PROF. CHAO QUAN (Orcid ID : 0000-0003-1040-3930)

Article type : Original Article

Encephalitis is an important clinical component of MOG-antibody-associated demyelination: a single-center cohort study in Shanghai, China

Liang Wang[1+], MD Jingzi ZhangBao[1+], MD Lei Zhou[1], MD Yue Zhang[1], MD Haiqing Li[2], MD Yuxin Li[2], MD Yongheng Huang[3], MD Min Wang[3], MD Chuanzhen Lu[1], MD Jiahong Lu[1], MD&PhD Chongbo Zhao[1], MD&PhD Chao Quan[1*], MD&PhD

* corresponding author

+ contributed equally

1. *Department of Neurology, Huashan Hospital, Shanghai Medical College, Fudan University, 12 Wulumuqi Zhong Road, Shanghai 200040, China*
2. *Department of Radiology, Huashan Hospital, Shanghai Medical College, Fudan University, 12 Wulumuqi Zhong Road, Shanghai 200040, China*
3. *Department of Ophthalmology, Eye and ENT Hospital, Shanghai Medical College, Fudan University, 83 Fen Yang Road, Shanghai 200031, China*

***Corresponding author: Chao Quan**, Tel 0086-21-52888159, Fax 0086-21-52887150, chao_quan@fudan.edu.cn.

Running title: Encephalitis in MOG-antibody-associated demyelination

Keywords Encephalitis; Myelin oligodendrocyte glycoprotein (MOG); Aquaporin 4 (AQP4); N-methyl-D-aspartate-receptor (NMDAR)

Conflicts of Interests None declared

Abstract

Background Besides a distinct spectrum of demyelinating syndromes, encephalitis was observed in patients with myelin oligodendrocyte glycoprotein antibodies (MOG-ab).

Methods We retrospectively reviewed the clinical records of 690 patients with idiopathic demyelinating diseases of the CNS seen in our center from 06/2015 to 12/2017. All underwent serum aquaporin 4 antibodies (AQP4-ab) and MOG-ab detection by cell-based assays as routine diagnostic approach. Patients with MOG-ab or AQP4-ab that had ever experienced an encephalitis-like illness during the course were sorted out. Whether the diagnoses of possible or definite autoimmune encephalitis (AE) could be reached with regard to these particular episodes of encephalitis were determined. The incidence and clinical features of encephalitis in anti-MOG disease were described in detail and compared with those in anti-AQP4 disease.

Results Among the 690 patients, 87 were MOG-ab-positive while 140 were AQP4-ab-positive. 20.7% (18/87) of the MOG-ab-positive patients had typical presentations of encephalitis. Unique cortical lesions (72.2%, 13/18) were observed; fever (55.6%), intracranial hypertension (41.2%) and CSF pleocytosis (64.7%) were common during MOG-ab-associated encephalitis. Sixteen of the 18 patients fulfilled the criteria of definite AE (specific disease with MOG-ab) during encephalitis, and 5 patients overlapped with anti-N-methyl-D-aspartate-receptor encephalitis (NMDARE). Only 3.6% (5/140) of the AQP4-ab-positive patients had encephalitis, and none overlapped with NMDARE. The Expanded Disability Status Scale scores and the Cerebral Functional System Scores at last follow-up were lower in patients with MOG-ab-associated encephalitis than in those with AQP4-ab-associated encephalitis.

Conclusions Encephalitis should be recognized as important clinical component in anti-MOG diseases.

Introduction

Myelin oligodendrocyte glycoprotein (MOG) is a membrane protein expressed on oligodendrocyte cell surfaces and the outermost surface of myelin sheaths. With the introduction of highly specific cell-based assays (CBA), conformation-sensitive anti-MOG antibodies have been detected in a distinct spectrum of central nervous system (CNS) inflammatory demyelinating diseases (IDDs) with clinical phenotypes partly overlapping acute disseminated encephalomyelitis (ADEM) [1] or aquaporin 4 antibody (AQP4-ab)-negative neuromyelitis optica spectrum disorders (NMOSD) [2]. However, the

pathology of MOG antibody (MOG-ab) diseases is characterized by prominent demyelination with astrocytes being preserved, fundamentally different from the astrocytopathy typically seen in AQP4-ab-positive NMOSD [3]. Notably, encephalitis and epilepsy are observed in patients with MOG-ab, which are seldom seen in patients with AQP4-ab [4-6].

