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# CONTENTS

<b>Shared rare immune-related variants in a family with MOGAD and MS: evidence from trio-based exome sequencing ....</b>	<b>1</b>
Karla Pinto Coelho Fadel, Renan Amphilophio Fernandes, Elielson Veloso da Silva, Andreza Salvio Lemos, Larissa Araujo Duarte, Elisa Gouvea Gutman, Helena França Alcaraz Ferreira, Valeria Pereira, Caio Faria Tardim, Soniza Vieira Alves-Leon	
<b>Anti-NMDA receptor encephalitis after herpes simplex encephalitis in a 51-year-old female: a diagnostic challenge ....</b>	<b>1</b>
Paula Oliveira Pinto, Luciane Perez Silveira, Samuel Brighenti Bergamashi, Patricia Santos, Daiane PAola Perin, Ricardo Weber Rocha	
<b>Caspr2 antibody-associated disease presenting as Morvan syndrome and concomitant titin and LGI1 antibodies: a case report .....</b>	<b>1</b>
Caio César Diniz Disserol, Camila Lorenzini Tessaro, Hélio Afonso Ghizoni Teive, Henry Koiti Sato, Mariana Sandri Schumacher Welling, Rosana Herminia Scola, Livia Almeida Dutra	
<b>Mimics of autoimmune encephalitis in Brazil: preliminary results from the BRAIN cohort .....</b>	<b>1</b>
Caio César Diniz Disserol, Paulo Ribeiro Nóbrega, Pedro Braga Neto, Aducto Wanderley da Nóbrega Junior, Alexandre Coelho Marques, Orlando Graziani Povoas Barsottini, Milena Sales Pitombeira, Fernanda Martins Maia Carvalho, Polyana Favero Ferreira Caetano, Livia Almeida Dutra	
<b>Progressive encephalomyelitis with rigidity and myoclonus (PERM) with anti-GAD antibodies: a case report.....</b>	<b>2</b>
Ana Beatriz de Matos Berg Abrantes, Lorena Oliveira Carneiro, Pedro Maia Nobre Rocha Saffi, Leonardo Jadyr Silva Rodrigues Alves, Marcelle Rodrigues Carneiro de Souza Reis, Lana Francischetto Rocha, Lucas Lourenço da Rocha Matos, Lucas Ferreira Alves, Felipe Von Glehn Silva, Priscilla Mara Proveti de Lima	
<b>The vanishing past: a LGI1 antibody encephalitis case report .....</b>	<b>2</b>
Vanessa Dantas Andrade, Cândida Driemeyer, Júlia Santos Soares, Alexandre Laisson Prado Taschetto, Marlise de Castro Ribeiro, Alexandre Balzano Maulaz	
<b>Trends of hospital admissions for viral encephalitis in Brazil from 2019 to 2024: possible COVID-19 impacts and neuroimmunological implications .....</b>	<b>2</b>
Bárbara Araújo Pereira Cabral	
<b>A pragmatic prognostic model for severe disability in patients with relapsing–remitting multiple sclerosis: evidence from a multicenter Brazilian cohort .....</b>	<b>2</b>
Felipe Toscano Lins Menezes, Nise Alessandra Carvalho Sousa, José Luiz Miranda Coelho Inojosa, Lis Campos Ferreira, Denise Sisterolli Diniz, Felipe von Glehn Silva, Victor Alexandre Dantas Miranda, Claudia Cristina Ferreira Vasconcelos, Marlise Castro Ribeiro, Enedina Maria Lobato Oliveira	
<b>Alemtuzumab in MS: frequency and severity of liver enzyme elevations and implications for hepatotoxicity monitoring</b>	<b>3</b>
Gabriela Abrahão Allioni, Alana Bacelar Limeira Sales, Henrique de Moraes Bernal, Lucas Alexandre Santos Marzano, Milena Lins Veiga, Thiago Ivan Vilchez Santillan, Tarso Adoni, Samira dos Apostolos Pereira, Dagoberto Callegaro, Guilherme Diogo Silva	
<b>Alemtuzumab: Is it failure or just the need of an extra infusion course? .....</b>	<b>3</b>
Alana Bacelar Limeira Sales, Milena Lins Veiga, Gabriela Abrahão Allioni, Lucas Alexandre Santos Marzano, Henrique de Moraes Bernal, Tarso Alana Adoni, Guilherme Diogo Silva, Dagoberto Callegaro, Samira Luisa Apóstolos Pereira	
<b>Case report of a patient with Miastenia Gravis associated with amyotrophic lateral sclerosis.....</b>	<b>3</b>
Bianca Teixeira, Hamilton Franco, Gustavo Lacerda, Max Sarmet, Vinicius Maldaner, Karla Xavier	
<b>Clinical, demographic and therapeutic profile of patients with multiple sclerosis managed at a public referral center in Florianópolis, Santa Catarina, Southern Brazil .....</b>	<b>3</b>
Rafael Mendes Marques, Gabriela da Silva Cremonese, Cristine Koehler, Mariana Costa Borges, Maria Eduarda Andreatta, Carolina Aparecida Donofrio Santos Costa, Gladys Lentz Martins, Ricardo Pereira Gonçalves	
Isabela Canedo Campos Schettino, Ana Julia Resende Rocha, Ana Carolina Santana Santos, Amanda Sanchez Machado, Cláudia Fideles Resende, Michel Moraes Soane, Rodrigo Isabela Kleinpaul, Flavio Guimaraes Fonseca, Fernanda Ludolf Ribeiro, Juliana Santiago Amaral	
<b>From diagnosis to intervention: how treatment timing influences broader outcomes in multiple sclerosis .....</b>	<b>4</b>
Leticia Pieroni Cavaglieri, Murilo Freire Pinoti Bernardo, Laura Barbosa Salome, Douglas de Moraes, João Victor Ferraiolli Gabrelon, Clayton Zoccoli, Olivia Pires, Isabella Avolio, Mateus Boaventura	
<b>High-efficacy MS drug access in the Amazon basin: distance doesn't tell the whole story.....</b>	<b>4</b>
Victoria Lin, Alexandre Coelho Marques, Luiz Eduardo Betti Paiva, Lucas Hernandes Corrêa, Marina Martins Siqueira, Gabriely Rangel Pereira, Doralina Guimarães Brum Souza, Livia Almeida Dutra	
<b>Impact of the 2021 PCDT update on multiple sclerosis medication dispensation patterns in Brazil: a big data analysis ..</b>	<b>4</b>
Alexandre Coelho Marques, Victoria Lin, Luiz Eduardo Betti Paiva, Lucas Hernandes Corrêa, Marina Martins Siqueira, Gabriely Rangel Pereira, Doralina Guimarães Brum Souza, Livia Almeida Dutra	
<b>Impact of the 2024 revised McDonald criteria on multiple sclerosis diagnosis in Brazilian patients .....</b>	<b>5</b>
João Victor Ferraiolli Gabrelon, Murilo Freire Pinoti Bernardo, Leticia Pieroni Cavaglieri, Douglas de Moraes, Laura Barbosa Salome, Clayton Zoccoli, Olivia Pires, Isabella Avolio, Mateus Boaventura	

<b>Multiple sclerosis drug access across Brazil's public health system between 2019 and 2023: a study using distance traveled by patients and dispensing centers .....</b>	<b>5</b>
Luiz Eduardo Betti Paiva, Alexandre Coelho Marques, Lucas Hernandes Corrêa, Marina Martins Siqueira, Gabriely Rangel Pereira, Victoria Lin, Doralina Guimarães Brum Souza, Lívia Almeida Dutra	
<b>Multiple sclerosis: analysis of initial treatment in a tertiary hospital .....</b>	<b>5</b>
Milena Vasconcelos Falcão, Paulo Henrique Martinelli Oliveira, Larissa Miyashiro, Laiz Helena de Pádua, Gustavo Carvalho Costa, Alexandre Coelho Marques, Raderi Luiz Cardoso dos Santos, Lucas Silva Dias, Renata Maiolo Rigonato, Lais Micheli de Souza	
<b>Ocrelizumab in multiple sclerosis: sustained effectiveness and low discontinuation rates in a Brazilian real-world cohort .....</b>	<b>5</b>
Murilo Bernardo, Douglas Morais, João Gabrelon, Laura Salome, Leticia Cavaglieri, Clayton Zoccoli, Olivia Pires, Isabella Avolio, Mateus Boaventura	
<b>Ocrelizumab-induced interstitial lung disease: case report with primarily progressive multiple sclerosis .....</b>	<b>6</b>
Marina Nolasco Manhaes Gomes Barreto, Claudia Cristina Ferreira Vasconcelos	
<b>Overlapping features of multiple sclerosis and neuromyelitis optica: a case report .....</b>	<b>6</b>
Rafael Marques Mendes, Gladys Lentz Martins, Gabriela da Silva Cremonese, Cristine Koehler, Mariana Costa Borges, Maria Eduarda Andreatta, Carolina Aparecida Donofrio Santos Costa, Ricardo Pereira Gonçalves	
<b>Prevalence of viral seropositivity in multiple sclerosis patients: focus on vaccine-preventable infections .....</b>	<b>6</b>
Ana Carolina Santana Santos, Isabela Canedo Campos Schettino, Ana Julia Resende Rocha, Quezia Dias Teixeira, Rodrigo Kleinpaul, Fernanda Ludolf Ribeiro, Juliana Santiago-Amaral	
<b>Quality of life evaluation in individuals with relapsing-remitting multiple sclerosis in a reference center .....</b>	<b>7</b>
Bianca Etelvina Santos Oliveira, Heyell Kevin Rodrigues Franklin Chacon, Naftaly Angélica Lopes Souza, Anne Caroline Oliveira Melo, Victor Camelo Vilar Sá Heim, Luiza Alves Monteiro Torreão Villarim, Davi Veloso Guerra, Mayra Beatriz Gomes Dêrio, Gabrielle Benício Araújo, Rebeca Ribeiro Paiva	
<b>Regional inequalities in hospitalizations due to multiple sclerosis in Brazil and the impact of the COVID-19 pandemic between 2017 and 2022 .....</b>	<b>7</b>
Bárbara Araújo Pereira Cabral	
<b>Understanding delayed diagnosis in multiple sclerosis: risk factors in a Brazilian cohort .....</b>	<b>7</b>
Leticia Pieroni Cavaglieri, Laura Barbosa Salome, João Victor Ferraiolli Gabrelon, Murilo Freire Pinoti Bernardo, Douglas de Morais, Clayton Zoccoli, Olivia Pires, Isabella Avolio, Mateus Boaventura	
<b>Use of Ofatumumab in Patients with Multiple Sclerosis at a Reference Center .....</b>	<b>7</b>
Bianca Etelvina Santos Oliveira, Luiza Alves Monteiro Torreão Villarim, Davi Veloso Guerra, Jeanina Cabral, Arthur Felipe Barbosa Vasconcelos, Ana Clara Guilherme, Francisco Anderson Sá Carvalho, José Felipe Lacerda Fernandes, Daniel Vicente Siqueira Lima Junior, Maria Clara Lucena Freire	
<b>Acute flaccid areflexic paraparesis in a pediatric patient: differential diagnosis between acute polyradiculoneuritis and neuromyelitis optica .....</b>	<b>8</b>
Larissa Miyashiro, Laiz Helena de Pádua, Milena Vasconcelos Falcão, Renata Maiolo Rigonato, Lais Micheli de Souza, Paulo Henrique Martinelli Oliveira, Raderi Luiz Cardoso dos Santos, Lucas Silva Dias, Gustavo Carvalho Costa, Alexandre Coelho Marques	
<b>FCGR3A Polymorphism in patients with AQP4 IgG-seropositive neuromyelitis optica spectrum disorder .....</b>	<b>8</b>
Bianca Etelvina Santos Oliveira, Fernando Paiva Melo Neto, Marinna Karla Cunha Lima Viana, Luiza Alves Monteiro Torreão Villarim, Davi Veloso Guerra, Ana Clara Guilherme Rodrigues, Jeanina Cabral, Arthur Felipe Barbosa Vasconcelos, Francisco Anderson Sá Carvalho, José Felipe Lacerda Fernandes	
<b>Optic neuritis and mucosal ulcers in a young woman: a case of dual autoimmune neuroinflammation .....</b>	<b>8</b>
Renata Vitorino Borges, Natalia Carvalho Fonseca, Rebeca Raissa Bezerra Oliveira, Pedro Hamilton Guimarães Leite, Reigson Alves Dias, Lais Reis Santos Abe, Julio Montes Garcia Barbosa, Samela Daiere Soares Mota Reis, Raquel Rios de Castro Pontes, Fernando Elias Borges	
<b>Pulmonary MALT lymphoma during long-term rituximab therapy in a patient with neuromyelitis optica: a rare and paradoxical association .....</b>	<b>8</b>
Gabriel Soares Dutra Souza, Nathalia Lindsay Pereira Queiroz, Francisco Gil Sarmiento Neto, Paulo Santiago Morais Brito, Mário Emílio Teixeira Dourado Júnior, Felipe Toscano Lins Menezes,	
<b>Real-world evaluation of rituximab effectiveness in reducing annualized relapse rate in AQP4-IgG-positive NMOSD patients .....</b>	<b>9</b>
Henrique de Moraes Bernal, Lucas Alexandre Santos Marzano, Thiago Ivan Vilchez Santillan, Guilherme Diogo Silva, Mateus Boaventura de Oliveira, Tarso Adoni, Roger Santana de Araújo, Eduardo Macedo de Souza Tieppo, Samira Apóstolos, Dagoberto Callegaro	
<b>The etiologies of optic neuritis in an outpatient clinic dedicated to atypical demyelinating diseases .....</b>	<b>9</b>
Lucas Alexandre Santos Marzano, Guilherme Diogo Silva, Thiago Ivan Vilchez Santillan, Douglas Kazuyoshi Sato, Tarso Adoni, Roger Santana, Sara Terrim, Dagoberto Callegaro, Samira Luisa dos Apostolos	
<b>The value of choroid plexus in differentiating Multiple Sclerosis from Neuromyelitis optica spectrum disorder .....</b>	<b>9</b>
Lucas Alexandre Santos Marzano, Julia Coutinho Cordeiro, Gabriel Augusto de Souza Figueiredo, Lia Araújo Guabiraba, Andre Veloso Souto Rocha, Carolina de Medeiros Rimkus, Samira Luisa dos Apostolos	

<b>A TNFRSF13B mutation presenting as immune dysregulation and chronic inflammatory polyneuropathy .....</b>	<b>9</b>
Marina Driemeier Cardoso, João Henrique Fregadolli Ferreira, Guilherme Fleury Perini, Mauricio Elias Nunes da Silva, Livia Almeida Dutra	
<b>Association between mortality from inflammatory polyneuropathies and the Zika virus epidemic in Brazil from 2010 to 2020.....</b>	<b>10</b>
Bárbara Araújo Pereira Cabral	
<b>Beyond anti-GAD65: atypical stiff-person syndrome presentation with anti-glycine receptor antibodies and CSF oligoclonal bands.....</b>	<b>10</b>
Pedro Maia Nobre Rocha Saffi, Leonardo Jadyr Silva Rodrigues Alves, Marcelle Rodrigues Carneiro de Souza Reis, Lorena Oliveira Carneiro, Ana Beatriz de Matos Berg Abrantes, Lana Francischetto Rocha, Felipe von Glehn Silva, Priscilla Mara Proveti de Lima, Keila Rejane Ferreira Galvão, Luciano Talma Ferreira	
<b>Beyond the cavernous sinus: expanding the clinical and radiological spectrum of Tolosa-Hunt syndrome .....</b>	<b>10</b>
Milena Lins Veiga, Graziella Aguiar Santos, Alana Bacelar Limeira Sales, Lucas Alexandre Santos Marzano, Gabriela Abrahao Allioni, Henrique de Moraes Bernal, Leandro Tavares Lucato, Luiz Henrique Martins Castro, Suely Kazue Nagahashi Marie, Guilherme Diogo Silva	
<b>Blurred lines: IgG4-related disease behind a case of vision loss.....</b>	<b>11</b>
Fernanda Nicoli Broch, Cândida Driemeyer, Laís Elizabete Favaretto, Alexandre Prado Taschetto, Amanda Fernanda Klajn Maycá, Vanessa Vanessa Dantas de Andrade, Julia Santos Soares, Marlise de Castro Ribeiro	
<b>Cerebellar ataxia as a clinical manifestation related to the use of oncological immunotherapy .....</b>	<b>11</b>
Raphaella Moura Cardoso, Arthur Cauã Silva Santos, Barbara Conceição Ferreira Moura	
<b>Challenges in attributing neuropsychiatric symptoms in SLE: validation of attribution models in a Brazilian cohort ....</b>	<b>11</b>
Fabiano Ferreira de Abrantes, Marianna Pinheiro Moraes de Moraes, Pedro Henrique Almeida Fraiman, José Luiz Pedroso, Edgard Torres dos Reis Neto, Orlando Graziani Povoas Barsottini	
<b>Dural Rosai-Dorfman disease in the differential diagnosis of pachymeningitis and hypophysitis .....</b>	<b>11</b>
Lucas Alexandre Santos Marzano, Gabriella Faria Nogueira, Alana Sales Bacelar, Gabriela Abrahão Allioni, Milena Lins veiga, Henrique de Moraes Bernal, Guilherme Diogo,	
<b>Epidemiological, clinical, and radiological assessment of hypertrophic pachymeningitis in a tertiary neurology center in Brazil.....</b>	<b>12</b>
Marianna Pinheiro Moraes de Moraes, Fabiano Ferreira de Abrantes, Pedro Henrique Almeida Fraiman, Stênio Burlin, Victor Hugo Rocha Marussi, José Luiz Pedroso, Orlando Graziani Povoas Barsottini	
<b>Identifying hidden inflammation: the role of FDG-PET/CT in pachymeningitis affecting the cavernous sinus .....</b>	<b>12</b>
Lucas Alexandre Santos Marzano, Graziella Aguiar Santos Faria, Artur Coutinho, Leandro Tavares Lucato, Luiz Henrique Martins Castro, Suely Kazue Nagahashi Marie, Guilherme Diogo Silva	
<b>Idiopathic hypertrophic pachymeningitis presenting as cranial palsy and headache: a case report .....</b>	<b>12</b>
Cândida Driemeyer, Vanessa Dantas de Andrade, Julia Santos Soares, Amanda Fernanda Klajn Maycá, Ana Letícia Amorim de Albuquerque	
<b>IgG4-related autoimmune disease with neurological manifestation: a case report.....</b>	<b>13</b>
Larissa Nóbrega Ribeiro da Silva, Octavio Morais Veloso, Monique Rodrigues Pereira Pinto, Poliana D'aurea Alfonso, Isabella Cristina Amate Dutra, Yasmin Martins Moreno, Victor Ezaki Alves Silva, Victor Assis Souza, Arthur de Medeiros Dias, Ana Claudia Piccolo	
<b>Mortality from inflammatory polyneuropathy in Brazil (2018–2023): possible neuroimmunological effects of COVID-19.....</b>	<b>13</b>
Bárbara Araújo Pereira Cabral	
<b>Neutrophilic meningoencephalitis with internuclear ophthalmoplegia: a rare manifestation of Neuro-Behçet.....</b>	<b>13</b>
Larissa Miyashiro, Laiz Helena de Pádua, Milena Vasconcelos Falcão, Renata Maiolo Rigonato, Laís Micheli de Souza, Gabriella Verardo Braga, Paulo Henrique Martinelli Oliveira, Alexandre Coelho Marques, Gustavo Carvalho Costa	
<b>Progressive leukoencephalopathy associated with pathogenic CSF1R mutation: case report .....</b>	<b>13</b>
Paula Oliveira Pinto, Luciane Perez Silveira, Pedro Henrique Andrade, Patricia Santos	
<b>Structured Functional and Clinical Profiling in Patients with GAD-SD spectrum disorders: a review of 22 cases from Brazilian Autoimmune Encephalitis Network .....</b>	<b>14</b>
Carolina Souza Sanchez, João Henrique Ferreira Fregadolli, Caio Disserol, Alexandre Coelho Marques, Alessandra Delavance, Luis Eduardo Coelho, Livia Almeida Dutra	
<b>Susac syndrome in a young woman: a diagnostic challenge in neuroimmunology .....</b>	<b>14</b>
Miguel Inácio Silva Gomes, Felipe Toscano Lins Menezes	
<b>Unmasking an inflammatory disorder: clues from the orbit and dura .....</b>	<b>14</b>
Larissa Braga Mendes, Maria Eduarda Slhessarenko Fraife Barreto, Fernanda Lustosa Cabral Gomez, Sofia Mônaco Gama, Marianna Pinheiro Moraes de Moraes, José Luiz Pedroso, Orlando Graziani Povoas Barsottini,	

