced by Brazilian patients. Those aspects can help in public management projects and in the development of a diagnosis and on-label treatment protocol aimed at the profile of NMOSD patients in Brazil.

DOI: 10.1055/s-0044-1789416

Sociodemographic profile of neuromyelitis optica spectrum disorder patients in Brazil

Bianca Oliveira[1], Daniel Lima Junior[2], Bruna Rocha[3], Cleide Pires[3], Wedson Santos[3], Juliana Almeida[3], Dulcila Torres[3]
[1]*Centro de Referência em Esclerose Múltipla da Paraíba, João Pessoa PB, Brazil.*
[2]*University of California San Diego, San Diego CA, United States.*
[3]*Associação Brasileira de Neuromielite Óptica, Salvador BA, Brazil.*

Address for correspondence: Bianca Oliveira (email: oliveira_bes@hotmail.com).

Abstract

Background: Neuromyelitis optica spectrum disorder (NMOSD) is a rare and severe inflammatory autoimmune disease of the central nervous system (CNS) that was identified as a distinct clinical entity with the discovery of aquaporin-4 immunoglobulin G antibodies (AQP4-IgG).
Objective: To assess the sociodemographic profile of the respondents of a self-reported questionnaire.
Methods: The present is a cross-sectional observational study that used a self-reported questionnaire composed of questions on sociodemographic aspects. General data were expressed through descriptive analysis, and count data were expressed through frequencies and percentages.
Results: The survey was answered by 50 people in 2023 through a partnership with the Brazilian Association of NMOSD (Associação Brasileira de Neuromielite Óptica, ABNMO, in Portuguese), and we obtained 41 valid filled-out questionnaires. In relation to sex, we found that 79% of the respondents were female, and, regarding skin color, 41% were Caucasians and 23% were Black. Assessing time since the NMOSD diagnosis, 13% had had it for 7 years, and 38%, for 1 year. Furthermore, despite the fact that 57% of the

respondents had completed higher education to a Ph.D., 56% were unemployed or on leave, receiving social security benefits.
Conclusion: The present the first collection of epidemiological and social data through ABNMO data. These features are important to know our the characteristics of Brazilian patients that may assist in the development of public management projects, as well as a diagnosis and treatment protocol aimed at the profile of NMOSD patients in Brazil.
!

DOI: 10.1055/s-0044-1789417

The importance of a psycho-emotional support group for the quality of life of people with NMO

Bruna Rocha[1], Cleide Pires[1], Wedson Santos[1], Juliana Almeida[1], Dulcila Torres[1], Bianca Oliveira[2]
[1]*Associação Brasileira de Neuromielite Óptica, Salvador BA, Brazil.*
[2]*Centro de Referência em Esclerose Múltipla da Paraíba, João Pessoa PB, Brazil.*

Address for correspondence: Bruna Rocha (email: bruna.rochasilveira@gmail.com).

Abstract
Background: In a quantitative survey carried out in 2024, 13% of NMO patients in Brazil did not use medication for psychological and emotional control before diagnosis, a rate that rises to 23% after diagnosis. In addition, 54% of the patients reported having psychological problems (depression, anxiety, mood swings) after their NMO diagnosis, demonstrating the need for psychotherapeutic support for this group.
Objective: To demonstrate how the Psycho-emotional Support Group (Grupo de Apoio Piscoemocional, GAP, in Portuguese), created in 2022, provides a virtual space for listening, talking, and emotional elaboration for patients diagnosed with NMO, as well as for sharing experiences and learning new coping strategies.
Methods: The GAP has 45 people registered, with virtual meetings twice a month, with an average of 10 participants per meeting, aged between 18 and 57 years. The meetings are coordinated by a psychologist who proposes dynamics to help participants develop their coping strategies.
Results: The participants' initial emotional demand revolves around the challenge of the onset of the first symptoms of NMO and the delay in concluding the diagnosis. This period is marked by high anxiety, depressive episodes, and a sense of emotional confusion. Another challenge is adapting to the new reality of the body, with symptoms such as fatigue, low vision, pain, limited movement, among others, which require that the patients develop a new perspective on themselves on and their relationship with their family, work, and society.
Conclusion: The exchange of experiences during the GAP meetings has led to an increase in the repertoire of strategies. One participant said: "I hadn't thought of this before", referring to the explanation given about the importance of clear communication between caregiver and the person being cared for. Another participant reported becoming aware of the possibility of continuing life after diagnosis, after hearing the story of overcoming a wheelchair user.

DOI: 10.1055/s-0044-1789418

Social and emotional support for men with NMO

Bruna Rocha[1], Wedson Santos[1], Juliana Almeida[1], Cleide Pires[1], Bianca Oliveira[2], Dulcila Torres[1]
[1]*Associação Brasileira de Neuromielite Óptica, Salvador BA, Brazil.*
[2]*Centro de Referência em Esclerose Múltipla da Paraíba, João Pessoa PB, Brazil.*

Address for correspondence: Bruna Rocha (email: bruna.rochasilveira@gmail.com).

Abstract
Background: Studies show a higher incidence of NMO in women compared to men. In a qualitative study carried out in 2024, data showed that, among the participants diagnosed with NMO, 21% were male, and 79% were female. Patients generally show emotional and psychological difficulties from the first symptoms to the conclusion of the diagnosis and afterwards with coping with their new life condition.
Objective: To point out the importance of the participation of men with NMO in the Psycho-emotional Support Group (Grupo de Apoio Piscoemocional, GAP, in Portuguese) created in 2023 by the Brazilian Neuromyelitis Optica Association (Associação Brasileira de Neuromielite Óptica, ABNMO, in Portuguese), which enables them to reframe their experience with the diagnosis and rebuild themselves, their masculinity, their sexuality, and their role in their families and in society.
Methods: The GAP has 13 members, with monthly virtual meetings, with an average per meeting of 4 participants aged between 18 and 48 years. The topics of the meetings are suggested by the patients according to their demands and are worked on through sharing experiences, conscious breathing and body awareness exercises, mindfulness exercises, and the development of new coping strategies.
Results: The participants are able to address their issues freely with the group, and they are welcomed by the others. According to one participant, hearing people share their experiences made it possible for him to reduce his anxiety, as he realized that there were others with demands similar to his own, and that there were possible ways of dealing with the new situation. Sexual impotence is a common and challenging issue for some, as it affects their concepts of masculinity.
Conclusion: The participation of men with NMO in the GAP provides a safe space for talking, listening, and working through issues related to masculinity. The possibility of being vulnerable in a group of equals helps these patients gain new perspectives on their lives after the diagnosis.

DOI: 10.1055/s-0044-1789419

Impact of motor and visual sequelae on the perception of functional performance in people with neuromyelitis optica

Bruna Rocha[1], Bianca Oliveira[2], Juliana Almeida[1], Dulcila Torres[1], Wedson Santos[1], Cleide Pires[1]
[1]*Associação Brasileira de Neuromielite Óptica, Salvador BA, Brazil.*
[2]*Centro de Referência em Esclerose Múltipla da Paraíba, João Pessoa PB, Brazil.*

Address for correspondence: Bruna Rocha (email: bruna.rochasilveira@gmail.com).

Abstract
Background: Neuromyelitis optica spectrum disorders (NMOSD) are a group of inflammatory, demyelinating diseases characterized by six main clinical syndromes, including acute myelitis and optic neuritis. On average, 50% of the cases present severe visual and motor sequelae after 5 years of evolution, with a significant impact on the functionality of these individuals.
Objective: To describe the perception of individuals with NMOSD about the impact of motor and visual sequelae on the performance of daily activities and locomotion.

Methods: The present was a cross-sectional observational study using a self-reported questionnaire created by health professionals who are members of the Brazilian Neuromyelitis Optica Association (Associação Brasileira de Neuromielite Óptica, ABNMO, in Portuguese). The questionnaire was developed with questions about sociodemographic and healthcare characteristics, and the presence of symptoms and their impact on the performance of daily activities and locomotion. It was made available for completion by people diagnosed with NMOSD via an online platform after informed consent was obtained. The general data was expressed through descriptive analysis, and the count data, through frequencies and percentages.
Results: A total of 41 of the 55 individuals contacted filled out the questionnaire: 79% were female, 38% had been diagnosed for up to 1 year, 35% had motor and visual sequelae (30% had only motor sequelae, and 25%, only visual sequelae), and 7.5% had no sequelae. Regarding the impact on daily activities, 60% of the individuals with motor sequelae needed help to perform them. Regarding locomotion, 32.5% needed to use some kind of aid (cane, walker or wheelchair).
Conclusion: The motor and visual sequelae caused by NMOSD have a considerable impact on independence regarding daily activities and locomotion, even in individuals who have been recently diagnosed.

