ROLE OF THE ANTI-MYELIN OLIGODENDROCYTE GLYCOPROTEIN (MOG) ANTIBODIES AND ANTI-AQUAPORIN 4 (AQP4) ANTIBODIES IN IDIOPATHIC ISOLATED OPTIC NEURITIS AND MYELITIS: SERUM BIOMARKERS OF SPECIFIC CLINICAL SYNDROMES?

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OBJECTIVE

Anti-AQP4 antibodies (AQP4-Abs) are well known pathogenetic biomarkers of Neuromyelitis Optica Spectrum Disorders (NMOSD). Anti-MOG antibody (MOG-Ab) has been associated with a broad spectrum of acquired Central Nervous System (CNS) demyelinating diseases ranging from NMOSD to variant of Multiple Sclerosis (MS).
The aim of our study was to compare clinical and paraclinical features of patients who experienced an optic neuritis (ON) or a myelitis as first clinical episode suggestive of demyelinating disease classified according to the presence/absence of AQP4-Ab and MOG-Ab.

PATIENTS AND METHODS

We included two cohorts of patients:
1) a prospective cohort of 57 patients followed for a mean period of 3.3±3.2 years;
2) a retrospective cohort of 19 AQP4-Ab positive NMOSD patients.
All patients were tested for both AQP4- and MOG-Ab using specific Cell-Based Assays.

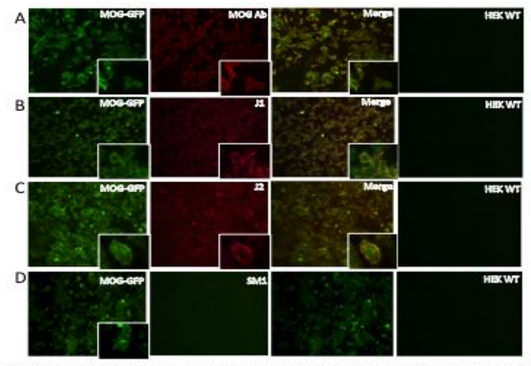

FIGURE. Cell Based Immunofluorescence Assay (CBA) performed on HEK 293 expressing human MOG Alpha-1 fused to GFP. The GFP tag was inserted to evaluate the expression levels of MOG (green staining). In red is shown the immunofluorescence staining using commercial antibody (A), two MOG-positive (J1, J2) patient's sera (B,C) and one negative serum of a MS patient (SM1). Non transfected cells (HEK WT) were used as negative control. Magnification 20X. *Inset* shows an higher magnification (100x) of the staining on a single transfected cell.

RESULTS

Table 1. Comparison of clinical findings between patients with MOG Abs, AQP4 Abs and without Abs with statistical analysis

	Tot.	MOG neg/AQP4 neg	MOG-Ab Positive	AQP4-Ab positive	p
N pts	76	38	19	19	
Sex (F), [n° of patients] (%)	47 (61.8%)	22 (57.9%)	7 (36.8%)	18 (95%)	<0.0001
Age at onset, ys [mean ±DS] (range)	35.4±11.3	33±9.3 (17-56)	40.7±12.7 (14-60)	35±12.4 (16-68)	0.05
Follow-up duration, ys (mean ±DS) (range)	4.8±4.5	3.5±3 (0.5-8.5 aa)	2.9±3.8 (0.5-13 aa)	9±5.3 (0.5-18.5 aa)	<0.0001
Onset Myelitis Optic Neuritis (ON)	 34 42	 13 (34.2%) 25 (65.8%)	 11 (57.9%) 8 (42.1%)	 10 (52.6%) 9 (47.4%)	ns
EDSS at onset (mean ±DS)	2.4±1.4	1.6±0.62	2.5±1	3.8±2	<0.0001
EDSS at last follow-up (mean ±DS)	2.4±1.8	1.7±0.7	2±1	4.3±2.5	<0.0001
DIS (clinical and/or paraclinical), [n° (%) of pazients]	61	37^ (97%)	11 (57%)	13 (68%)	<0.0001
Clinical DIT [n° (%) of pazients]	43	17 (44%)	8 (42%)	18(95%)	0.001
DIT (clinical and/or paraclinical), [n° (%) of pazients]	49	20 (52%)	11 (57%)	18 (95%)	0.006
Time between first and second attack, ys (mean±DS)	1.9±2.1	1.2±1	2±2.7	2.4±2.5	ns
Second relapse ON Myelitis Other	 18 18 7	 9 (53%) 6 (35.3%) 2 (11.7%)	 4 (50%) 1 (12.5%) 3 (37.5%)	 8 (44.4%) 8 (44.4%) 2 (11.2%)	ns

DIS Dissemination in Space; DIT Dissemination in Time

Table 2. Comparison of CerebroSpinal Fluid (CSF) findings between patients with MOG Abs, AQP4 Abs and without Abs with statistical analysis

	Tot.	MOG-Ab negative/AQP4-Ab negative (n. 38)	MOG-Ab Positive (n. 19)	AQP4-Ab Positive (n. 19)	p
CSF WBC (mean ±DS)	10±26.1	7,5±9,4	5.6±5.5	20.2±51.8	ns
CSF Proteins (mean ±DS)	52.3±67.6	45,3±13,3	74±132.4	44.4±23	ns
CSF Oligoclonal Bands, [n° (%) of pazients]	40	28 (73.6%)	6 (31.5%)	6 (31.5%)	0.001

Table 3. Comparison of MRI findings between patients with MOG Abs, AQP4 Abs and without Abs with statistical analysis

	Tot.	MOG-Ab negative/AQP4-Ab negative (n. 38)	MOG-Ab Positive (n. 19)	AQP4-Ab Positive (n. 19)	p
Presence of MS-like brain lesions, [n° (%) of pazients]	40	30 (79%)	7 (37%)	3 (16%)	<0.0001
N° of brain lesions 0-1 2-9 >9	 19 47 10	 1 (3%) 30 (79%) 7 (18%)	 9 (47.4%) 7 (36.8%) 3 (15.8%)	 9 (47%) 10 (53%) 0	<0.0001
Presence of spinal cord lesions [n° (%) of pazients]	41	17 (45%)	11 (58%)	13 (68%)	ns
LETM, [n° (%) of pazients]	17	1 (6%)	4 (36%)	12 (92%)	<0.0001
MRI follow-up Stable New lesions Reduction/disappearing	70 27 39 4	35 13 (37%) 21 (60%) 1 (3%)	16 9 (56.3%) 5 (31.2%) 2 (12.5%)	19 5 (26.3%) 13 (68.4%) 1 (5.3%)	ns
MRI DIT and DIS at follow-up [n° (%) of pazients]	33	25 (66%)	8 (42%)	0	<0.0001
MS diagnosis, [n° (%) of pazients]	27	24 (63%)	3 (16%)	0	<0,0001

LETM Long Extensive Transverse Myelitis

CONCLUSION

The presence of serum MOG-Ab is not a rare event in ON and myelitis suggestive of CNS demyelinating syndrome. Clinical and paraclinical characteristics of these patients overlap partially those of NMOSD and MS. The possibility for MOG-Ab positive patients to reach MRI dissemination in space and time claim attention on differential diagnosis with "typical" MS and may suggest B-cell specific therapeutic long-term strategy.

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