<b>Vanishing white matter disease without neurological deficits: a case report .....</b>	<b>14</b>
Lucas Lourenço Rocha Matos, Lucas Ferreira Alves, Ana Beatriz Matos Berg Abrantes, Leonardo Jadyr Silva Rodrigues Alves, Pedro Maia Nobre Rocha Saffi, Lorena Oliveira Carneiro, Marcelle Rodrigues Carneiro Souza Reis, Lana Francischetto Rocha, Priscilla Mara Proveti Lima, Felipe Von Glehn Silva	
<b>Vogt-Koyanagi-Harada syndrome with recurrent neuroretinitis: a case report .....</b>	<b>15</b>
Milena Vasconcelos Falcão, Larissa Miyashiro, Laiz Helena de Pádua, Renata Maiolo Rigonato, Lais Micheli de Souza, Paulo Henrique Martineli Oliveira, Alexandre Coelho Marques	
<b>When livedo reticularis is the key: ADA2 deficiency .....</b>	<b>15</b>
Pedro Henrique Almeida Fraiman, Marianna Pinheiro Moraes de Moraes, Thiago Yoshinaga Tonholo Silva, Fabiano Ferreira de Abrantes, Anne Carolina Barbosa Teixeira, Renata Moldenhauer Minillo, Tatiana Ferreira de Almeida, José Luiz Pedroso, Orlando Graziani Povoas Barsottini	



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**ABSTRACTS**

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**Área Técnica do trabalho:** Doença associada a MOG

### Shared rare immune-related variants in a family with MOGAD and MS: evidence from trio-based exome sequencing

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**Background:** Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and multiple sclerosis (MS) are inflammatory demyelinating diseases of the central nervous system (CNS) with overlapping clinical features but distinct immunopathogenic mechanisms. Familial clustering of these diseases is rare, raising the hypothesis of shared genetic susceptibility influencing immune regulation and neuroinflammation. **Objective:** To explore the genetic architecture underlying CNS autoimmunity by performing whole-exome sequencing (WES) in a family presenting distinct inflammatory demyelinating diseases, with MOGAD in the proband and MS in his mother, aiming to identify candidate variants potentially contributing to disease susceptibility. **Methods:** WES was performed in a non-consanguineous family comprising a proband with MOGAD, his mother with MS, a healthy father, and an unaffected sister. Variant filtering prioritised rare nonsynonymous variants (allele frequency <0.01 in gnomAD and ABraOM) with high pathogenicity prediction supported by multiple *in silico* tools. Candidate genes were further annotated based on literature-curated evidence of involvement in neuroinflammation and immune response. **Results:** Seven rare heterozygous variants were identified, shared exclusively by the proband and his mother, in NTN4, ATP7B, PIP5K1C, CCDC150, TAAR2, CELA3A, and DHRS7B. All were ultra-rare or absent in public databases and predicted as deleterious. These genes participate in processes relevant to CNS autoimmunity, including immune cell signalling, extracellular matrix remodelling, neurovascular integrity, and oxidative stress response. Notably, PIP5K1C regulates immune signalling via PIP2 synthesis upstream of BTK activation. NTN4 is involved in axon guidance and blood-brain barrier integrity. ATP7B regulates copper homeostasis and oxidative stress. TAAR2 modulates neutrophil migration and lymphocyte responses. CCDC150 was recently described as a negative regulator of TGFB expression, a cytokine with context-dependent roles in neuroinflammation. **Conclusion:** We identified rare coding variants co-segregating with MOGAD and MS phenotypes within the same family, reinforcing the hypothesis of shared genetic susceptibility mechanisms in CNS autoimmunity. These findings provide novel candidate genes for future functional studies aimed at elucidating their role in the pathophysiology of MOGAD and MS, and at uncovering shared pathogenic mechanisms within the neuroinflammatory spectrum.

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**Área Técnica do trabalho:** Encefalite autoimune

### Anti-NMDA receptor encephalitis after herpes simplex encephalitis in a 51-year-old female: a diagnostic challenge

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**Case Presentation:** A 51-year-old female patient with a history of bariatric surgery, alcoholism, and depression was admitted due to acute confusion and seizures. Prior to admission, she reported headache, fever, and disorientation. Physical and neurological examinations at admission were unremarkable. Laboratory tests revealed hyponatremia. Cerebrospinal fluid (CSF) analysis showed leukocytes of 35/mm<sup>3</sup>, erythrocytes of 20/mm<sup>3</sup>, glucose of 106 mg/dL, and protein of 103 mg/dL; Gram stain was negative. CSF PCR tested positive for herpes simplex virus type 1. Brain MRI demonstrated extensive signal changes involving the medial temporal lobes, hippocampi, right thalamus, insular cortex, frontal lobes, and cingulate gyri, predominantly on the right side. ECG showed no abnormalities. The patient received acyclovir for 21 days. On day 10, she experienced worsening headache and fever, and a brain CT scan revealed a large intraparenchymal hemorrhage. Despite this, her seizures resolved, and she was discharged after 41 days on levetiracetam 1000 mg/day. Thirty days later, she returned with fever, insomnia, hallucinations, echolalia, and aggression. Olanzapine and diazepam were introduced, and the antiepileptic therapy was switched to valproic acid. A new CSF analysis showed leukocytes of 15/mm<sup>3</sup>, erythrocytes of 2/mm<sup>3</sup>, glucose of 56 mg/dL, and protein of 178 mg/dL; Gram stain was negative. Follow-up brain MRI showed reduced edema and hemorrhage in the previously noted lesions. Persistent agitation and insomnia led to further investigation. A transvaginal ultrasound identified an ovarian teratoma. CSF testing revealed oligoclonal bands and positive anti-NMDAR antibodies. Pulse therapy with methylprednisolone 1 g/day was administered. The patient underwent surgical removal of the tumor, followed by treatment with methylprednisolone and monthly cyclophosphamide (1 g/month for 9 months), resulting in gradual clinical improvement. After ten months, she continued to have mild disorganized speech; however, insomnia, suicidal ideation, and hallucinations had resolved. **Discussion:** This case illustrates the diagnostic complexity in patients with anti-NMDAR encephalitis, particularly in atypical age groups and when overlapping with or following prior viral encephalitis. **Final Comments:** Anti-NMDAR encephalitis should be considered even in uncommon age groups and complex clinical contexts. Early diagnosis is crucial for appropriate management and improved prognosis.

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**Área Técnica do trabalho:** Encefalite autoimune

### Caspr2 antibody-associated disease presenting as Morvan syndrome and concomitant titin and LGI1 antibodies: a case report

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**Case Presentation:** a 73-year-old male with a previous smoking history presented with polyneuropathy, ataxia, imbalance, agrypnia excitata, peripheral neuronal hyperexcitability, dysautonomia and cognitive complaints that evolved over a few weeks. Neurological examination

revealed an amnesic and dysexecutive syndromes, normal strength, hypoactive reflexes, diffuse myokymias, mild distal sensory loss, global ataxia and prominent autonomic signs (palmar and plantar erythema alternating with cyanosis, and sudoresis). MRI was normal, while CSF analysis revealed mild protein elevation. EMG showed prominent myokymias and neuromyotonic discharges. TBA and CBA for neuronal autoantibodies in serum and CSF were done, revealing a strong positivity to Caspr2 anti titin antibodies, and mild positivity for LGI1 antibodies, only in serum. The patient received IVIg and corticosteroids with partial improvement, followed by an excellent response to Rituximab. Paraneoplastic screening was negative, including a thoracic MRI and a PET-scan. **Discussion:** Morvan syndrome (MS) is an autoimmune neurological condition that affects predominantly older males and involves peripheral nerve hyperexcitability, autonomic dysfunction, movement disorders, and prominent neuropsychiatric and sleeps symptoms. It is mostly associated with Caspr2 antibodies, and the concomitant occurrence of other neuronal antibodies, specially LGI1, enhances the probability of presentation as Morvan syndrome with diverse movement disorders. Co-occurrence with LGI1 and titin augments the possibility of finding a tumor, specially thymoma. Then, regular tumor screening is highly recommended in these cases. **Final Comments:** we report a case of Caspr2 antibody-associated disease with the presence of other neuronal antibodies. This association augments the risk of a paraneoplastic disorder and may alert for more frequent paraneoplastic investigation. Moreover, second-line therapies may benefit cases with partial response to corticosteroids and IVIg in this disease.

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**Área Técnica do trabalho:** Encefalite autoimune

### Mimics of autoimmune encephalitis in Brazil: preliminary results from the BRAIN cohort

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**Background:** possible autoimmune encephalitis (AE) criteria proposed in 2016 aid early recognition to AE cases. However, their specificity varies considerably. In 2023, a new diagnostic algorithm was proposed to improve suspected AE classification and distinguish true AE cases from mimics. **Objective:** to apply the 2023 algorithm for possible AE cases, to characterize mimics and compare them to seropositive AE (sAE) cases. **Methods:** we retrospectively analyzed 114 suspected AE cases from the BRAIN database from 2018 to 2023. Clinical, imaging, CSF, EEG, and antibody data were reviewed. The cohort was classified using the updated algorithm. Statistical comparisons and multivariate models between sAE and mimics were performed. **Results:** 29 sAE, 10 probable seronegative AE, 5 ADEM, and 58 mimics were found (12 excluded). Mimics were mainly inflammatory (15%), epileptic (15%), undetermined (13%) and degenerative (12%) disorders. There were no differences between groups regarding gender, presence of prodromal symptoms, or

EEG changes. Patients with sAE were younger (mean age: AE 25 years x mimics 44 years;  $p < 0,001$ ), had more frequently movement disorders (AE 72% x mimics 38%;  $p = 0,03$ ), dysautonomia (AE 38% x mimics 10%;  $p = 0,001$ ), pleocytosis (AE 62% x mimic 33%;  $p = 0,006$ ), response to immunotherapies (AE 76% x mimics 53%;  $p = 0,03$ ), and a normal brain MRI (AE 66% x mimics 34%;  $p = 0,03$ ). In contrast, mimics had more comorbidities (AE 34% x mimics 69%;  $p = 0,001$ ). **Conclusion:** mimics constitute a heterogeneous spectrum of disorders - inflammatory, epileptic and degenerative causes were the most common in the group of patients with a final diagnosis. In suspected AE cases, the absence of movement disorders and dysautonomia — particularly in older patients with comorbidities presenting brain MRI abnormalities, pleocytosis, and poor response to immunotherapies — should prompt consideration of alternative diagnoses.

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**Área Técnica do trabalho:** Encefalite autoimune

### Progressive encephalomyelitis with rigidity and myoclonus (PERM) with anti-GAD antibodies: a case report

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**Case Presentation:** A 46-year-old man with vitiligo and no prior comorbidities presented in 2013 with insidious low back pain that progressed to thoracic and cervical pain, accompanied by axial and limb rigidity, fatigue, and functional limitation. Since 2022, he experienced generalized muscle spasms, including during sleep, triggered by auditory, visual, and emotional stimuli. He developed spontaneous myoclonus, lost 10 kg in one year, and reported constipation, urinary dysfunction, and gastric fullness. In 2024, cognitive decline emerged, with memory impairment, acalculia, anomia, agnosia, mild dysphagia, and chronic dysphonia. He received methylprednisolone pulse therapy in September 2024, with partial relief of spasms; a second infusion in November was ineffective. In March 2025, upon tertiary hospital admission, he showed myoclonic spasms triggered by loud noises, left patellar hyperreflexia, mild axial hypertonia, and hypopigmented patches. Electroneuromyography revealed continuous paravertebral muscle activity suppressed by benzodiazepines. EEG showed left temporal slowing. CSF and standard labs were unremarkable. Anti-GAD65 antibodies were positive by ELISA (213 UI/mL), but negative by IHC-TBA. ENT exam revealed vocal sulci due to chronic vocal strain. He was treated with intravenous immunoglobulin, with improvement in cognition, fatigue, myoclonus, and rigidity. **Discussion:** Progressive Encephalomyelitis with Rigidity and Myoclonus (PERM) is a rare, severe variant of Stiff Person Spectrum Disorder (SPSD), featuring axial and limb rigidity, painful spasms, reflex or spontaneous myoclonus, autonomic dysfunction, and central nervous system involvement, including cognitive decline and seizures. PERM is often associated with autoantibodies (anti-GAD, GlyR, DPPX, AMPA-R), though seronegative forms are increasingly recognized. Diagnosis is based on clinical signs and electrophysiology. Benzodiazepine responsiveness suggests GABAergic dysfunction of immune origin. The presence of vitiligo may reflect systemic autoimmunity. Treatment involves symptom control with benzodiazepines and immunotherapy, such as corticosteroids, IVIG, rituximab, or cyclophosphamide, with varying outcomes. **Final Comments:** This case aligns with PERM, evidenced by progressive rigidity, spasms, myoclonus, autonomic and cognitive symptoms, and electromyographic features. The presence of anti-GAD65 by ELISA further supports the diagnosis. It highlights the need

to consider PERM in atypical SPSP cases with CNS and systemic features. Early recognition and timely immunotherapy are essential for better outcomes

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**Área Técnica do trabalho:** Encefalite autoimune

### The vanishing past: a LGI1 antibody encephalitis case report

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**Case Presentation:** A 67-year-old male physician developed involuntary movements and emotional lability. He initially experienced orofacial and tongue movements described as dystonia. His wife observed cognitive decline, including forgetting past trips and work commitments. On examination, he exhibited faciobrachial dystonic seizures (FBDS). His medical history included terbinafine use for onychomycosis and ischemic cardiovascular disease. Laboratory tests showed positive antinuclear antibodies (ANA 1:640) and hyponatremia (sodium 127 mEq/L). Cranial MRI and cerebrospinal fluid (CSF) analysis were normal, with negative infectious serologies and no evidence of malignancy. An antibody panel revealed the presence of anti-LGI1 antibodies. Treatment began with corticosteroid pulse therapy and intravenous immunoglobulin, leading to progressive improvement of orofacial dystonia, emotional symptoms, and cognition. Rituximab was subsequently introduced, normalizing ANA titers and sodium levels. The patient remains asymptomatic under follow-up, with a planned rituximab infusion to evaluate the need for continued immunomodulatory therapy. **Discussion:** This case illustrates autoimmune encephalitis mediated by anti-LGI1 antibodies, presenting with orofacial dystonia, emotional lability, cognitive impairment, and hyponatremia. The leucine-rich glioma-inactivated 1 (LGI1) protein is highly expressed in the hippocampus, playing a key role in regulating presynaptic voltage-gated potassium channels and postsynaptic AMPA receptors. First described in 2010 by Irani et al., anti-LGI1 antibodies define a spectrum of limbic encephalitis marked by seizures and cognitive deficits. A distinct seizure type, faciobrachial dystonic seizures (FBDS), is highly specific to this condition and typically responds well to immunosuppressive therapy. Memory complaints, especially involving short-term recall, are common in LGI1 antibody-mediated disease. **Final Comments:** Early diagnosis of anti-LGI1 encephalitis is vital, as prompt immunotherapy often results in significant clinical improvement. Long-term monitoring is necessary to detect relapses and to guide the duration of immunomodulatory treatment.

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**Área Técnica do trabalho:** Encefalite autoimune

### Trends of hospital admissions for viral encephalitis in Brazil from 2019 to 2024: possible COVID-19 impacts and neuroimmunological implications

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**Background:** Viral encephalitis refers to inflammation of the brain parenchyma caused by direct viral invasion or immune-mediated responses triggered by viral antigens and is a notifiable disease in Brazil. The COVID-19 pandemic, which began in 2020, posed challenges for epidemiological surveillance, as the virus became associated with neurological manifestations. Recent studies suggest that viruses such as Herpes and SARS-CoV-2 may act as immunological triggers for autoimmune encephalitis, which is often underdiagnosed or misinterpreted as infectious. The absence of a specific ICD-10 code data for autoimmune encephalitis further complicates case identification. Evaluating the trends in viral encephalitis-related hospitalizations during the COVID-19 pandemic may support discussions on the underdiagnosis of neuroimmunological conditions. **Objective:** To analyze the trend of hospital admissions for unspecified viral encephalitis (ICD-10 A86) in Brazil between 2019 and 2024, considering possible effects of the COVID-19 pandemic on case notifications and differential diagnosis with autoimmune encephalitis. **Methods:** This was an ecological, retrospective, cross-sectional study based on secondary data from the Brazilian Hospital Information System (SIH) covering the period from 2019 to 2024. Records of hospitalizations due to unspecified viral encephalitis were included and stratified by year and geographic region. Temporal trends and comparisons were conducted across three periods: pre-pandemic (2019), during the pandemic (2020–2021), and post-pandemic (2022–2024). Only records with complete data on date and location were considered; duplicate and inconsistent entries were excluded. Bar and line graphs were used to illustrate trends and regional distributions. **Results:** A total of 12,022 hospitalizations for unspecified viral encephalitis were recorded in Brazil between 2019 and 2024. A drop in hospitalizations was observed in 2020 (1,689 cases) and 2021 (1,647 cases), compared to 2,436 cases in 2019. From 2022 onwards, there was a steady increase: 1,977 cases in 2022, 2,072 in 2023, and 2,201 in 2024. The Northeast and Southeast regions had the highest number of hospitalizations, with 4,774 and 3,263 cases, respectively. **Conclusion:** Hospitalizations for viral encephalitis decreased in the first two years of the COVID-19 pandemic, possibly due to limited access to healthcare services and the reallocation of medical resources. The subsequent increase from 2022 may reflect the resurgence of neurotropic viral infections or undiagnosed autoimmune encephalitis cases presenting with similar clinical features. Current literature supports the hypothesis that SARS-CoV-2 may act as a trigger for autoimmune encephalitis, potentially contributing to the observed trend. These findings highlight the need for enhanced epidemiological surveillance and diagnostic capabilities to better differentiate between viral and autoimmune encephalitis and improve clinical outcomes.

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**Área Técnica do trabalho:** Esclerose Múltipla

### A pragmatic prognostic model for severe disability in patients with relapsing-remitting multiple sclerosis: evidence from a multicenter Brazilian cohort

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**Background:** Disability progression is a major concern in relapsing-remitting multiple sclerosis (RRMS), yet predictive models derived from Latin American populations are scarce. Understanding the influence of early clinical factors and treatment response may support individualized, risk-based decisions. **Objective:** To develop and validate a predictive model for sustained Expanded Disability Status Scale (EDSS) 6 in Brazilian RRMS patients, integrating baseline clinical characteristics and treatment-related mediators. **Methods:** We conducted a retrospective, multicenter cohort study including RRMS patients aged  $\geq 18$  years from 11 multiple sclerosis (MS) centers across Brazil (1994–2023). Exclusion criteria were: time to first specialized appointment  $> 10$  years, baseline EDSS  $\geq 6$ , follow-up  $< 1$  year, or time to EDSS 6  $< 6$  months. Patients were split into training (85%) and validation (15%) cohorts. Predictors included demographic, clinical, radiologic, and laboratory variables available at baseline. Treatment-related variables were assessed as potential mediators. Statistical analysis included: (1) descriptive statistics; (2) univariate and multivariate logistic regression; (3) mediation analysis using generalized structural equation modeling; and (4) model performance evaluation using area under the curve (AUC) and validation in an independent cohort. **Results:** Among 785 database entries, 654 patients met eligibility criteria (556 in training; 98 in validation). The training cohort included 76.8% females and 61.4% White individuals, with a median follow-up of 6.0 years. Sustained EDSS 6 occurred in 17.1%. Initial multivariate analysis identified early predictors: first appointment between 1994–2010 (adjusted odds ratio [aOR] 5.91; 95% confidence interval [CI] 3.42–10.23, vs. 2011–2023), incomplete recovery from first relapse (aOR 2.03; 95% CI 1.07–3.84), number of relapses before first appointment (aOR 1.30 per relapse; 95% CI 1.09–1.56), and baseline EDSS score (aOR 1.64 per point; 95% CI 1.26–2.14). In the mediation analysis, failure to achieve no evidence of disease activity-3 (NEDA-3) within one year of treatment (aOR 3.94; 95% CI 1.77–8.73) and initiating disease-modifying therapy (DMT) only after EDSS 3 (aOR 13.2; 95% CI 6.32–27.58) significantly increased disability risk and attenuated the effects of early predictors. The 1994–2010 period was associated with both higher disability risk (aOR 7.29; 95% CI 3.68–14.42) and lower NEDA-3 rates (aOR 2.95; 95% CI 1.92–4.54). The final model performance showed: AUC of 0.84, 81.8% sensitivity, 73.5% specificity, 95.2% negative predictive value, and 69.9% overall accuracy when applied in the validation cohort. **Conclusion:** Baseline clinical characteristics strongly predict disability risk in Brazilian RRMS patients. However, early DMT initiation and disease control (NEDA-3) mitigate high-risk profiles. The proposed model facilitates early risk stratification and clinical decisions in real-world MS care.

