MOG-antibodies associated diseases:
clinical features and prognostic factors in 197 adult patients

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Introduction

Myelin oligodendrocyte glycoprotein antibodies (MOG-Ab) in adults are mainly associated to neuromyelitis optica spectrum disorders (NMOSD).[1,2] However, the clinical phenotype could be broader than expected, and prognostic factors of poor outcome have not yet been identified.

Methods and subjects

Inclusion criteria and recruitment

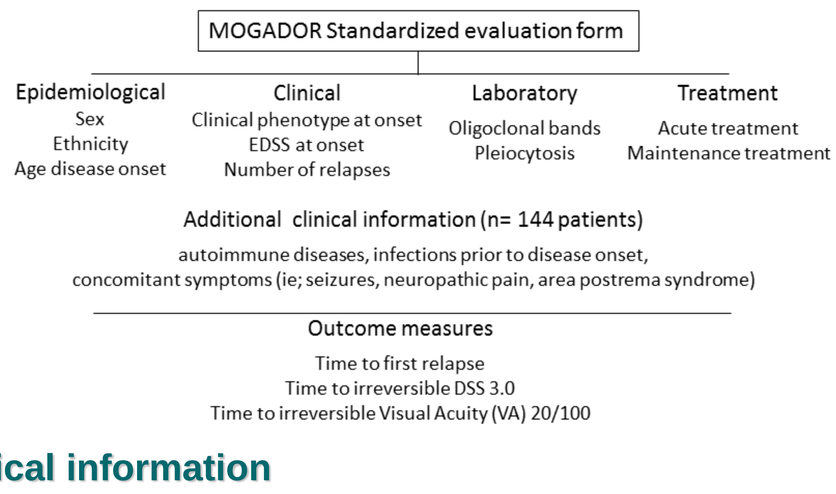
This is a multicentric retrospective study from all the French referral centers within the scope of *observatoire français de la sclérose en plaques* (OFSEP) performed between January 2014-January 2017. Patients were included when fulfilling the following inclusion criteria: 1) diagnosis of Acute Demyelinating Syndrome (ADS), 2) presence of MOG-Ab in serum detected either at onset of disease or during follow-up, 3) age ≥ 18 years at onset of disease.

Clinical information

Information was prospectively collected in standardized evaluation forms dedicated to the present study: MOGADOR study. Additional epidemiological and clinical features were assessed when available (n=144) (**figure1**).

At last follow-up patients were classified as ADEM, NMOSD, other limited NMO-like phenotypes (i.e; isolated monophasic or relapsing transverse myelitis [TM] or optic neuritis [ON]), Multiple Sclerosis (MS), and brainstem syndromes. Patients with short TM and ON who did not strictly fulfilled NMOSD criteria were classified as optico-spinal phenotype.

Figure 1. Baseline variables and outcome measures.



Radiological information

Available brain magnetic resonance imaging (MRI) within three months from onset of symptoms were evaluated, and features known to be associated with NMOSD and MOG-Ab registered.[3,4] As controls, we used the most recent available abnormal brain MRI from our cohort of AQP4-Ab-positive patients.[5]

Autoantibody detection

Within the period of the study, 16.181 serum samples were tested for AQP4-Ab and MOG-Ab by cell-based assay with live HEK293.

Prognosis analysis

For motor disability, we included all patients who presented with ON phenotypes, and for visual disability we only included those who presented with ON, at first ADS.

Results

Epidemiological and clinical features

We identified 197 MOG-Ab-positive patients. Among them, 50.8% were males and the median age of presentation was 36.5 years (interquartile range, 28.2-47.7). Patients were predominantly Caucasian (92.9%). The most frequent clinical phenotypes at onset were ON (60.9%), then myelitis (22.3%).

The proportion of relapsing patients increased with time from 54/74 (73.0%) to 38/44 (90.5%) when considering only patients with a minimum follow-up of two and five years, respectively.

At last follow-up, 38 (19.3%) of patients fulfilled criteria for NMOSD, and 3 (1.5%) patients for MS (**table 1**).

