Case report

Neuromyelitis Optica Spectrum Disorder in a Pediatric Patient: Literature Review with Case Report

Doença do espectro da neuromielite óptica em paciente pediátrico: revisão de literatura com relato de caso

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ABSTRACT

Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a severe autoimmune astrocytopathy of the central nervous system (CNS) with secondary demyelination, often associated with the anti-aquaporin-4 (anti-AQP4) antibody. Approximately 5–10% of NMOSD cases begin before the age of 18. However, the scarcity of available studies hampers a comprehensive understanding of pediatric NMOSD, particularly regarding treatment.
Objectives: To present a case report of a pediatric patient with NMOSD and to conduct an integrative literature review on treatments already used in pediatric patients, as well as ongoing clinical trials in this population.
Case report: We describe the case of an 11-year-old female patient who presented with NMOSD.
Methods: This is a case report and integrative literature review conducted between October 2024 and January 2025 using the PubMed, Web of Science, Embase, Scopus, EBSCO, LILACS, and SciELO databases.
Results: Eight articles were included in this study after a series of screenings. Additionally, four clinical trials involving pediatric patients were found to be ongoing or recently completed in clinicaltrials.gov.
Conclusion: The management of pediatric NMOSD requires a stepwise approach in the acute phase and effective immunosuppression for relapse prevention. Satralizumab is indicated for patients aged 12 years and older, Rituximab proved to be the most effective option; however, its limited availability in the Brazilian public health system (SUS) hinders its application. The clinical case highlights the importance of early diagnosis and appropriate control to prevent sequelae and minimize treatment-related adverse effects.

Keywords: Neuromyelitis optica. Child. Central nervous system.

RESUMO

Introdução: A doença do espectro da neuromielite óptica (DENMO) é uma astrocitopatia autoimune grave do SNC com desmielinização secundária frequentemente associada ao anticorpo anti-aquaporina 4 (anti-AQP4). Cerca de 5 a 10% dos casos da DENMO têm início antes dos 18 anos. Porém, a escassez de estudos disponíveis dos dados dificulta a compreensão abrangente da DENMO em pacientes pediátricos, principalmente relacionados ao tratamento.
Objetivos: Descrever um relato de caso de paciente pediátrico com DENMO e realizar uma revisão integrativa da literatura sobre os tratamentos já utilizados em pacientes pediátricos e os ensaios clínicos em andamento nesta população.
Caso clínico: Descrevemos o caso de uma paciente do sexo feminino, de 11 anos, que apresentou quadro de DENMO. Métodos: Trata-se de um relato de caso e uma revisão integrativa da literatura realizada no período de outubro/2024 a janeiro/2025 nas bases de dados PubMed, Web Of Science, Embase, Scopus, EBSCO, LILACS e SciELO.
Resultados: A partir da busca bibliográfica, 8 artigos foram incluídos neste estudo após uma série de triagens. 4 ensaios clínicos foram encontrados no clinicaltrials.gov em andamento ou recém finalizados em pacientes pediátricos.
Conclusão: O manejo da DENMO pediátrico exige abordagem escalonada na fase aguda e imunossupressão eficaz na manutenção. O Satralizumabe tem indicação em pacientes acima de 12 anos. O rituximabe mostrou-se superior na prevenção de recaídas, mas o acesso restrito no SUS limita sua aplicação. O caso clínico evidencia a importância do diagnóstico precoce e do controle adequado para evitar sequelas e minimizar efeitos adversos do tratamento.

Palavras-chave: neuromielite óptica, criança, sistema nervoso central.

ARTICLE INFO

DOI: https://doi.org/10.46979/rbn.v61i3.68271

Conflict of Interest: The authors declare that there is no conflict of interest associated with the conduct of this study.

Funding: This research did not receive any specific funding from public, commercial or non-profit funding agencies.

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INTRODUCTION

Neuromyelitis optica spectrum disorder (NMOSD) is a severe autoimmune astrocytopathy of the central nervous system (CNS) with secondary demyelination, often associated with the anti-aquaporin-4 (anti-AQP4) antibody. It is mainly characterized by recurrent episodes of optic neuritis and longitudinally extensive transverse myelitis[1]. In 2015, the diagnostic criteria for NMOSD were revised to incorporate stratification based on AQP4-IgG positivity, consolidating a more precise diagnostic approach aligned with immunopathological findings[2].

According to the most recent criteria, the clinical presentation of NMOSD includes neurological deficits in six typical topographies: optic neuritis, transverse myelitis, area postrema syndrome, acute brainstem syndrome, acute diencephalic syndrome, and symptomatic cerebral syndrome[2].

Although more prevalent in adults, particularly in women aged 30 to 40, around 5–10% of cases have onset before age 18. Clinical manifestations in pediatric patients are similar to those seen in adults, and the latest diagnostic criteria also apply to this age group. However, due to the rarity of the disease in the pediatric population, there is limited data available regarding the treatment of NMOSD in children and adolescents, with most treatment recommendations based on retrospective case series studies[3].

Treatment of NMOSD involves management of acute events, preventive therapy, and symptom control[4]. Therapeutic decisions in pediatric patients are generally based on experience with adult cases using immunosuppressants and monoclonal antibodies, with already established efficacy and side effect profiles[5].

This study aims to present a case report of a pediatric patient with NMOSD and to conduct an integrative literature review on treatments already used in pediatric patients, as well as ongoing clinical trials in this population.