In fact, MOG-ab was integrated into the clinical approach to the diagnosis of autoimmune encephalitis (AE) as one of the specific auto-antibodies in a recent position paper [7]. An epidemiologic survey conducted in Olmsted County, Minnesota, USA showed that the prevalence of definite AE with MOG-ab was 1.9/100,000, higher than that of leucine-rich glioma-inactivated-protein-1 (LGI1) (0.7/100,000) and N-methyl-D-aspartate-receptor (NMDAR) (0.6/100,000) antibody-associated AE [8]. In our clinical practice, we are encountering more patients with anti-MOG diseases that have experienced encephalitis, some overlap with anti-NMDAR encephalitis (NMDARE).

In the current study, we aim to further characterize the incidence and clinical features of encephalitis in anti-MOG diseases, and to compare the features and outcomes of MOG-ab-associated encephalitis with those of AQP4-ab-associated encephalitis.

Patients and methods

Patients

From 06/2015 to 12/2017, 690 consecutive patients (all of Han Chinese ethnicity) with suspected CNS-IDDs were seen in the NMO-MS clinic at Huashan Hospital, Shanghai Medical College, Fudan University (Shanghai, China). All of them underwent serum MOG-ab and AQP4-ab detection using CBA as part of the routine diagnostic approach

(Figure 1).

Upon reviewing the clinical, magnetic resonance imaging (MRI) and laboratorial records of these patients, patients with MOG-ab or AQP4-ab that had ever experienced an encephalitis-like illness during the course were sorted out. Whether the diagnoses of possible or definite AE could be reached with regard to these particular episodes of encephalitis were determined. The incidence and clinical features of encephalitis in anti-MOG disease were described in detail and compared with those in anti-AQP4 disease. The Expanded Disability Status Scale (EDSS) score, the Cerebral Functional System Score (CFSS), and the modified Rankin scale (mRS) score at last follow-up were utilized to estimate the disease outcome of the patients with encephalitis.

We obtained written informed consent from each participant. The study was approved by the Medical Ethics Committee of Huashan Hospital, Shanghai Medical College, Fudan University.

Methods

Details of the methods are shown in Appendix S1.

Results

Demographic data

Among the 690 patients with CNS-IDDs, 87 were MOG-ab-positive, while 140 were AQP4-ab-positive (Figure 1). The demographic data of the anti-MOG and anti-AQP4 cohort were listed in Table S1.

Eighteen of the 87 (20.7%) MOG-IgG-positive patients had presented with acute or subacute onset of psychiatric symptoms, decreased or altered level of consciousness, lethargy, personality change, or working memory deficits during the course based on clinical records. Among them, 8 were female while 10 were male. The median disease onset age was 22 years (mean 21.3 ± 8.4 years, range: 9-38 years). Disease started in childhood (<14 years) in 5 patients. Combined with the CSF findings, electroencephalograph (EEG) alterations and MRI features, all of the 18 patients met a diagnosis of encephalitis (Table S2).

Five of the 140 (3.6%) AQP4-ab-positive patients had experienced an encephalitis episode. All of them were females, with a median onset age of 38 years (range: 16-52 years).

Disease course and onset presentation

The median disease duration of the 18 MOG-ab-positive patients with encephalitis was 24 months (mean: 28.4 months; range: 5-114 months). Until the last follow-up, 72.2% (13/18) had a relapsing remitting course, whereas 27.8% (5/18) had a monophasic course (Table S2).

Twelve of the 18 (66.7%) patients presented with encephalitis during their first episode. The remaining 6 (33.3%, 6/18) patients initially presented with unilateral or bilateral optic neuritis (ON) at onset, and then developed encephalitis during subsequent episodes. Two patients (patient 7 and patient 18) experienced two episodes of encephalitis during the course; the remaining 16 patients (88.9%, 16/18) had only one episode of encephalitis till the last follow-up (Table S2).