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**Área Técnica do trabalho:** Esclerose Múltipla

### Alemtuzumab in MS: frequency and severity of liver enzyme elevations and implications for hepatotoxicity monitoring

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**Background:** Alemtuzumab is a high-efficacy therapy for relapsing-remitting multiple sclerosis (RRMS), with

well-known hematologic, renal, and thyroid adverse events. However, hepatotoxicity remains poorly understood, and drug-induced liver injury (DILI) is rarely reported. **Objective:** To assess the frequency and severity of transaminase elevation in RRMS patients treated with alemtuzumab. **Methods:** We conducted a retrospective observational study including 58 consecutive RRMS patients treated with alemtuzumab. Liver enzymes (ALT and AST) were measured at baseline, on day 3, and at the end of the treatment cycle. Elevations were graded using CTCAE v5.0: grade 1 (above ULN to  $3 \times$  ULN), grade 2 ( $3-5 \times$  ULN), grade 3 ( $5-20 \times$  ULN), and grade 4 ( $> 20 \times$  ULN). All patients underwent routine screening for viral hepatitis and documentation of concomitant medications. **Results:** Among 55 patients with baseline data, none had elevated transaminases. On day 3, 6 of 49 (12.2%) had elevated ALT and 5 (10.2%) elevated AST, all overlapping. At the end of the cycle, 19 of 51 (37.2%) had elevated ALT and 15 (29.4%) elevated AST. Among 45 patients with both measurements, 20.0% reached grade 1, 15.5% grade 2, and 4.4% grade 3. No patient reached grade 4 or showed clinical signs of liver dysfunction. All cases resolved spontaneously. No case was attributable to infectious hepatitis. **Conclusion:** Transaminase elevations were common but typically mild, asymptomatic, and reversible, rarely justifying treatment discontinuation.

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**Área Técnica do trabalho:** Esclerose Múltipla

### Alemtuzumab: Is it failure or just the need of an extra infusion course?

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**Background:** Alemtuzumab is a high efficacy DMD newly included in the Brazilian public healthcare system for MS treatment. Data concerning the frequency and risk factors for clinical relapse in between or after the two first cycles is still scarce specially in developing countries. **Objective:** This study aims to evaluate the need of extra alemtuzumab courses a Brazilian large tertiary public MS treatment center. **Methods:** This is a pilot observational prospective longitudinal study performed between 01-2023 and 06-2025. **Results:** In our service, 58 patients are in use of Alemtuzumab, 14 of which completed 1 year after the second cycle and 3 had clinical relapses after or in between the two infusion cycles, accounting for 21,4% of our sample. Patient 1: 27 y-o white male with 7 years of multiple sclerosis (MS) diagnosis and previous clinical failure with natalizumab. At the first Alemtuzumab cycle, 2023-07, the EDSS score was 6.5. After 8 months of the second cycle, worsening of ataxia and gait with three new MRI lesions were observed. Immunophenotyping showed B-cell repopulation and T-cell depletion. Patient 2: 25 y-o black male with 8 years of MS diagnosis and previous clinical failure with natalizumab. The EDSS score at the first cycle of alemtuzumab, in 2023-04, was 2.5. After 10 months of the first infusions, the patient presented a central vertigo syndrome with improvement after high dose corticosteroid therapy. The second cycle was anticipated, and clinical stability was attained. Patient 3: 41 y-o white male with 7 years of MS diagnosis and previous use of natalizumab, changed due to high risk of PML, and fingolimod, changed due to clinical relapse. At the first cycle of alemtuzumab, in 2023-09, the EDSS score was 3.0. After 6 months of the second cycle, the patient presented paresis of the left leg without improvement after high dose corticosteroid therapy. **Conclusion:** We highlight the importance of monitoring clinical and radiological relapses in between and after the completion of the two cycles, as the need of extra courses is not rare.

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**Área Técnica do trabalho:** Esclerose Múltipla

### Case report of a patient with Myasthenia Gravis associated with amyotrophic lateral sclerosis

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**Case Presentation:** A 45-year-old male patient began experiencing symptoms in February 2023. Initially, he reported muscle weakness and atrophy in the hands, associated with cramps, with lower limbs involvement appearing approximately two months after symptom onset. The condition progressed with thenar and hypothernar muscle atrophy in the hands and significant asymmetric atrophy in the upper limbs. Following the diagnosis of amyotrophic lateral sclerosis (ALS) and initiation of riluzole treatment, the patient developed dysphagia accompanied by ptosis, with a positive ice pack test. Cerebrospinal fluid analysis, ganglioside antibodies, and light chain levels were normal. High levels of acetylcholine receptor antibodies, positive decremental response, and improvement with immunoglobulin and prednisone. Good response with pyridostigmine, based on the clinical and neurophysiological findings. A diagnostic hypothesis of Myasthenia Gravis associated with Amyotrophic Lateral Sclerosis (ALS) was proposed. **Discussion:** The relevance of this case lies in the rare and complex association between Myasthenia Gravis (MG) and Amyotrophic Lateral Sclerosis (ALS), two distinct neurological conditions with overlapping symptoms, which complicates diagnosis and management. MG is a chronic autoimmune disorder characterized by fluctuating muscle weakness and fatigue. At the same time, ALS is a progressive and fatal neurodegenerative disease affecting motor neurons, leading to muscle weakness and atrophy. The overlap typically manifests in the bulbar region (dysarthria, dysphagia) and ocular region (ptosis, diplopia). Diagnosis is based on clinical evaluation, electromyography (EMG), repetitive nerve stimulation (RNS) tests, and serological assays. Prognosis varies depending on the sequence of disease onset and the extent of neurological involvement. Immunomodulatory therapy may improve MG symptoms and prevent disability. This case underscores the importance of heightened awareness among healthcare professionals to enable early and accurate diagnosis, supported by comprehensive assessment and careful interpretation of test results. **Final comments:** Although rare, Myasthenia Gravis in association with motor neuron disease - Amyotrophic Lateral Sclerosis (ALS). Treatment may include immunosuppressive drugs for MG, or can be non-invasive, like speech therapy, for ALS, to help with the prognosis of the condition. The diagnosis can be facilitated by antibody serology, Anti-ACh and MuSK-Ab, and neurological physical examination with a well-written anamnesis. Finally, this case report is important to highlight the clinical relevance of recognizing overlapping syndromes and contributes to meaningful discussion in the neuromuscular field.

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**Área Técnica do trabalho:** Esclerose Múltipla

### Clinical, demographic and therapeutic profile of patients with multiple sclerosis managed at a public referral center in Florianópolis, Santa Catarina, Southern Brazil

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**Background:** Multiple sclerosis is a chronic inflammatory disease of the central nervous system that usually affects young adults and follows a variable course in terms of relapses and disability progression. Real-world clinical and epidemiological data from Brazilian public healthcare centers are still scarce and may contribute to improving local care planning. **Objective:** To describe the clinical, demographic, and therapeutic characteristics of patients diagnosed with multiple sclerosis treated at a public neuroimmunology clinic in southern Brazil. **Methods:** This was a retrospective observational study based on the updated registry of the Neuroimmunology Clinic of Hospital Governador Celso Ramos, a tertiary public hospital located in Florianópolis, Santa Catarina. All patients with a confirmed diagnosis of multiple sclerosis under regular follow-up were included. The following variables were collected: sex, age at diagnosis and at last evaluation, ethnicity, clinical phenotype, functional disability scores at the first and last appointments, and current use of disease-modifying therapies. **Results:** A total of 103 patients were included. The majority were female (75.7%), and the median age at evaluation was 36 years, with a median age at diagnosis of 30 years. Most patients self-identified as white (86.4%). The relapsing-remitting clinical form was predominant (85.4%), followed by the primary progressive (6.8%) and secondary progressive forms (2.9%). Among patients with the relapsing-remitting form, optic neuritis was the most frequent initial manifestation, observed in 18 of 88 individuals (20.5%). Among those with progressive forms, no single symptom predominated. The median disability score, measured using the Expanded Disability Status Scale, was 2.0 at both the first and the most recent consultation, with a slight mean increase of 0.12 points. A total of 92 patients (89.3%) were under disease-modifying therapy at the time of data collection, while 11 patients (10.7%) were not receiving any treatment. High-efficacy therapies were commonly prescribed, with natalizumab used by 34.0% of patients, followed by fingolimod (16.5%) and ocrelizumab (11.7%). **Conclusion:** The cohort presented in this study reflects the demographic and clinical profile typically described in multiple sclerosis, with a predominance of young adult women with relapsing forms and low disability. The therapeutic strategy adopted in this public healthcare center aligns with contemporary standards, emphasizing the use of high-efficacy drugs. These findings reinforce the relevance of structured clinical registries and may support the optimization of care delivery and policy development within the public health system.

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Área Técnica do trabalho: Esclerose Múltipla

EBV serology in multiple sclerosis: a profile of chronic infection

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**Background:** Several viral infections have been implicated in the pathogenesis of autoimmune diseases, including multiple sclerosis (MS). Epstein-Barr virus (EBV), a highly prevalent DNAlymphotropic herpesvirus, has been consistently associated with MS onset. Antibodies targeting different EBV antigens such as IgM, IgA, or IgG against viral capsid antigen (VCA), early antigen (EA), and EBV nuclear antigen (EBNA) may reflect the timing of infection and its potential association with MS development. **Objective:** To evaluate the seroprevalence and IgM/VCA and IgG profiles against EBV antigens in patients

with multiple sclerosis in Brazil. **Methods:** A total of 57 patients with a confirmed diagnosis of MS, according to the 2017 McDonald criteria, and 25 healthy controls were included. From the MS group, 105 serum samples were collected, either in a single visit or across multiple follow-up appointments. IgM(VCA) and IgG (VCA, EA-D, and EBNA-1) antibodies were measured using semiquantitative ELISA kits from Euroimmun. **Results:** Among patients with MS (n = 57), all tested negative for IgM antibodies against EBV VCA, with no positive cases identified. Regarding IgG antibodies, the most frequent seropositivity was for anti-EBNA-1, with 54 patients testing positive, 1 negative, and 2 inconclusive. Anti-VCA IgG was positive in 54 patients, with 2 negative results and 1 inconclusive. Anti-EA-D IgG appeared in only 2 patients; 54 were negative and 1 inconclusive. **Conclusion:** The absence of anti-VCA IgM in the cohort indicates that no individuals were in the acute phase of EBV infection at the time of sampling. Furthermore, the low prevalence of anti-EA-D antibodies suggests limited viral reactivation among patients with MS. The high seropositivity rates for anti-VCA IgG and anti-EBNA-1 are consistent with prior EBV exposure and support the interpretation that the majority of patients were in a chronic phase of EBV infection, without serological evidence of active viral replication.

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Área Técnica do trabalho: Esclerose Múltipla

From diagnosis to intervention: how treatment timing influences broader outcomes in multiple sclerosis

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**Background:** Multiple sclerosis (MS) is the most common non-traumatic cause of disability in young adults. The growing prevalence contributes significantly to the socioeconomic impact of the disease, largely driven by physical and cognitive impairments. Early diagnosis and the timely initiation of treatment are crucial for minimizing the daily limitations and quality of life deterioration experienced by those affected. **Objective:** Clarify statistically the long-term impact of the interval between symptom onset and the initiation of treatment and high efficacy therapy on prognosis. **Methods:** This is a multicenter study involving MS patients from three outpatient clinics, analyzed through an ambispective design. The time from disease onset to the initiation of the first disease-modifying therapy (TFDT), as well as the time to the first high-efficacy treatment (TFET), were calculated. Sociodemographic and clinical data were collected and disease progression was assessed using conventional physical and cognitive disability scales, along with symptom burden, employability and quality of life questionnaires. **Results:** A total of 249 MS patients were included in the baseline analysis: 77.9% females; mean/standard deviation (SD) age at analysis was 39.9(11.5) years; mean/SD age at disease onset was 29.4(9.5) years; mean disease duration of 10.7(8.1) years; median baseline EDSS score was 2.0. A longer TFDT was associated with worse processing speed ( $r=-0.214$ ;  $p=0.014$ ) and visual memory ( $r=-0.266$ ;  $p=0.002$ ), and was also significantly correlated to worse EDSS scores ( $r=0.363$ ;  $p<0.001$ ). TFET was also significantly correlated to EDSS ( $r=0.482$ ;  $p<0.001$ ) and SymptoMScreen ( $r=0.273$ ;  $p<0.001$ ). Early usage of high-efficacy therapy was associated with significantly higher MSQOL-54 scores (median 72.6 vs. 61.42;  $p=0.0357$ ). Longer time to high-efficacy treatment was significantly associated with impaired employability (median: 8.89 vs. 3.2 years;  $p<0.001$ ). **Conclusion:** A delay in treatment introduction is associated with cognitive

dysfunction, symptom severity and worse physical disability. Furthermore, longer time to start high efficacy therapy was significantly associated to impaired employability and lower quality of life.

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Área Técnica do trabalho: Esclerose Múltipla

High-efficacy MS drug access in the Amazon basin: distance doesn't tell the whole story

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**Background:** Multiple sclerosis (MS) in the Amazon Basin presents challenges for diagnosis and treatment with high efficacy disease-modifying drugs (DMDs) due to its vast geography. **Objective:** To analyze the dispensation of DMDs by the public healthcare system in the Amazon Basin between 2019 and 2023, and to evaluate the association between the distance traveled by patients and the dispensation of high efficacy DMDs. **Methods:** Using Big Data, we analyzed DATASUS's APAC data from 2019–2023 for seven Amazon Basin states (AC, AM, AP, PA, RO, RR, MT). Natalizumab and Alemtuzumab were classified as high efficacy. DMD dispensation frequencies were compared using Wilcoxon test. In 2023, distance traveled by patients was calculated using the OSRM API, excluding patients living in the same city as the dispensing centers. A Spearman correlation analysis was conducted to assess the association between distance traveled by patients and high efficacy DMD dispensation. **Results:** In 2023, 710 patients received DMDs, a 35.7% increase from 2019 (n = 523). AC held 4.23% of cases, AM 16.90%, AP 2.25%, PA 28.31%, RO 10.42%, RR 3.52%, MT 34.37%. High efficacy DMD dispensation increased (2019: 497; 2023: 1555,  $p=0.03$ ). The mean distance traveled by patients in the Amazon Basin was  $127.9 \pm 78.11$  km, average distances were: AC  $141.20 \pm 42.3$  km, AM  $152.60 \pm 20.0$  km, AP  $176.83 \pm 57.0$  km, PA  $119.56 \pm 83.0$  km, RO  $129.92 \pm 43.73$  km, RR  $0 \pm 0$  km, and MT  $130.41 \pm 81.3$  km. The Spearman correlation analysis did not show an association between distance traveled by patients and high efficacy DMD dispensation ( $\rho = -0.14$ ,  $p = 0.76$ ). **Conclusion:** In the Amazon Basin between 2019 and 2023 there was an increase of MS cases and an increase in high efficacy dispensation, with regional disparities. Distance traveled by patients was not associated with high efficacy dispensation, indicating that barriers beyond distance are limiting access to high efficacy DMDs in the Amazon Basin.

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Área Técnica do trabalho: Esclerose Múltipla

Impact of the 2021 PCDT update on multiple sclerosis medication dispensation patterns in Brazil: a big data analysis

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**Background:** Multiple Sclerosis (MS) treatment is offered by the Brazilian Unified Health System through a Clinical Protocol and Therapeutic Guidelines updated in 2021 to include high-efficacy drugs such as natalizumab (NTZ) and alemtuzumab (ALE) as initial and escalation treatments, respectively. Despite these updates, data regarding regional differences in dispensation of drugs after PCDT update are unknown. **Objective:** To evaluate differences in dispensation of MS drugs in Brazil after PCDT update, emphasizing high-efficacy drugs and regional variabilities. **Methods:** We conducted a Big Data analysis using High-Cost Ambulatory Procedures Authorization (APAC) from 2019 to 2023 from DATASUS. The number of patients were compiled for each region and year. Disease Modifying Drugs (DMDs) by region were compiled and grouped as high-efficacy (NTZ, ALE) and moderate/low-efficacy (FNG, DME, TERI, AZA, AG, IFN). The average number of APACs from 2019 to 2021 (pre-PCDT) was compared with the data from 2023 (post-PCDT), and frequency of DMD dispensation were compared using X2. **Results:** NTZ dispensation increased from 12.7% pre-PCDT to 20.07% post-PCDT ( $p < 0.05$ ), while IFN dispensation decreased from 29.6% to 16.07% ( $p < 0.05$ ). The North and Central-West regions had the largest increases in high-efficacy DMD dispensation (13.12% and 9.7%, respectively), with notable reductions in low-efficacy treatments (North -20.5%, Central-West -14.6%). Additionally, the frequency of switches to high-efficacy DMDs increased from 18.05% to 33.67% ( $p < 0.05$ ). In 2023, 28,521 received DMD, a 25.91% of increased between 2019 and 2023. The Southeast region held 56.23% of MS patients. **Conclusion:** The 2021 PCDT update has influenced MS DMD dispensation patterns across Brazil with a shift toward high-efficacy therapies. However, regional disparities in DMD dispensation persist, indicating the need for further investigation to ensure equitable access to MS treatments across Brazil.

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Área Técnica do trabalho: Esclerose Múltipla

### Impact of the 2024 revised McDonald criteria on multiple sclerosis diagnosis in Brazilian patients

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**Background:** Multiple sclerosis (MS) is a chronic immune-mediated disease of the central nervous system, characterized by inflammation, demyelination, and neurodegeneration. Early diagnosis is critical for timely initiation of disease-modifying therapies, which can delay progression and improve long-term outcomes. In 2024, the McDonald diagnostic criteria (McD) were revised to increase sensitivity and accuracy, as underdiagnosis and misdiagnosis can have serious consequences for patients. **Objective:** To evaluate the impact of the 2024 McD on MS prevalence in patients initially classified with clinically isolated syndrome (CIS), radiologically isolated syndrome (RIS), or recurrent demyelinating episodes (RDE), comparing rates before and after implementation and identifying which criteria changes led to reclassification. **Methods:** This retrospective multicenter study included patients from three Brazilian clinics initially diagnosed with MS (2017 McD), RIS, CIS, or RDE not meeting 2017 McD. All were reassessed using both 2017 and 2024 McD.

New variables were assessed according to proposals presented at ECTRIMS (European Committee for Treatment and Research in Multiple Sclerosis) 2024. Clinical data, the five anatomical topographies, cerebrospinal fluid (CSF) data—including oligoclonal bands (OCB) and kappa free light chains (KFLC)—and MRI findings—including paramagnetic rim lesions (PRL) and central vein sign (CVS)—were evaluated. Pediatric and late-onset cases were reviewed for misdiagnosis. Diagnosis changes and prevalence shifts were recorded. **Results:** Among 301 patients (78.4% female; mean age 32.1 years; mean disease duration 9.1 years; median EDSS 2.0), initial diagnoses included MS ( $n=271$ ), while 30 did not fulfill 2017 McD: CIS ( $n=14$ ), RIS ( $n=15$ ), and RDE ( $n=1$ ). Fifteen of these 30 patients (50%) were reclassified as MS under 2024 criteria. RIS mainly drove reclassification: 13/15 (86.7%) became MS-McD2024; one CIS and the RDE case were also reclassified. Seven of 30 (23.3%) showed dissemination in time by MRI, 11 (36.7%) had optic nerve involvement, 5/19 (26.3%) had  $\geq 1$  PRL, none had quantitative CVS data, 17/29 (58.6%) had positive OCB, and 1/3 (33.3%) had positive KFLC. MS prevalence increased by 5.5%, from 271 to 286 patients. No misdiagnoses were found among pediatric-onset ( $n=27$ ) or late-onset ( $n=9$ ) cases. **Conclusion:** The 2024 McD increased MS diagnosis mainly by reclassifying RIS cases, with no misdiagnoses in pediatric or late-onset patients. Focused reassessment of RIS and CIS patients is recommended. Structured MRI reports—including optic nerve evaluation, PRL, and CVS—are essential. KFLC can be helpful, especially where OCB are less reliable or unavailable. Caution is needed in centers lacking specialists, high-quality imaging, standardized MRI reports, or biomarker access. These updates support earlier, accurate diagnosis and timely treatment, improving outcomes.