CASE REPORT

A female patient, 11 years old, mixed race, with no significant medical history, began presenting in June 2024 with a sudden onset of pain and limited movement in her left upper limb. The condition progressed to involve her lower limbs, impairing her ability to walk. After one week, she also experienced nausea, vomiting, persistent hiccups, total bilateral anopsia, scalp and facial pruritus, as well as urinary and fecal incontinence.

Hospitalized in July 2024 at a state hospital, where she remained for one month. During hospitalization, she developed bilateral visual acuity loss. Due to clinical suspicion of an autoimmune etiology, she received pulse therapy with methylprednisolone, leading to resolution of vomiting and hiccups and partial recovery of visual acuity. However, the patient developed a hypertensive crisis and orotracheal intubation. Patient with no history of obstetric or neonatal complications, exhibiting appropriate neurological development, and no previous hospitalizations or family history of neurological or autoimmune diseases.

Brain MRI during hospitalization revealed diffuse and heterogeneous signal changes involving the midbrain, pons, and medulla, without contrast enhancement and almost no mass effect. It also showed involvement of the cerebellar peduncles and the prechiasmatic region of the optic tract, as well as the area postrema of the brainstem (Figure 1).

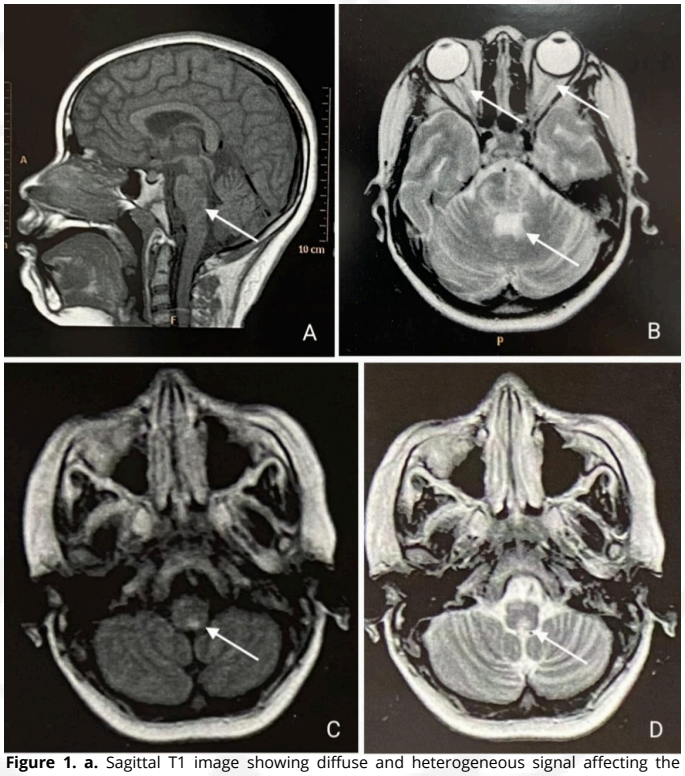

Figure 1. a. Sagittal T1 image showing diffuse and heterogeneous signal affecting the brainstem (arrow) b. Hyperintensity in the area postrema and optic neuritis (arrows) c. Hyperintensity in the medulla oblongata adjacent to the fourth ventricle in FLAIR (arrow) d. Hyperintensity in the medulla oblongata adjacent to the fourth ventricle in T2 (arrow).

Spinal MRI revealed several intramedullary lesions extensively affecting the cervicomedullary junction and cervical and thoracic spinal cord, without mass effect and with a slight area of contrast enhancement. These findings characterized longitudinally extensive transverse myelitis, with markedly hyperintense T2 signals within the lesions (Figure 2). Testing for anti-AQP4 antibody was positive (1:20). After stabilization, two months later, she was discharged on August 23, 2024, prescribed 40 mg/day prednisone and 100 mg/day azathioprine. After six months on azathioprine 2 mg/kg/day and lymphocyte count below 1500, prednisone was gradually tapered with the aim of discontinuation.

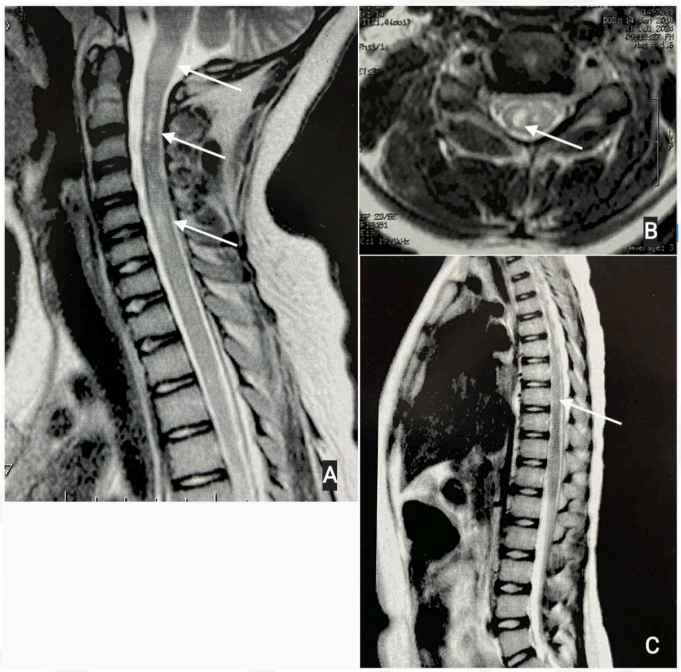

Figure 2. a. Longitudinally extensive transverse myelitis (LETM) with hyperintense T2 signal (arrow) b. Axial T2-weighted image at the C3–C4 level showing hyperintense signal involving both gray and white matter (arrow) c. Longitudinally extensive transverse myelitis involving the thoracic spinal cord with hyperintense T2 signal (arrow).