Clinical manifestations throughout the disease duration

During the particular episodes of encephalitis, all of the 18 MOG-ab-positive patients

presented with typical symptoms, such as headache, decreased level of consciousness, lethargy, disorientation, irritability, euphoria, abnormal behavior or speech, hallucination, psychosis, change of personality, social withdrawal, memory decline or cognitive decline. Ten (55.6%, 10/18) patients had fever, 9 (50.0%, 9/18) patients had seizure, and 1 patient (patient 1) had trunk dyskinesias and hypoventilation during encephalitis (Table S2).

Furthermore, 13 of the 18 (72.2%) MOG-ab-positive patients had ON attacks, 2 patients (11.1%) had myelitis, and 6 patients (33.3%) had acute brainstem syndromes throughout the disease duration (Table S2).

Neuro-imaging

The brain MRI images of the 18 MOG-ab-positive patients obtained during the episodes of encephalitis were reviewed. Cortical lesions were the most frequently observed and were best depicted by T2-fluid-attenuated inversion recovery (FLAIR) images. Altogether, 13 of the 18 (72.2%) patients had cortical involvement. Among them, 6 patients (33.3%, 6/18) had frontal and/or parietal cortical lesions close to the cerebral falx (Figures 2A-2H); striking serpentine or twisting enhancement along the cortical lesion was observed in 3 of the 6 patients (Figures 2B-D,2F, and 2H). Five patients (27.8%, 5/18) had diffuse cortical lesions located in the unilateral hemisphere (Figures 2I-2L), with or without corresponding leptomeningeal enhancement (Figure 2J). In the remaining 2 patients (patient 6 and patient 9), cortical lesions were invisible on MRI, but were confirmed by positron emission computed tomography (PET-CT) (Figure 2M, 2N). Moreover, cortical lesions were seen to develop alone (7/13), or were accompanied by lesions with demyelination features in deeper structures (6/13).

During encephalitis, brain lesions were also observed in the temporal lobe or limbic system (38.9%, 7/18) (Figures 2O, 2P); in the subcortical white matter of the parietal lobe (33.3%, 6/18), frontal lobe (16.7%, 3/18), or occipital lobe (5.6%, 1/18); in the deep white matter adjacent to the lateral ventricle (5.6%, 1/18); or in the corpus callosum (11.1%, 2/18).

The involvement of deep midline structure, such as brainstem and brachium pontis (44.4%, 8/18), thalamus (27.8%, 5/18), or peri-third ventricle area (16.7%, 3/18) were also observed during encephalitis (Table S3).

Laboratory findings

The serum MOG-ab titers ranged from 1:10 to 1:320 in the 18 patients with encephalitis. For patient 3 and patient 5, MOG-ab was tested during a subsequent ON attack following encephalitis; the remaining patients were tested for MOG-ab during the acute phase of encephalitis (Table S4).

Lumbar punctures were performed at the earliest available time in 17 of the 18 patients during encephalitis. Seven patients (41.2%, 7/17) had an increased intracranial pressure over 200 mmH_2O, 11 patients (64.7%, 11/17) had CSF pleocytosis and 3 patients (25%, 3/12) exhibited a positive CSF oligo-clonal band (OB). Anti-nuclear antibody (ANA) was positive in 5 patients (27.8%, 5/18) and Ro-52 was mildly positive in 1 patient (Table S4).

The CSF and serum anti-NMDAR (GluN1 subunit), LGI1, anti-contactin-associated-protein-2 (CASPR2), anti-alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) and anti-γ-aminobutyric acid-B receptor (GABA(B)R) IgGs were tested in 15 of the 18 patients. Among them, 5 were positive for CSF anti-NMDAR antibody during

encephalitis. One patient (patient 5) exhibited negative result during encephalitis, but became anti-NMDAR positive during a subsequent ON. No patients were positive for the LGI1, CASPR2, AMPAR, or GABA(B)R antibodies (Table S4).