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Área Técnica do trabalho: Esclerose Múltipla

### Multiple sclerosis drug access across Brazil's public health system between 2019 and 2023: a study using distance traveled by patients and dispensing centers

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**Background:** Multiple sclerosis (MS) patients often have motor and cognitive impairments that are barriers to treatment. Disease-modifying drugs (DMDs) are provided by the Unified Health System (SUS); however, analysis of geographic distribution of dispensing centers (DCs) and distance traveled by patients to access them are unknown. **Objective:** To analyze the number of DCs and MS patients between 2019 and 2023, the geographic distribution of DCs and its correlation with distance traveled by patients in 2023. **Methods:** We analyzed the APACs (High-Cost Procedure Authorizations) (2019–2023) for DMD dispensation and identified MS patients (ICD G35). We extracted home cities, and DC's locations. Then, DCs/100,000 km<sup>2</sup> were calculated by region. Distance traveled by patients was estimated via Open Source Routing Machine (OSRM) API using distances between city centroids and DCs; patients living in the same city as the DC were excluded from this analysis. Kruskal-Wallis compared distances traveled by patients between regions. Spearman correlation between DCs/100,000 km<sup>2</sup> and distance traveled by patients was calculated. **Results:** From 2019 to 2023, the number of MS patients treated by SUS increased by 25.9%

(22,651 to 28,521), while the number of DCs rose only 4.8% (187 to 196). In 2023, Brazil had 2.30 DCs/100,000 km<sup>2</sup> and a mean distance traveled by patients of 76.5 ± 55.6 km. The distance traveled by patients differed across regions (North 128.5 ± 71.8 km; Midwest 119.2 ± 78.8 km; Northeast 103.9 ± 67.0 km; South 83.6 ± 59.4 km; Southeast 64.7 ± 43.6 km;  $p < 0.001$ ). DCs/100,000 km<sup>2</sup> by region were: Midwest 0.31; North 0.62; Northeast 3.15; South 7.11; Southeast 8.33. There was a negative correlation between DC density and distance traveled by patients ( $\rho = -0.90$ ,  $p = 0.037$ ). **Conclusion:** In Brazil, the number of DCs did not match the growth of MS patients. There were regional differences in the distribution of DCs, and long distances traveled by patients were correlated with low DC densities. A way to improve the distance traveled by patients would be to increase DCs for MS patients served by the public health system.

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Área Técnica do trabalho: Esclerose Múltipla

### Multiple sclerosis: analysis of initial treatment in a tertiary hospital

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**Background:** The initial therapeutic strategy in multiple sclerosis (MS) plays a crucial role in long-term prognosis. There is increasing evidence that initiating high-efficacy therapies (HET) early provides superior disease control compared to escalation approaches with low- to moderate-efficacy therapies (LMET). **Objective:** To evaluate the impact of initial treatment with HET versus LMET on disability progression in patients with relapsing-remitting MS (RRMS) followed in a Brazilian public tertiary hospital. **Methods:** A retrospective observational study was conducted based on electronic medical records of 35 RRMS patients treated between December 2021 and December 2023. Patients were stratified by initial therapy into HET or LMET groups. Demographic data, lesion topography, time to diagnosis and treatment, and changes in the Expanded Disability Status Scale (EDSS) after one year were analyzed. Statistical comparisons and effect size estimations were performed using appropriate tests. **Results:** The HET group showed a significantly greater reduction in EDSS after one year ( $-0.33 \pm 0.53$ ) compared to an increase in the LMET group ( $+0.5 \pm 1.1$ ;  $p = 0.00498$ ). Despite having a higher baseline EDSS (4.08 vs. 1.5;  $p = 0.0002$ ), the HET group demonstrated superior control of disease progression. Delays in diagnosis (mean 34.16 months) and treatment initiation (14.08 months) were observed in both groups, reflecting systemic barriers in the Brazilian Unified Health System (SUS). **Conclusion:** Early initiation of HET was associated with better disability outcomes, even in patients with more severe baseline presentations. These findings support the adoption of early, high-efficacy interventions and underscore the need for structural improvements in MS care within the SUS.

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Área Técnica do trabalho: Esclerose Múltipla

### Ocrelizumab in multiple sclerosis: sustained effectiveness and low discontinuation rates in a Brazilian real-world cohort

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**Background:** Ocrelizumab, a humanized anti-CD20 monoclonal antibody, selectively depletes B cells involved in the pathogenesis of multiple sclerosis (MS). Although widely used for both relapsing-remitting and primary progressive MS, real-world data from Brazil—particularly in treatment-naïve patients, those switching from natalizumab due to progressive multifocal leukoencephalopathy (PML) risk, or transitioning from other therapies due to inadequate response or adverse events—remain limited. **Objective:** This study provides a descriptive analysis of patient profiles and main treatment indications, and evaluates the sustained effectiveness of ocrelizumab in preventing relapses, along with discontinuation rates and their causes. **Methods:** In this prospective observational study, MS patients initiating ocrelizumab were stratified into four groups: (1) treatment-naïve; (2) switchers from natalizumab due to progressive multifocal leukoencephalopathy (PML) risk; (3) switchers from other disease-modifying therapies (DMTs) due to treatment failure or adverse events (AEs); and (4) patients undergoing prognostic reassessment under clinical stability. Outcomes included annualized relapse rate (ARR), relapse-free survival, and treatment discontinuation rates and reasons. **Results:** Among 102 MS participants (mean age 38.1 ± 10 years; 72.5% female; median disease duration 9.9 years; median EDSS 2.0; median treatment cycles 6, range 1–12), 20.6% were treatment-naïve, 33.3% switched due to PML risk, 44.1% switched from other DMTs (42.1% due to treatment failure, 2% due to adverse events), and 2% due to prognostic reassessment. Over a median follow-up of 33.2 months, 95.9% of patients remained relapse-free, representing a 90.7% reduction in annualized relapse rate (ARR) from 0.37 to 0.034 ( $p < 0.001$ ). Notably, the PML-risk subgroup achieved 100% relapse-free status after switching from natalizumab, following the strategy of a maximum 4-week washout period. Discontinuation rates were very low, with no discontinuations due to treatment failure or serious adverse events; one patient discontinued by personal preference, and three (3.2%) due to loss of insurance coverage. **Conclusion:** Ocrelizumab demonstrated robust and sustained effectiveness across all subgroups, with excellent relapse control. Given the absence of anti-CD20 therapies in the Brazilian public health system, these data support its essential role as a treatment option. Additional findings on efficacy in slowing disease progression and a favorable safety profile in national cohorts may further strengthen confidence in translating RCT results into everyday clinical practice.

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Área Técnica do trabalho: Esclerose Múltipla

### Ocrelizumab-induced interstitial lung disease: case report with primarily progressive multiple sclerosis

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**Case Presentation:** Woman, 49 years old, diagnosed with Primary Progressive Multiple Sclerosis (PPMS) in 2017 after a progressive case of weakness in the lower limbs, paresthesias, and hypoesthesia, starting in the left lower limb. MRI showed hyperintense lesions on T2 in periventricular and juxtacortical regions, as well as spinal foci. The cerebrospinal fluid demonstrated positive oligoclonal bands. Other laboratory tests were negative. Since 2019, she has been using ocrelizumab regularly. In June 2024, she presented an acute episode of fever, chest pain, and asthenia. The chest tomography showed bilateral infiltrates consistent with pneumonia. She was

admitted to the ICU, receiving broad-spectrum antibiotic therapy. Despite the therapy, she progressed to respiratory failure, requiring intubation and mechanical ventilation. A comprehensive investigation was carried out for infectious agents, including acid-fast bacilli (AFB), fungi, atypical bacteria, and respiratory viruses, with negative results. In the absence of infectious etiology and the history of exposure to ocrelizumab, a lung biopsy was performed, which confirmed organized pneumonia associated with the use of the immunobiological. Ocrelizumab was discontinued and, after recovery, was replaced by ofatumumab in November 2024. The patient shows stabilization of the neurological and pulmonary condition, maintaining rigorous monitoring. **Discussion:** Primary Progressive Multiple Sclerosis (PPMS) has a pathophysiology that is not yet fully understood, but B cells play a central role. Ocrelizumab, an anti-CD20 monoclonal antibody, has shown efficacy in reducing the clinical progression of PPMS, according to the ORATORIO study. Its adverse effects include infusion reactions, respiratory infections, and severe events such as drug-induced interstitial lung disease (DIILD), a rare and potentially severe complication. 1 The diagnosis is challenging, requiring the exclusion of other infectious, autoimmune, or environmental etiologies, as well as a temporal correlation with the use of the medication. 2 Although reports of DIILD from ocrelizumab are scarce, this reaction is described in treatments with other anti-CD20s, such as rituximab, usually occurring within two weeks following the infusion, with a good response to corticosteroids. 3,4 In the presence of a compatible pulmonary condition, it was decided to suspend ocrelizumab and start ofatumumab, another anti-CD20. Although not approved for EMPP, its subcutaneous application and lower pulmonary distribution suggest a potentially more favorable safety profile in these cases. **Final Comments:** The use of anti-CD20 therapies, such as ocrelizumab, represents an advance in the treatment of primarily progressive multiple sclerosis. However, close follow-up of patients is critical, with special attention to potential adverse effects, including serious and infrequent complications such as drug-induced interstitial lung disease.

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Área Técnica do trabalho: Esclerose Múltipla

### Overlapping features of multiple sclerosis and neuromyelitis optica: a case report

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**Case Presentation:** An 18-year-old male was referred with a six-month history of central scotoma in the left eye and progressive visual loss, with ocular pain worsened by movement. Examination revealed a left afferent pupillary defect, visual acuity of 20/800 in the left eye and 20/60 in the right, and hypoesthesia in the left lower limb. CSF analysis showed normal cell count, protein, and glucose, with negative infectious tests and presence of oligoclonal bands. Brain MRI revealed multiple ovoid, periventricular T2/FLAIR lesions, including Dawson's fingers and involvement of the corpus callosum and callosseptal interface. Orbital MRI showed enhancement of the left optic nerve and chiasm, suggesting optic neuritis. Subtle signal changes were also noted in the right optic nerve and tracts, without enhancement. Spinal MRI identified demyelinating lesions in the left medulla and cervical spinal cord bilaterally. AQP4 and MOG antibodies were negative. The patient received intravenous methylprednisolone (1 g/day, 5 days) followed by five plasmapheresis sessions, improving left visual acuity to 20/100. Despite optic chiasm involvement, the diagnosis of MS was favored based on imaging and CSF, and natalizumab was initiated. **Discussion:** MS

and NMOSD share overlapping features such as optic neuritis and myelitis. NMOSD typically involves bilateral optic nerves and the chiasm, often with longitudinally extensive transverse myelitis. In contrast, MS shows periventricular, ovoid lesions perpendicular to the ventricles (Dawson's fingers) and involvement of the corpus callosum. Chiasmal involvement is more suggestive of NMOSD but may rarely appear in MS. In this case, the absence of AQP4 and MOG antibodies did not rule out NMOSD, but the presence of oligoclonal bands and the lesion distribution strongly supported MS. The diagnostic process underscores the importance of detailed radiological evaluation, especially in antibody-negative cases. **Final Comments:** This case highlights the relevance of integrating clinical, radiological, and laboratory data in distinguishing MS from NMOSD. Despite optic chiasm enhancement, the MRI pattern and CSF profile were more consistent with MS. Early treatment led to partial visual recovery, and initiation of a high-efficacy disease-modifying therapy like natalizumab aims to reduce relapse risk and disability accumulation. Such cases exemplify the complexity and nuance required in diagnosing demyelinating diseases, particularly when classic features overlap.

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Área Técnica do trabalho: Esclerose Múltipla

### Prevalence of viral seropositivity in multiple sclerosis patients: focus on vaccine-preventable infections

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**Background:** Viral infection screening is a crucial step in the differential diagnosis of multiple sclerosis (MS) and has become increasingly relevant with the introduction of disease-modifying therapies (DMTs). These immunosuppressive or immunomodulatory agents may reactivate latent viral infections, making it essential to understand the viral serological profile of MS patients to ensure safe therapeutic management. **Objective:** To analyze the prevalence of viral seropositivity in MS patients, focusing on vaccine-preventable viruses. **Methods:** A descriptive and retrospective study was conducted to investigate the seroprevalence of infections caused by 3 viruses in 54 patients with a confirmed MS diagnosis according to the 2017 McDonald criteria. Serological records included IgM and IgG results for Varicella Zoster Virus (VZV) and Rubella Virus (RV) and Hepatitis B Virus (HBV), evaluated through HBsAg and anti-HBs. **Results:** IgG seropositivity was highest for VZV (77.4%), followed by RV (76.5%) and anti-HBs (30.8%). IgM positivity for VZV was low (3.4%), suggesting a low prevalence of recent or active infections. No recent infections were observed for RV or active infections for HBV (HBsAg). Serological analysis by sex showed that 80% of women and 66.7% of men had reactive VZV IgG results ( $p = 0.596$ ). For HBV (anti-HBs), 32.3% of women and 25% of men were reactive ( $p = 1.000$ ). For RV (IgG), 71.4% of women and 100% of men were reactive ( $p = 0.541$ ). Serological analysis by age group showed VZV IgG reactivity in 50% of individuals under 30, 83.3% in those aged 30–49, and 85.7% in those aged 50 or older ( $p = 0.316$ ). HBV anti-HBs was reactive in 42.9% of individuals under 30 and 30–49, but absent in those aged 50 or older ( $p = 0.037$ ). RV IgG reactivity was 75% in individuals under 30, 80% in the 30–49 group, and 66.7% in those 50 or older ( $p = 1.000$ ). **Conclusion:** In this cohort of MS patients, most individuals showed prior exposure or immunization against VZV and RV, while HBV seropositivity was notably lower, particularly among individuals aged 50 or older. The findings highlight the importance of systematically assessing vaccine-related

viral immunity in MS patients, especially before initiating immunosuppressive treatments, to reduce the risk of reactivating latent viral infections.

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Área Técnica do trabalho: Esclerose Múltipla

### Quality of life evaluation in individuals with relapsing-remitting multiple sclerosis in a reference center

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**Background:** Multiple sclerosis (MS) is the most common disabling pathology of the CNS in young adults. Patients with MS have an impaired quality of life (QOL). The Short Form Health Survey 36 (SF-36) is the most widely used questionnaire to assess quality of life in patients with MS. **Objective:** to evaluate the quality of life of patients diagnosed with multiple sclerosis in the relapsing-remitting form, in order to understand how patients evaluate themselves in this regard. **Methods:** this is a cross-sectional field study with a quantitative approach, of a descriptive and exploratory nature. The study was carried out on people with MS followed at the MS Reference Center of the State of Paraíba (CREMPB). The Short Form Health Survey 36 (SF-36) questionnaire was used and sociodemographic data were evaluated. **Results:** The survey obtained 85 responses to the questionnaire. The sample consisted of 77.58% females and 22.42% males. The overall mean age of the participants was 36.77 (SD=9.65) years. Regarding the time since diagnosis in years, the mean obtained was 6.14 years (SD=4.94). Regarding the level of education, we observed that 93.11% (N=54) of the participants had completed high school. Regarding the position in the job market, 68.96% (N=37) of the participants declared themselves to be active in the job market. Regarding the analysis of the patients' quality of life, the domains with the greatest impairment were limitation due to emotional aspects, followed by vitality and limitation due to physical aspects. **Conclusion:** Patients with Relapsing Remitting Multiple Sclerosis have a decreased perception of Quality of Life. Gender influences the quality of life of patients with RRMS.

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Área Técnica do trabalho: Esclerose Múltipla

### Regional inequalities in hospitalizations due to multiple sclerosis in Brazil and the impact of the COVID-19 pandemic between 2017 and 2022

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**Background:** Multiple Sclerosis (MS) is a rare, chronic, autoimmune demyelinating disease that affects the brain, optic nerves, and spinal cord, leading to motor and sensory impairments. One of its main features is the unpredictable occurrence of relapses, which may include symptoms such as severe fatigue, depression, muscle weakness, impaired coordination, joint pain, and bowel and bladder dysfunction. Early diagnosis and specialized management are essential for adequate care. Therefore, inequalities in

access to healthcare contribute to increased frequency of disease exacerbations and hospital admissions. In this context, the COVID-19 pandemic, which began in 2020, posed additional challenges to the continuity of care, especially for complex and chronic conditions such as MS. The analysis of hospitalization data can offer insights into the pandemic's impact and identify regions in the country that are more vulnerable in terms of neurological healthcare coverage. **Objective:** To analyze the regional distribution and temporal trends of hospitalizations for Multiple Sclerosis in Brazil between 2017 and 2022, with a focus on the possible repercussions of the COVID-19 pandemic on access to specialized care. **Methods:** This is an ecological, retrospective, cross-sectional, and quantitative study based on secondary data extracted from the Brazilian Hospital Information System (SIH/SUS). Hospital admissions for Multiple Sclerosis (ICD-10 G35) from 2017 to 2022 were included. Variables analyzed were year of processing and region of hospitalization. Bar and line graphs were used to illustrate trends and regional proportions. **Results:** A total of 35,444 hospitalizations for Multiple Sclerosis were recorded between 2017 and 2022. The Southeast region accounted for 71% of cases (25,166), followed by the Midwest (8.4%) and South (12%). The North and Northeast regions together represented only 8.3% of hospitalizations. In 2020, there was a 10% drop in total admissions (from 4,374 to 3,972), coinciding with the onset of the pandemic in Brazil. However, hospitalization numbers rose again in 2021, peaking in 2022 (7,299 hospitalizations). This increase was especially prominent in the Southeast region, while areas such as the North remained stable. **Conclusion:** This study reveals significant regional disparities in hospitalizations for Multiple Sclerosis in Brazil, with a clear concentration in the Southeast. The decline in admissions in 2020, followed by an uneven recovery, suggests that the pandemic may have worsened existing barriers to early diagnosis and adequate hospital care, particularly in historically underserved regions. These findings highlight the urgent need to expand specialized public healthcare services and strengthen neurological health surveillance across the country.

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Área Técnica do trabalho: Esclerose Múltipla

### Understanding delayed diagnosis in multiple sclerosis: risk factors in a Brazilian cohort

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**Background:** Multiple sclerosis is a chronic autoimmune disorder of the central nervous system that affects daily life through a wide range of symptoms and long standing limitations. Understanding the factors associated with delayed diagnosis, besides the evolution of diagnostic criteria, offers important insights for improving the diagnostic process and identifying predictors of worse outcomes. **Objective:** Widen the analysis of factors contributing to a delay in MS diagnosis, beyond only the evolution of diagnostic criteria. **Methods:** A prospective cohort was conducted with relapsing-remitting multiple sclerosis patients who underwent consultations from 2015-2024 in three participating outpatient centers. Clinical, demographic, and neuropsychological data were collected and analyzed. Diagnostic delay was defined as more than 12 months from disease onset. **Results:** 288 patients were included in the analysis (77.3% female) with a mean age at diagnosis of 30.5 years, mean disease duration of 7.8 years, and a median EDSS score of 2.0. Univariate analysis revealed that late diagnosis was significantly associated with older age at diagnosis ( $p < 0.001$ ), male sex ( $p = 0.041$ ), and

absence of health insurance at symptom onset ( $p = 0.001$ ). Family history of autoimmune diseases and involvement of the sensory functional system showed a trend toward earlier diagnosis but did not reach statistical significance ( $p = 0.097$  and  $p = 0.056$ , respectively). In multivariate logistic regression, older age increased the odds of late diagnosis (OR = 1.05; 95% CI: 1.02-1.08;  $p = 0.001$ ), while having health insurance at symptom onset reduced the odds by 84.2% (OR = 0.158; 95% CI: 0.034-0.541;  $p = 0.007$ ). Additionally, after this second analysis, having a family history of autoimmune diseases was independently associated with lower odds of delayed diagnosis (OR = 0.487; 95% CI: 0.257-0.900;  $p = 0.024$ ). However, in the adjusted model, sex, sensory dysfunction, education level, and race were not significantly associated with delayed diagnosis. **Conclusion:** Factors associated with a longer time to diagnosis include older age, absence of healthcare insurance and no family history of autoimmune diseases. By knowing the population at risk for delayed diagnosis, it is possible to target public policies to improve earlier detection of the disease and the access to specialized care. This approach would help reduce the overall disease burden associated with treatment delays.