Table 1. Epidemiological and clinical characteristics in MOG-Ab-positive patients

Variables from MOGADOR standardized evaluation form	MOG-Ab-positive patients n=197
Females, n (%)	97 (49.24)
Age at onset, y median (range)	36.46 (18.97-76.75)
Caucasian, n (%)	183 (92.89)
Follow-up, m median (range)	15.77 (1-556.64)
Phenotype at onset, (%)	
All ON	120 (60.91)
Unilateral ON	70 (35.53)
Bilateral ON	50 (25.38)
Myelitis	44 (22.34)
ON & myelitis	15 (7.61)
Brainstem syndrome	8 (4.06)
Encephalopathic syndrome	5 (2.54)
Brainstem & encephalopatic syndrome	4 (2.03)
Brainstem syndrome & ON	1 (0.51)
EDSS at onset, median (range)	3 (0-9.5)
Relapsing disease, n (%)	83 (42.13)
Maintenance therapy at final follow-up, n (%)	115 (58.38)
Laboratory data	
CSF OCB, n (%)	10/175 (5.71)
CSF pleiocytosis (>5 cells/mm^3)	61/138 (44.20)
IgG index, n (%)	7/96 (7.29%)
Autoantibodies, n (%)	29/144 (20.13)
Clinical phenotype at last follow-up	
Isolated ON	106 (53.81)
Monophasic-ON	72 (36.55)
Recurrent-ON	34 (17.26)
NMOSD	38 (19.29)
Isolated LETM	24 (12.18)
Monophasic-LETM	20 (10.15)
Recurrent-LETM	4 (2.03)
ADEM	9 (4.57)
MS	3 (1.52)
Isolated Non- LETM	8 (4.06)
Monophasic-Non-LETM	5 (2.54)
Recurrent-Non-LETM	3 (1.52)
Monophasic brainstem syndrome	5 (2.54)
Optico-spinal phenotype	4 (2.03)
Disability at last follow-up, n (%)	
[a]DSS 3.0	19/77 (24.68)
[a]DSS 6.0	8/77 (10.39)
[b]VA 20/100	11/136 (8.09)
Patients who died	1 (0.51)
Additional features from reviewed clinical reports	
Autoimmune disease, n (%)	16/144 (11.11)
Previous infection, n (%)	29/144 (20.14)
Other symptoms at onset, n (%)	
Area postrema symptoms	3/144 (2.08)
Fever	13/144 (9.02)
Seizures	2/144 (1.39)
Neuropathic pain	11/144 (7.64)

[a]For motor disability comparison (DSS = 3.0 and DSS = 6.0), patients who presented with non-ON phenotypes at first ADS were included

[b]For visual disability (AV 20/100), only patients who presented with ON at first ADS were included

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Radiological features

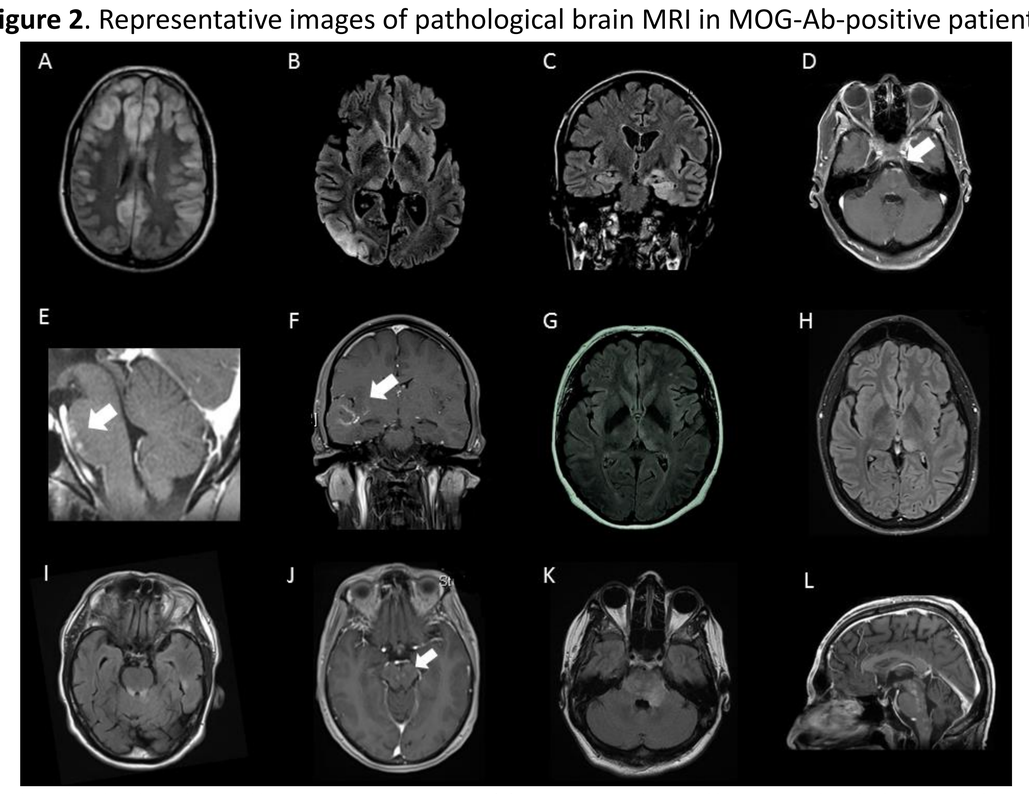
Lesions in thalamus and pons were more frequently seen in the MOG-Ab group (p=0.031 and p=0.007, respectively), while lesions in medulla oblongata and area postrema were more frequently observed in AQP4-group (p=0.004 and p<0.001, respectively) (**table 2**). Other findings associated with MOG-Ab were cortical involvement in 8 (16.3%) and leptomeningeal enhancement in 3 patients (6.1%) (**figure 2**).