Treatment response

All of the 18 MOG-ab-positive patients received high-dose methyprednisolone therapy, with or without intravenous immunoglobulin G, during the acute phase of encephalitis. Four patients were empirically treated with ganciclovir on the basis of immunotherapy. Before treatment, the mRS and CFSS values were 3.75±0.64 (range: 3-5) and 3.70±0.80 (range: 2-5), respectively, and by the last follow-up, these values dropped significantly to 0.89±0.83 (range: 0-3; $p < 0.001$) and 1.17±1.10 (range: 0-3; $p < 0.001$). Faint residual white matter lesion was observed in patient 2 and temporal lobe atrophy was observed in patient 16 and 18 in follow-up MRI studies. In the remaining patients, the lesions acquired during encephalitis were completely resolved after treatment.

Diagnostic determination

The diagnoses with respect to these particular episodes of encephalitis were determined according to the diagnostic criteria of AE [7]. Combined with the clinical context as well as MRI and CSF changes, a diagnosis of possible AE was reached in all the 18 MOG-ab-positive patients (Table S1).

To obtain a more specific diagnosis, we further included the MOG-ab status on the basis of a preliminary possible AE diagnosis following the proposed clinical approach [7]. It turned out that 16 patients fulfilled the criteria for definite AE (specific disease with MOG-ab), whereas

2 patients (patient 3 and patient 5) did not because their MOG-abs were not tested during encephalitis (Figure 1, Table S1).

Six of the 18 MOG-ab-positive patients were positive for CSF anti-NMDAR antibody. Based on the proposed diagnostic criteria, 5 of the 6 patients were diagnosed as having overlapping NMDARE [7]. The remaining patient (patient 5) was not diagnosed as NMDARE because his anti-NMDAR antibody was negative at the time of encephalitis (Figure 1, Tables S1 and S4).

Accordingly, the 5 AQP4-ab-positive patients with encephalitis also conformed to the criteria of definite AE (specific disease with AQP4-ab) [7]. However, none of them overlapped with NMDARE, as anti-NMDAR antibodies were absent in their CSF or serum (Figure 1, Table S1).

The comparison between encephalitis in patients with MOG-ab and AQP4-ab

Episodes of encephalitis were much more common in patients with MOG-ab than in patients with AQP4-ab (20.7% vs. 3.6%; $p < 0.001$); and the proportion of overlapping NMDARE was higher in MOG-ab-positive cohort than in AQP4-ab-posotive cohort (5.7% vs. 0%; $p = 0.008$) (Figure 1, Table S1).

MOG-ab-positive patients tended to have more frequent cortex involvement during encephalitis ($p = 0.052$), whereas deep cerebral white matter and corpus callosum lesions were more common in patients with AQP4-ab during encephalitis ($p = 0.017$). The outcomes of MOG-ab-positive patients with encephalitis seemed to be better, with significantly lower EDSS ($p = 0.022$) and CFSS ($p = 0.005$) scores at last follow-up. 94.4% of the MOG-ab-positive patients with encephalitis and 60% of the AQP4-ab-positive patients with

encephalitis achieved a favorable outcome (mRS score = 0-2 at last follow-up), although the comparison did not reach a statistical significance (p = 0.102) (Table 1).

Discussion

The whole clinical spectrum of anti-MOG diseases still needs to be clearly defined. Recently, unique cortical encephalitis was reported in 5 Japanese cases with MOG-ab [4, 5]. In a cohort study in the United Kingdom, seizure and encephalitis were observed in 5 out of 34 patients with MOG-ab [6]. In our cohort, nearly one fifth (20.7%) of the MOG-ab-positive patients had encephalitis, all conformed to the diagnostic criteria of possible AE, and 18.4% fulfilled the diagnostic criteria of definite AE (specific disease with MOG-ab). These findings strongly suggest that encephalitis is an important clinical component of MOG-ab-associated demyelination, making the clinical spectrum of anti-MOG diseases wider than imagined.

In more complicated situations, MOG-IgG disease can co-exist with NMDARE [10, 11]. Herein, 5 of the 18 patients with MOG-ab-associated encephalitis had overlapping NMDARE. In these particular cases, it is extremely difficult, even impossible, to tell whether the encephalitis or seizure is attributed to MOG or NMDAR antibodies. However, this problem does not affect the direction of treatment. Considering that oligodendrocytes do contain NMDAR [12], it is reasonable to speculate that the immune attack targeting myelin may simultaneously involve NMDAR, and vice versa.