One month after hospitalization, the patient was able to walk independently, although requiring bilateral support. There was improvement in lower limb paresis and partial recovery of visual acuity, but persistent spasticity in the left hand.

Two months after discharge, the patient presented with cushingoid facies, spasticity with reduced range of motion and distal-predominant paresis in the left upper limb; mild reduction in range of motion and muscle strength (grade 4/5) in the lower limbs; preserved tactile and pain sensitivity.

She also showed partial visual acuity loss with fatigable nystagmus; noticeable shoulder asymmetry at rest and during movement, with the left side lower. Finger-to-finger dysmetria with fragmented movement and difficulty walking. She began rehabilitation and gradual tapering of prednisone.

After one month, the patient showed motor improvement but continued to experience wrist pain and reduced visual acuity persisted. Nocturnal enuresis was reported, along with significant weight gain. The patient showed complete improvement in gait following full recovery of lower limb strength and upper limb range of motion, with persistent distal limitation on the left side. Azathioprine dosage was maintained, and prednisone was adjusted to 40 mg and a new MRI was requested.

The most recent brain MRI showed a tumefactive lesion in the medulla and pons, especially in the dorsal and periaqueductal regions, along with mild enhancement of the right optic nerve sheath (Figure 3). Cervical spine MRI between C2 and C6 showed a small post-contrast enhancement at C3–C4 (Figure 3). Due to the significant weight gain, azathioprine was increased to 125 mg/day.

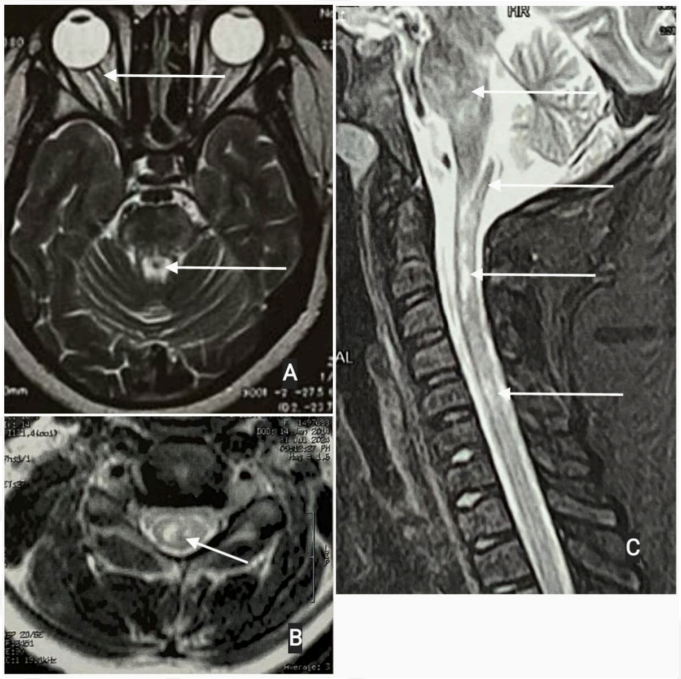

Figure 3. a. Post-contrast enhancement of the right optic nerve and area postrema (arrows) b. Axial post-contrast image of the cervical spine at the C3–C4 level showing focal enhancement (arrow) c. T2-weighted image demonstrating extensive myelitis involving the medulla oblongata and cervicothoracic spinal cord.

Currently, the patient remained on 40 mg daily prednisone and 125 mg (2.11 mg/kg/day) azathioprine. She has experienced significant weight gain, developed acanthosis nigricans on the neck, hypertrichosis, boutonniere deformity in the left hand, cushingoid facies and persistence of strength and movement limitation in the left upper limb. No new clinical events have occurred over seven months of follow-up under combined immunosuppressive therapy.

METHODS

Formulation of the Research Question

The integrative review followed adapted PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist guidelines[6]. The guiding question was structured using the PICO strategy (Population, Intervention, Comparison, Outcome). Based on this, the research question was defined as: "What is the effectiveness and clinical outcomes of the available treatments for neuromyelitis optica in pediatric patients?"

Data Collection and Search Strategy

The literature search was conducted on the following databases: PubMed, Web of Science, Embase, Scopus, EBSCO, LILACS, and SciELO from October 2024 to January 17, 2025. Additional searches were conducted on ClinicalTrials.gov to identify ongoing studies.

The following search terms were used, according to Medical Subject Headings (MeSH): (("Neuromyelitis Optica" OR "Neuromyelitis Optica Spectrum Disorder") AND ("Child" OR "Children")). These terms were adapted according to each database (Figure 4).