DOI: 10.1055/s-0044-1789420

Retinal evaluation with spectral domain-optical coherence tomography in eyes with previous optic neuritis and neuromyelitis optica spectrum disorders or anti-myelin oligodendrocyte glycoprotein antibody-associated disease

Clarissa dos Reis Pereira[1], Thais de Souza Andrade Benassi[1], Luiz Guilherme Marchesi Mello[2], Thiago Gomes Filgueiras[1], Ana Beatriz Ayroza Galvão Ribeiro Gomes[3], Laila Kulsvehagen[3], Anne-Katrin Proebstel[3], Samira Luisa Apóstolos-Pereira[4], Dagoberto Callegaro[5], Mario Luiz Ribeiro Monteiro[1]
[1]*Universidade de São Paulo, São Paulo SP, Brazil.*
[2]*Universidade Federal do Espírito Santo, Vitória ES, Brazil.*
[3]*University Hospital Basel, Basel, Switzerland.*
[4]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.*
[5]*Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.*

Address for correspondence: Clarissa dos Reis Pereira (e-mail: clarissa_rp@yahoo.com.br).

Abstract
Objective: To compare the thickness of retinal layers using spectral domain-optical coherence tomography (SD-OCT) in patients with previous optic neuritis (ON) and neuromyelitis optica spectrum disorders (NMOSD) who have positive anti-aquaporine4 antibody (AQP4) or anti-myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), or who are negative for both IgG antibodies.
Methods: We included 49 patients who were divided into 3 groups: ON-AQP4 (n = 21), ON-MOGAD (n = 19), and ON double-IgG seronegative (ON-DSN; n = 9). The control group was composed of 19 patients. The patients were submitted to a complete ophthalmic evaluation, including 24-2 standard automated perimetry and SD-OCT with acquisition of peripapillary retinal nerve fiber layer (pRNFL), macula full-thickness (mFT), and the following segmented retinal layers: macular-RNFL (mRNFL), ganglion cells (GCLs), inner plexiform (IPL), inner nuclear (INL), outer plexiform (OPL), outer nuclear (ONL), and photoreceptors (PhL). The mean thickness was obtained for each layer, and the visual field mean sensitivity (VFMS) was also calculated. Data were compared using GEE models, and values of $p < 0.001$ were considered statistically significant.
Results: The difference previously observed that the OPL was thinner in the eyes of ON-AQP4 patients than in the eyes of ON-MOGAD patients was not confirmed, with strong statistical significance ($p = 0.04$). Yet, the inner retina until the INL was thinner than that of the controls in all three ON groups, but the measurements were similar among the affected groups. The pRNFL was thinner than that of the controls only among the eyes of the ON-AQP4 and in the ON-MOGAD groups, but also equivalent between these two ON groups. The VFMS of the ON-AQP4 patients was significantly lower compared with that of the other two affected groups ($p < 0.001$). All three groups had reduced VFMS compared to that of the controls ($p < 0.001$).
Conclusion: The visual function of the ON-AQP4 group was more severely compromised than that of the other ON groups, but the structural OCT retinal measurements were similar among the affected groups. Hence, we still need to unravel the evidence of structural-functional dissociation in these cases.

DOI: 10.1055/s-0044-1789421

Challenges in the diagnosis and management of MOG-IgG associated disease (MOGAD) in Brazil

Daissy Liliana Mora Cuervo[1], Douglas Kazutoshi Sato[1], Pamela Hellen Fussinger Novaz[2]
[1]*Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil.*
[2]*Universidade do Vale do Rio dos Sinos, São Leopoldo RS, Brazil.*

Address for correspondence: Daissy Liliana Mora Cuervo (email: lilianamoracuervo@yahoo.com).

Abstract
Background: In January 2023, the International Panel proposed diagnostic criteria for myelin oligodendrocyte glycoprotein (MOG)-IgG-associated disease (MOGAD). The criteria require positivity for serum MOG-IgG using live or fixed cell-based assays (CBAs), as well as the definition of the groups into clear positives and low positives based on the antibody titers. Accessing and reporting the MOG-IgG assays are challenging.
Objective: To identify the status of the access to MOG-IgG assays and treatments in reference centers in Brazil.
Methods: We conducted an online survey for MS neurologists in Brazil based on referral centers using the RedCap platform. Only one response per center was included. We collected information about the center and the state of origin. We investigated the availability and the type of MOG-IgG assay, and if the report included quantitative information. We also collected information about the treatment options offered to MOGAD patients.
Results: We received responses from 15 centers based in 9 Brazilian states: Bahia, the Federal District, Paraná, Paraíba, Pernambuco, Rio de Janeiro, Rio Grande do Sul, Santa Catarina, and São Paulo. We found that the rate of availability of MOG-IgG assays in their local labs was 23.5%, with 17.6% reporting no access to the tests. All centers had access to aquaporin-4 IgG for the diagnosis of neuromyelitis optica spectrum disorder. Only 13.3% reported ELISA or WB for testing MOG-IgG. The MOG-IgG titers were reported in 40% of the centers, as well as positive/negative results in 46.7%. Most centers start chronic treatments only after a relapse, such as rituximab, immunoglobulin, oral steroids, and/or oral immunosuppressive drugs.

Conclusion: We found that there is a lack of availability of MOG-IgG assays in local labs. There is still use of methods that are not recommended, such as ELISA for MOG-IgG, which increases the risk of false-positive results. The MOG-IgG titers or clear/low positive reporting is low.

DOI: 10.1055/s-0044-1789422

Susac syndrome: remember to see and hear

Elisangela Ferraz Pazinato[1], Alex Eduardo Silva[1], Marlos Aureliano Dias de Sousa[1], Ana Luisa Rufino de Sousa[1], Amanda Soares Pimenta[1], Daniela Aparecida Lima Viana[1], Giovani Zago Borges[1], Joao Henrique da Matta Clementino[1]
[1]*Universidade Federal do Triângulo Mineiro, Uberaba MG, Brazil.*

Address for correspondence: Elisangela Ferraz Pazinato (email: elisangelapazinato@gmail.com).

Abstract
Case Presentation: We herein report the case of a 23-year-old male patient, with complaints of dysarthria, paresthesia in the right hand, tinnitus in the right ear, diplopia, and sudden scotoma in the left eye, without associated cognitive complaints, but with a report of slowing of thought observed by the family. On a magnetic resonance imaging scan of the skull, there was evidence of involvement of the corpus callosum by "snow ball"; on arteriography, there was occlusion of branches of the ophthalmic arteries bilaterally; audiometry showed sensorineural deafness; and fluorescent retinography showed occlusion of the arteriolar branch of the right eye and arteriole branches in the lower arch and temporal periphery of the left eye. The clinical presentation and results of the complementary exams were related with Susac syndrome. Immunosuppression was performed with corticosteroids, azathioprine, and immunoglobulin, with partial response. After two months, the patient evolved with short- and long-term memory changes, headache, paresthesias, and bilateral tinnitus, and immunosuppression was adjusted for corticosteroids, immunoglobulin, and cyclophosphamide, with stabilization of the disease.
Discussion: Susac syndrome is a rare and severe disease, of probable autoimmune etiology, which, due to the occlusion of microvessels, causes small infarctions in the central nervous system, inner ear, and retina. It is characterized by the clinical triad of encephalopathy, sensorineural hearing loss, and visual impairment. The treatment is based on long-term immunosuppression.
Final Comments: The diagnosis of Susac syndrome is challenging, given its rarity and the incomplete presentation of the initial phase, which expands the possibilities of differential diagnoses, which include demyelinating, autoimmune, and vascular-occlusion diseases. In addition to other neurological pathologies, psychiatric and otorhinolaryngological pathologies are also among the hypotheses to be considered throughout the propedeutics.

DOI: 10.1055/s-0044-1789423

Water channelopathies beyond NMOSD: a pathophysiological discussion on two real-world clinical cases

Gustavo Figueira[1], Paula Soares[1], Raquel Silveira[1], Viviane Carvalho[1], Alexandra Seide Cardoso Vidal[1], Matheus Castro[1], Fernando Faria Andrade Figueira[1]
[1]*Hospital São Francisco na Providência de Deus, Rio de Janeiro RJ, Brazil.*

Address for correspondence: Gustavo Figueira (email: gustavo@ffigueira.net).