Table 2. Radiological features in MOG-Ab-positive patients with an initial abnormal brain MRI

	MOG-Ab group N=49	AQP4-Ab group N=22	p- value
Radiological features, n (%)			
Predominantly cortical grey matter	8 (16.33)	1 (4.55)	0.257
Confined to brainstem and/or basal ganglia	14 (28.57)	8 (36.36)	0.511
Hazy/poor demarcated lesions	10 (20.41)	3 (13.64)	0.741
Tumefactive lesions	5 (10.20)	2 (9.09)	0.884
Nonspecific white matter lesions	7 (14.29)	3 (13.64)	0.942
Gadolinium enhancement	6 (12.24)	5 (22.73)	0.298
Lesion location at onset, n (%)			
Bilateral	22 (44.90)	11 (54.54)	0.563
[a]Leptomeningeal enhancement	3 (6.12)	0 (0)	0.236
Juxtacortical	20 (40.82)	7 (31.82)	0.599
Deep white matter	24 (48.98)	13 (59.09)	0.455
Periventricular	13 (26.53)	6 (27.27)	0.948
U or S shape	5 (10.20)	1 (4.55)	0.658
Dawson finger	4 (8.16)	0 (0)	0.303
Corpus callosum	5 (10.20)	2 (9.09)	0.884
Thalamus	9 (18.37)	0	**0.031**
Brainstem	18 (36.73)	13 (59.09)	0.079
Midbrain	5 (10.2)	3 (13.64)	0.672
Pons	17 (34.69)	1 (4.55)	**0.007**
Medulla oblongata	7 (14.29)	10 (45.45)	**0.004**
Area postrema	1 (2.04)	7 (31.82)	**<0.001**
Adjacent to four ventricle	11 (22.45)	3(13.64)	0.388
Cerebellar peduncles	9 (18.37)	4 (18.18)	0.985
Cerebellum	2 (4.08)	2 (9.09)	0.397

[a]Leptomeningeal enhancement was located in brainstem in two and in the temporal-parietal lobe in one patient.

Figure 2. Representative images of pathological brain MRI in MOG-Ab-positive patients



(A-B) Bilateral and unilateral cortical lesions on FLAIR sequences. (C) Temporomesial cortical lesion mimicking limbic encephalitis on FLAIR sequence. (D-F) Pontine and cortical leptomeningeal gadolinium enhancement. (G-H) Thalamic lesions on FLAIR sequence. (I-K) Brainstem lesions involving the mesencephalic tegmentum and pons. (L) "Salt and pepper" brainstem pattern in CLIPPERS-like imaging

Baseline factors related to outcome

After performing a univariate and multivariate analysis, we found that age (Hazard Ratio [HR], 0.96; 95%Confidence interval [95%], 0.94-0.99; p=0.032) and higher disability at onset (HR, 0.80; 95%CI, 0.66-0.96; p=0.022) were protective baseline factors to reach a first relapse.

A higher EDSS at onset of symptoms was related to time to reach DSS 3.0 (HR, 1.33; 95%CI, 1.04-1.70; p=0.022) and time to reach VA 20/100 (HR, 1.73; 95%CI, 1.24-2.50; p=0.002).

Discussion

As previously reported, MOG-Ab had a predilection for optic nerve and spinal cord in more than 80% of patients,[1,2] but only 19% of patients fulfilled the 2015 criteria for NMOSD. In the future, to avoid diagnostic overlapping between both groups, NMOSD would be better defined by the term AQP4-Ab or MOG-Ab-associated diseases, regardless of the clinical phenotype.

Interestingly, we observed that a not depreciable proportion of patients with abnormal MRI displayed cortical involvement (16%). Some of them fulfilled encephalitis criteria since they presented with encephalopathy, retrograde amnesia and seizures (data not shown).[6] MOG-Ab-encephalitis has been recently characterized in patients with unilateral or bilateral cortical affection, epilepsy and good response to steroids.[7,8]

Finally, we observed that, overall, a higher disability at onset predicted a worse motor and visual outcome, with no other clear baseline prognostic factor.

Conclusion

In this MOG-Ab cohort of adult patients, most of patients presented either with ON or myelitis at onset, and a high proportion of them relapsed at long-term. We identified higher disability at onset as the only predictor of poor outcome.

References

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