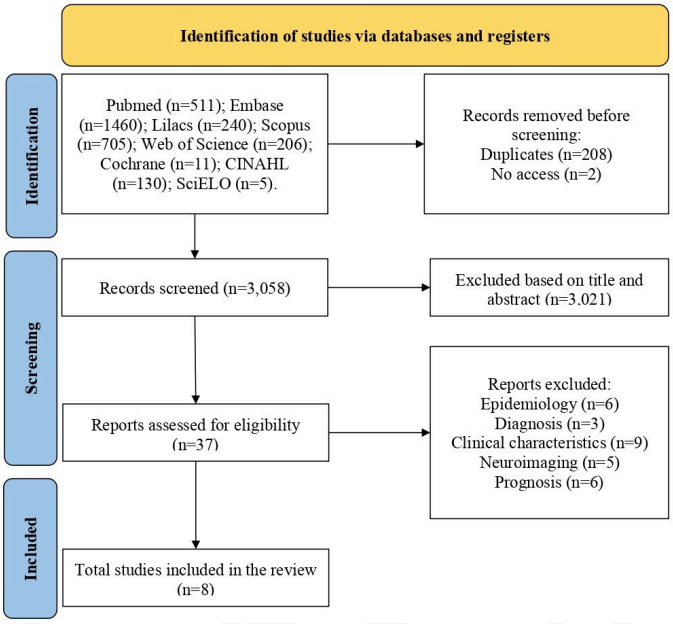

Figure 4. Identification: initial data collection based on descriptors. Screening: full-text reading of articles with inclusion or exclusion according to the established criteria. Included: articles selected to be part of the study.

Inclusion Criteria:

1. Studies involving only pediatric patients (<18 years) diagnosed with neuromyelitis optica spectrum disorder based on the 2015 or 2006 diagnostic criteria.
2. Original articles with primary data, case series with at least 5 patients, and observational studies.
3. Publications in Portuguese, English, or Spanish, published between 2015 to 2024 with full-text available.

Exclusion Criteria:

1. Studies without clear age group separation;
2. Systematic reviews, case reports, editorials, opinion pieces, animal or in vitro studies, and conference abstracts; articles with irrelevant data for the topic.

Data Extraction

To extract estimated data from selected studies, the authors used a standardized data collection form. Collected data included: First author's name, Year of publication, Country of origin, Study design, Sample size, Sex distribution, Mean age at onset, Percentage of AQP4-IgG positive patients, Type and dose of treatment, Follow-up duration, Primary outcomes, Annualized Relapse Rate (ARR), Expanded Disability Status Scale (EDSS), with reported means before and after treatment, Adverse effects. Any discrepancies were reviewed again and resolved by consensus.

To assess the treatment effect, the primary indicators used were the mean ARR and mean EDSS before and after the initiation of therapy.

RESULTS

The literature search identified a total of 3,268 articles on the treatment of NMOSD, of which 8 were included in this study after a series of screenings, as shown in Figure 4. The main characteristics of the included studies are presented in Tables 1 and 2. A total of 365 pediatric patients with NMOSD were included.

Table 1. Characteristics of the 8 articles included in the integrative review.

N	Author	Year	Study design	PT	AQP 4 +/ DS	F:M	Follow-up time
1	Zhichao Li et al[7]	2023	Case series	6	6/0	6:0	46,6 m (33-81m)
2	Umeton et al[11]	2023	Multicenter retrospective	91	77/14	78:13	RTX: 2,46 y, MMF e AZA: 2,26 y, IVIg: 1,84 y
3	Martins et al[8]	2022	Multicenter retrospective	20	6/1	12:8	2 y
4	Zhou et al[5]	2019	Retrospective cohort	31	23/5	4,2:1	AZA: 20 m / RTX: 13 m / 22m
5	Baghbanian et al[9]	2019	Retrospective cohort	10	7/ NR	4:1	2 y (1-3y)
6	Fragomeni et al[13]	2018	Retrospective cohort	11	8	2,6:1	6,7 y (±5)
7	Gmuca et al[10]	2018	Retrospective cohort	180	NR	129:51	12 m
8	Nosadini et al[12]	2016	Multicenter retrospective	16	15	14:2	6,1y

PT: patients; AQP4-IgG+: anti-aquaporin-4 antibody positive; DS: double-seronegative; F: female; M: male; RTX: rituximab; MMF: mycophenolate mofetil; AZA: azathioprine; IVIG: intravenous immunoglobulin; M: months; Y: years; NR: not reported.

Table 2. Data on the treatment performed in each study.

Nº	Type of treatment	Dose	Adverse effects	ARR B / A	EDSS B / A
1	IVIg e PLEX	PLEX: 40 mL/kg per cycle (5 sessions) / IVMP: 10-20mg/day.	Severe thrombocytopenia , acute jugular vein thrombosis, and skin irritation.	NR	3,6 / 3,5
2	RTX, MMF, AZA, IVIg	NR	Risk of hypogammaglobulinemia and infections with RTX.	NR / NT: 0,97; RTX: 0,28; MMF: 0,39; AZA: 0,41; IVIg: 0,54	AQP4+: 2; DS and NT: 3 / NSSD
3	IVMP, IVIg, PLEX, AZA, RTX	NR	NR	NR / AQP4+: 0,5 (0,25-1.0)	NR / AQP4+: 2,3
4	AZA / RTX / MMF	AZA: 2 mg/kg/day / RTX: 375 mg/m² per infusion / MMF: 1g/day	No complications were reported	AZA: 0.89 - 0.65 / MMF: 0.98 - 0.28/ RTX: 1 - 0	NR - AQP4+: 2; Totaly: 1,5
5	AZA, RTX, IVMP	IVMP: 30 mg/kg/day per 5 days (maximum of 1000 mg/day); AZA: 2–3 mg/kg; RTX: 1 g IV every 6 months	No severe complications were reported with RTX.	1/year (0.6-2); AZA: 1 - 0,5; RTX: 1 - 0	3 (0-5) / 2,5 (0-5)
6	AZA	AZA: 1,9 (0,5–3) mg/kg/day / Prednisone: 0.4 (0.2–1) mg/kg/day.	No severe complications were reported	1.26 / 0,41	3 (1-8,5) / 4 (1-8,5)
7	RTX	NR	NR	NR	NR
8	RTX	1.000 mg; 375 mg/m²; 750 mg/m² Redosing on average every 7.9 months.	Mild infusion reactions, infections, case of immunoglobulin deficiency without associated infection.	2,2 / 0,4	2,4 - NR