Abstract
Background: The functions of water channels have been clarified since the 1950s, and their disorders are now well recognized as autoimmune, toxic or vascular. Neuromyelitis optica remains as one of the most significant neurological water channelopathies, involving immune attack of a well-defined autoantibody to water channels not only on the optic nerves and spinal cord but also on the brain. On the other hand, a more diffuse pattern of dysfunction triggered by toxicity and/or vascular insult targeting the structures of water channel evolves acutely as an encephalopathy syndrome, potentially but not always reversible.
Objectives: We herein present two cases of posterior reversible encephalopathy syndrome (PRES), its different pathophysiological mechanisms, and the possible correlations to NMOSD management.
Methods: In the first case, a patient with hypertensive renal disease on hemodialysis was admitted to the ER on a hypertensive crisis and with generalized convulsive epileptic status. In the second case, a woman with bilateral nephrectomy and renal transplantation, immunosuppression with tacrolimus and steroids, was also admitted to the ER with a generalized convulsive epileptic status.
Results: Both patients shared comorbidities. They were admitted to the ICU due to acute encephalopathy, and they had good outcomes after proper management. The first patient showed parieto-occipital cortical linear areas of hyperintense signal on T2W/FLAIR with patches of diffusion restriction, while the second exhibited a holohemispheric watershed pattern involving cortical and periventricular areas with hyperintense signal on T2W/FLAIR and no diffusion restriction.
Conclusion: We present two hypotheses for PRES pathophysiology: the hemodynamic hypothesis, in which rapid increase in blood pressure leads to hyperperfusion, breakdown of autoregulation, vascular leakage, and vasogenic edema; and the neurotoxicity hypothesis, which suggests endothelial dysfunction due to endogenous or exogenous toxins, also leading to vascular leakage and vasogenic edema. We finally discuss the possible implication of PRES on NMOSD patients, some of whom have undergone rituximab treatment, as well as a possible role of anti-aquaporin 4 antibody on its mechanism.

DOI: 10.1055/s-0044-1789424

Exploring the relationship between ibrutinib therapy and neuromyelitis optica spectrum disorders: a case report

Ana Carolina Mourão Passos[1], Antônia Quarti de Andrade[1], Isabella de Oliveira Santana[1], Gutemberg Augusto Cruz dos Santos[2]
[1]*Instituto de Educação Médica, Rio de Janeiro RJ, Brazil.*
[2]*Universidade Federal Fluminense, Niterói RJ, Brazil.*

Address for correspondence: Gutemberg Augusto Cruz dos Santos (email: gutemberg.c.santos@gmail.com).

Abstract
Case Presentation: We herein present the case of a 58-year-old female patient diagnosed with CLL in 2021, who had been undergoing ibrutinib therapy and, in May 2023, experienced paresthesia and dysesthesia in her lower limbs, accompanied by sensory disturbance. Furthermore, muscle weakness was observed in her lower limbs and right upper limb, leading to difficulties in mobility and urinary retention. Subsequently, she was admitted to the hospital in July 2023 for

comprehensive examinations, including laboratory tests, infectious screenings, autoimmune assessments, imaging studies, cerebrospinal fluid (CSF) analysis, serological tests, and blood cultures. She was diagnosed with longitudinal transverse myelitis (TM) and commenced pulse therapy with corticosteroids, exhibiting partial improvement before being discharged for further outpatient investigation. Presently, she exhibits paraparesis with indications of pyramidal release. In January 2024, her serum tested positive for anti-aquaporin 4 antibodies at a titer of 1/10, confirming the diagnosis of neuromyelitis optica spectrum disorders (NMOSD), leading to the initiation of rituximab treatment.
Discussion: An autoimmune disease that primarily affects the optic nerves and the spinal cord, NMOSD is characterized by recurrent attacks of inflammation in the optic nerves and the spinal cord. Ibrutinib is a medication used in the treatment of certain types of cancer, acting through the inhibition of Bruton tyrosine kinase (BTK), which plays a key role in B-cell signaling. By inhibiting BTK, ibrutinib reduces the production of certain immune cells. Therefore, it is important to recognize that ibrutinib may have effects on the immune system.
Conclusion: Ibrutinib, like any medication affecting the immune system, can influence the development or progression of NMOSD. There is no conclusive evidence establishing a direct relationship between its use and the development of the disease. Therefore, if a patient experiences symptoms suggestive of NMOSD, it is essential to recognize the risk and perform appropriate tests.

DOI: 10.1055/s-0044-1789425

Brain lesions characteristic of NMOSD and the impact of treatment on radiological evolution: a case report

Isadora Cunha Leão Figueredo[1]
[1]*Hospital do Servidor Público Estadual de São Paulo, São Paulo SP, Brazil.*

Address for correspondence: Isadora Cunha Leão Figueredo (email: isacunhadora@gmail.com).

Abstract
Case Presentation: A 36-year-old woman presented with tetraparesis associated with paresthesia of her hands and feet. One year before, she had been experiencing significant weight loss associated with nausea and vomiting. Upon physical examination, she presented weakness of grade 3 in the upper and lower limbs. Her visual acuity was of 20/20 bilaterally. The rest of the neurological exam was normal. She underwent a cranial MRI scan, which evidenced hypersignal in the medulla, pons, periaqueductal predominance, and area postrema, in addition to involvement in the hypothalamus. The MRI scans of the orbit and spinal cord did not show changes. Anti-aquaporin 4 antibody was positive in the blood. Even before the antibody result, treatments with intravenous methylprednisolone for 5 days and plasmapheresis also for 5 days were started. The patient presented complete improvement of the symptoms, walking without changes, without other sequelae. We decided to start rituximab as a maintenance treatment. In a control MRI scan, the patient showed a significant reduction in signal changes in previously-presented lesions.
Discussion: Neuromyelitis optica spectrum disorder (NMOSD) is characterized by preferential involvement of the optic nerve and spinal cord. However, brain involvement can occur in at least half of the cases, generally with non-specific lesions. In less than 10% of the cases, it may present with typical and more serious lesions, in regions rich in aquaporin 4 channels, periaqueductal gray matter, the hypothalamus, and the periventricular region, lesions such as those presented by the patient herein described.
Final Comments: Rapid clinical suspicion based on typical brain lesions and introduction of treatment at an optimal time change the clinical outcome and reduce morbidity and mortality in patients with NMOSD, in addition to the impact on the radiological evolution of MRI lesions.

DOI: 10.1055/s-0044-1789426

Evaluation of neuromyelitis optica spectrum disorder in patients under rituximab and applicability of no responsiveness criteria for first-line therapies: real-world data in settings with limited resources

Ivna Lacerda Pereira Nóbrega[1], José Artur Costa D'Almeida[2], Igor Bessa[2], Gabriela Martins[2], Lucas Silvestre[2], Milena Sales Pitombeira[2]
[1]*Hospital Geral de Fortaleza, Fortaleza CE, Brazil.*
[2]*Hospital Geral de Fortaleza, Departamento de Neuroimunologia, Fortaleza CE, Brazil.*

Address for correspondence: Ivna Lacerda Pereira Nóbrega (email: ivnalacerda@gmail.com).

Abstract
Background: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune astrocytophaty that primarily affects the optic nerve, spinal cord, and periventricular areas. Although new medications have been approved for the management of NMOSD, to date there is no universal treatment protocol, and accessibility is heterogeneous, especially in resource-limited settings. The current treatment options include classic immunosuppressants (IS) and rituximab (RTX).
Objective: To analyze the clinical and epidemiological profile of patients with NMOSD using RTX, and to evaluate whether patients who have failed classic IS and were escalated to RTX can be identified early based on clinical and demographic criteria.
Methods: The present was a single-center retrospective study which included NMOSD patients under classic IS and RTX treatment from 1995 to November 2022. Failure was considered as one severe relapse. In the population receiving RTX as a second-line therapy, the clinical predictors of non-responsiveness to classic IS used as criteria were age under 35 years and severe attack at disease onset.
Results: Out of 105 NMOSD patients regularly followed up at our reference center, 26% (n = 27) were under RTX treatment, with median follow-up of 108 months. Out of those, 96% (n = 26) were female, with a median age of 41 (range: 21–77) years, and a median EDSS score of 4 (range: 1–8.5); 85% (n = 23) were anti-AQP4 seropositive, and 88.8% (n = 24) were relapse-free under RTX treatment. Out of the 20% (n = 21) using RTX as a second-line therapy, 30.7% met both criteria: disease onset under 35 years of age and severe attack that determined a risk of 22.5% of not responding to classic IS, while the absence of both criteria was associated with a 4.6% risk.
Conclusion: Rituximab is likely an effective drug for NMOSD treatment in a resource-limited and real-world setting. Younger age and severe attack at disease onset can be used as predictors of poor response to classic IS and support the early initiation of highly-effective medications.