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Área Técnica do trabalho: Esclerose Múltipla

### Use of Ofatumumab in Patients with Multiple Sclerosis at a Reference Center

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**Background:** Multiple sclerosis (MS) is a chronic, autoimmune, demyelinating disease of the central nervous system. The primary goal of treatment is to prevent disease progression and disability accumulation. Ofatumumab (Kesimpta®), a recombinant human anti-CD20 monoclonal antibody, has proven effective in treating relapsing forms of MS. **Methods:** A retrospective study based on the review of medical records from 10 patients treated with Ofatumumab at a multiple sclerosis reference center in Brazil. **Results:** Data from 10 patients using Ofatumumab were analyzed. Seven had relapsing-remitting MS, and three had secondary progressive MS. Seven patients had previously used disease-modifying therapies, with six switching from natalizumab and one from dimethyl fumarate. Three patients were naïve, having used only corticosteroids. Reasons for switching to Ofatumumab varied: four patients had positive JCV serology while using natalizumab, one developed lymphopenia <500 with positive JCV, three had worsening disability and EDSS scores, and two had new relapses and MRI lesions. Regarding adverse effects (AEs), only mild symptoms (myalgia, headache, and fever) were observed on the day of the first dose. There were no changes in immunoglobulin G or M levels. A reduction in annualized relapse rates, MRI-detected lesion activity, and disability progression was observed, similar to the results seen in the ASCLEPIOS I and II trials. Adverse effects were consistent with phase II trial data, where subcutaneous ofatumumab was well tolerated, and similar findings were seen in phase III trials, where AEs were reported in 83.6% of patients treated with ofatumumab. **Conclusion:** The results of this study suggest that the use of Ofatumumab in patients with relapsing MS is safe, with a low incidence of adverse

events, and is effective in controlling disease relapses in both naïve and previously treated patients. This promising profile may reduce disability accumulation in the medium to long term.

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**Área Técnica do trabalho:** Espectro da Neuromielite Óptica

### Acute flaccid areflexic paraparesis in a pediatric patient: differential diagnosis between acute polyradiculoneuritis and neuromyelitis optica

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**Case Presentation:** We present the case of a previously healthy 13-year-old female patient who developed ascending flaccid paraparesis, global areflexia, ataxia, dysarthria, and dysphagia. She was initially diagnosed with acute polyradiculoneuritis and treated with intravenous immunoglobulin, with no significant improvement. Approximately 20 days before symptom onset, the patient had received the Pfizer COVID-19 vaccine, raising the possibility of an immune-mediated trigger. During disease progression, signs of pyramidal tract involvement emerged, raising suspicion of central nervous system involvement. Complementary examinations revealed inflammatory supratentorial and infratentorial lesions on magnetic resonance imaging, and serology demonstrated AQP4-IgG positivity, confirming the diagnosis of NMOSD. The patient showed significant clinical improvement after pulse therapy with methylprednisolone, followed by immunosuppressive treatment with azathioprine. **Discussion:** Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory autoimmune disease of the central nervous system, frequently associated with anti-aquaporin-4 antibodies (AQP4-IgG). Its clinical presentation can vary, and atypical manifestations may delay diagnosis, leading to delayed therapy and unfavorable prognosis. This case highlights the diagnostic challenges of NMOSD in pediatric patients, particularly when initial symptoms mimic acute polyradiculoneuropathies. **Final Comments:** We emphasize the importance of early recognition of central nervous system involvement and the need for targeted investigation to prevent delays in treatment and minimize permanent neurological sequelae.

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**Área Técnica do trabalho:** Espectro da Neuromielite Óptica

### FCGR3A Polymorphism in patients with AQP4 IgG-seropositive neuromyelitis optica spectrum disorder

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**Background:** Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare autoimmune disease of the central nervous system, characterized by severe attacks of optic neuritis, transverse myelitis, and/or area postrema syndrome. Latin America (LATAM) is known for its extensive racial and genetic diversity, stemming from historical interactions among Indigenous populations, European colonizers, and African slaves. A polymorphism in the low-affinity IgG Fc receptor III-A gene (FCGR3A) has been associated with reduced efficacy of monoclonal antibody treatments in various diseases, including NMOSD. **Objective:** To determine the presence and type of FCGR3A polymorphism in patients diagnosed with NMOSD. **Methods:** This was a descriptive, cross-sectional study conducted with patients diagnosed with NMOSD receiving follow-up care at a neurology outpatient reference center in Latin America. The study was approved by the institutional ethics committee, and all participants provided informed consent prior to enrollment. Patients with a confirmed diagnosis of NMOSD were invited to participate. Genotyping for polymorphism in the low-affinity IgG Fc receptor III-A gene was performed using buccal swab samples. Samples were collected using sterile swabs and stored at appropriate temperatures until processing. Genotypes were classified as homozygous valine (VV), heterozygous valine/phenylalanine (VF), or homozygous phenylalanine (FF). Descriptive statistical analysis was used to determine the frequency of each genotype among the participants. The results were expressed as absolute numbers and percentages. **Results:** Fourteen patients diagnosed with NMOSD, all receiving different therapeutic regimens, underwent buccal swab testing to detect the FCGR3A polymorphism. 80% were female and 20% male. And based on self-identification, 8 participants were White, and 8 were mixed ethnicity or Black. Among those who consented to genotyping, 1 (7%) was homozygous for the VV allele, 6 (44%) were heterozygous (VF), and 7 (49%) were homozygous for the FF allele. The majority of participants were women, and most tested positive for serum AQP4-IgG antibodies. **Conclusion:** The distribution of FCGR3A polymorphisms in this cohort suggests potential implications for individualized treatment approaches in NMOSD. Understanding genetic variability may help optimize therapeutic strategies and improve clinical outcomes in genetically diverse populations, such as those in Latin America.

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**Área Técnica do trabalho:** Espectro da Neuromielite Óptica

### Optic neuritis and mucosal ulcers in a young woman: a case of dual autoimmune neuroinflammation

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**Case Presentation:** A 27-year-old woman presented with a two-year history of arthralgia affecting the hands, feet, and knees, associated with complaints of alopecia, xerophthalmia, and xerostomia. Systemic Lupus Erythematosus (SLE) was initially considered. Laboratory evaluation revealed a positive antinuclear antibody (ANA) at a titer of 1:160 with a homogeneous nuclear pattern, while other autoantibodies (anti-RNP, anti-SM, anti-Ro, anti-La, lupus anticoagulant, anticardiolipin, and anti-dsDNA) were non-reactive. Infectious serologies were negative. One year later, she developed painful, self-limiting but recurrent oral and genital mucosal ulcers. During this period, she

also exhibited neurological manifestations including persistent holocranial headache, bilateral tonic-clonic seizures, asymmetric tetraparesis, urinary retention, dysarthria, and blurred vision. Complementary investigations revealed retrobulbar neuritis confirmed on brain and orbital MRI, lymphocytic pleocytosis in cerebrospinal fluid (CSF), and positivity for the HLA-B51 allele on etiologic screening. Imaging of the cervical, thoracic, and lumbar spinal cord showed no significant abnormalities. CSF biochemistry revealed no other relevant changes. The pathology test was negative, and serological tests for anti-MOG and anti-aquaporin-4 antibodies were also negative. Based on these findings, a dual diagnosis of Neuro-Behçet's disease (NB) and double-seronegative neuromyelitis optica spectrum disorder (NMOSD) was proposed. The patient underwent immunosuppressive therapy, initially with pulse methylprednisolone, followed by azathioprine and subsequently cyclophosphamide, resulting in significant clinical improvement. **Discussion:** The present case describes a patient with clinical and laboratory findings supporting a concurrent diagnosis of Neuro-Behçet's disease (NB) and neuromyelitis optica spectrum disorder (NMOSD), which may share overlapping neurological manifestations. The coexistence of these autoimmune neuroinflammatory entities, potentially involving dysregulated T-cell activation and proinflammatory cytokine production, may reflect converging immunopathogenic mechanisms in genetically predisposed individuals. Although this association remains rare in the literature, autoimmune diseases commonly coexist in the same patient. On one hand, despite the absence of spinal cord lesions on MRI, the combination of CSF lymphocytic pleocytosis and HLA-B51 positivity supports NB as a diagnostic hypothesis, particularly in the context of systemic features such as oral/genital ulcers, uveitis, and cutaneous lesions. On the other hand, the presence of optic neuritis along with urinary retention, tetraparesis, and dysarthria reinforces the suspicion of NMOSD. **Final Comments:** This case highlights the importance of recognizing neuroimmune overlap syndromes, for which close monitoring, early identification, and effective management can significantly improve clinical outcomes.

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**Área Técnica do trabalho:** Espectro da Neuromielite Óptica

### Pulmonary MALT lymphoma during long-term rituximab therapy in a patient with neuromyelitis optica: a rare and paradoxical association

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**Case Presentation:** A 61-year-old male with aquaporin-4-positive neuromyelitis optica spectrum disorder (NMOSD) since 2009 presented with a history of five relapses, including episodes of optic neuritis and myelitis between 2009 and 2015, resulting in significant visual impairment. From 2015 to 2023, he received annual rituximab infusions (1 g/year) with no further relapses. In 2023, during latent tuberculosis screening, an abnormal chest X-ray prompted suspension of rituximab. Although the Interferon Gamma Release Assay was negative, chest CT revealed multiple bilateral pulmonary nodules with variable morphology and contrast enhancement. In late 2024, lung biopsy followed by immunohistochemistry confirmed extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT), involving bronchus-associated lymphoid tissue (BALT). Despite the histological diagnosis, the patient remained asymptomatic from an oncologic perspective (no B symptoms). Given the indolent nature of the disease and his preserved general condition, rituximab was reintroduced at a full

dose of 2 g every 6 months, targeting both NMOSD and BALT lymphoma. A conservative approach was adopted, maintaining rituximab monotherapy without initiating chemoimmunotherapy. **Discussion:** The simultaneous occurrence of NMOSD and pulmonary MALT lymphoma is extremely rare. Even more paradoxical is the development of a lymphoproliferative disorder under long-term anti-CD20 therapy, which is routinely used in the treatment of both NMOSD and indolent B-cell lymphomas. This case raises important hypotheses regarding immune escape, clonal evolution, or a potential oncogenic effect of chronic immunosuppression in predisposed individuals. The clinical stability, absence of systemic symptoms, and histologic features supported a non-aggressive treatment strategy, with anti-CD20 monotherapy addressing both underlying conditions. **Final Comments:** This report describes a rare and paradoxical association between NMOSD and pulmonary MALT lymphoma emerging during rituximab therapy. It emphasizes the importance of malignancy surveillance in patients undergoing prolonged immunosuppressive treatment, even with agents recognized for their antineoplastic efficacy. Further studies are warranted to understand the mechanisms underlying lymphomagenesis in autoimmune settings.

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**Área Técnica do trabalho:** Espectro da Neuromielite Óptica

### Real-world evaluation of rituximab effectiveness in reducing annualized relapse rate in AQP4-IgG–positive NMOSD patients

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**Background:** Rituximab effectively reduces annualized relapse rates (ARR) in neuromyelitis optica spectrum disorder (NMOSD) globally. Despite newer on-label drugs for AQP4-IgG+ patients, rituximab remains the most prescribed medication in low-income countries with limited financial resources. Because real-world data from Latin America populations are lacking, regional studies are essential. **Objective:** To assess rituximab's effectiveness in reducing ARR in AQP4-IgG-seropositive NMOSD patients. **Methods:** Retrospective cohort analysis, based on medical records from a tertiary hospital, from 2010 to 2025, including patients diagnosed with NMOSD according to the 2015 International Panel Criteria and seropositive for AQP4-IgG. All patients received rituximab for at least 6 months. Baseline demographic characteristics were described. Two comparative analyses were performed: (1) Intra-patient evaluation of ARR at different treatment time points, comparing the period of prior oral immunosuppressant use with the period after rituximab, assessed by the Wilcoxon test. (2) Inter-patient comparison of post-rituximab ARR between patients who initiated rituximab as first-line therapy and those who received it as escalation therapy, using Mann-Whitney test. Statistical significance was set at  $p < 0.05$ . **Results:** We identified 69 AQP4-IgG+ NMOSD patients (median age 45.42 [IQR 36.92–58.84]; 95.7% female); 14 initiated rituximab as first-line therapy, 55 had prior oral immunosuppressants (median duration 71.00 [IQR 38.74–123.48]; ARR 0.38 [IQR 0.23–0.77]), primarily azathioprine (83.6%) and mycophenolate mofetil (18.2%). Rituximab median duration was 52.00 [IQR 19.50–65.50] months. Post-treatment ARR was significantly lower in the rituximab group (0.00 [IQR 0.00–0.21]) compared to immunosuppressant group (0.33 [IQR 0.15–0.75]),  $p < 0.001$ . Among 52 patients with 24-month follow-up, therapeutic failure rate was 26.9% in rituximab versus 47.1% in oral immunosuppressants ( $p < 0.05$ ). No significant difference

in ARR was found between first-line and escalation therapy users ( $p = 0.463$ ). Rituximab discontinuation rate was 4.29%. **Conclusion:** This Latin American real-world study confirms rituximab's effectiveness in reducing relapses in AQP4-IgG+ NMOSD, emphasizing its importance where access to newer drugs is restricted.

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**Área Técnica do trabalho:** Espectro da Neuromielite Óptica

### The etiologies of optic neuritis in an outpatient clinic dedicated to atypical demyelinating diseases

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Atypical demyelinating diseases (ADD) are rare conditions that differ from Multiple Sclerosis (MS) due to unusual clinical or imaging findings or poor responses to treatments used for MS. According to global prevalence, there are different frequencies of etiology of ADD according to location. The most common etiologies described in Brazilian population are Neuromyelitis optica spectrum disorder (NMOSD) and Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOGAD), with NMOSD being more frequent than MOGAD. Optic neuritis (ON) represents inflammation of the optic nerve which could manifest as an initial clinical symptom of an ADD. However, there are few descriptions associating the first demyelinating event to specific etiologies of ADD, which includes ON. The objective is to describe the frequency of etiological diagnosis in patients with ON as the first clinical symptom in an outpatient clinic dedicated to ADD. Retrospective medical record analysis of patients described with atypical demyelinating symptoms using frequency of events and description analysis of the population. 79 patients presenting ON as initial presentation were selected from a population of 196 patients with ADD. 52 cases of unilateral ON, in which 3 (5.7%) were due to MS, 17 (32.6%) were due to MOGAD, 16 (30.7%) were due to NMOSD and 15 (28.8%) without specific etiology. 27 cases of bilateral ON, in which 7 (25.9%) were due to NMOSD, 13 (48.1%) were due to MOGAD, and 8 (29.6%) were indeterminate. Although the most frequent etiology of ON in our study were MOGAD and NMOSD there were many patients with indeterminate etiology, highlighting the need for investigation of new biomarkers for ADD

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**Área Técnica do trabalho:** Espectro da Neuromielite Óptica

### The value of choroid plexus in differentiating Multiple Sclerosis from Neuromyelitis optica spectrum disorder

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**Background:** Recent literature has highlighted a potential role of choroid plexus as a biomarker for demyelinating diseases, such as Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorder (NMOSD). Considering that MS pathogenesis includes histopathological changes in choroid plexus that result in edema, it is expected that the larger volume of choroid plexus is correlated with the diagnosis of multiple sclerosis. However, in other demyelinating diseases like NMOSD these findings are not reported. Therefore, it could be hypothesized that the volume of choroid plexus could be useful in differentiating these conditions. **Objective:** Analyze articles in literature in a systematic review that evaluates the volume of plexus choroid as a possible imaging biomarker capable of differentiating MS from NMOSD and to describe the methods of imaging in studies. **Methods:** This systematic review was conducted according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The inclusion criteria considered eligible cross-sectional, and cohort studies that evaluated plexus choroid volume in MS and NMOSD using PubMed and BIREME as a database. The MeSH search terms were “multiple sclerosis” AND “neuromyelitis optica,” OR “alternative diagnosis” AND “choroid plexus” in all fields of publication. **Results:** An initial screening to remove duplicate studies yielded 10 articles. After excluding all articles that did not meet the inclusion criteria, 4 studies were gathered. The imaging methods of evaluating CP varied between studies. One study reported a measurement of CP of the lateral and fourth ventricles was bilaterally in the axial and coronal views, while 2 studies measured CP volume relative to the total intracranial volume and 1 study reported radiomics features from CP. Two studies reported significant differences between CP from MS and NMOSD. Two studies reported Sensitivity and specificity analysis, that ranged from 0.5 to 0.86 of sensitivity and ranged from 0.76 to 0.84 of specificity. **Conclusion:** Choroid plexus imaging is a promising specific imaging biomarker that can differentiate MS from NMOSD according to the type of imaging method.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### A TNFRSF13B mutation presenting as immune dysregulation and chronic inflammatory polyneuropathy

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Immune dysregulation comprises a heterogeneous group of disorders marked by immunodeficiency, autoimmunity, cancer predisposition. We present a case of chronic inflammatory demyelinating polyneuropathy (CIDP) with TACI phenotype secondary to TNFRSF13B mutation. TACI describes a clinical presentation characterized by autoimmunity and immune dysregulation with lymphoproliferation in individuals with TNFRSF13B mutations, regardless of the presence of classical immunodeficiency. **Case Presentation:** 37-year-old female presented with nocturnal fevers, sweating, and splenomegaly. She developed joint pain, hyperchromic skin lesions in inferior limbs and pancytopenia. Bone marrow biopsy excluded lymphoproliferative disorders and skin biopsy excluded vasculitis but showed lymphocytic infiltration. PET-CT also showed lymphoproliferation with para-aortic lymphadenopathy. After a year she developed muscle weakness,

cyanosis, hyperemia, burning sensations, in the lower limbs. Electroneuromyography showed sensory-motor asymmetric demyelinating peripheral polyneuropathy in the lower limbs. Workup for systemic autoimmune diseases, amyloidosis, nutritional deficiencies, and toxic-metabolic disorders were negative. Genetic testing identified a pathogenic TNFRSF13B mutation, associated with common variable immunodeficiency (CVID), consistent with a TACI phenotype. She was treated with IVIG and cyclophosphamide without improvement. Later rituximab treatment showed response. **Discussion:** The TNFRSF13B gene encodes the TACI protein, involved in B-cell regulation. Mutations are linked to CVID, autoimmunity, and lymphoproliferative disorders. **Final Comments:** This case is notable for CIDP associated with TNFRSF13B mutation in the absence of classical CVID, highlighting the importance of evaluating patients with inflammatory polyneuropathies and systemic symptoms for underlying immune dysregulation syndromes.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Association between mortality from inflammatory polyneuropathies and the Zika virus epidemic in Brazil from 2010 to 2020