The MRI imaging herein during MOG-ab-associated encephalitis is impressive and unique, with cortical lesions observed the most frequently. Frontal and/or parietal cortical lesions that were close to the cerebral falx, with serpentine enhancement along the cortical lesion, were

striking and quite similar to a previous report [4]. Another type of cortical lesion located in the unilateral hemisphere and can be accompanied by corresponding leptomeningeal enhancement. Unilateral cortical lesions, when developed in the temporal or occipital lobes, can mimic those seen in Creutzfeldt-Jakob disease or mitochondrial encephalomyopathy. Except for cortical involvement, lesions in the temporal lobe or limbic system also have been observed and are similar to those seen in limbic or HSV encephalitis.

Notably, the clinical diagnosis of AE can overlap with ADEM, as they share clinical features of encephalopathy. In the MOG-ab-positive encephalitis cohort, patients 2, 14, and 17 met the criteria of ADEM by having large white matter lesions. However, patient 2 had cortical involvement, which is atypical for ADEM (Figure2E, asterisk). Patient 17 had only one larger, swelling white matter lesion, but a single unilateral lesion is also atypical of ADEM, which usually exhibits multifocal lesions. If we strictly follow the diagnostic algorithm [7], these 3 patients would be considered to have AE rather than ADEM because of having specific auto-antibodies.

The role of infectious agents in triggering MOG-ab production is still a matter of debate. During MOG-ab-associated encephalitis, fever (55.6%), elevated intracranial pressure (ICP) (41.2%), and CSF pleocytosis (64.7%) are common. However, none of the patients had a confirmed infectious pathogen. Given the distinctive lesions found on the MRI, which mimicked those in previously reported MOG-ab-positive encephalitis cases; the typical demyelination episode, such as ON or myelitis following or preceding the encephalitis; and the definite presence of MOG-IgG in the serum, as well as the immunotherapy

responsiveness, we consider the encephalitis to be mainly of autoimmune origin.

As was also seen in previous studies [11], the frequency of encephalitis (3.6%) and coexistence of anti-NMDAR antibody (0%) was much lower in AQP4-ab-positive cohort than in MOG-ab-positive cohort. Deep cerebral white matter and corpus callosum lesions were the most commonly seen during encephalitis associated with AQP4-ab, different from the anti-MOG encephalitis in which cortex was the most frequently involved. The EDSS and CFSS of anti-MOG encephalitis at last follow-up were lower, indicating a better prognosis compared to AQP4-ab-associated encephalitis.

In summary, our study showed that encephalitis should be recognized as an important clinical phenotype of anti-MOG diseases. Further verification of the results in prospective, larger-scale, multicenter studies is warranted.

Acknowledgements

This research was supported by the National Natural Science Foundation of China (Grant No. 81771296, 81801196) and the National Key Research and Development Program of China (2016YFC0901504).

References

*Cited in Appendix S1

1. Baumann M, Sahin K, Lechner C, et al. Clinical and neuroradiological differences of paediatric acute disseminating encephalomyelitis with and without antibodies to the myelin oligodendrocyte glycoprotein. *Journal of Neurology, Neurosurgery, and Psychiatry* 2015;86(3):265-272.