ARR: Annual Relapse Rate, EDSS: Expanded Disability Status Scale, B/A: before and after the start of therapy, IVIg: intravenous immunoglobulin, PF: plasmapheresis, IVMP: intravenous methylprednisolone, RTX: rituximab, MMF: mycophenolate mofetil, AZA: azathioprine, NT: no treatment, NSSD: no statistically significant difference, AQP4+: anti-aquaporin 4 positive antibody, NR: not reported, DS: double-seronegative;

In the acute phase, the articles reported the use of intravenous methylprednisolone (IVMP), plasma exchange (PLEX), and intravenous immunoglobulin (IVIG). The most commonly reported maintenance treatments were rituximab (RTX), azathioprine (AZA), and mycophenolate mofetil (MMF), classified as disease-modifying therapies (DMTs), with or without oral prednisone. Table 3 presents the 4 clinical trials found on ClinicalTrials.gov that are either ongoing or recently completed in pediatric patients.

DISCUSSION

The treatment of NMOSD is divided into two phases: the acute phase, aimed at halting inflammation and demyelination and restoring neurological function; and the maintenance phase, which focuses on preventing relapses. During acute events, high-dose IVMP therapy (15–30 mg/kg/day, up to 1 g/day for 3 to 5 days) remains the first-line treatment. There is strong evidence of rapid clinical improvement and inflammatory control in most cases[5, 7-9].

This was the approach adopted in the reported clinical case, with significant neurological benefits observed during hospitalization.

In patients who are refractory to corticosteroid therapy or present with severe relapses, additional therapies have shown promise for use during the initial acute episode or in the exacerbation of pre-existing disease. These therapies are considered as adjuvant treatments, such as IVIG and PLEX[5,7-9]. PLEX has been associated with more favorable outcomes when performed early, shortly after symptom onset, or as a rescue therapy when the response to initial IVMP treatment is inadequate[7].

Li et al. supported this finding in their study, demonstrating better outcomes with early initiation of PLEX, especially within the first ten days of an acute event. After this period, the therapeutic response was similar to that of IVMP. In their study of six participants, one patient showed a visual acuity improvement from 0.06 to 0.6 and a reduction in EDSS from 4 to 3, precisely the patient who began therapy on the tenth day of the acute episode[7].

The combination of IVMP and PLEX has demonstrated therapeutic superiority in severe cases[7,10]. IVIg has been primarily used in patients who are refractory or intolerant to conventional therapies. Its mechanism involves modulation of the immune response and neutralization of autoantibodies. Evidence suggests it is effective in alleviating symptoms and preventing relapses[5,7,8,11]. Pizzolato et al. investigated IVIG as monotherapy in first-line treatment as a DMT and found a reduction in symptom duration and required treatment time when compared to other DMTs[11].

The therapies used for relapse prevention in the studies were RTX, AZA and MMF. The response to immunosuppressive and immunobiologic treatment in pediatric NMOSD patients is variable but generally favorable, especially with RTX. Most studies showed a significant reduction in the ARR after initiation of maintenance therapy, as well as improvement or stabilization in the EDSS[5,8,9,11,12].

RTX, an anti-CD20 monoclonal antibody that depletes B lymphocytes, was the most frequently mentioned biologic in the reviewed articles. The average dose reported was 375 mg/m² per infusion every 6 months. In the evaluated studies, ARR dropped from 0.91–2.2 before RTX to 0.6–0 after therapy[5,8,11,12]. In a study by Nosadini et al., involving 16 pediatric patients, ARR was reduced from 2.2 to 0.6, representing the greatest difference reported in the review[12].

RTX showed sustained benefit even in patients with severe prior relapses, with better responses than AZA and MMF[5,9,11]. In several studies, patients treated with RTX achieved sustained remission without serious adverse effects during follow-up[5,9]. There is a correlation between B-cell repopulation and relapse, indicating that monitoring B-cell counts is crucial for timely administration of a new cycle of RTX to prevent relapses, as demonstrated in the study by Nosadini et al. Individualizing dosing intervals through rigorous CD19 monitoring may represent a promising strategy to optimize efficacy and safety in pediatric use[12].

AZA remains widely used in the public healthcare system as a maintenance agent due to its availability and low cost. The dose used in studies was 2–3 mg/kg/day[5,9,13], similar to that used in the case report. Despite its frequent use, AZA has lower efficacy, with a less significant reduction in ARR and a higher incidence of adverse effects such as hepatotoxicity, leukopenia, and gastrointestinal intolerance. AZA appears to have a less robust response in children compared to adults[11].

The effectiveness of AZA treatment varies across studies, based on the difference in ARR before and after therapy, suggesting potential benefits but requiring careful monitoring. Combining AZA with prednisone may enhance relapse control, representing a viable strategy, especially when monotherapy is insufficient. Fragomeni et al. evaluated the use of AZA combined with prednisone (average dose: 0.4 mg/kg/day) in a subset of patients, showing a significant reduction in disability progression (from 1.04 to 0) and in ARR (from 1.26 to 0.41)[13].

