



Clinical and MRI Characteristics of Double-Seronegative NMO Phenotype in Brazil

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INTRODUCTION

Neuromyelitis optica (NMO) syndrome is defined by the combination of optic neuritis (ON) and acute myelitis (MY). Despite advancements, the nature of the disease in AQP4-Ab and MOG-Ab seronegative patients is most frequently unknown. Studying double seronegative NMO (DN-NMO) may reveal subtypes within this group, enabling targeted therapies.

Objective

To assess the clinical and MRI characteristics of DN-NMO based on the 2015 IPND.

METHODS

We selected a cohort of patients who presented NMO phenotype and AQP4-Ab negative serostatus at a tertiary Center in Brazil. Patients were categorized into two groups based on whether they fulfilled the 2015 International criteria for NMOSD without AQP4-Ab. Demographic, clinical, and imaging data were compared.

RESULTS

The cohort included 25 DN-NMO patients (median age at onset 30 years (2–60); 21 (80%) female and non-Caucasian). Ten patients (40%) met the 2015 diagnostic criteria for NMOSD without AQP4-Ab (8 females, non-Caucasians). These patients more frequently had simultaneous ON and MY at onset (60% vs. 13.3%, $p=0.028$), higher median EDSS scores at the last visit (4.0 vs. 3.25), and normal brain MRI ($p=0.049$). No significant differences were observed in time to first relapse, median ARR, prevalence of extensive optic nerve lesions, or LETM. Median disease durations were 16.2 and 8.35 years, respectively. Data are summarized in the table.

CONCLUSION

Our findings suggest that DN-NMO represents a heterogeneous group of conditions. A subgroup fulfilling the 2025 IPND criteria for NMOSD without AQP4-Ab differs in having a lower prevalence, more frequent simultaneous ON and MY at onset ($p<0.05$), more frequent normal brain MRI ($p<0.05$), and higher EDSS scores (though not statistically significant). Collaborative multicenter studies are needed to better understand DN-NMO subgroups, explore the impact of genetic/environmental factors on their expression, and improve management strategies based on their specific pathogenesis.

Table: Clinical and MRI Characteristics of NMO patients according to the classical phenotype of neurites and myelitis			
	NMO phenotype (n= 15)	DN NMO (n= 10)	p
Sex, F:M	13:2	8:2	>0.05
Age at disease onset, median	27 (2-60)	34.5 (19-55)	>0.05
Race/ ethnicity			
Mixed race, n	8	6	>0.05
Black, n	5	2	>0.05
Caucasian, n	2	2	>0.05
Presenting symptoms			
ON	8	1	0.04
MY	5	1	0.345
Simultaneous ON+MY	2	6	0.028
BS	1	2	0.543
CS/APS/HS	1	0	-
EDSS at first evaluation, median	4 (0-6.5)	3 (1-7.5)	0.08
Relapsing course	13	7	0.458
Time to first relapse, months	12 (2-47)	18 (4-58)	>0.05
ARR	0.2 (0.06-1.0)	0.25 (0.13-0.33)	>0.05
MRI, T2-Hyperintension lesion			
Brain	Normal (4)	Normal (7) Atypical for MS (3)	0.049
Orbits	Normal (7) ON >50% or chiasma involved (5) Short ON (3)	Normal (4) ON > 50% or chiasma involved (4) Short ON (2)	>0.05
Spinal	LESCL (6) Normal (5) Short MY (2) NA (2)	LESCL (10)	>0.05
Disease duration, yrs, median	16.2 (4-51.2)	8.35 (3.5-17)	0.04
Maintenance treatment	AZA (8) None (5) R (2)	AZA (5) None (3) TER (1) Vit. D (1)	-
Most recent EDSS	4 (0-8)	3.25 (1-8)	>0.05

REFERENCES