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**Background:** Inflammatory polyneuropathies, especially Guillain-Barré Syndrome (GBS), are rare, severe, and immune-mediated neurological conditions. The most common form of GBS involves autoimmune destruction of peripheral nerves, leading to ascending flaccid paralysis, with a risk of death due to respiratory failure, arrhythmias, and hospital-acquired sepsis. Commonly associated with viral infections, GBS gained prominence during the Zika virus epidemic in Brazil (2015–2017), when studies reported a significant increase in compatible neurological manifestations. Due to the lack of specific mortality data for GBS (ICD-10 G61.0) in the DATASUS system, this study used mortality records from inflammatory polyneuropathies (ICD-10 G61.x) as a proxy to indirectly estimate the impact of GBS during the analyzed period. Considering GBS as the main clinical and epidemiological representative within this category, the study sought to explore possible correlations between polyneuropathy mortality and the Zika epidemic. **Objective:** To analyze the trends in mortality from inflammatory polyneuropathies in Brazil between 2010 and 2020 and their possible temporal and geographical association with reported cases of Zika virus during the same period. **Methods:** This is an ecological, retrospective, cross-sectional, and quantitative study based on secondary data from the Mortality Information System (SIM) for deaths due to inflammatory polyneuropathies (ICD-10 G61.x), and from the Notifiable Diseases Information System (SINAN) for Zika virus cases, both available through the DATASUS platform, covering 2010 to 2020. All records with complete data on the date and location of occurrence were included; duplicates and inconsistencies were excluded. The analyses compared the number of deaths before (2010–2014), during (2015–2017), and after (2018–2020) the epidemic, and assessed regional distribution. Bar and line graphs were used to illustrate temporal trends and possible regional overlaps. **Results:** Between 2010 and 2020, 2,283 deaths from inflammatory polyneuropathies were recorded in Brazil, with an average of 171.4 deaths per year from 2010 to 2014. In 2016, a peak of 263 deaths was observed, representing a 53% increase compared to the pre-epidemic average and coinciding with the peak of the Zika outbreak, with approximately 281,464 reported cases. The Southeast and Northeast regions had the highest numbers of both Zika cases and deaths from inflammatory polyneuropathies, suggesting an association with GBS. From 2017

onwards, both Zika cases and polyneuropathy-related deaths declined. **Conclusion:** The findings suggest a temporal and regional correlation between mortality from inflammatory polyneuropathies and the Zika epidemic in Brazil. The results highlight the need for strengthened neurological surveillance during viral outbreaks and the implementation of effective public health policies for the prevention and management of these potentially severe conditions.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Beyond anti-GAD65: atypical stiff-person syndrome presentation with anti-glycine receptor antibodies and CSF oligoclonal bands

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**Case Presentation:** A 33-year-old female patient attended her first consultation in March 2024, reporting hip pain associated with the femoral head rotation, which began in June 2023. Over time, she developed pain extending from the thoracic to the sacral region and rigidity predominantly in the right lower limb (RLL), with difficulty walking due to inversion and plantar flexion of the right foot. She stated that her left foot was starting to show similar symptoms. She denied having any complaints regarding her upper limbs. During the consultation, she also reported urinary urge incontinence, bowel urgency, and a burning sensation in both feet. Physical examination revealed global hyperreflexia, 3+/4+ in the upper limbs (UL) and 4+/4+ in the lower limbs (LL), with an increased reflexogenic area. Muscle strength was grade III in the RLL for right foot dorsiflexion and right thigh extension and grade IV for leg flexion and extension, thigh flexion, and right foot plantar flexion, with hypertonia in the RLL (2+/4+). Muscle strength was grade V in the left lower limb (LLL). Bilateral extensor plantar reflex and positive bilateral Hoffmann's sign were observed. Anti-GAD65 was requested and came back negative. At the following consultation, she reported worsening pain in the LL, arthralgia in the knees and ankles bilaterally, and progression of rigidity in the abdomen and LL. She experienced two episodes of falls during this period. A lumbar puncture was performed, revealing oligoclonal bands restricted to the cerebrospinal fluid. Other tests, such as mammography and contrasted CT scans of the abdomen, pelvis, and chest, showed no abnormalities. During the same consultation, she presented weak positive results for anti-glycine receptor antibodies, and hospitalization for immunoglobulin therapy was requested. **Discussion:** Stiff Person Syndrome (SPS) is characterized by dysfunction in the GABAergic inhibitory pathway, presenting symptoms such as rigidity and painful muscle spasms, primarily in axial and proximal limb muscles. It is associated with high levels of anti-glutamic acid decarboxylase (anti-GAD) antibodies, with other antibodies such as anti-glycine receptor antibodies (anti-GlyR) also described. The classic form of the disease has an estimated prevalence of 1 to 2 cases per million, affecting more women than men. Diagnosis is based on recognizing the symptoms and is corroborated by serologies, response to diazepam, and electromyography (EMG) studies results, which show continuous motor unit activity. Symptomatic treatment involves the use of GABA-stimulating medications, such as benzodiazepines and baclofen, to reduce rigidity and painful muscle spasms. Immunotherapy aims to reduce or remove the antibodies, usually through intravenous immunoglobulin.

**Final Comments:** Stiff Person Syndrome is progressive and generally ensues varying levels of disability. Early diagnosis and treatment initiation significantly impact the patient's prognosis.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Beyond the cavernous sinus: expanding the clinical and radiological spectrum of Tolosa-Hunt syndrome

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**Background:** Tolosa-Hunt syndrome (THS) is a rare neurological condition initially described as a painful ophthalmoplegia due to an inflammatory process confined to the cavernous sinus. Over time, diagnostic criteria have evolved to include additional sites such as the superior orbital fissure and orbit. Despite the refinements, there is growing recognition that the current criteria remain insufficient due to the variability in clinical presentations and radiological findings. Therefore, further characterization of the clinical and radiological features of THS is needed. **Objective:** To characterize the frequency of clinical and radiological features of THS described in the International Criteria for Headache Disorders-3 (ICHD-3). **Methods:** We conducted a retrospective analysis of medical records from consecutive patients at the outpatient pachymeningitis clinic between 2016 and April 2025. We included patients with orbital apex syndrome or cavernous sinus syndrome and excluded those with tumors, vasculitis, basal meningitis, sarcoidosis, or diabetes mellitus, in accordance with ICHD-3 criteria. We assessed the frequency of the individual components of the ICHD-3 criteria: (a) unilateral orbital or periorbital headache; (b) paresis of one or more of the ipsilateral III, IV, and/or VI cranial nerves; (c) inflammation of the cavernous sinus, superior orbital fissure, or orbit, as demonstrated by MRI or biopsy. We also evaluated the concordance between lesion laterality and clinical symptoms, as well as the response to corticosteroid therapy. **Results:** We examined 58 patients presenting with orbital apex or cavernous sinus syndrome. Of these, 46 were excluded due to alternative diagnoses. We re-evaluated 13 patients with a prior diagnosis of THS using the ICHD-3 criteria. The most common pain pattern was unilateral orbital pain (n=10, 77%), followed by unilateral headache (n=8, 61%); one patient presented with a bipartite headache. The most frequently affected cranial nerves were the III (n=10, 76.9%) and VI (n=10, 79.3%), followed by the IV (n=5, 38%). The cavernous sinus was involved in all cases; however, extension to adjacent anatomical regions was also observed: optic nerve (n=5, 38%), oculomotor nerve (n=4, 30%), inferior orbital fissure (n=3, 23%), and foramen ovale (n=3, 23%). The lesion was ipsilateral to the symptoms in all patients. Corticosteroid therapy was administered to all patients, predominantly intravenously (n=12, 92%), and all experienced significant pain relief within the first week. **Conclusion:** Our findings highlight that most patients initially suspected of THS were ultimately diagnosed with other inflammatory disorders, underscoring the importance of thorough etiologic investigation. The imaging showed involvement of the cavernous sinus, frequently extending to adjacent structures. These observations challenge the view of THS as an isolated cavernous sinus process and support its interpretation as a focal form of pachymeningitis.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Blurred lines: IgG4-related disease behind a case of vision loss

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**Case Presentation:** A 32-year-old woman was referred to the emergency department with decreased visual acuity in her left eye. She reported a year-long progression of blurred vision, worsening significantly two months prior, culminating in unilateral amaurosis. A CT scan from a previous hospitalization revealed optic nerve infiltration, and a presumptive diagnosis of neuromyelitis optica (NMO) was made. She was treated with corticosteroid pulse therapy and discharged on 80 mg/day of prednisone. One month later, at our hospital, she presented with persistent headache, pain on left eye movement, and blurred vision in the right eye. A new investigation showed pachymeningitis on brain MRI, with normal rheumatologic labs except for a positive ANA (1:640). Lumbar puncture results were unremarkable. The constellation of findings prompted suspicion of a granulomatous disease, leading to a meningeal biopsy. Histopathological and immunohistochemical analysis confirmed IgG4-related disease (IgG4-RD), with dense lymphoplasmacytic infiltrate and an IgG4:IgG ratio >60%. **Discussion:** IgG4-RD is a rare, immune-mediated inflammatory condition that can involve nearly any organ, leading to fibrosis and functional impairment. Commonly affected sites include the pancreas, bile ducts, salivary, and lacrimal glands. Neurological involvement, though less frequent, may impact the orbits, pituitary, meninges, peripheral nerves, and brain. The condition typically affects individuals aged 50–80, and autoimmune pancreatitis (a common manifestation) has a male predominance (4:1). Though often indolent, IgG4-RD can present acutely, especially with vascular or neurological involvement. In this case, MRI revealed pachymeningeal thickening with bilateral optic foramen involvement—more prominent on the left—extending to the orbital apex and retropharyngeal space. Infectious causes were excluded. Although the patient's serum IgG4 was normal, biopsy confirmed the diagnosis. CSF IgG4 was not available. Treatment began with corticosteroids, followed by biannual Rituximab infusions. **Final Comments:** Early recognition of IgG4-RD is essential, especially in atypical cases, as timely corticosteroid therapy can significantly alter the disease course. Delayed diagnosis risks irreversible fibrosis and permanent damage. In our patient, more than a year elapsed from symptom onset to diagnosis. Despite targeted anti-CD20 therapy, her condition continues to progress, underscoring current limitations in treatment and the urgent need for more robust evidence-based strategies.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Cerebellar ataxia as a clinical manifestation related to the use of oncological immunotherapy

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**Case Presentation:** A 53-year-old male patient, diagnosed in September/2022 with metastatic melanoma through left axillary lymph node biopsy, started in November/2022 combined therapy with immune checkpoint inhibitors (ICIs), ipilimumab and nivolumab. In March/2023, he developed myocarditis resulting from the use of ICIs, however, after adequate management, it was decided to maintain the medication for 24 cycles. The patient received the last dose of ICIs in November/2024 and has been oncological remission since then. In March/2025, he began to show progressive imbalance, ataxic gait and incoordination. The neurological examination upon admission presented nystagmus, scandile dysarthria, dysmetria, dyssynergia, axial ataxia and cerebellar gait. A cranial MRI with contrast was performed, which showed multiple foci of signal alteration in T2/FLAIR in cerebellar peduncles, with contrast uptake and no diffusion restriction. Analysis of the cerebrospinal fluid showed hyperproteinorrhachia with absent oligoclonal bands (OCB) and negative infectious screening. A panel to test for autoantibodies was not performed due to costs. The decision was made to start pulse therapy with methylprednisolone 1g/day for 5 days, followed by another 5 days of IV human immunoglobulin 2g/kg, with partial clinical and radiological response. The patient continued to use prednisone orally in a tapered regimen, with improvement in gait and dysarthria, while maintaining discreet nystagmus. **Discussion:** ICIs, such as ipilimumab (anti-CTLA-4) and nivolumab (anti-PD-1), potentiate the antitumor immune response, improving the survival of patients with metastatic melanoma. However, sustained blockade of these regulation points is associated with the development of immune-mediated adverse events (AEs), including rare but potentially serious neurological toxicities. These neurological manifestations have a median latency of 4 weeks after the start of immunotherapy and their incidence varies between 1% and 10% of all AEs, depending on the cohort evaluated, the ICI class and the type of underlying neoplasia. In the literature, the use of anti-CTLA-4 alone or in combination with anti-PD-1, especially in patients with melanoma and lung cancer, seems to lead to a higher risk of neural toxicity. Among neurological AEs, cerebellar alteration is a rare presentation, described to date as isolated ataxia or, in a few cases, associated with scandile dysarthria and nystagmus. Among the complementary exams, it usually presents cerebrospinal fluid findings of an inflammatory pattern (hyperproteinorrhachia, pleocytosis and OCB), and MRI without relevant findings or with nonspecific alterations (hyperintensity, atrophy or cerebellar edema). **Final Comments:** Cerebellar alterations resulting from the use of oncological immunotherapy must be recognized as it is a rare entity that requires appropriate and prompt investigation and treatment.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Challenges in attributing neuropsychiatric symptoms in SLE: validation of attribution models in a Brazilian cohort

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**Background:** Neuropsychiatric symptoms significantly contribute to morbidity and diminished quality of life in systemic lupus erythematosus (SLE). Early recognition and accurate attribution are essential but challenging, given symptom heterogeneity and potential confounding by disease activity, comorbidities, or treatments. To address this, standardized attribution models have been proposed. The Systemic Lupus International Collaborating

Clinics (SLICC) developed two models (A: more stringent; B: less stringent) based on timing relative to SLE diagnosis, exclusion of alternative causes, and identification of “minor” symptoms. Additionally, an algorithm by Bortoluzzi et al. uses a probability score incorporating temporal relationships, confounding factors, minor events, and supportive clinical or laboratory findings. These models are also valuable for patient classification in clinical studies, enhancing inclusion consistency. However, external validation remains limited, especially in Latin American populations. **Objective:** To evaluate the diagnostic performance of the SLICC models A and B and the Italian algorithm in attributing neuropsychiatric events to SLE, using multidisciplinary clinical assessment as the reference standard. **Methods:** We retrospectively analyzed 304 patients diagnosed with SLE according to the 2019 SLICC criteria. Eighty patients experienced at least one neuropsychiatric symptom, totaling 113 distinct events. Each event was evaluated by a multidisciplinary team, whose consensus served as the reference standard. The three attribution models (SLICC model A, SLICC model B, and the Italian algorithm) were applied by a single researcher using clinical data retrieved from medical records. Diagnostic performance of these models was compared to the multidisciplinary assessment. **Results:** Of the 113 events, 64 (56.6%) were attributed to SLE by multidisciplinary assessment. Diagnostic performance varied significantly among the models. SLICC model A had sensitivity of 50%, specificity of 95.9%, and moderate agreement ( $\kappa=0.428$ ). SLICC model B showed sensitivity of 71.9%, specificity of 69.4%, and moderate agreement ( $\kappa=0.410$ ). The Italian algorithm had the highest sensitivity (95.3%) but lowest specificity (57.1%), achieving moderate agreement ( $\kappa=0.548$ ). **Conclusion:** The attribution models showed only moderate agreement with multidisciplinary assessment, indicating limited standalone diagnostic value. Variability in sensitivity and specificity highlights the necessity of complementing these models with clinical judgment, especially in diverse populations where neuropsychiatric SLE is diagnostically complex.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Dural Rosai-Dorfman disease in the differential diagnosis of pachymeningitis and hypophysitis

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A 52 year old female presented in the emergency department in May 2022 with complaints of conjunctival erythema on the left eye, associated with pulsating periorbital pain for 1 week. In neurological examination it was noted the presence of corkscrew vessels in the left eye, as well as more evident proptosis on the left and partial eyelid ptosis on the left and exophoria on the left. Skin exam showed papules and nodules on her thighs. Brain and sellar magnetic resonance imaging showed rounded images in the parenchyma of the adenohypophysis on the left with adjacent pachymeningeal enhancement. Cerebrospinal fluid analysis was unremarkable. Later, patient reported she also had a history of early menopause (at 38 years old) and that the skin lesion was biopsied in 2017, rendering the diagnosis of Rosai Dorfman disease (RDD). Treatment with high-dose steroids led to improvement of pain and visual complaints. Rosai-Dorfman disease is a rare histiocytic proliferative disorder that may involve the dura mater and diencephalon, presenting with headache, cranial nerve palsies, and pachymeningeal enhancement on neuroimaging.

This clinical-radiological picture can closely mimic other systemic inflammatory conditions such as IgG4-related disease, sarcoidosis, and ANCA-associated vasculitis. This case underscores the importance of a thorough evaluation for current or prior systemic disease in patients with focal pachymeningitis, as this may reveal safer and more accessible biopsy targets. In our patient, a prior skin biopsy revealed characteristic findings of RDD—S100-positive, CD68-positive, and CD1a-negative histiocytes—providing a definitive diagnosis and obviating the need for a high-risk CNS biopsy. Although RDD most commonly presents with painless lymphadenopathy, this case highlights that extranodal manifestations, such as dural and cutaneous involvement, may occur in isolation. Recognizing this pattern was critical for initiating appropriate immunosuppressive therapy, which led to clinical improvement, including resolution of headache and visual symptoms. This case underscores the diagnostic challenges of focal pachymeningitis and the need to include RDD in the differential diagnosis—even in the absence of lymphadenopathy. Recognition of other extranodal manifestations, such as skin lesions, can provide safer biopsy targets and facilitate diagnosis, helping to avoid invasive CNS procedures and guide appropriate treatment.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Epidemiological, clinical, and radiological assessment of hypertrophic pachymeningitis in a tertiary neurology center in Brazil

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**Background:** Hypertrophic pachymeningitis (HP) is a rare inflammatory disease characterized by localized or diffuse thickening of the dura mater. It manifests with varied neurological symptoms, especially persistent headache and cranial nerve palsies. Etiologies include infections, autoimmune diseases, neoplasms, and idiopathic forms. MRI with gadolinium enhancement is the imaging method of choice, while dural biopsy remains the diagnostic gold standard. Early identification is crucial to prevent permanent deficits, but diagnosis is often delayed due to its nonspecific presentation. **Objective:** This study aims to describe the clinical, epidemiological, and radiological profile of HP in a tertiary neurology center in Brazil. **Methods:** Data from 51 patients with HP were retrospectively analyzed. All underwent blood tests, HIV serology, autoantibody panels, chest CT, and gadolinium-enhanced brain MRI. Cerebrospinal fluid (CSF) analysis included routine parameters and specific microbiological stains. **Results:** Among the 51 patients, 14 were men and 37 women, with a mean age of 47.85 years (range 19–74); 49% were aged 40–60. Headache was the initial symptom in 80.39%, followed by cranial nerve involvement in 84.31%—notably nerves II, VI, and V. ESR was elevated in 15.7%, CRP in 19.6%, and both in 39.2%. ANA was positive in 16% of patients. MRI showed localized dural thickening in 74.5%, predominantly in the tentorial, parasellar, and falx regions. Hypertelorism was present in 51%. Etiologic classification identified 9 cases of granulomatosis

with polyangiitis, 7 of neurosarcoidosis, and 7 idiopathic; 14 remained undefined. **Conclusion:** This study highlights the clinical heterogeneity of HP and the diagnostic value of combining imaging, laboratory, and CSF data. The findings support the creation of a structured diagnostic approach to improve early recognition and management of this rare condition.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Identifying hidden inflammation: the role of FDG-PET/CT in pachymeningitis affecting the cavernous sinus

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Hypertrophic pachymeningitis (HP) is an uncommon inflammatory disorder characterized by localized or diffuse thickening of the cranial or spinal dura mater. Inflammatory involvement of the orbital apex and cavernous sinus is frequently observed in HP, often presenting with symptoms such as headache, vision loss, and ophthalmoplegia. Although dural biopsy remains the gold standard for establishing a definitive diagnosis, accessing the cavernous sinus for biopsy poses significant technical challenges due to its deep location and proximity to critical neurovascular structures. Consequently, there is increasing interest in identifying alternative, safer biopsy sites outside the cavernous sinus that can still yield diagnostic tissue. In this context, 18F-fluorodeoxyglucose positron emission tomography combined with computed tomography (FDG-PET/CT) has emerged as a valuable imaging modality for detecting subclinical systemic disease and guiding targeted biopsies. This study aims to assess the diagnostic utility of FDG-PET/CT in patients with inflammatory orbital apex and cavernous sinus syndromes. We retrospectively screened patients evaluated between 2016 and 2025 at a specialized outpatient clinic for pachymeningitis. We included patients presenting with inflammatory orbital apex or cavernous sinus syndromes who underwent FDG-PET/CT as part of their diagnostic workup to investigate possible systemic disease and to guide biopsy. We recorded the frequency of scans showing hypermetabolic activity, indicative of abnormal findings. We then assessed how often these scans led to biopsy, and in how many cases the biopsy site was identified solely by FDG-PET/CT, as opposed to conventional imaging modalities such as brain MRI, chest CT, or abdominal CT. Finally, we reported the definitive etiological diagnoses obtained from the biopsies. A total of 27 patients with pachymeningeal disease underwent FDG-PET/CT imaging. Of these, 23 were female (85.2%), with a mean age of 46.1 ± 13.0 years. Ten patients (37%) had abnormal FDG-PET/CT findings, demonstrating areas of increased metabolic activity. In three cases (30%), FDG-PET/CT identified a biopsy site that had not been detected on routine imaging. In the remaining seven cases (70%), the biopsy site had already been suggested by conventional imaging and was subsequently confirmed by FDG-PET/CT. Seven patients proceeded to biopsy, which established the following diagnoses: four cases of idiopathic hypertrophic pachymeningitis, two cases of IgG4-related disease, and one case of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis. FDG-PET/CT revealed abnormal findings in over one-third of patients with inflammatory orbital apex and cavernous sinus syndromes. Importantly, it guided biopsies in a subset

of patients of inflammatory orbital apex and cavernous sinus syndromes where conventional imaging failed to localize a target lesion.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Idiopathic hypertrophic pachymeningitis presenting as cranial palsy and headache: a case report