Similarly, in the maintenance phase of the patient in our case report, AZA combined with prednisone was used from the beginning—a regimen commonly seen in Brazilian studies, particularly due to the lack of standardized SUS protocols for RTX use in NMOSD. As discussed by Fragomeni et al. and reflected in the case report, this combination may offer relapse control, although with a higher risk of adverse effects such as weight gain, acanthosis nigricans, and hypertrichosis[13], consistent with the patient's clinical picture. Nonetheless, the patient remained relapse-free during the study period, demonstrating this as an effective therapeutic option.

MMF showed better efficacy than AZA, with lower relapse rates, though slightly inferior to RTX[5,11]. A 1 g/day

dose demonstrated better relapse control compared to 0.25 g/day[5]. Its adverse effect profile includes gastrointestinal issues and leukopenia, requiring regular hematologic monitoring. The persistence of motor sequelae, despite overall clinical improvement, highlights the importance of early treatment and access to more effective therapies such as RTX, which—as shown in the studies by Zhou et al. and Pizzolato Umeton et al.—yielded better results in relapse prevention and EDSS stabilization[5,11].

One of the main current challenges is the development of clinical trials specifically focused on the pediatric population. Currently, four clinical trials involving new therapies are listed on ClinicalTrials.gov (Table 3). The study involving Eculizumab was discontinued due to difficulties in recruiting participants, highlighting the challenges of conducting clinical trials in patients with rare diseases. Ongoing studies are currently evaluating the efficacy and safety of Satralizumab, Ravulizumab and Inebilizumab in the pediatric population[14,15,16,17].

Table 3. Ongoing or recently completed clinical trials in the treatment of NMO in pediatric patients.

Tratament	ID	Antibody	Mechanism of action	Route	Dose	Age range	IgG-AQP4	Date of completion
Eculizumabe	NCT04155424	Anti-C5	Complement inhibition	IV	Based on weight	2-17	(+)	july, 2023
Ravulizumabe	NCT05346354	Anti-C5	Complement inhibition	IV	Based on weight	2-17	(+)	January, 2029
Satralizumabe	NCT05199688	Anti-IL-6	Reduces the production of AQP4-IgG.	SC	Based on weight	2-11	(+)	September, 2029
Inebilizumab	NCT05549258	Anti-CD19	Reduces immatures B cells	IV	NR	2-17	(+)	april, 2027

ID: study identification, IgG-AQP4: anti-aquaporin 4 antibody, IV: intravenous, SC: subcutaneous, NR: not reported.

The SakuraSky study was a randomized controlled trial that compared satralizumab to placebo in patients with NMOSD, demonstrating efficacy and safety in this population. Patients aged 12 years and older were included, and they were allowed to continue their previous treatments with azathioprine or mycophenolate mofetil in combination with corticosteroids[18].

Satralizumab is a humanized monoclonal antibody (IgG2) that blocks the interleukin-6 receptor (IL-6), a cytokine involved in the pathophysiology of NMOSD. Administration is subcutaneous (120 mg), with biweekly dosing for the first three doses, followed by monthly injections[19].

Currently, the SAkuraSun phase 3 study is ongoing to evaluate the safety and efficacy of satralizumab in children aged 2 to 11 years with AQP4-IgG positivity. This multicenter study aims to expand the indication of the medication to the pediatric population under 12 years of age[16].

Ravulizumab is a second - generation terminal complement inhibitor derived from eculizumab, with a prolonged half-life, allowing for infusions every 8 weeks—an important advance for treatment adherence and patient quality of life. In adult trials such as CHAMPION-NMOSD, ravulizumab showed strong efficacy in reducing acute events in AQP4-IgG-positive patients and improved functional outcomes like EDSS and the Hauser Ambulation Index, with an acceptable safety profile[19].

Based on these promising results, a multicenter, open-label, controlled clinical trial (NCT05346354) was launched to assess ravulizumab's safety and efficacy in children and adolescents aged 2–17 years with AQP4-IgG positivity. The protocol includes weight-adjusted doses administered on days 1, 15, and then every 8 weeks, for up to 104 weeks. Primary completion is expected in March 2026[15].

Inebilizumab is an anti-CD19 monoclonal antibody targeting B cells, including plasmablasts and short-lived plasma cells. In adults, it has shown significant efficacy in reducing relapses in AQP4-IgG-positive patients, as demonstrated in the N-MOmentum trial. The annualized relapse rate was significantly reduced, with most patients remaining relapse-free for up to 4 years of follow-up. The safety profile was also acceptable, with a low incidence of serious adverse events and no need for treatment discontinuation[19].

Despite promising results in adults, the application of inebilizumab in the pediatric population is still in its early stages. A phase 2, open-label, multicenter clinical trial (NCT05549258) has been launched to evaluate the safety and efficacy of the drug in children and adolescents aged 12 to 17 years with AQP4-IgG-positive NMOSD and a history of at least one relapse in the past year or two in the past two years. The study outlines a 28-week treatment period, with recruitment starting in September 2022[17].

In Brazil, despite the clinical severity of NMOSD and advances in scientific evidence regarding its therapeutic options, the Unified Health System (SUS) still does not have a Clinical Protocol and Therapeutic Guidelines (PCDT) specific to this condition. The National Committee for Health Technology Incorporation (CONITEC) acknowledged the lack of national guidelines for NMOSD and highlighted the absence of incorporated medications in the public network for this purpose[20]. As a result, patients diagnosed with NMOSD are often left without standardized access to essential immunosuppressive therapies, which are critical for preventing relapses and disease progression.

