RITUXIMAB IS EFFECTIVE REGARDLESS EVOLUTION TIME IN SEROPOSITIVE AQP4 IgG NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOsd) PATIENTS

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Introduction

Neuromyelitis Optica spectrum disorders (NMOsd) are a group of inflammatory disorders of the CNS characterized by episodes of demyelination and immunomodulated axonal damage and are usually associated with the presence of serum anti-aquaporin-4 antibodies (AQP4). Rituximab (RTX) is a monoclonal antibody directed against CD20 that has long-term reduction in AQP4-IgG titers and the relapse rate in patients with NMOsd.

Objective

Defining the efficacy of RTX treated AQP4 seropositive NMOsd patients.

Methods

In an observational and retrospective study, all patients treated in our institution diagnosed with NMOsd by 2015 criteria, with recurrent clinical phenotype, seropositive for anti-AQP4 antibodies under treatment with RTX at least 2 years were included. the Student's t-test, survival curves and log analysis were performed. Rank Values of $p \leq 0.05$ were considered statistically significant.

Results

A total of 22 patients (100% female) were identified. Mean age at onset weas 34 years (SD 11) with a mean time of disease of 8.11 years and mean of 7 relapses during the same period. 15 patients received an immunosuppressive agent before RTX (AZA 40%, CFM 46%, MMF 6.7%, MTX 6.7%). The mean age at treatment initiation with RTX was 37 years (SD 12), with a mean treatment time of 52 months (SD 28). The mean ARR before and after treatment with RTX was 2.55 and 0.35 (5 vs 1 relapses before and after the start of RTX); with a difference of -2.20 ($p = 0.006$)

Table 1. Basal clinical characteristics

		N=15
Sex	Male [a]	0 (0%)
	Female [a]	15 (100%)
Age at disease onset (years)[b]		34 (11)
Age at disease diagnosis (years)[b]		36 (12)
Disease duration (years)[b]		8.11 (4.05)
Number of relapses [b]		7 (5)
CSF glucose(mg/dl) [b]		52 (12)
CSF proteins (mg/dl) [b]		84 (120)
CSF cell count [b]		12 (21)
OCB	Present [a]	3 (20%)
	Absent [a]	4 (26.7%)
	Untested [a]	8 (53.3%)
Previously immunotherapy	Azathioprine (AZA) [a]	6 (40%)
	Cyclophosphamide (CYC) [a]	7 (46.7%)
	Methotrexate (MTX) [a]	1 (6.7%)
	Mycophenolate mofetil (MMF) [a]	1 (6.7%)
Age at RTX treatment onset (years) [b]		37 (12)
Evolution time before the RTX treatment (years) [b]		45 (34
RTX treatment duration [b]		52 (28)
Relapses before RTX treatment		5 (4)
Relapses during RTX treatment		1 (3)

a. Frequency (%).
b. Mean (standard deviation).

Discusion

We observed a significant ARR reduction (-2.20) with RTX treatment. These findings are very similar to what is found in the first report of RTX in NMOsd[16] (-2.60 ARR reduction), and a greater ARR reduction compared to the previously reported in two meta-analysis (-1.56 and -0.79) and the clinical study of AZA vs RTX (-1.09) [7],[8],[9]. This difference in the reduction of ARR may be related to two situations: the design of this study that aims to assess the effect in seropositive AQP4-IgG+ patients (although in the study by Mealy et al[14] it had already been suggested that presence of AQP4-IgG does not modify the response to treatment) and to the highest proportion of patients in our study who had a short term previously immunomodulatory treatment. During the time observed, patients undergoing RTX treatment achieved a relapse-free rate of 66.7%, which is similar to that previously reported in the aforementioned meta-analysis (62%).

Table 2. Annualized relapse rate (ARR) before and during RTX treatment

N=15		Mean	Standard deviation	p
ARR	Before RTX treatment	2.55	2.57	0.006
	During RTX treatment	0.35	0.74	
Relapse-free status	Before RTX treatment	5 (33.3%)		0.054
	During RTX treatment	10 (66.7%)		

Conclusion

This study shows a statistically significant reduction in the ARR and an increase in the relapse-free rate in AQP4+ NMOsd patients treated with RTX. The benefit seems to be maintained independent of the time of evolution or prior treatment. These findings support the use of rituximab in our population, and indirectly suggests that the early use of rituximab would modify the course of the disease .

References

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