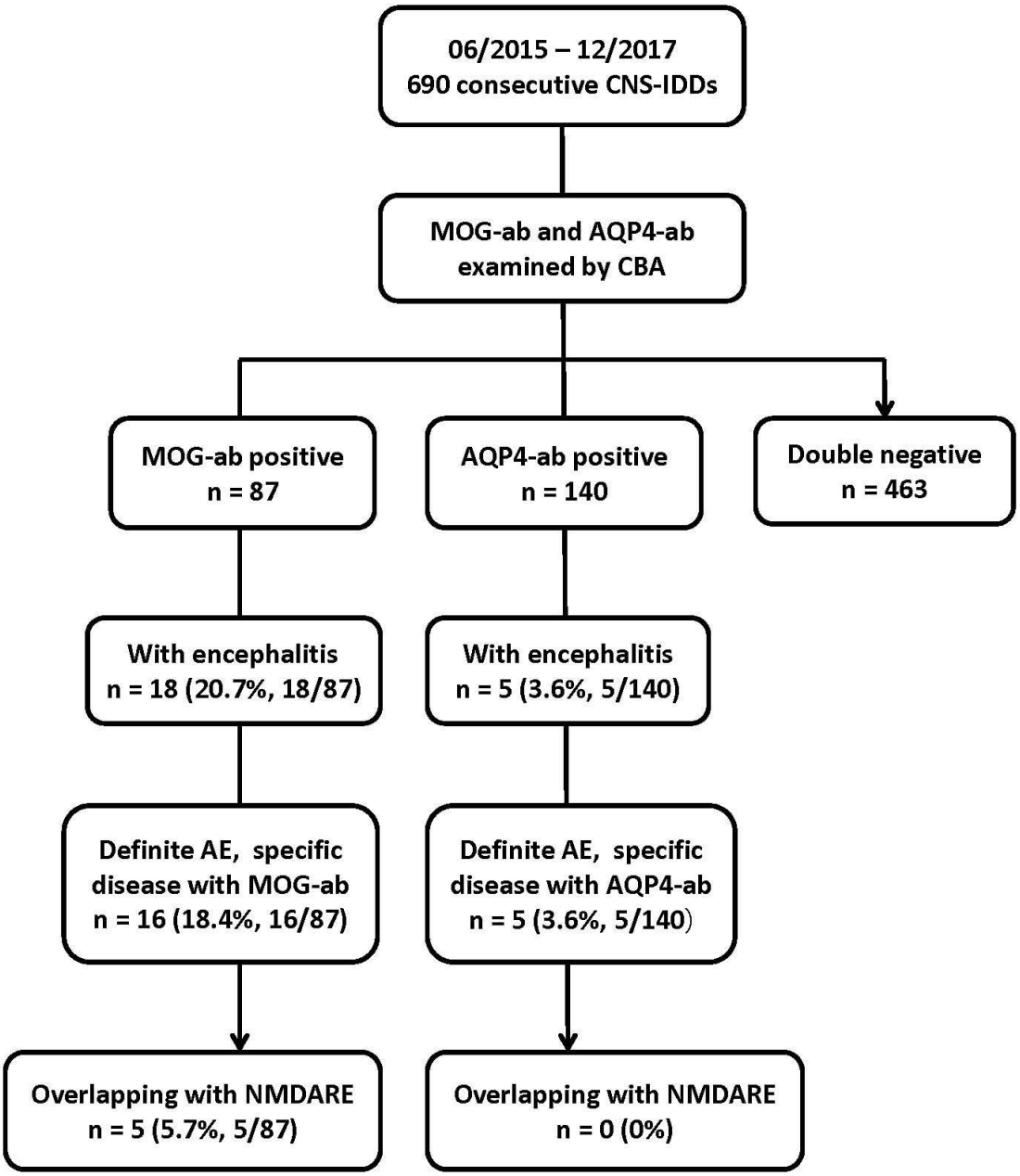
2. Kitley J, Waters P, Woodhall M. Neuromyelitis optica spectrum disorders with aquaporin-4 and myelin-oligodendrocyte glycoprotein antibodies: a comparative study. *JAMA Neurology* 2014;71(3):276-283.
3. Zhou L, Huang Y, Li H, et al. MOG-antibody associated demyelinating disease of the CNS: a clinical and pathological study in Chinese Han patients. *Journal of Neuroimmunology* 2017; 305:19-28.
4. Fujimori J, Takai Y, Nakashima I, et al. Bilateral frontal cortex encephalitis and paraparesis in a patient with anti-MOG antibodies. *Journal of Neurology, Neurosurgery, and Psychiatry* 2017;88:534-536.
5. Ogawa R, Nakashima I, Takahashi T, et al. MOG-antibody-positive, benign, unilateral, cerebral cortical encephalitis with epilepsy. *Neurology Neuroimmunology & Neuroinflammation* 2017;4:e322.
6. Zhou Hamid SHM, Whittam D, Saviour M, et al. Seizures and Encephalitis in Myelin Oligodendrocyte Glycoprotein IgG Disease vs Aquaporin 4 IgG Disease. *JAMA Neurology 2018*;75(1):65-71.
7. Graus F, Titulaer MJ, Balu R, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurology* 2016;15:391-404.
8. Dubey D, Pittock SJ, Kelly CR, et al. Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. *Annals of Neurology* 2018;83(1): 166-177.
9. *Simon JH, Li D, Traboulsee A, et al. Standardized MR imaging protocol for multiple sclerosis: Consortium of MS Centers consensus guidelines. *American Journal of Neuroradiology* 2006;27(2):455-461.