RTX is considered off-label in Brazil, as it is not formally approved for NMOSD treatment in its drug label[20]. Nevertheless, the drug has strong scientific evidence supporting its effectiveness in reducing relapses, with superior efficacy compared to other therapies such as azathioprine, and is regarded as the first-choice treatment when available[5,9,11]. Currently, the NMOSD treatments officially registered in Brazil are inebilizumab, ravulizumab, and satralizumab. However, none are available through SUS, due to unfavorable budgetary impact and low cost-effectiveness, as stated in CONITEC's evaluations[20].

Because NMOSD is a rare disease, especially in children, this review faced some limitations. First, there is limited literature available in the indexed databases, which led to the inclusion of retrospective and observational studies—most with relatively small sample sizes and some incomplete data, which restricts the generalizability of findings and increases the risk of selection bias.

Additionally, there was significant heterogeneity in the diagnostic criteria used and in the length of follow-up. The scarcity of clinical trials in pediatric NMOSD underscores the urgent need for more prospective, multicenter studies to enable greater methodological standardization and generate high-quality evidence to guide clinical decisions in this population. Nevertheless, this study contributes to the systematization of knowledge on pediatric NMOSD treatment by gathering and critically analyzing dispersed data and contrasting it with clinical practice through a detailed case report.

CONCLUSION

The review highlights that, in the acute phase of pediatric NMOSD, IVMP combined with PLEX is the preferred therapeutic approach, particularly in cases of longitudinally extensive transverse myelitis and severe optic neuritis. This strategy, guided by clinical response, has been shown to optimize immediate neurological outcomes. As maintenance therapy, satralizumab is indicated for patients aged 12 years and older, while rituximab has demonstrated superior efficacy in reducing the ARR and stabilizing the EDSS, outperforming AZA and MMF.

In the maintenance phase, RTX showed the highest efficacy in reducing the ARR and stabilizing EDSS, outperforming AZA and MMF, although MMF showed intermediate performance. AZA, despite being widely used, was less effective and had a higher incidence of adverse effects, being better suited for combination therapy with corticosteroids in settings where access to RTX is limited.

Emerging targeted therapies satralizumab, ravulizumab and inebilizumab have shown promising results in adults, and ongoing pediatric trials may broaden the range of available treatment options, with better tolerability and cost-effectiveness profiles. The lack of clinical protocols and specific therapeutic guidelines within SUS remains a significant barrier to the universalization of treatment.

The clinical case discussed underscores the importance of early diagnosis and continuous follow-up, highlighting that despite the side effects associated with long-term glucocorticoid use, the patient remained relapse-free for seven months under combined immunosuppressive therapy, demonstrating the effectiveness of the proposed management.

REFERENCES

1. WINGERCHUK, DM; LUCCHINETTI, CF. Neuromyelitis Optica Spectrum Disorder. N Engl J Med. Aug 18; v.387, n.7, p.631-639, 2022. Disponível em: 10.1056/NEJMra1904655. Acesso em: 07 de outubro de 2025.
2. WINGERCHUK, DM; BANWELL, B.; BENNETT, JL; CABRE, P.; CARROLL, W.; CHITNIS, T.; et al. International Panel for NMO Diagnosis. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. v.85, n.02, p.177–189, 2015.
3. TENEMBAUM, S.; CHITNIS, T.; NAKASHIMA, I.; COLLONGUES, N.; MCKEON, A.; LEVY, M.; et al. Neuromyelitis optica spectrum disorders in children and adolescents. Neurology. v.87, n.9, Suppl 2, p.S59–S66, 2016.
4. CARNERO, Contentti. E.; ROJAS, JI.; CRISTIANO, E.; MARQUES, VD.; FLORES-RIVERA, J.; LANA-PEIXOTO, M.; NAVAS, C.; PAPAIS-ALVARENGA, R.; SATO, DK.; SOTO DE CASTILLO, I.; CORREALE, J. Latin American consensus recommendations for management and treatment of neuromyelitis optica spectrum disorders in clinical practice. Mult Scler Relat Disord. Oct; v. 45, p.102428, 2020. Disponível em: 10.1016/j.msard.2020.102428. Acesso em: 07 de outubro de 2025.
5. ZHOU, Y.; ZHONG, X, SHU, Y.; CUI, C.; WANG, J.; WANG, Y.; LI, X.; CHEN, Z.; PENG, L.; KERMODE, A.; QIU, W. Clinical course, treatment responses and outcomes in Chinese paediatric neuromyelitis optica spectrum disorder. Mult Scler Relat Disord. Feb; v.28, p.213-220, 2019. Disponível em: 10.1016/j.msard.2018.12.038. Acesso em: 07 de outubro de 2025.
6. PAGE, Matthew J., MCKENZIE, Joanne E., BOSSUYT, Patrick M., BOUTRON, Isabelle.; HOFFMANN, Tammy C., MULROW, Cynthia D. et al. A declaração PRISMA 2020: diretriz atualizada para relatar revisões sistemáticas. Epidemiol. Servir. Saúde. v. 31, n.2, p. e2022107, 2022. Disponível em: http://dx.doi.org/10.1590/s1679-4974202200020003. Acesso em: 07 de outubro de 2025.
7. LI, Z.; WAN, L.; LIU, X.; WANG, J.; SHI, X.; ZHOU, H.; XU, Q.; WEI, S.; YANG, G. Safety and efficacy of plasma exchange treatment in children with AQP4-IgG positive neuromyelitis optica spectrum disorder. Front Immunol. Jan 5, v.13, p.1113406, 2023. Disponível em: 10.3389/fimmu.2022.1113406. Acesso em: 07 de outubro de 2025.
8. MARTINS, C.; MOURA, J.; FIGUEIROA, S.; GARRIDO, C.; MARTINS, J.; SAMÕES, R.; GUIMARÃES, J.; MELO, C.; SOUSA, R.; PALAVRA, F.; FERREIRA, J.; SILVA, AM.; SÁ, MJ.; SANTOS, E. Pediatric neuromyelitis optica spectrum disorders in Portugal: A multicentre retrospective study. Mult Scler Relat Disord. Mar; v.59, p.103531, 2022. Disponível em: 10.1016/j.msard.2022.103531. Acesso em: 07 de outubro de 2025.
9. BAGHBANIAN, SM.; SAHRAIAN, MA.; NASER, Moghadasi A.; ASGARI, N. Disability and Therapeutic Response in Paediatric Neuromyelitis Optica Spectrum Disorder: A Case Series from Iran. Iran J Child Neurol. v.13, n.3, p.99-104, 2019.
10. GMUCA, S.; XIAO, R.; WEISS, PF.; WALDMAN, AT.; GERBER JS. Use of Rituximab and Risk of Re-hospitalization for Children with Neuromyelitis Optica Spectrum Disorder. Mult Scler Demyelinating Disord. Apr; v.3, p.3, 2018. Disponível em: 10.1186/s40893-018-0035-9. Acesso em: 07 de outubro de 2025.
11. PIZZOLATO, Umeton R.; WALTZ, M.; AAEN, GS.; BENSON, L, GORMAN, M.; et al.; US Network of Pediatric MS Centers. Therapeutic Response in Pediatric Neuromyelitis Optica Spectrum Disorder. Neurology. Feb 28; v.100, n.9, p. e985-e994, 2023. Disponível em: 10.1212/WNL.0000000000201625. Acesso em: 07 de outubro de 2025.