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**Case Presentation:** A 47-year-old female presented to the emergency department with a 45-day history of bilateral pulsatile headache and left-sided peripheral facial palsy, with acute worsening over the past 24 hours. At that point, she also developed gaze palsy. Initially evaluated by an ophthalmologist, no acute ocular pathology was identified, and she was referred to the emergency. When symptoms first began, she was clinically diagnosed with Bell's palsy, presumed secondary to herpes zoster, and treated empirically with acyclovir and prednisone both for 7 days, without clinical improvement. No cutaneous lesions were observed at any point. Neurological examination revealed left infranuclear facial palsy, left eye ptosis, complete paralysis of all left ocular extrinsic muscles, and impaired convergence. Right eye examination and pupillary reflexes were normal. Magnetic resonance angiography revealed left-sided pachymeningeal thickening, predominantly in the frontoparietal region and adjacent to the ipsilateral cavernous sinus, though findings were nonspecific. An extensive workup was conducted. Infectious serologies (HIV, VDRL, HBsAg, anti-HCV) and neoplasm screening were negative. Autoimmune testing showed mildly elevated complement C4 (40 mg/dL; ref: 12–36) with no other abnormalities. Lumbar puncture revealed elevated opening pressure (354 mmH<sub>2</sub>O), 1 cell/mm<sup>3</sup>, protein of 32 mg/dL, and glucose of 71 mg/dL (with corresponding serum glucose 106 mg/dL). CSF cultures, VDRL, and AFB staining were negative. PCR testing for HSV-1, HSV-2, and *Mycobacterium tuberculosis* was also negative. Other investigations include cryptoantigen, protein electrophoresis, immunophenotyping, and cytology which were negative. Given the inconclusive findings, a meningeal biopsy was performed. Histopathology revealed marked mononuclear infiltration with focal perivascular aggregation, consistent with idiopathic hypertrophic pachymeningitis (IHP). **Discussion:** The patient's headache improved early during hospitalization with non-steroidal anti-inflammatory drugs. After the diagnosis of IHP, she was treated with intravenous methylprednisolone (1 g/day for 5 days), followed by oral corticosteroid tapering. Progressive improvement in ocular motility and facial weakness was observed. The differential diagnosis of pachymeningeal thickening includes infectious etiologies (e.g., tuberculosis, syphilis), systemic autoimmune diseases, neurosarcoidosis, neoplastic infiltration, and IgG4-related disease. In this context, histopathological examination remains critical, particularly to exclude IgG4-related pachymeningitis, which may mimic idiopathic forms. **Final Comments:** This case highlights the importance of thorough investigation in patients presenting with persistent headache and cranial neuropathies. Despite advanced imaging and laboratory tools, meningeal biopsy remains the definitive method for diagnosing idiopathic hypertrophic pachymeningitis and for ruling out IgG4-related disease.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### IgG4-related autoimmune disease with neurological manifestation: a case report

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**Case Presentation:** A 35-year-old female presented in September 2024 with progressive pulsatile headache localized to the left frontotemporal and occipital regions, associated with nausea, vomiting, and nocturnal awakenings. Brain CT and MRI showed a right expansive lesion involving the temporal bone, extending to the cerebellum, with mild mass effect and ipsilateral sigmoid sinus thrombosis. Surgical resection resolved the headache but led to right facial palsy, hoarseness, and limited right shoulder abduction. Histopathology revealed infiltration by >30 IgG4-positive plasma cells. No postoperative immunosuppressive therapy was started. Six months later, the patient returned with recurrent headache and diplopia. MRI demonstrated new thrombosis of the right transverse and sigmoid sinuses; serum IgG4 levels were elevated. Corticosteroid therapy was introduced, resulting in clinical improvement. **Discussion:** IgG4-Related Disease (IgG4-RD) is an immune-mediated fibroinflammatory disorder affecting multiple organs, with dense lymphoplasmacytic infiltrates rich in IgG4-positive plasma cells. Diagnosis is often challenging due to heterogeneous presentations and absence of specific serological markers; up to 30% of patients may have normal serum IgG4. Although it predominantly affects males, head and neck involvement is more frequent in females. Neurological manifestations, including hypertrophic pachymeningitis, intracranial lesions, or cranial neuropathies, are uncommon but relevant. In this case, the patient presented an intracranial lesion mimicking neoplasm, complicated by venous sinus thrombosis, likely from local inflammation or mass effect. Histopathology with >10 IgG4-positive plasma cells per high-power field and an IgG4/IgG ratio >40% is the gold standard for diagnosis. Early treatment helps prevent irreversible neurological damage. First-line therapy usually consists of glucocorticoids like prednisone 0.5–1 mg/kg/day, tapered gradually. For refractory or relapsing cases, DMARDs and rituximab are options. Maintenance therapy may be necessary in patients with multiorgan disease or higher recurrence risk. Considering IgG4-RD in the differential of intracranial masses, especially with inflammatory features or atypical evolution, can change clinical approach and outcome. **Final Comments:** This case illustrates a rare neurological manifestation of IgG4-RD as an intracranial expansive lesion associated with cerebral venous sinus thrombosis. Lack of early immunosuppressive therapy may have favored recurrence and new vascular events. Histopathology remains crucial for definitive diagnosis. Prompt recognition and corticosteroid therapy are key to improving prognosis and reducing recurrence. Including IgG4-RD in the differential diagnosis of intracranial lesions can guide timely intervention and better results.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Mortality from inflammatory polyneuropathy in Brazil (2018–2023):

### possible neuroimmunological effects of COVID-19

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**Background:** Guillain-Barré Syndrome (GBS) is a disorder of the peripheral nervous system characterized by progressive autoimmune demyelination with significant severity potential, and represents the main cause of inflammatory polyneuropathy, classified under ICD-10 code G61. Recent studies highlight the association between SARS-CoV-2 infections and the onset of GBS, framing it as a manifestation of post-COVID-19 syndrome. However, in the Brazilian context, data assessing the morbidity patterns of inflammatory polyneuropathy, with GBS as its main representative, throughout the pandemic remain scarce. Thus, analyzing mortality trends from inflammatory polyneuropathy may indirectly reflect the neuroimmunological repercussions associated with COVID-19. **Objective:** To analyze the trend in mortality from inflammatory polyneuropathy (ICD-10 G61) in Brazil between 2018 and 2023, considering possible changes related to the COVID-19 pandemic and its neuroimmunological impact. **Methods:** This is an ecological, retrospective, and cross-sectional study based on secondary data extracted from the Brazilian Mortality Information System (SIM) covering the period from 2018 to 2023. Death records classified under ICD-10 G61 (Inflammatory Polyneuropathy) were included and stratified by year and geographic region. Temporal trends and comparisons were made across three periods: pre-pandemic (2018–2019), pandemic (2020–2021), and post-pandemic (2022–2023). Records with incomplete or inconsistent data were excluded. **Results:** A total of 1,632 deaths from inflammatory polyneuropathy were recorded in Brazil between 2018 and 2023. A progressive increase in mortality was observed following the onset of the pandemic: 214 deaths in 2018, 269 in 2019, 255 in 2020, 254 in 2021, 338 in 2022, and 302 in 2023. The Southeast region accounted for the highest number of deaths (734), followed by the Northeast (343) and South (298). The data reveal a significant rise in mortality from inflammatory polyneuropathy in the years following the COVID-19 pandemic. **Conclusion:** There was an increase in mortality from inflammatory polyneuropathy in Brazil between 2022 and 2023, during the period following the peak of the COVID-19 pandemic. Considering that Guillain-Barré Syndrome is the main clinical form of ICD-10 G61 and is associated with autoimmune processes often triggered by viral infections, the findings suggest a possible delayed neuroimmunological impact of SARS-CoV-2, consistent with post-COVID-19 syndrome. The lack of a specific ICD-10 subclassification for GBS hampers direct analysis of these cases, reinforcing the need for more critical epidemiological surveillance that values post-infectious neurological syndromes in the context of COVID-19.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Neutrophilic meningoenzephalitis with internuclear ophthalmoplegia: a rare manifestation of Neuro-Behçet

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**Case Presentation:** A 38-year-old male patient with a history of migraine was admitted with headache, fever and decreased consciousness. Cerebrospinal fluid (CSF)

analysis revealed neutrophilic pleocytosis, elevated protein and preserved glycochorrhachia. Empirical antibiotics and acyclovir were initiated. The patient improved clinically, but after 14 days, pseudofolliculitis-like skin lesions appeared. Cultures and viral panel results were negative. Considering the neurological symptoms, sterile CSF and dermatological findings, Neuro-Behçet was suspected. Ophthalmological evaluation showed no uveitis or fundoscopic abnormalities. He was discharged with oral prednisone (1 mg/kg/day) but developed right-sided INO two days later. Brain magnetic resonance imaging (MRI) with gadolinium revealed an inflammatory lesion at the central of bulbopontine junction (T2/FLAIR hypersignal, restricted diffusion and absence of gadolinium enhancement). Oligoclonal bands were absent. IV methylprednisolone (1 g/day for 5 days) was administered, with partial improvement. **Discussion:** Neuro-Behçet's disease is a chronic inflammatory vasculitis of unknown etiology, with neurological manifestations occurring in up to 10% of cases. This report describes an uncommon case of Neuro-Behçet, initially presenting with neutrophilic meningoenzephalitis and progressing to internuclear ophthalmoplegia (INO). This case illustrates a rare form of Neuro-Behçet, initially indistinguishable from a viral or bacterial infection, with an unusual neurological progression. Neurological involvement in Behçet's disease typically occurs 3–6 years after the initial systemic symptoms. However, in about 6% of cases, neurological symptoms may precede systemic features. The clinical diagnosis underscores the importance of considering Behçet's disease in the differential diagnosis of sterile meningoenzephalitis with atypical neurological manifestations. **Final Comments:** This case reinforces the need for high clinical suspicion of Neuro-Behçet's disease in patients presenting with sterile neutrophilic meningoenzephalitis and atypical neurological signs, especially in the absence of definitive infectious or autoimmune markers. Early recognition and prompt immunosuppressive therapy are essential to avoid neurological sequelae and improve patient outcomes.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Progressive leukoencephalopathy associated with pathogenic CSF1R mutation: case report

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**Case Presentation:** A previously healthy 28-year-old female patient presented with progressively worsening gait disturbances and behavioral changes, beginning three months prior to hospital admission. Subsequently, she developed involuntary limb movements, generalized rigidity, hyperreflexia, urinary incontinence, and affective flattening, initially managed as treatment-resistant depression. Family history was negative for known neurological disorders. The parents were non-consanguineous. One sibling had died at the age of nine from an undetermined cause, and her father had died at age 30 due to a motor vehicle accident. Neurological examination revealed bradykinesia, preserved muscle strength, asymmetric choreoathetoid movements, generalized rigidity, and hyperreflexia. No skeletal abnormalities were noted. Initial laboratory tests were unremarkable. Cerebrospinal fluid (CSF) analysis showed only mild pleocytosis (10 cells/mm<sup>3</sup>). Brain magnetic resonance imaging revealed extensive periventricular leukoencephalopathy characterized by T1 hypointensity, T2/FLAIR hyperintensity, and multiple interspersed hemorrhagic foci. Initial differential diagnoses included vasculitis, infectious, and inflammatory disorders. Pulse therapy with methylprednisolone was administered without clinical response. Additional investigations, including cerebral arterial CT angiography, thoracoabdominal CT, and comprehensive

hematologic and autoimmune assessments, were unremarkable. Given the progressive clinical deterioration and absence of a defined etiology, a genetic panel for leuko-dystrophies was performed. Heterozygous variants were identified in the CSF1R gene (colony-stimulating factor 1 receptor): c.1441C>T (p.Gln481\*), a nonsense mutation resulting in a premature stop codon, classified as likely pathogenic; and c.1693C>T (p.Asp565Tyr), a missense variant of uncertain significance, with in silico analyses suggesting potential deleterious effects. After 18 months of follow-up, the patient exhibited marked motor and cognitive decline, loss of ambulation, dysphagia, dysarthria, diffuse spasticity, pathological reflexes, and complete dependence for activities of daily living. **Discussion:** This case illustrates a severe and rapidly progressive form of CSF1R-associated leukoencephalopathy, presenting initially with nonspecific neuropsychiatric symptoms followed by significant motor and cognitive deterioration. The broad and nonspecific differential diagnosis emphasizes the diagnostic challenge of this condition. Early identification of genetic mutations is crucial, allowing for early interventions and genetic counseling. The lack of clinical response to empirical immunotherapy underscores the importance of precise etiological diagnosis through genetic testing in patients with atypical and progressive neurological conditions, especially rapidly progressive leukoencephalopathy. **Final Comments:** This case emphasizes early genetic testing in progressive adult-onset leukoencephalopathy.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Structured Functional and Clinical Profiling in Patients with GAD-SD spectrum disorders: a review of 22 cases from Brazilian Autoimmune Encephalitis Network

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**Background:** GAD antibody-spectrum disorders (GAD-SD) include stiff person syndrome (SPS), autoimmune epilepsy (AE), cerebellar ataxia, progressive encephalomyelitis with rigidity and myoclonus (PERM), and limbic encephalitis (LE). Their course varies by phenotype and often responds to immunotherapy, but Brazilian data are still scarce. **Objective:** To describe Brazilian patients with GAD-SD from the BRAIN network. **Methods:** Patients with anti-GAD CSF (+) from the BRAIN registry were assessed via a structured questionnaire using clinical records and follow-up, covering demographics, phenotype, workup, treatment, and outcomes. **Results:** Mean age at onset was 39.2 years (18–67); 65.2% female. Phenotypes included SPS (n=8, 2 PERMs), LE (n=7), cerebellar ataxia (n=4), and AE (n=1). Prodromes occurred in 30.4%, mostly fever or respiratory symptoms; psychiatric symptoms in 43.5%; cognitive impairment in 34.8%, especially in LE. CSF (n=21) showed pleocytosis (n=12) and OCB (n=8). MRI was abnormal in 56.5% (T2/FLAIR hyperintensities); EEG in 11 (focal slowing or epileptiform discharges). Autoimmune comorbidities were found in 21.7%. Immunotherapy was used in 20 patients: methylprednisolone (n=16), IVIg (n=10), plasmapheresis (n=6), rituximab (n=7). One received monthly IVIg. Rituximab was used in 3 with ataxia, 3 with LE, 1 with SPS. BZDs were used in 6 SPS/PERM. Most began treatment within 12 months. Five completed follow-up: 2 with SPS; 3 with LE. All received immunotherapy. Three had full independence (mRS 1), one mild (mRS 2), and one moderate disability (mRS 3). **Conclusion:** In the cohort,

most GAD-SD in Brazil were female, with SPS and LE. Neuropsychiatric symptoms were frequent for all phenotypes. Treatment patterns shows predominant use of steroids, suggesting adoption of AIE protocols for GAD-SD.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Susac syndrome in a young woman: a diagnostic challenge in neuroimmunology

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**Case Presentation:** A 33-year-old Brazilian pediatric dentist, previously healthy, developed recurrent headaches and nausea during a study trip to the Netherlands. Over three months, her family observed progressive cognitive slowing and difficulty understanding speech. She also reported transient right-sided weakness and right-sided hearing loss. Low-dose prednisone was started abroad. Upon returning to Brazil in October 2024, she exhibited mild encephalopathy, right hemiparesis, and hearing loss. Hospitalized for extensive workup, she received intravenous methylprednisolone with complete resolution of hemiparesis and partial cognitive improvement. MRI revealed multiple small T2-hyperintense lesions, some with restricted diffusion, and rounded lesions in the corpus callosum. CSF showed mild lymphomononuclear pleocytosis (7 cells/mm<sup>3</sup>) without intrathecal synthesis. Angio-MRI and vessel wall study were normal. Audiometry confirmed bilateral sensorineural hearing loss. Infectious and autoimmune encephalitis panels, aquaporin-4 IgG, MOG-IgG, and CSF oligoclonal bands were negative. In December, fluorescein angiography revealed retinal arteriolar occlusions with segmental leakage and ischemia, confirming Susac syndrome. Monthly intravenous immunoglobulin (IVIg) was initiated. She currently has mild executive dysfunction, 60% hearing loss, and episodic dizziness. Rituximab initiation is pending. **Discussion:** This case fulfilled clinical and radiologic criteria for Susac syndrome, a rare autoimmune endotheliopathy affecting the brain, retina, and cochlea. The subacute and multifocal presentation initially mimicked more common conditions such as migraine, vestibular dysfunction, or psychiatric syndromes. A rigorous diagnostic strategy was essential, integrating MRI findings (including restricted diffusion and callosal snowballs), CSF profile, retinal angiography, and systematic exclusion of differentials—particularly multiple sclerosis, systemic vasculitis, and autoimmune/paraneoplastic encephalitides. Negative immunological and infectious panels reinforced the diagnosis and guided the escalation of therapy. This highlights the importance of structured reasoning and broad investigation in atypical neuroinflammatory presentations. **Final Comments:** This case underscores the need for early recognition and comprehensive diagnostic workup in patients with subacute encephalopathy and multisystem neurologic symptoms. Timely access to high-intensity immunotherapy is crucial to avoid permanent neurological damage. Despite a definitive diagnosis, treatment remains challenging due to real-world barriers in both public and private healthcare systems. Nonetheless, early and aggressive intervention should be pursued in rare neuroimmunologic syndromes such as Susac syndrome.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Unmasking an inflammatory disorder: clues from the orbit and dura

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A 32-year-old woman presented with new-onset headache and focal motor onset seizures. Over the preceding year she had been evaluated for painless left-sided proptosis with no definitive cause identified. Physical examination showed unilateral proptosis with normal visual acuity and preserved extra-ocular motility. Orbital computed tomography disclosed a contrast-enhancing soft-tissue mass infiltrating the inferolateral extraconal fat and abutting the inferior rectus and inferior oblique muscles, while brain magnetic resonance imaging demonstrated a pseudotumoral dural thickening in the left parieto-occipital region surrounded by vasogenic edema. Extensive metabolic, endocrine, infectious and rheumatologic testing was unrevealing except for a ANA titer of 1:320 with fine-speckled pattern, retroperitoneal lymph node enlargement on body computed tomography. Cerebral spinal fluid studies, including metagenomic sequencing, were normal. Meningeal biopsy showed storiform fibrosis with a dense lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells (IgG4/IgG > 40%), establishing the diagnosis of IgG4-related disease with hypertrophic pachymeningitis and orbital involvement. High-dose corticosteroid therapy (1 g/day intravenous methylprednisolone for 5 days followed by oral prednisone 1 mg/kg/day) was followed by rituximab induction and maintenance, producing marked clinical and radiological improvement, including partial headache resolution, seizure control, and regression of both dural and orbital lesions. IgG4-related disease is a chronic fibroinflammatory disease marked by the formation of slow-growing, often pseudotumoral lesions that may affect a single site or present with multi-organ involvement. Classically, four clinical phenotypes are recognized: pancreato-hepato-biliary involvement, retroperitoneal fibrosis and/or aortitis, head and neck-limited disease, and the Mikulicz syndrome with systemic involvement. Histopathologically, IgG4-RD is characterized by a dense lymphoplasmacytic infiltrate composed of T cells, B cells, eosinophils, and IgG4-positive plasma cells, along with storiform fibrosis and often obliterative or non-obliterative phlebitis. Immunohistochemistry typically reveals an elevated IgG4+/IgG+ plasma cell ratio, frequently exceeding 40%, which supports—but does not confirm—the diagnosis, as several other conditions may present with increased IgG4+ cells. IgG4-related disease is rare and can present with various clinical manifestations, many of which impact patient's quality of life and lead to a worse prognosis for the disease. It remains a diagnostic challenge, requiring a comprehensive and multidisciplinary approach that synthesizes clinical presentation with serological, radiological, and histopathological findings. Therefore, early recognition is crucial so that treatment can be effective in improving patient outcomes.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Vanishing white matter disease without neurological deficits: a case report