DOI: 10.1055/s-0044-1789427

Pediatric patient with acute disseminated encephalomyelitis with MRI scans characteristic of multiple sclerosis

Joana Laurindo da Silva[1], Olga Cassol Silva[1], Pablo Wanrick Silva Ferreira[1], André Luiz Pereira Martins[1], Eduardo Ferracioli Fusão[2]
[1]*Hospital Governador Celso Ramos, Florianópolis SC, Brazil.*
[2]*Hospital Infantil Joana de Gusmão Florianópolis SC, Brazil.*

Address for correspondence: Joana Laurindo da Silva (email: joanalaurindo@hotmail.com).

Abstract
Case Presentation: A 6-year-old boy presented to the Emergency Room of a Hospital in the city of Florianópolis, Brazil, with behavioral arrest and staring eyes that lasted more than two hours and progressed with lowered level of consciousness. He was being treated for an upper-respiratory-tract infection with symptomatics. Antiepileptic drugs were administered, with resolution of the seizures. The brain magnetic resonance imaging (MRI) scan performed was compatible with acute disseminated encephalomyelitis (ADEM). He was treated with intravenous methylprednisolone, exhibiting great recovery. A control MRI scan after three months of the hospitalization showed many white matter lesions, some of them with enhancement, consistent with MS. The patient was asymptomatic during this period. The test for MOG autoantibody was negative. The boy was diagnosed with possible MS and started on interferon beta. After three years, he maintained an EDSS score of zero, although the MRI showed that he continued to accumulate new brain lesions. Therefore, when the boy becomes older, changing to a more effective drug is under consideration.
Discussion: Acute disseminated encephalomyelitis is a rare initial presentation of MS, especially if compared to other demyelinating diseases; therefore, it is important to exclude alternative diagnoses. In this case, the McDonald criteria should not be applied, and the child has not had other non-ADEM attacks to fulfill the criteria; nevertheless, he has juxtacortical, periventricular, and infratentorial lesions on MRI and, in follow-up images, shows enhancement of certain lesions. We decided to initiate treatment, despite fulfilling the diagnostic criteria for MS, since it is a highly-active disease with lesions that can result in disability in the future, even with no clinical relapse.
Final Comments: The present case report is a reminder that ADEM may be a first presentation of MS, and that it could be suspected mostly by MRI pattern.

DOI: 10.1055/s-0044-1789428

Immune-mediated neurological complications and dengue

João Henrique da Matta Clementino[1], Alex Eduardo Silva[1], Marlos Aureliano Dias de Sousa[1], Ana Luisa Rufino de Sousa[1], Amanda Soares Pimenta[1], Daniela Aparecida Lima Viana[1], Elisangela Ferraz Pazinato[1], Giovani Zago Borges[1]
[1]*Universidade Federal do Triângulo Mineiro, Uberaba MG, Brazil.*

Address for correspondence: João Henrique da Matta Clementino (email: joaoclementino96@hotmail.com).

Abstract
Case Presentation: Case 1: After 15 days of dengue infection confirmed by detection of the NS1 antigen in the blood, a 50-year-old woman started to present intense asthenia, paresthesia, and ascending paresis. She underwent electroneuromyography, which was compatible with acute demyelinating polyradiculoneuritis – Guillain-Barré Syndrome, and liquor with proteinocytological dissociation. After treatment with human immunoglobulin, she showed significant improvement in symptoms. Case 2: A 23-year-old man had dengue virus infection confirmed by serology. After 20 days, he evolved with paresthesia and upward paresis, hypoesthesia with a sensory level on T1, and urinary retention. On a magnetic resonance imaging scan of the skull and cervical spine, multiple lesions with hypersignal in T2/FLAIR were evident in the white, supra- and infratentorial substance, in the brainstem, and in the cervical and thoracic spinal cord, with acute disseminated encephalomyelitis (ADEM) being the first diagnostic hypothesis. In the cerebrospinal fluid, pleocytosis, proteinorrachia, and IgM immunoglobulin reagent for the dengue virus were observed.
Discussion: The neuropathogenesis of dengue infection is due to the direct invasion of the virus into the central nervous system, immune-mediated reactions, or metabolic changes. The neurological complications of dengue include encephalopathy, meningitis, myelitis, ADEM, optic neuromyelitis, optic neuritis, Guillain-Barré syndrome and neuro-ophthalmic complications. After infection by the dengue virus, our patients had neurological complications in the peripheral and central nervous system which, in both cases, are probably secondary to the immune-mediated mechanisms.
Final Comments: The dengue virus is considered non-neurotropic; however, the presence of viral particles in the cerebrospinal fluid, as well as damage to the blood-brain barrier, suggest viral neurotropism. Acute febrile diseases with neurological manifestations should be included in the diagnostic investigation, especially in endemic regions of arboviruses, such as tropical and subtropical countries.

DOI: 10.1055/s-0044-1789429

Overlapping NMOSD-AQP4 and Bickerstaff encephalitis: an intriguing case report

João Marcus Alves[1], Vanessa Lauanna Lima Silva[1], João Pedro Izidoro Gomes[1], Charles Mantovani[1], Camila Aquino Cruz[1], Katharina Messias[2], Vanessa Daccach[1]
[1]*Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Ribeirão Preto SP, Brazil.*
[2]*Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Hospital das Clínicas, Ribeirão Preto SP, Brazil.*

Address for correspondence: João Marcus Alves (email: joaomarcuspm@gmail.com).

Abstract
Case Presentation: A 50-year-old, previously healthy, male patient presented with sudden malaise, blurred vision, imbalance, nausea, and vomiting. During an ENT consultation, ischemic causes were ruled out with CT and MRI scans. Despite the initial treatment with betahistine and cinnarizine, the symptoms persisted, evolving to drowsiness, dysphonia, dysphagia, and urinary retention, prompting a neurology evaluation. The patient reported experiencing recurrent sharp pain on the lateral aspect of his right thigh ten days prior to symptom onset. Upon physical examination, he presented with skew deviation, multidirectional nystagmus, right internuclear ophthalmoplegia, globally-increased and symmetric reflexes, right dysmetria, and significant dysbasia. A lumbar puncture revealed significant pleocytosis (50 cells), raising the suspicion of possible rhombencephalitis of infectious or inflammatory etiology. Empirical treatment with intravenous antibiotics was initiated. The patient's symptoms remained refractory, and viral PCRs and cultures were negative. An MRI scan performed at our facility revealed

multiple inflammatory lesions with periventricular and perivenular distribution, associated with perivascular diffusion restriction in the right cerebellar peduncle, corpus callosum, and subcortical regions, with contrast enhancement. A new lumbar puncture showed increased pleocytosis (110 cells), presence of oligoclonal bands of IgG, IgG index > 0.5, and positive anti-GQ1b. Additionally, AQP4-IgG was positive in the serum. Given the anti-AQP4 positivity and neuroimaging findings, the diagnosis of NMOSD-AQP4 was established. The patient underwent pulse therapy with methylprednisolone, plasmapheresis, and maintenance therapy with rituximab.
Discussion: Anti-GQ1B syndromes are well-documented, with specific diagnostic criteria, which typically exclude NMOSD. There is only one other similar case reported in the literature, involving Miller Fisher syndrome with AQP4-IgG positivity.
Final Comments: The present case report demonstrates a clinical and serological overlap between NMOSD-AQP4 and Bickerstaff encephalitis (anti-GQ1B syndromes), which is unique in the literature. This case raises the hypothesis of whether there is an overlap of diseases or if there is a disease spectrum related to AQP4-IgG.

DOI: 10.1055/s-0044-1789430

Unveiling inflammatory optic neuropathy with silicone oil endotamponade: a clinical case

João Marcus Alves[1], Vanessa Lauanna Lima Silva[1], Jorge Alberto Martins Pentidado Júnior[1], Iago Blanco Bacchiega[1], Renata Moreto[2], Lucas Ravagnani[1]
[1]*Hospital São Lucas de Ribeirão Preto, Ribeirão Preto SP, Brazil.*
[2]*Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Hospital das Clínicas, Ribeirão Preto SP, Brazil.*

Address for correspondence: João Marcus Alves (email: joaomarcuspm@gmail.com).