10. Titulaer MJ, Höftberger R, Iizuka T, et al. Overlapping demyelinating syndromes and anti–N-methyl-D-aspartate receptor encephalitis. *Annals of Neurology* 2014; 75(3):411-428.
11. Fan S, Xu Y, Ren H, et al. Comparison of myelin oligodendrocyte glycoprotein (MOG)-antibody disease and AQP4-IgG-positive neuromyelitis optica spectrum disorder (NMOSD) when they co-exist with anti-NMDA (N-methyl-D-aspartate) receptor encephalitis. *Multiple Sclerosis and Related Disorders* 2018;20:144-152.
12. Lipton SA. NMDA receptors, glial cells, and clinical medicine. *Neuron* 2006; 50:9-11.

Table 1. The comparison of the clinical features between the 18 MOG-ab-positive and the 5 AQP4-ab-positve patients with encephalitis.

	MOG-ab-associated encephalitis n=18	AQP4-ab-associated encephalitis n=5	*p*
Age at onset, median (range), y	22 (9-38)	38 (16-52)	0.028*
Female, % (n/total)	44.4 (8/18)	100.0 (5/5)	0.038*
Disease duration, median (range), mo	24 (5-114)	26 (6-135)	0.737
Seizure, % (n/total)	50.0 (9/18)	20.0 (1/5)	0.212
Cortical lesion, % (n/total)	72.2 (13/18)	20.0 (1/5)	0.052
Temporal lobe or limbic system lesion, % (n/total)	38.9 (7/18)	20.0 (1/5)	0.325
Deep cerebral white matter and corpus callosum lesion, % (n/total)	16.7 (3/18)	80.0 (4/5)	0.017*
Deep midline structure lesion [a], % (n/total)	61.1 (11/18)	80.0 (4/5)	0.325
CSF NMDAR-ab positive, % (n/total)	40.0 (6/15)	0 (0/5)	0.129
CSF pleocytosis, % (n/total)	64.7 (11/17)	40.0 (2/5)	0.249
Intracranial hypertension, % (n/total)	41.2 (7/17)	0 (0/5)	0.114
Anti-ENA antibodies, % (n/total)	5.6 (1/18)	80.0 (4/5)	0.003*
EDSS at last follow up, mean±SD	1.6±1.1	3.1±1.6	0.022*
CFSS at last follow up, mean±SD	1.2±1.1	3.2±1.6	0.005*
Favorable outcome, mRS 0-2, % (n/total)	94.4 (17/18)	60.0 (3/5)	0.102

MOG-ab, myelin oligodendrocyte glycoprotein antibody; AQP4-ab, aquaporin 4 antibody; y, year; mo, month; CSF, cerebrospinal fluid; NMDAR-ab, anti-N-methyl-D-aspartate-receptor antibody; ENA, extractable nuclear antigens; EDSS, Expanded Disability Status Scale; CFSS, Cerebral Functional System Score ; mRS, modified Rankin scale score; *, with statistical significance; [a], refers to lesions in brainstem/brachium pontis, thalamus or peri-third ventricle area.