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**Case Presentation:** A 34-year-old woman with a history of tension type headaches and a first degree family

history of cerebral aneurysm was referred for outpatient neurological evaluation. Her medical history included generalized anxiety disorder and asthma, and she had been on long-term treatment with zolpidem, escitalopram, sodium valproate, and a combined oral contraceptive. A brain MRI performed in 2019 during routine evaluation revealed nonspecific white matter changes without accompanying clinical symptoms. A follow-up MRI in 2021 demonstrated symmetric T2 weighted and FLAIR hyperintensities predominantly affecting the frontoparietal white matter, sparing the U fibers and corpus callosum, with extension into the corticospinal tracts. No diffusion restriction, cavitation, or calcifications were observed. Serial neurological examinations showed no motor, sensory, cerebellar, or cognitive deficits. Neuropsychological assessments conducted on two separate occasions were within normal limits across all domains. Further diagnostic workup, including cerebrospinal fluid analysis, infectious and autoimmune serologies, cervical spine MRI, and nerve conduction studies, yielded unremarkable results. Whole exome sequencing identified a likely pathogenic heterozygous variant (c.338G>A) in exon 3 of the EIF2B5 gene, confirming the diagnosis of vanishing white matter disease (VWM). **Discussion:** VWM is a rare autosomal recessive leukodystrophy caused by mutations in EIF2B1 through EIF2B5, which encode subunits of eukaryotic initiation factor 2B (eIF2B), a key modulator of protein synthesis during cellular stress. It typically presents in childhood with progressive motor and cognitive impairment, cerebellar ataxia, and spasticity, often worsened by physiological or emotional stressors such as fever or minor trauma. Adult onset VWM is less common and tends to follow a more heterogeneous and indolent course, with a female predominance. This case is noteworthy due to the extensive radiological abnormalities in the absence of any neurological or cognitive symptoms, suggesting a subclinical or attenuated phenotype. Such findings may reflect incomplete penetrance or variable expressivity, phenomena increasingly recognized in adult onset leukodystrophies. Minor physical stressors, such as horseback riding, could potentially trigger disease progression in genetically predisposed individuals. **Conclusion:** This report describes a genetically confirmed case of adult onset VWM in an asymptomatic woman, representing a rare non progressive phenotype. It underscores the importance of neuroimaging in detecting silent leukoencephalopathies and highlights the diagnostic value of genomic testing in atypical presentations. Long term clinical monitoring and genetic counseling remain essential, especially in cases involving variants with uncertain phenotypic expression.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### Vogt-Koyanagi-Harada syndrome with recurrent neuroretinitis: a case report

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**Case Presentation:** A 45-year-old woman with a history of migraine and bariatric surgery presented in March 2023 with bilateral ocular hyperemia, retro-orbital pain, and scotoma in the right eye. She was initially diagnosed with central neuroretinitis and empirically treated with doxycycline for four weeks. Due to lack of improvement, she sought emergency care and was evaluated by neurology. A thorough workup was conducted, including serologies (HIV, HTLV, syphilis, toxoplasmosis, CMV), rheumatologic panel, CSF analysis with oligoclonal band testing, brain and cervical spine MRI, and chest CT. CSF showed mononuclear pleocytosis (15 cells/mm<sup>3</sup>, 76% mononuclear); other tests were unremarkable. Her vision improved after a five-day course of intravenous methylprednisolone. Between 2023 and 2024, she experienced recurrent episodes of pain, hyperemia, and decreased visual acuity. Ophthalmologic exams revealed macular microaneurysms, right-sided neuroretinitis, and hyperreflective retinal foci on OCT. Repeat MRIs remained normal. In 2025, she developed hypopigmented macules on her lower limbs and scalp poliosis, leading to the diagnosis of Vogt-Koyanagi-Harada (VKH) syndrome. **Discussion:** VKH is a rare autoimmune inflammatory disease with tropism for melanocytes, presenting with ocular, neurologic, auditory, and cutaneous manifestations. In this case, the disease followed a progressive and relapsing course, with bilateral neuroretinitis, mononuclear pleocytosis, and initial responsiveness to corticosteroids. The absence of subsequent immunosuppressive therapy likely contributed to recurrence and progression to later disease phases. The CSF pleocytosis observed in 2023 was consistent with the prodromal phase, while the cutaneous depigmentation (poliosis and hypopigmented macules) marked the convalescent phase. Though uncommon, the presence of macular microaneurysms may indicate chronic retinal inflammation. Hyperreflective foci on OCT signaled ongoing inflammatory activity. Repeatedly normal MRIs supported a primarily ocular and tegumentary presentation, distinguishing VKH from demyelinating diseases. **Final Comments:** This case underscores the importance of early recognition of Vogt-Koyanagi-Harada syndrome, particularly in atypical or incomplete presentations. Prompt initiation of immunosuppressive therapy alongside corticosteroids is essential to prevent disease progression and preserve visual function.

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**Área Técnica do trabalho:** Outras doenças da neuroimunologia

### When livedo reticularis is the key: ADA2 deficiency

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<sup>2</sup>Projeto Brasileiro do Genoma de Doenças Raras, São Paulo SP, Brazil. **Case Presentation:** A previously healthy 19-year-old male born to non-consanguineous parents presented with recurrent, self-limited acute neurological deficits, including ataxia, bilateral internuclear ophthalmoplegia, unilateral facial palsy, contralateral appendicular sensory loss, and non-painful left-eye visual loss. He reported partial recovery, with persistent ophthalmoplegia. These episodes were initially considered autoimmune, and high-dose intravenous corticosteroids were administered. He was referred to our unit with a diagnosis of multiple sclerosis (MS). On re-examination, he exhibited bilateral internuclear ophthalmoplegia, bilateral sensorineural hearing loss, and livedo reticularis. Laboratory tests showed elevated inflammatory markers. Cerebrospinal fluid (CSF) analysis was normal, with negative oligoclonal bands (type 1). Rheumatologic and infectious workups were unremarkable. Brain MRI revealed perivenular lesions involving the corpus callosum and periventricular white matter. Audiometry confirmed bilateral low- and high-frequency sensorineural hearing loss. Visual evoked potentials and fluorescein angiography were normal. Given atypical features—sensorineural hearing loss, hyper-acute recurring deficits, negative oligoclonal bands, and livedo reticularis—alternative diagnoses were considered, including genetic and auto-inflammatory syndromes. Whole genome sequencing identified a pathogenic autosomal recessive variant in the ADA2 gene (NM\_001282225.2:c.139G>C; p.Gly47Arg), confirming Adenosine Deaminase 2 Deficiency (DADA2), a monogenic autoinflammatory disorder with Sneddon-like features. **Discussion:** Autoinflammatory syndromes like DADA2 stem from innate immune dysregulation and often present with systemic inflammation, vasculopathy, and neurologic manifestations—including strokes and sensorineural deficits. In this case, the recurrent neurological episodes and brain lesions initially resembled MS, but key differences—bilateral hearing loss, livedo reticularis, negative CSF findings, and rapid onset—raised suspicion for a distinct etiology. DADA2 can closely mimic MS but requires distinct management. Tumor necrosis factor inhibitors are the mainstay treatment, significantly reducing the risk of stroke and systemic complications. Acute episodes may benefit from anti-inflammatory therapy. The use of antiplatelet or anticoagulant therapy remains controversial due to hemorrhagic risk. **Final Comments:** This case underscores the need to consider autoinflammatory diseases in young patients with atypical or multisystem neurological presentations. While MS is a frequent initial diagnosis in demyelinating syndromes, systemic features such as livedo reticularis, hearing loss, and absence of intrathecal IgG synthesis should prompt further investigation, including genetic testing for rare conditions like DADA2.



**28 A 30 DE AGOSTO DE 2025 | BRASÍLIA**

**INDEX OF AUTHORS**

ABE, Lais Reis Santos	8	COSTA, Gustavo Carvalho	5, 8, 13	MACHADO, Amanda Sanchez	4
ABRANTES, Ana Beatriz de Matos Berg	2, 10	COUTINHO, Artur	12	MALDANER, Vinicius	3
ABRANTES, Ana Beatriz Matos Berg	14	CREMONESE, Gabriela da Silva	3, 6	MARIE, Suely Kazue Nagahashi	10, 12
ABRANTES, Fabiano Ferreira de	11, 12, 15	DELAVANCE, Alessandra	14	MARQUES, Alexandre Coelho	1, 4, 5, 8, 13, 14, 15
ADONI, Tarso	3, 9	DÉRIO, Mayra Beatriz Gomes	7	MARQUES, Rafael Mendes	3
ADONI, Tarso Alana	3	DIAS, Arthur de Medeiros	13	MARTINS, Gladys Lentz	3, 6
ALBUQUERQUE, Ana Letícia Amorim de	12	DIAS, Lucas Silva	5, 8	MARUSSI, Victor Hugo Rocha	12
ALFONZO, Poliana D'aurea	13	DIAS, Reigson Alves	8	MARZANO, Lucas Alexandre Santos	3, 9, 10, 11, 12
ALLIONI, Gabriela Abrahão	3, 10, 11	DINIZ, Denise Sisterolli	2	MATOS, Lucas Lourenço da Rocha	2
ALMEIDA, Tatiana Ferreira de	15	DIOGO, Guilherme	11	MATOS, Lucas Lourenço Rocha	14
ALVES, Leonardo Jadyr Silva Rodrigues	2, 10, 14	DISSEROL, Caio	14	MAULAZ, Alexandre Balzano	2
ALVES-LEON, Soniza Vieira	1	DISSEROL, Caio César Diniz	1	MAYCÁ, Amanda Fernanda Klajn	11, 12
ALVES, Lucas Ferreira	2, 14	DOURADO JÚNIOR, Mário Emílio Teixeira	8	MELO, Anne Caroline Oliveira	7
AMARAL, Juliana Santiago	4	DRIEMEYER, Cândida	2, 11, 12	MELO NETO, Fernando Paiva	8
ANDRADE, Pedro Henrique	13	DUARTE, Larissa Araujo	1	MENDES, Larissa Braga	14
ANDRADE, Vanessa Dantas	2	DUTRA, Isabella Cristina Amate	13	MENDES, Rafael Marques	6
ANDRADE, Vanessa Dantas de	12	DUTRA, Livia Almeida	1, 4, 5, 9, 14	MENEZES, Felipe Toscano Lins	2, 8, 14
ANDRADE, Vanessa Vanessa Dantas de	11	FADEL, Karla Pinto Coelho	1	MINILLO, Renata Moldenhauer	15
ANDREATTA, Maria Eduarda	3, 6	FALCÃO, Milena Vasconcelos	5, 8, 13, 15	MIRANDA, Victor Alexandre Dantas	2
APÓSTOLOS, Samira	9	FARIA, Graziella Aguiar Santos	12	MIYASHIRO, Larissa	5, 8, 13, 15
APOSTOLOS, Samira Luisa dos	9	FAVARETTO, Laís Elizabete	11	MORAES, Marianna Pinheiro Moares de	11, 12, 14, 15
ARAÚJO, Gabrielle Benício	7	FERNANDES, José Felipe Lacerda	7, 8	MORAIS, Douglas	5
ARAÚJO, Roger Santana de	9	FERNANDES, Renan Amphiphio	1	MORAIS, Douglas de	4, 5, 7
AVOLIO, Isabella	4, 5, 7	FERREIRA, Helena França Alcaraz	1	MORENO, Yasmin Martins	13
BACELAR, Alana Sales	11	FERREIRA, João Henrique Fregadolli	9	MOURA, Barbara Conceição Ferreira	11
BARBOSA, Julio Montes Garcia	8	FERREIRA, Lis Campos	2	NÓBREGA JUNIOR, Aducto Wanderley da	1
BARRETO, Maria Eduarda Shlessarenko Fraife	14	FERREIRA, Luciano Talma	10	NÓBREGA, Paulo Ribeiro	1
BARRETO, Marina Nolasco Manhaes Gomes	6	FIGUEIREDO, Gabriel Augusto de Souza	9	NOGUEIRA, Gabriella Faria	11
BARSOTTINI, Orlando Graziani Povoas	1, 11, 12, 14, 15	FONSECA, Flavio Guimaraes	4	OLIVEIRA, Bianca Etelvina Santos	7, 8
BERGAMASHI, Samuel Brighenti	1	FONSECA, Natalia Carvalho	8	OLIVEIRA, Enedina Maria Lobato	2
BERNAL, Henrique de Moraes	3, 9, 10, 11	FRAIMAN, Pedro Henrique Almeida	11, 12, 15	OLIVEIRA, Mateus Boaventura de	9
BERNAL, Henrique de Moraes	3	FRANCO, Hamilton	3	OLIVEIRA, Paulo Henrique Martineli	15
BERNARDO, Murilo	5	FREGADOLLI, João Henrique Ferreira	14	OLIVEIRA, Paulo Henrique Martinelli	5, 8, 13
BERNARDO, Murilo Freire Pinoti	4, 5, 7	FREIRE, Maria Clara Lucena	7	OLIVEIRA, Rebeca Raissa Bezerra	8
BOAVENTURA, Mateus	4, 5, 7	GABRELON, João	5	PÁDUA, Laiz Helena de	5, 8, 13, 15
BORGES, Fernando Elias	8	GABRELON, João Victor Ferraiolli	4, 5, 7	PAIVA, Luiz Eduardo Betti	4, 5
BORGES, Mariana Costa	3, 6	GALVÃO, Keila Rejane Ferreira	10	PAIVA, Rebeca Ribeiro	7
BORGES, Renata Vitorino	8	GAMA, Sofia Mônaco	14	PEDROSO, José Luiz	11, 12, 14, 15
BRAGA, Gabriella Verardo	13	GOMES, Miguel Inácio Silva	14	PEREIRA, Gabriely Rangel	4, 5
BRAGA NETO, Pedro	1	GOMEZ, Fernanda Lustosa Cabral	14	PEREIRA, Samira dos Apostolos	3
BRITO, Paulo Santiago Moraes	8	GONÇALVES, Ricardo Pereira	3, 6	PEREIRA, Samira Luisa Apóstolos	3
BROCH, Fernanda Nicoli	11	GUABIRABA, Lia Araújo	9	PEREIRA, Valeria	1
BURLIN, Stênio	12	GUERRA, Davi Veloso	7, 8	PERIN, Daiane PAola	1
CABRAL, Bárbara Araújo Pereira	2, 7, 10, 13	GUILHERME, Ana Clara	7	PERINI, Guilherme Fleury	9
CABRAL, Jeanina	7, 8	GUTMAN, Elisa Gouvea	1	PICCOLO, Ana Claudia	13
CAETANO, Polyana Favero Ferreira	1	HEIM, Victor Camelo Vilar Sá	7	PINTO, Monique Rodrigues Pereira	13
CALLEGARO, Dagoberto	3, 9	INOJOSA, José Luiz Miranda Coelho	2	PINTO, Paula Oliveira	1, 13
CARDOSO, Marina Driemeier	9	KLEINPAUL, Rodrigo	6	PIRES, Olivia	4, 5, 7
CARDOSO, Raphaella Moura	11	KLEINPAUL, Rodrigo Isabela	4	PITOMBEIRA, Milena Sales	1
CARNEIRO, Lorena Oliveira	2, 10, 14	KOEHLER, Cristine	3, 6	PONTES, Raquel Rios de Castro	8
CARVALHO, Fernanda Martins Maia	1	LACERDA, Gustavo	3	QUEIROZ, Nathalia Lindsay Pereira	8
CARVALHO, Francisco Anderson Sá	8	LEITE, Pedro Hamilton Guimarães	8	REIS, Marcelle Rodrigues Carneiro de Souza	2, 10
CARVALHO, Francisco Anderson Sá	7	LEMOS, Andreza Salvio	1	REIS, Marcelle Rodrigues Carneiro Souza	14
CASTRO, Luiz Henrique Martins	10, 12	LIMA JUNIOR, Daniel Vicente Siqueira	7	REIS NETO, Edgard Torres dos	11
CAVAGLIERI, Letícia	5	LIMA, Priscilla Mara Proveti	14	REIS, Samela Daiere Soares Mota	8
CAVAGLIERI, Letícia Pieroni	4, 5, 7	LIMA, Priscilla Mara Proveti de	2, 10	RESENDE, Cláudia Fideles	4
CHACON, Heyell Kevin Rodrigues Franklin	7	LIN, Victoria	4, 5	RIBEIRO, Fernanda Ludolf	4, 6
COELHO, Luis Eduardo	14	LUCATO, Leandro Tavares	10, 12		
CORDEIRO, Julia Coutinho	9				
CORRÊA, Lucas Hernandez	4, 5				
COSTA, Carolina Aparecida Donofrio Santos	3, 6				

XXXI Congresso Brasileiro de Neurologia

RIBEIRO, Marlise Castro	2	SARMENTO NETO, Francisco Gil	8	TARDIM, Caio Faria	1
RIBEIRO, Marlise de Castro	2, 11	SARMET, Max	3	TASCHETTO, Alexandre Laisson Prado	2
RIGONATO, Renata Maiolo	5, 8, 13, 15	SATO, Douglas Kazuyoshi	9	TASCHETTO, Alexandre Prado	11
RIMKUS, Carolina de Medeiros	9	SATO, Henry Koiti	1	TEIVE, Hélio Afonso Ghizoni	1
ROCHA, Ana Julia Resende	4, 6	SCHETTINO, Isabela Canedo Campos	4, 6	TEIXEIRA, Anne Carolina Barbosa	15
ROCHA, Andre Veloso Souto	9	SCOLA, Rosana Herminia	1	TEIXEIRA, Bianca	3
ROCHA, Lana Francischetto	2, 10, 14	SILVA, Elielson Veloso da	1	TEIXEIRA, Quezia Dias	6
ROCHA, Ricardo Weber	1	SILVA, Felipe von Glehn	2, 10, 14	TERRIM, Sara	9
RODRIGUES, Ana Clara Guilherme	8	SILVA, Guilherme Diogo	3, 9, 10, 12	TESSARO, Camila Lorenzini	1
		SILVA, Larissa Nóbrega Ribeiro da	13	TIEPPO, Eduardo Macedo de Souza	9
SAFFI, Pedro Maia Nobre Rocha	2, 10, 14	SILVA, Mauricio Elias Nunes da	9		
SALES, Alana Bacelar Limeira	3, 10	SILVA, Thiago Yoshinaga Tonholo	15	VASCONCELOS, Arthur Felipe Barbosa	7, 8
SALOME, Laura	5	SILVA, Victor Ezaki Alves	13	VASCONCELOS, Claudia Cristina Ferreira	2, 6
SALOME, Laura Barbosa	4, 5, 7	SILVEIRA, Luciane Perez	1, 13	VEIGA, Milena Lins	3, 10, 11
SANCHEZ, Carolina Souza	14	SIQUEIRA, Marina Martins	4, 5	VELOSO, Octavio Morais	13
SANTANA, Roger	9	SOANE, Michel Moraes	4	VIANA, Marinna Karla Cunha Lima	8
SANTIAGO-AMARAL, Juliana	6	SOARES, Julia Santos	2, 11, 12	VILLARIM, Luiza Alves Monteiro Torreão	7, 8
SANTILLAN, Thiago Ivan Vilchez	3, 9	SOUSA, Nise Alessandra Carvalho	2		
SANTOS, Ana Carolina Santana	4, 6	SOUZA, Doralina Guimarães Brum	4, 5	WELLING, Mariana Sandri Schumacher	1
SANTOS, Arthur Cauã Silva	11	SOUZA, Gabriel Soares Dutra	8		
SANTOS, Graziella Aguiar	10	SOUZA, Lais Micheli de	5, 8, 13, 15	XAVIER, Karla	3
SANTOS, Patricia	1, 13	SOUZA, Naftaly Angélica Lopes	7		
SANTOS, Raderi Luiz Cardoso dos	5, 8	SOUZA, Victor Assis	13	ZOCCOLI, Clayton	4, 5, 7

