Early clinical predictors of failure to oral immunosuppressive therapies in NMOSD

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Introduction

Neuromyelitis Optica Spectrum Disease (NMOSD) is an autoimmune astrocitophaty that primarily affects the optic nerve, spinal cord and periventricular areas, such as the area postrema. Although new medications have been approved for the management of NMOSD, to date there is no universal treatment protocol and access to new therapies is heterogeneous, especially in resource-limited settings. Current treatment options include classic immunosuppressants (IS), such as azathioprine, methotrexate and mycophenolate usually used as first line therapies due to their availability, and rituximab (RTX), an anti-CD20 monoclonal antibody, widely used to control the disease, despite the lack of consensus in the literature regarding the indication, dose and frequency of administration.

Objectives

To analyze the clinical and epidemiological profile of patients with NMOSD using RTX, diagnosed, and evaluate whether patients who failed classic IS and were escalated to RTX can be identified early based on clinical and demographic criteria.

Methods

This was a single-center retrospective study which included NMOSD patients under classic IS and RTX treatment from 1995 to November 2022. Failure was considered as one severe relapse. In the population whether RTX was a second line therapy, clinical predictors for non-responsiveness to classic IS used as criteria were age under 35 years and severe attack at disease onset.

Results

From 105 patients with NMOSD regularly followed-up at our reference center, 26% (n=27) were under RTX treatment during the study period, with median follow-up of 108 months. From those, 96% (n=26) were female, median age was 41 years (range 21-77), median EDSS was 4 (range 1-8.5), 85% (n=23) were anti-AQP4 seropositive and 88,8% (n=24) were relapse free under RTX treatment. From the 20% (n=21) using RTX as second-line therapy, 30.7% met both criteria, where disease onset under 35 years-old and severe attack determine a risk of 22.5% to not respond to classic IS, while the absence of both criteria was associated with a 4.6% risk.

NMO patients under oral IST or switched to RTX.

Age ≤ 35 years	Severe first relapse	n	Oral IST / RTX	% Non-responsive oral IST phenotype	RR (%)
✓	✓	52	36 / 16	30.7	22.5
✓	✗	6	6 / 0	0	0
✗	✓	29	24 / 5	17	4.6
✗	✗	12	12 / 0	0	0

IST = immunosuppressive therapies; RR = relative risk

Prognostic value of criteria for no responsiveness oral IST and specific variables

	Sensitivity (%)	Specificity (%)	PPV (%)	PNV (%)
Age ≤ 35 years + Severe relapse	100	25	30	100
Severe relapse criteria	100	33	17	100

PPV: Predictive positive value; PNV: predictive negative value.

Conclusion

Rituximab is likely an effective drug for NMOSD treatment in a resource-limited and real-world setting, given the high proportion of relapse-free patients in our cohort. Younger age and severe attack at disease onset can be used as predictors of poor response to classic IS and support the early initiation of highly effective medications.

References

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