Abstract
Case Presentation: A 59-year-old patient had a history of retinal detachment in the right eye, and was undergoing surgical retinopexy and silicone oil use, with progressive worsening of vision in that eye, despite multiple oil changes and cataract surgery aimed at improving vision, without success. About 4 months the before evaluation, she developed progressive, painless worsening of vision in the contralateral eye. Referral to a Neuro-ophthalmologist revealed finger counting visual acuity in the left eye at 50 cm, right optic nerve atrophy, and left optic nerve hyperemia. The OCT showed no changes in RNFL thickness, and an MRI scan showed T2 hyperintensity throughout the right optic nerve, chiasm, and optic tracts, with no contrast enhancement. She was then hospitalized for further investigation. The Workup showed normal CSF, negative AQP4-IgG, absent oligoclonal bands, and spinal cord MRI without demyelinating plaques. Considering a possible atypical optic neuritis in the patient's single eye, pulse therapy with methylprednisolone for 5 days and gradual oral prednisone tapering were initiated, resulting in partial improvement in visual acuity (now finger counting at 1.5 m), reduction of central scotoma, and even slight improvement in the right eye.
Discussion: Limited reports in the literature have documented the diffusion of silicone oil into the CNS, with only one reported case of optic neuritis in the contralateral eye. We speculate whether this condition resulted from the direct toxic and inflammatory effects of silicone oil or triggered autoimmune activity targeting the optic pathways. The partial response to corticosteroid, initiated 4 months after the onset of symptoms and in the absence of gadolinium enhancement, could support the presence of a sustained local inflammatory component.
Final Comments: The case report underscores significant concerns regarding the neurological risks associated with silicone oil endotamponade in retinal surgeries. It also reinforces the existing literature highlighting the potential adverse and treatable effects on the CNS following such procedures.

DOI: 10.1055/s-0044-1789431

Efficacy and safety of inebilizumab in patients aged 50 years and older with neuromyelitis optica spectrum disorder: N-MOmentum study subgroup analysis

Marilia Kanegae[1], Yang Mao-Draayer[1], Dean Wingerchuk[1], Jennifer Graves[1], Amy Kunchok[1], Elijah Lackey[1], Friedemann Paul[1], Kazuo Fujihara[1], Douglas Kazutoshi Sato[1], Zhong Wang[1], Dan Cimbora[1], Kristina Patterson[1], Bruce Cree[1]
[1]*Amgen Inc. São Paulo SP, Brazil.*
[2]*Oklahoma Medical Research Foundation, Oklahoma City OK, United States.*
[3]*Mayo Clinic Health System, Rochester MN, United States.*
[4]*University of San Diego, San Diego CA, United States.*
[5]*Cleveland Clinic, Cleveland OH, United States.*
[6]*Duke University Hospital, Durham NC, United States.*
[7]*Max Delbrück Center for Molecular Medicine, Berlin, Germany.*
[8]*Fukushima Medical University Hospital, Fukushima, Japão.*
[9]*Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil.*
[10]*Amgen Inc., Thousand Oaks CA, United States.*
[11]*University of California, San Francisco, School of Medicine, San Francisco CA, United States.*
Address for correspondence: Marilia Kanegae (email: mkanegae@amgen.com).

Abstract
Background: In older adults, the clinical features of neuromyelitis optica spectrum disorder (NMOSD) and the response to the treatment are scarce. Inebilizumab (INEB), an anti-CD19 B cell-depleting antibody, is approved for the treatment of NMOSD in adults seropositive for aquaporin-4 antibody (AQP4-IgG+).
Objective: To evaluate the efficacy and safety of INEB in AQP4-IgG+ participants aged ≥ 50 years with NMOSD.
Methods: N-MOmentum was a double-blinded, phase-2/3 trial that assessed the efficacy and safety of INEB in adults (aged between 18 and 74 years) with NMOSD, with a 28-week randomized controlled period (RCP; intravenous INEB 300 mg or placebo [PBO] on days 1 and 15), and an open-label period (OLP) of ≥ 2 years.
Results: Out of 213 AQP4-IgG+ participants, 65 (30.5%) were aged ≥ 50 years, and 148(69.5%) were aged < 50 years. In the RCP, the risk of attack for patients aged ≥ 50 years receiving INEB (n = 48) compared to PBO (n = 17) was of 0.26 (0.07–0 0.97; $p = 0.05$), whereas in participants aged < 50 years, it was of 0.21 (0.10–0.42; $p < 0.0001$). In the OLP, the annualized attack rate (AAR) in those aged ≥ 50 years was of 0.08 (0.04–0.14), and, in those aged < 50 years, it was of 0.11 (0.08–0.16), indicating no statistical difference. Worsening of the EDSS score in the RCP was significantly different between those aged ≥ 50 years (odds ratio [OR] = 0.56; 95% confidence interval [95%CI] = 0.14–2.30) and those aged < 50 years (OR = 0.33; 95%CI = 0.13–0.82). However, in the OLP, there was no statistical difference: ≥ 50 years, – OR = 0.68; 95%CI = 0.20–2.28; < 50 years – OR = 0.86; 95%CI = 0.30–2.43. The NMOSD-related annualized hospitalization rate in the OLP for participants aged ≥ 50 and < 50 years was of 0.16 (95%CI = 0.06–

0.42) and 0.13 (95%CI = 0.08–0.22) respectively. Among participants aged ≥ 50 years receiving INEB in the RCP, 31.3% (15/48) reported ≥ 1 IP-TEAE, versus 35.3% (6/17) in the PBO group; and, among participants aged < 50 years, the IP-TEAE was of 22.1%(25/113) in the INEB group, and of 20.0% (7/35) in the PBO group. No IP-related serious adverse events or deaths occurred in the participants aged ≥ 50 years in the INEB or PBO groups of the RCP.
Conclusion: This data supports the efficacy and safety of INEB in AQP4-IgG+ NMOSD patients aged ≥ 50 years, although evaluations of larger populations are needed to confirm these results.

DOI: 10.1055/s-0044-1789432

Looking beyond optic disc drusen: the concealment of relapsing isolated optic neuritis

Grazielle Fialho Souza[1], Ana Cristina Cotta-Queiroz[1], Anna Christina Higino Rocha[1], Natália Cirino Talim[1], Thales Ponsá Pinto[1], Paulo Pereira Christo[1], Marco Lana-Peixoto[1]
[1]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract
Optic disc drusen (ODD) are congenital anomalies characterized by calcified acellular deposits within the head of the optic nerve. They frequently mimic papilledema, which emphasizes the importance of an accurate diagnosis to avoid unnecessary investigations and inappropriate treatment. The aim of the present study was to describe a patient with ODD who developed bilateral relapsing isolated optic neuritis (RION). The presence of ODD led to delayed diagnosis and treatment of RION. A 35-year-old woman presented with headache and painless visual loss in the right eye (RE). An examination disclosed visual acuity (VA) of 20/200 OU and "bilateral papilledema". She experienced full recovery of vision following IV pulses of methylprednisolone. Three subsequent attacks of blurred vision resulted in a VA of 20/40 in the RE, and hand movements in the LE, associated with bilateral optic disc atrophy. A brain MRI scan was unrevealing, and lumbar puncture showed normal CSF opening pressure. A diagnosis of anterior ischemic optic neuropathy was initially made, and the patient was referred to our center. Although autofluorescence testing and ultrasound of the head of the optic nerve were unrevealing, EDI-OCT disclosed the presence of ODD. A new optic nerve MRI scan showed hyperintense lesions in both optic nerves. The visual evoked potentials examination showed P100 with normal amplitude values and marked latency delays. The diagnosis of RION associated with ODD was established, and the patient was started on immunosuppressive treatment. This case illustrates the delay in diagnosing and treating RION, leading to a severe outcome. It underlies the need for a meticulous neuro-ophthalmologic examination associated with appropriate imaging techniques such as EDI-OCT for ODD diagnosis, and optic nerve MRI scans to search for demyelinating lesions.