12. NOSADINI, M.; ALPER, G.; RINEY, CJ.; BENSON, LA.; MOHAMMAD, SS.; RAMANATHAN, S.; et al. Rituximab monitoring and redosing in pediatric neuromyelitis optica spectrum disorder. Neurol Neuroimmunol Neuroinflamm. 2016 Jan 21;3(1):e188, 2016. Disponível em: 10.1212/NXI.0000000000000188. Acesso em: 07 de outubro de 2025.
13. FRAGOMENI, MO.; BICHUETTI, DB.; OLIVEIRA, EML. Pediatric-onset multiple sclerosis in Brazilian patients: Clinical features, treatment response and comparison to pediatric neuromyelitis optica spectrum disorders. Mult Scler Relat Disord. Oct; v.25, p. 138-142, 2018. Disponível em: 10.1016/j.msard.2018.07.036. Acesso em: 07 de outubro de 2025.
14. Alexion Pharmaceuticals, Inc. A Study of the Safety and Activity of Eculizumab in Pediatric Participants With Relapsing Neuromyelitis Optica Spectrum Disorder [Internet]. Bethesda (MD): ClinicalTrials.gov; 2019 [acesso em 2025 abr. 22]. Disponível em: https://clinicaltrials.gov/study/NCT04155424
15. Alexion Pharmaceuticals, Inc. Efficacy and Safety Study of Ravulizumab IV in Pediatric Participants With NMOSD [Internet]. Bethesda (MD): ClinicalTrials.gov; 2022 [acesso em 2025 abr. 22]. Disponível em: https://clinicaltrials.gov/study/NCT05346354
16. Hoffmann-La Roche, Inc. A Study to Evaluate Pharmacokinetics, Efficacy, Safety, Tolerability, And Phamacodynamics of Satralizumab In Pediatric Patients With Aquaporin-4 Antibody Positive Neuromyelitis Optica Spectrum Disorder (NMOSD) [Internet]. Bethesda (MD): ClinicalTrials.gov; 2022 [acesso em 2025 abr. 22]. Disponível em: https://clinicaltrials.gov/study/NCT05199688
17. Amgen, Inc. Study of Inebilizumab in Pediatric Subjects With Neuromyelitis Optica Spectrum Disorder [Internet]. Bethesda (MD): ClinicalTrials.gov; 2022 [acesso em 2025 abr. 22]. Disponível em: https://clinicaltrials.gov/study/NCT05549258
18. Hoffmann-La Roche, Inc. Efficacy and Safety Study of Satralizumab (SA237) as Add-on Therapy to Treat Participants With Neuromyelitis Optica (NMO) and NMO Spectrum Disorder (NMOSD).Clinicaltrials.gov. 2025 [cited 2025 Jul 25]. Available from: https://clinicaltrials.gov/study/NCT02028884?cond=%22Neuromyelitis%20Optica%20Spectrum%20Disorder%22&term=%22Child%22&rank=23
19. Anderson M, Levy M. Advances in the long-term treatment of neuromyelitis optica spectrum disorder. J Cent Nerv Syst Dis. 2024 Feb 1;16:11795735241231094. doi: 10.1177/11795735241231094 20. Ministério da Saúde (BR). Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde – Conitec. Relatório para a sociedade nº 457: Inebilizumabe para distúrbio do espectro da neuromielite óptica. Brasília: Conitec; 2024 [acesso em 22 abr. 2025]. Disponível em: https://www.gov.br/conitec/pt-br/midias/consultas/relatorios/2024/sociedade/relatorio-para-a-sociedade-n-457-inelizumabe/view