Contrasting Pre- and Post-Pubertal Pediatric NMOSD in the NMO-RG Cohort

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INTRODUCTION

Puberty typically begins between ages 9 and 14 and plays a critical role in the onset and expression of various autoimmune conditions due to hormonal changes and increased cytokine and antibody production. Data from the Brazilian pediatric neuromyelitis optica spectrum disorder (NMOSD) cohort show that children present distinct features compared with adults. To examine whether these differences result from the effects of puberty on the immune system, we compared disease characteristics between pre- and post-pubertal patients within our pediatric cohort. .

MATERIALS AND METHODS

Children with NMOSD registered in the NMO-RG by November 30, 2024, were divided into pre-pubertal (pre-p; age <11 years) and post-pubertal (post-p; age 11–18 years) groups. We compared demographic and clinical features in each pediatric group. Both pediatric subgroups were also compared separately with the adult NMOSD group. All patients fulfilled the 2015 International Diagnostic Criteria for NMOSD.

RESULTS

Of 111 pediatric patients, 41 (36.9%) were pre-p, and 70 (63.1%) were post-p. Relative to post-p patients, the pre-p group had more females, fewer individuals of African descent, more frequent optic neuritis and brainstem/cerebral symptoms, higher AQP4-antibody seropositivity and CSF-OCB rates, and higher EDSS scores at the last visit, though these differences did not reach statistical significance. Compared with adults, both pre-p and post-p groups had more frequent brainstem, diencephalic, and cerebral symptoms, as well as area postrema syndrome, but fewer general symptoms and pain (p<0.05; table). The AQP4-antibody rate, ARR, and EDSS were similar across all groups.

Table. Comparison of demographic and clinical characteristics across different age groups

	Age groups						
				P Value			
	Pre-P n=41	Post-P n=70	Adult n=754	All	Pre-P, Pos-P	Pre-P, Adult	Post-P, Adult
Age at onset, yr							
Median [IQR]	9.0 [6.0-10.0]	15.0 [13.0-16.0]	35.5 [27.0-45.0]	NA	NA	NA	NA
Range	1-10	11-18	19-79				
Mean±SD	7.8±2.5	14.5±2.0	37.0±12.5				
Female gender, no./total no. (%)	34 (82.9)	55 (79.7)	640/749 (85.4)	NS	NS	NS	NS
Ethnicity, no./total no. (%)				NS	NS	NS	NS
Caucasian	16 (41.0)	29 (45.3)	279/656 (42.5)				
Mixed	21 (53.8)	22 (34.4)	239/656 (36.4)				
African descent	2 (5.1)	12 (18.8)	128/656 (19.5)				
Asian/Other	0 (.0)	1 (1.6)	10/656 (1.5)				
Presenting symptoms, no./total no. (%)							
Optic neuritis (ON)	24 (58.5)	27 (39.7)	368/752 (48.9)	NS	NS	NS	NS
Myelitis (MY)	16 (39.0)	33 (48.5)	378/752 (50.3)	NS	NS	NS	NS
Area postrema syndrome (APS)	8 (19.5)	21 (30.9)	111/752 (14.8)	**0.002**	NS	NS	**0.002**
Brainstem (BS)	7 (17.1)	11 (16.2)	64/752 (8.5)	**0.029**	NS	0.084	**0.046**
Diencephalon	2 (4.9)	1 (1.5)	5/752 (0.7)	**0.021**	NS	**0.046**	NS
Cerebral	3 (7.3)	3 (4.4)	12/752 (1.6)	**0.017**	NS	**0.038**	NS
Optic neuritis and myelitis	4 (9.8)	6 (8.8)	84/752 (11.2)	NS	NS	NS	NS
Exclusive ON+MY	1 (2.4)	3 (4.4)	64/752 (8.5)	NS	NS	NS	NS
Exclusive ON	17 (41.5)	15 (22.1)	262/752 (34.8)	**0.062**	NS	NS	NS
Exclusive MY	9 (22.0)	21 (30.9)	260/752 (34.6)	NS	NS	NS	NS
Exclusive APS	2 (4.9)	8 (11.8)	42/752 (5.6)	NS	NS	NS	NS
Exclusive BS	1 (2.4)	3 (4.4)	25/752 (3.3)	NS	NS	NS	NS
General Symptoms, no./total no. (%)							
No general symptoms	12 (44.4)	34 (56.7)	240/664 (36.1)	**0.006**	NS	NS	**0.002**
Pain	6 (22.2)	12 (20.0)	284/664 (42.8)	**<0.001**	NS	**0.045**	**0.001**
Pruritus	0 (0.0)	1 (1.7)	22/664 (3.3)	NS	NS	NS	NS
Fatigue	2 (7.4)	9 (15.0)	123/664 (18.5)	NS	NS	NS	NS
Anxiety/depression	6 (22.2)	15 (25.0)	185/664 (27.9)	NS	NS	NS	NS
Cognitive symptoms	3 (11.1)	2 (3.3)	38/664 (5.7)	NS	NS	NS	NS
Annual relapse rate, relapses/yr	n=41	n=70	n=751				
Median [IQR]	0.42 [0.15-1.01]	0.46 [0.25-0.94]	0.39 [0.19 – 0.77]	NS	NS	NS	NS
Range	0.00-3.58	0.00-4.36	0 – 10.00				
Mean±SD	0.68±0.73	0.75±0.83	0.80±1.25				
EDSS at last visit	n=38	n=68	n=724				
Median [IQR]	4.75 [3.38-7.00]	4.00 [2.13-6.00]	4.00 [3.00 – 6.50]	NS	NS	NS	NS
Range	1.00-8.00	0.00-10.00	0.00 – 10.00				
Mean±SD	4.76±2.16	4.29±2.41	4.60±2.41				
AQP4-Ab positivity, no./total no. (%)	32 (84.2)	48 (73.8)	550/714 (77.0)	NS	NS	NS	NS
OCB/high IgG index, no./total no. (%)	4 (19.0)	6 (15.0)	60/416 (14.4)	NS	NS	NS	NS