DOI: 10.1055/s-0044-1789433

Multiple sclerosis-related optic neuritis is an outlier in the autoimmune optic neuritis group. The 2022 International panel classification needs a prompt revision

Marco A. Lana-Peixoto[1], Natália Cirino Talim[1], Thales Ponsá Pinto[1], Paulo Pereira Christo[1]
[1]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract
Background: Optic neuritis (ON) manifests in a range of demyelinating diseases of the central nervous system (DDCNS), offering crucial insights for early diagnosis and tailored treatment strategies. However, the current 2022 International Panel classification of ON fails to adequately distinguish multiple sclerosis-related ON (MSON) from other forms of immune-mediated ON (IMON).
Objective: To propose a revised classification for immune-mediated ON emphasizing the distinctions between MSON and other forms of IMON.
Methods: Patients diagnosed with DDCNS presenting with ON as their initial symptom were selected. The ON cases were categorized into two groups: MSON, including single isolated ON and ON in MS; and non-MS IMON, encompassing other IMON subtypes. Demographic, clinical, and imaging features, as well as outcomes, were compared between the groups.
Results: The analysis of 271 DDCNS patients revealed 101 (37.5%) with MSON and 170 (62.5%) with non-MS IMON at disease onset. The non-MS IMON group included NMOSD-ON, MOG-ON, recurring idiopathic ON, chronic relapsing inflammatory optic neuropathy, ADEM-ON, systemic autoimmune disease-related ON, parainfectious ON, vaccine-related ON, and IMON of unknown etiology. The significant differences ($p < 0.05$) between MS-related ON (MS-ON) and non-MS ON included age at onset, race, simultaneous bilaterality, severity of visual impairment, presence of CSF-specific OCB, and MRI lesions in the brain and optic nerve. These differences underscore the need for a revised classification, distinct from the 2022 International Panel classification. The present revision proposes the classification of MS-ON as a separate entity, distinguished from other autoimmune ON (AION) forms. Additionally, the AION group should be renamed IMON group to encompass parainfectious ON, vaccine-related ON, and cancer-related ON.
Conclusion: The proposed revision of the 2022 International Panel Classification of ON could assist clinicians in more accurately identifying MSON within the expanding spectrum of identifiable IMON etiologies, thereby facilitating tailored treatment for patients' conditions.

DOI: 10.1055/s-0044-1789434

The peculiar implications of immune-mediated optic neuritis at disease presentation in Brazil: study of 271 patients

Marco A. Lana-Peixoto[1], Natália Cirino Talim[1], Alice Horta Azevedo de Castro[1], Paulo Pereira Christo[1]
[1]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract
Background: Immune-mediated optic neuritis (IMON) is an initial symptom in various demyelinating diseases of the CNS (DDCNS). These conditions exhibit different epidemiological and clinical features in Brazil compared to other Western countries. Understanding the characteristics and frequencies of these underlying conditions in Brazil is crucial to develop public health strategies aimed at early intervention and prevention of more severe outcomes.
Objective: To describe the characteristics and frequencies of IMON as the presenting symptom of DDCNS.
Methods: We retrospectively selected a cohort of patients with IMON at onset of a DDCNS. Multiple sclerosis-related IMON (MSRON) comprised single isolated ON (SION), and ON in multiple sclerosis (MSON). The ON subtypes no related to MS-ON comprised recurring isolated ON (RION), chronic recurring inflammatory on (CRION), myelin oligodendrocytic glycoprotein-associated ON (MOGAD-ON), neuromyelitis optica ON (NMOSD-ON), ON in association with systemic autoimmune diseases (SAD-ON), parainfectious ON (PION), and vaccine-related ON (VON). The Severity of ON was measured by Kurtzke Visual Function System Scores (KVFSS).
Results: The analysis of 271 IMON patients revealed a mean age of 31.3±13 years, and 214 (79%) women. Non-Caucasians comprised 52%, and 13.3% had an associated autoimmune disease. Isolated ON occurred in 70.8%, and bilateral simultaneous ON, in 32.5%. The median KVFSS was of 2 (range: 1–5). In total, MSRON was identified in 101 (37.3%) patients, AQP4-seropositive NMOSD-ON, in 36 (13.3%), RION, in 26 (9.6%), MOGAD-ON, in 14 (5.2%), CRION, in 2 (0.7%), ADEM-O, in 7 (2.6%), PION, in 7 (2.6%), PV-ON, in 14 (5.2%), and SAD, in 7 (2.6%) patients. The etiology remained undetermined in 20 (7.4%) patients.
Conclusion: Compared to data from other Western populations, in Brazil IMON is more prevalent in non-Caucasians and NMOSD-ON, less so in MS and MOGAD, and it is associated with more severe outcomes. These findings underscore the need for tailored healthcare policies in the country.

DOI: 10.1055/s-0044-1789435

Optic neuritis as an initial presentation of granulomatosis with polyangiitis: two case reports

Ana Cristina Cotta-Queiroz[1], Anna Christina Higino Rocha[1], Grazielle Fialho Souza[1], Natália Cirino Talim[1], Paulo Pereira Christo[1], Marco A. Lana-Peixoto[1]
[1]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Divisão de Neuro-Oftalmologia, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract
Background: Granulomatosis with polyangiitis (GPA) is a rare systemic vasculitis predominantly involving the respiratory tract and kidneys. While ocular manifestations occur in approximately 50% of the cases, optic neuritis at disease onset is rare. We describe two cases in which optic neuritis was the initial presentation of GPA.
Case Presentation: Case 1: A 51-year-old, previously healthy man presented with headache and visual loss in the left eye (LE). An examination revealed a visual acuity (VA) of 20/20 in the right eye (RE) and counting fingers in the LE. A relative afferent pupillary defect was observed in the LE. Brain and orbit MRI scans showed pachymeningitis, an expansive lesion in the left orbital apex, and an enhanced lesion in the left optic nerve. The biopsy findings were consistent with GPA. Despite treatment with corticosteroids and cyclophosphamide, he developed loss of vision in the RE. The VA declined to counting fingers in the RE and no light perception in the LE. Case 2: A 56-year-old man developed painful visual loss in the RE. The diagnosis of optic neuritis was made, and he received IV pulses of methylprednisolone, resulting in RE amaurosis. Four months later, he developed painful LE amaurosis with no response to IV methylprednisolone. He was then referred to our center. An examination revealed bilateral amaurosis, ophthalmoplegia in both eyes, and necrotizing scleritis, leading to perforation of the RE. An MRI scan demonstrated bilateral optic nerve enhancement and hyperintense lesions in the apex of both orbits. A biopsy confirmed GPA. No improvement was observed following treatment with cyclophosphamide and steroids. Treatment was subsequently changed to rituximab.
Conclusion: These cases highlight that optic neuritis may occur at the onset of GPA, contributing to its severe outcomes. Early identification of the nature of the optic neuritis and appropriate treatment are essential to avoid catastrophic outcomes.

DOI: 10.1055/s-0044-1789436

Broadening NMOSD etiology: neurosyphilis as a mimicry factor

Paulo Pereira Christo[1], Anna Christina Higino Rocha[1], Natália Cirino Talim[1], Ana Cristina Cotta-Queiroz[1], Grazielle Fialho[1], Thales Ponsá Pinto[1], Marco Lana-Peixoto[2]
[1]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract
Neuromyelitis optica spectrum disorders (NMOSD) are autoimmune conditions most commonly associated with aquaporin-4 or MOG autoimmunity. Double-seronegative NMOSD encompasses a group of heterogenous diseases that may express typical manifestations of seropositive NMOSD. Neurosyphilis can manifest with a broad range of neurological symptoms, including optic neuritis and longitudinally-extensive transverse myelitis. We herein present a case of a patient who developed simultaneous bilateral optic neuritis and myelitis due to neurosyphilis. A 31-year-old man presented with subacute painful visual loss in both eyes accompanied by weakness and dysesthesia in the upper and lower limbs, as well as sphincter disturbances. Upon examination, his visual acuity (VA) was of 20/80 in the right eye and of 20/200 in the left eye. The fundoscopic examination was unremarkable. The neurological examination revealed quadriparesis and loss of light touch and vibration sense in the lower limbs. The EDSS score was of 5.0. A Brain MRI scan showed T2/FLAIR large lesions in both cerebral hemispheres, cerebellar peduncles, and the pontomesencephalic junction. A spinal MRI scan showed a longitudinally-extensive T2 lesion from the cervicomedullary junction to the level of T2. The patient tested negative for AQP4-IgG and positive for syphilis; MOG-IgG was not tested. The CSF analysis demonstrated 13 white blood cells/mm^3 with 8% of neutrophils, and protein content of 93 mg%, with a negative VDRL test. The patient was treated with IV crystalline penicillin but did not return for follow-up examinations. This case highlights the challenges in identifying the underlying cause in seronegative NMOSD. Clinicians should remain vigilant for alternative diagnoses to facilitate timely and appropriate

treatment. A limitation to this report was the absence of MOG-IgG testing, despite MRI findings suggesting the possibility of MOGAD. This case could represent an instance of MOGAD coexisting with neurosyphilis.

DOI: 10.1055/s-0044-1789437

MOG-IgG is rare in AQP4-IgG-seronegative NMOSD in Brazil: insights from a single-center cohort

Denison A. Pedrosa[1], Gustavo Bruniera Peres Fernandes[1], Natália Cirino Talim[2], Paulo Pereira Christo[2], Eliane Aparecida Rosseto Welter[1], Alexandre Gimenes Marques[1], Thales Ponsá Pinto[2], Carolina Reis Araújo Abrantes[2], Ana Cristina Cotta-Queiroz[2], Anna Christina Higino Rocha[2], Grazielle Fialho[2], Marco Lana-Peixoto[2]

[1]*Hospital Israelita Albert Einstein, São Paulo SP, Brazil.*
[2]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract

Background: Neuromyelitis optica spectrum disorders (NMOSD) are rare inflammatory conditions primarily associated with aquaporin-4 (AQP4) autoimmunity. Clinically, the disease mostly often manifests with optic neuritis and longitudinally-extensive transverse myelitis. AQP4-IgG-seronegative NMOSD encompasses MOG-IgG NMOSD and other heterogenous conditions, many of which with unknown etiopathogenesis. The frequency and features of MOG-IgG NMOSD remain unclear in Brazil.

Objective: To study the frequency and characteristics of MOG-IgG NMOSD in a Brazilian cohort.

Methods: MOG-IgG testing was performed on AQP4-IgG-seronegative patients with NMOSD, atypical optic neuritis, or transverse myelitis of unknown cause, using the 2015 IPND criteria. Commercially-available fixed CBA kits (Euroimmun, Luebeck, Germany) were employed for testing.

Results: Out of 118 AQP4-IgG-seronegative patients, 25 exhibited NMOSD phenotype. Serum MOG-IgG was detected in 3 patients (12%), all of whom were women aged 11, 26, and 34 years. The presenting symptoms included myelitis, unilateral optic neuritis, and a combination of unilateral optic neuritis, myelitis, and brainstem symptoms. The period between disease onset and the last follow-up varied from 8 to 17 (median: 11.2) years. The number of relapses reported were 1, 3, and 7, with a median interval of 1 month between the first and second attacks (range: 0–32 months). The EDSS scores at the last visit were of 0, 1.5, and 2.0. One patient was receiving oral prednisone and azathioprine, while two were on azathioprine at the time of MOG-IgG testing. The MOG-IgG titers were of 1/10 in 2 patients and of 1/32 in 1 subject.

Conclusion: Our findings suggest that MOG-IgG rarely occurs in AQP-4-IgG-seronegative NMOSD patients in Brazil as compared with other populations. However, the limitations to the present study include the time elapsed between the first attack and the testing, the use of immunosuppressants, and the small cohort. Collaborative multicenter studies in Brazil are needed to further clear the issue.

DOI: 10.1055/s-0044-1789438

Schistosomiasis mansoni-associated neuromyelitis optica: an unprecedent case report

Paulo Pereira Christo[1], Natália Cirino Talim[1], Thales Ponsá Pinto[1], Carolina Reis Araújo Abrantes[1], Ana Cristina Cotta-Queiroz[1], Anna Christina Higino Rocha[1], Grazielle Fialho[1], Marco Lana-Peixoto[1]

[1]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract

Despite a significant decline in the incidence of schistosomiasis mansoni (Sm) in Brazil's once-endemic regions, sporadic cases persist. Myelitis is the most common neurological complication during Sm's chronic phase, with optic neuritis and chiasmitis also observed as acute parainfectious reactions. We herein report a case of an Sm patient who developed neuromyelitis optica (NMO) syndrome, an association not previously documented. A 34-year-old male patient had an 18-month history of headaches and bitemporal hemianopsia, progressing rapidly to visual acuity (VA) of hand movement in both eyes. The fundoscopy showed mild pallor of the left eye's temporal rim; the right eye was normal. A brain MRI scan revealed T2/FLAIR and T1-enhanced lesions in the sellar region and optic chiasm thickening. Despite intravenous methylprednisolone treatment, the vision did not improve. A biopsy revealed non-necrotizing granulomatous inflammation with fibrosis, lymphocytes, macrophages, and epithelioid cells, but no Schistosoma eggs. The patient received oral prednisone for four months. Fourteen months later, he developed severe lumbar pain, bladder retention, and pronounced paraparesis with sensory loss in both legs. The VA was of 20/25 in the right eye and of 20/30 in the left eye. A spinal MRI scan showed a central non-enhancing lesion from C6 to T3 and another lesion in the conus medullaris. Cerebrospinal fluid analysis revealed 35 WBC/mm^3 with 38% eosinophils, a protein content of 60 mg%, glucose content of 50 mg%, and positive schistosomiasis serology. Treatment with oral prednisone and praziquantel led to partial myelitis recovery, with an EDSS score of 3.0. The association of chiasmitis and longitudinally-extensive transverse myelitis with schistosomiasis has not been previously reported. It highlights the broad concept of NMO syndrome, whose etiopathogenesis extends beyond autoimmune conditions to include various infectious diseases, some of which, such as schistosomiasis, are exclusively found in developing countries.

DOI: 10.1055/s-0044-1789439

Confusion in diagnosis: NMOSD patients mistakenly treated for multiple sclerosis

Juliana Santiago-Amaral[1], Natália Cirino Talim[1], Marco Lana-Peixoto[1]

[1]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract

Background: Neuromyelitis optica spectrum disorders (NMOSD) and multiple sclerosis are inflammatory

immune-mediated diseases of the central nervous system with relapsing attacks of neurological signs related to involvement of multiple functional systems. However, they have distinct treatments and, alarmingly, many drugs effective for MS can exacerbate NMOSD, highlighting the importance of an accurate diagnosis.
Objective: To assess the frequency of misdiagnosis and inappropriate treatment of NMOSD as MS.
Methods: We conducted a retrospective analysis of the medical records from a cohort of NMOSD patients consecutively evaluated at our MS Center, all meeting the 2015 IPND criteria. We assessed demographic and clinical data, with a focus on patients previously diagnosed with MS and treated with MS-specific therapies.
Results: The study included 85 patients, 15 (17.6%) of whom had been previously treated for MS. Among these cases, most subjects were female (86.7%), 8 (53.3%) were white, and 7 (46.7%) were of mixed race. The mean age at NMOSD onset was of 28.2 (range: 5–55) years. Aquaporin-4 antibodies (AQP4-IgG) tested positive in 8 (53.3%) patients and negative in 6 (40%). One patient (6.7%) lacked data on AQP4-IgG serum status. The average EDSS score at the last evaluation was of 4.96 (range: 0–8.0), and the mean disease duration was of 110.9 (range: 42–264) months.
Conclusion: The symptoms of NMOSD can mimic those of MS, leading to potential misdiagnosis, which poses significant risks to patients with NMOSD. Misdiagnosing NMOSD as MS can result in inappropriate treatment with disease-modifying drugs, which can exacerbate NMOSD symptoms and potentially lead to severe relapses or disability progression in NMOSD patients. Our findings underscore the urgent need for increased awareness and education among clinicians.

DOI: 10.1055/s-0044-1789440

Time between the first symptom and treatment of NMOSD in a Brazilian cohort

Juliana Santiago-Amaral[1], Natália Cirino Talim[1], Marco A. Lana-Peixoto[1]
[1]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract

Introduction: Neuromyelitis optica spectrum disorders (NMOSD) are a severe inflammatory immune-mediated disease of the central nervous system mainly characterized by relapsing attacks of optic neuritis and longitudinally extensive transverse myelitis. Disability is related to attacks and to start prophylactic treatment can change the course of the disease.
Objectives: The main aim of this study was to estimate the mean time between the first relapse and initiation of prophylactic treatment in a cohort of Brazilian NMOSD patients.
Methods: We reviewed the medical records of 85 patients with 2015 NMOSD diagnostic criteria. Demographic and clinical data were assessed.
Results: In the study of 85 patients, most were female (82.3%). Racial distribution was: white 40%, black 21.1%, mixed race/ethnicity 36.5%, and Asian 2.4%. The median age at NMOSD onset was 29 (5-68) years old. AQP4-IgG was positive in 54.1% and negative in 34.1%. AQP-4 antibody status was unknown for 11.8%. The median EDSS score was 5.0 (range 0-8.5), with a median disease duration of 96 months (range 9-360). The median time to treatment initiation was 24 months (IQR 9-60)(range: 0-324), with 15.5% starting within 6 months, 20.8% between 6 and 12 months, 15.5% between 12 and 24 months, and 48.0% after 24 months. Only 3.8% began treatment at symptom onset.
Conclusion: NMOSD is a severe and disabling disease, however the beginning of prophylactic treatment is still late in your country. This data support the importance to aware physicians and community about the illness with the aim to reduce time to diagnosis and treatment.