CONCLUSION

While both pre-p and post-p pediatric NMOSD differ from adult-onset disease, no significant differences emerged between these two pediatric subgroups. Factors beyond puberty likely contribute to the distinctive features of pediatric-onset NMOSD compared with the adult-onset disease.

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Disclosures
MALP has received funding for travel and speaker honoraria from Novartis, Horizon Therapeutics and Roche. NCT- Nothing to disclose; PPC has received funding for speaker honoraria from Roche; TP- Nothing to disclose; TF - Nothing to disclose, JACD - Nothing to disclose; MSP- In the last year has received support for scientific meetings, speaker fees or scientific consultancy from: Astrazeneca, Amgen, Novartis, Roche, Biogen and Merck; MLBF for this production nothing to disclose, however, has received support from Roche, Merck, Alexion, Horizon, Novartis, EMS for other activities; VDM - Participation in advisory boards at Horizon and Alexion; MFM - Nothing to disclose; AD - Received advisory board and/or research/travel grants from: Alexion, Bayer, Biogen, Horizon, Janssen, Merck Serono, Novartis, Roche, Sanofi and Teva; JB has received speaking honoraria and research or travel grants from Alexion, Bayer, Biogen, EMS, Horizon, Janssen, Merck, Novartis, Roche, Sanofi, Shire and TEVA; PG - Nothing to disclose; SG - Nothing to disclose; MG - Nothing to disclose; HKS has received funding for travel and speaker honoraria from Biogen, Roche, Novartis, AstraZeneca, Merck Serono; GF - Nothing to disclose; CT - Nothing to disclose; SLAP has eventual Sponsorship link for participation in clinical trials: Roche ; Contributions or consulting activities: Biogen, Genzyme, Novartis, AMGEN, Alexion; Educational support for participation in congresses: Merck Serono, Alexion, AMGEN, Roche; Board advisory: Merck, Novartis, Roche, Horizon-AMGEN, Alexion; Employment relationship with the institution: HC FMUSP; VAS - Nothing to disclose; BP - Nothing to disclose; LMA - Nothing to disclose; KM - Nothing to disclose; RPCH has received funding for travel grant da Horizon(2022); DG - Nothing to disclose.