DOI: 10.1055/s-0044-1789441

Analyzing the association between cancer and neuromyelitis optica: a case series

Felipe B. Brunheroto[1], Natália Cirino Talim[1], Juliana Santiago-Amaral[1], Paulo Pereira Christo[1], Marco A. Lana-Peixoto[1]
[1]*Universidade Federal de Minas Gerais, Faculdade de Medicina, Centro de Investigação de Esclerose Múltipla, Belo Horizonte MG, Brazil.*

Address for correspondence: Marco A. Lana Peixoto (email: marco.lanapeixoto@gmail.com).

Abstract

Background: Neuromyelitis optica spectrum disorders (NMOSD) are immune-mediated disorders of the central nervous system, with anti-aquaporin 4 antibodies most often detected in serum. The increasing number of reports associating cancer and NMOSD raises questions about their interconnectedness, especially when considering a cross-reactive mechanism of tumor cells triggering autoimmunity.
Objective: To investigate the prevalence and characteristics of patients with both cancer and NMOSD, to gain insights into those under care at the CIEM MS Research Center.
Methods: We reviewed the medical records of patients at our center diagnosed with NMOSD with a history of cancer.
Results: In a cohort of 281 patients with NMOSD, 8 met the established criteria (2.8%); 4 (50%) of them tested positive for anti-AQP-4 antibodies, and 6 (75%) were female subjects. The tumors identified included breast and cervical cancers (25% each), multiple myeloma (12.5%), pheochromocytoma (12.5%), prostate cancer (12.5%), and bladder cancer (12.5%). The patients presented heterogeneous phenotypes, with initial symptoms such as myelitis (62.5%), optic neuritis (50%), area postrema syndrome (50%), and brainstem syndrome (12.5%). Longitudinally-extensive transverse myelitis (LETM) was prominent, occurring in 7 (87.5%) patients, whereas optic neuritis occurred in 6 (75%) subjects.
Conclusion: Our findings are in line with those reported in the literature, indicating an association pf 3 to 12% between NMOSD and cancer, predominantly in female patients. The most prevalent symptom was LETM. In agreement with other published series, breast and genitourinary cancers were frequently-reported histological types.

DOI: 10.1055/s-0044-1789442

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) treated with IL-6 inhibitor (tocilizumab): experience of a neuroimmunology reference center in a hospital in the city of São Paulo

Pedro Pontes[1], Tainá Gonçalves[1], Herval Neto[1], Sonia Maria Azevedo[1]
[1]*Hospital do Servidor Público Estadual de São Paulo, São Paulo SP, Brazil.*

Address for correspondence: Pedro Pontes (email: pedroalmeida.pontes@gmail.com).

Abstract

We herein report two cases of acute optic neuritis diagnosed as myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) after extensive etiological investigation at a neuroimmunology reference center in the city of São Paulo, Brazil. Both patients were young men, aged 39 and 43 years, and presented with acute unilateral visual loss, ocular pain when moving the eye, relative afferent pupillary defect, and visual acuity impairment. The two patients presented with visual acuity defects in the left eye. One of them had acuity of 20/400, while the other one's was of 20/30, with normal visual acuity (20/20) in the right eye in both cases. An extensive etiological investigation was performed, including serum laboratory tests (anti-aquaporin 4 antibody by the cell-based assay method, and dosage of myelin oligodendrocyte glycoprotein-immunoglobulin G, MOG-IgG) and cerebrospinal fluid tests (with evaluation of oligoclonal bands), as well as cranial and orbital magnetic resonance imaging (MRI) scans. In both cases, AQP4-Ab showed negative results. The orbital MRI scan showed unilateral optic neuropathy, with intense and extensive optic nerve inflammation and edema, while also showing paramagnetic contrast enhancement. These findings, in this clinical context, are compatible with inflammatory optic neuritis. In the acute phase, treatment was immediately initiated with methylprednisolone 1 g for 5 days, resulting in significant improvement in visual acuity and symptoms, followed by hospital discharge. During the outpatient follow-up, the result of the MOG-IgG became available, which was positive. Therefore, both patients started receiving tocilizumab (an anti-IL-6 medication, used for 12 months in 1 patient, and for 5 months in the other subject) monthly, without any continued corticosteroid therapy. Since the initiation of this treatment, both patients have been undergoing regular outpatient follow-up, remaining free from recurrence of any symptom possibly attributable to MOGAD.

DOI: 10.1055/s-0044-1789443

Results of social media and in-person NMOSD awareness campaigns: how can we measure their impact?

Raquel Vassão Araujo[1], Gustavo San Martin[1], Giulia Gamba[1]

[1]Associação Crônicos do Dia a Dia (organização sem fins lucrativos), Guarulhos SP, Brazil.

Address for correspondence: Raquel Vassão Araujo (email: raquelvassao@yahoo.com.br).

Abstract

Background: Since 2021, various social media and in-person campaigns for NMOSD awareness in Brazil were held, and the results regarding the numbers of reach, impressions, and the peak in Google searches for the terms *NMO*, *NMOSD*, *neuromielite óptica* and *neuromielite* in Brazil in 2023 may reveal their impact.

Objective: To describe the results of social media and in-person awareness campaigns in 2023 compared to Google trends findings, especially during March and April of that year.

Methods: Numbers of impressions, reach, engagement, and of people impacted by in-person actions were compared to the Google trends searches of the aforementioned terms.

Results: Several actions were promoted, such as a subway station campaigns, thematic lighting of the Iguaçu Falls, a ferry boat action, a friendly soccer game, informative virtual live streaming with specialists, campaign with influencers and actors, local actions in association with NMO centers, specific hashtags and official videos for "Março Verde" ("Green March"), and stories published in the press. In total, more than 30 million people were reached by all actions. The most viewed actions were the subway station and ferry boat campaigns, with 8.5 million views (29.9%), the stories in the press, with 15.9 million views, and impressions (56%) on Instagram and Facebook, with 4 million (14%) views. The actions took place concomitantly with the highest Google trends peak of searches in 2023, around March and April. The Brazilian State with the highest index was Paraíba.

Conclusion: The Google trends index of 100 during March and April 2023 shows that the actions impacted the intrinsic number of people and were effective for people to show interest and search the terms on Google. Social media and in-person campaigns combined with stories published in the press may help increase NMOSD awareness in Brazil. The state of Paraíba developed an impactful campaign, and the Google searches reflected this. The next step is to determine how could we measure the impact of campaigns involving new diagnosis of NMOSD and social participation engagement.

DOI: 10.1055/s-0044-1789444

Therapeutic plasma exchange for neuromyelitis optica attacks: evidence and challenges from a real-world cohort from Brazil

Guilherme Almeida[1], Roger Araujo[1], Bruno Castrillo[1], Guilherme Diogo Silva[1], Ida Fortini[1], Marcia Gonçalves[1], Luiz Henrique Martins Castro[1], Nelson Tatsui[1], Tarso Adoni[1], Douglas Kazutoshi Sato[2], Samira Luisa Apóstolos-Pereira[1], Dagoberto Callegaro[3]

[1]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, São Paulo SP, Brazil.

[2]Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil.

[3]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia, São Paulo SP, Brazil.

Address for correspondence: Roger Araujo (email: rogersantana.araujo@gmail.com).

Abstract

Therapeutic plasma exchange (TPE) can improve disability recovery after neuromyelitis optica spectrum disease (NMOSD) attacks, but its effectiveness and safety in Latin-American patients with access barriers and diverse ethnicity is underexplored. We carried out a retrospective cohort study with NMOSD patients that underwent TPE. We evaluated 84 NMOSD attacks in 68 patients. Despite a median 25-day delay from symptom onset to TPE, 65.5% of the patients showed significant improvement. Adverse events occurred in 39% of the patients, usually transitory, and with no fatalities.