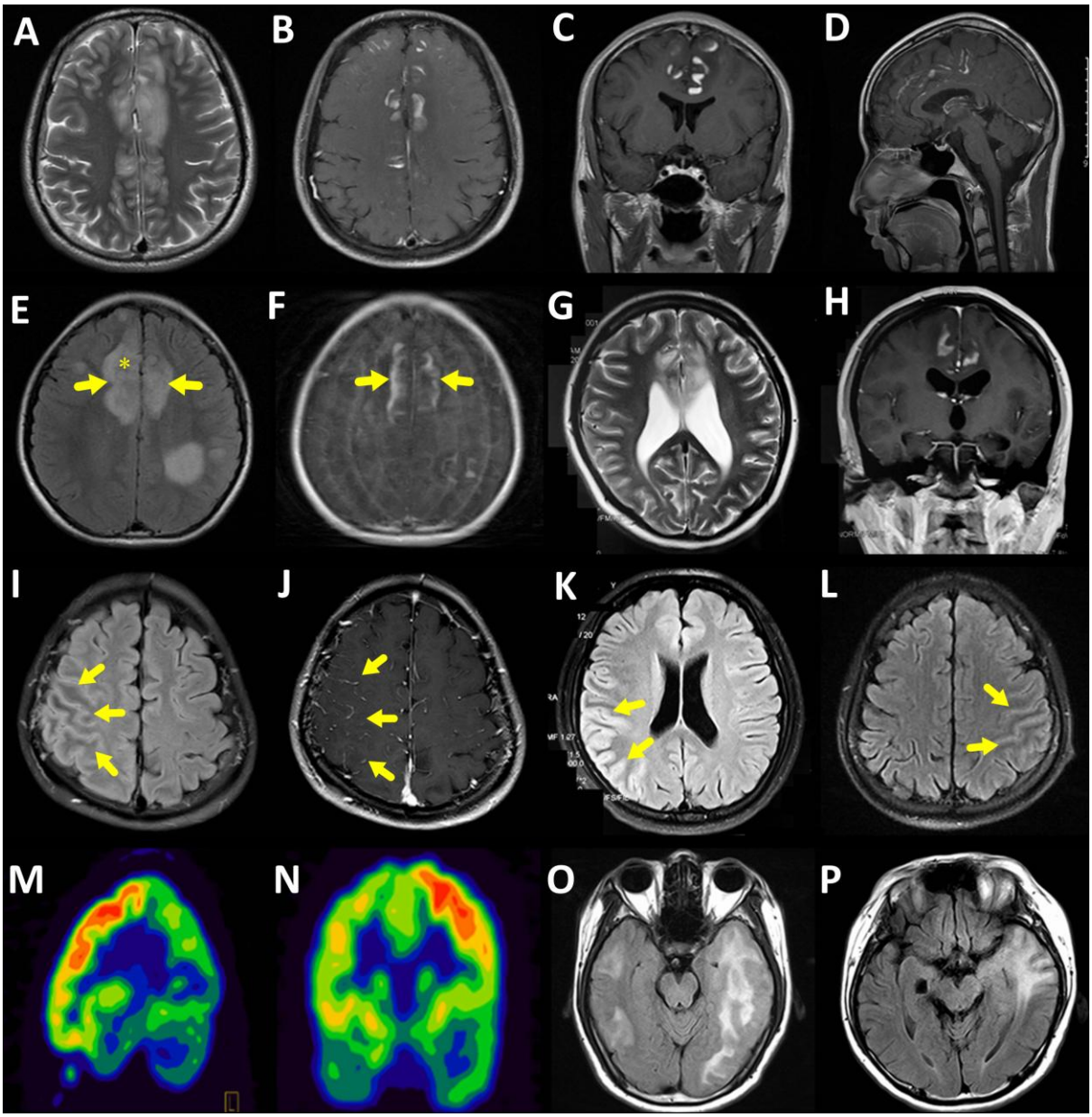


Figure 1. The proportions of encephalitis in the MOG and AQP4 antibody-positive groups.

MOG, myelin oligodendrocyte glycoprotein; AQP4, aquaporin 4; CNS, central nervous system; IDDs, idiopathic demyelinating diseases; CBA, cell-based assay; AE, autoimmune encephalitis; NMDARE, anti-N-methyl-D-aspartate-receptor encephalitis

Figure 2. Neuro-imaging during MOG-ab-associated encephalitis

(A) Axial T2 -weighed imaging shows bilateral cortical and juxtacortical lesions in the frontal and parietal lobe aside the cerebral flax in patient 1; (B-D) Axial, coronal and sagittal T1-weighed imagings show serpentine or twisting Gd enhancement along the cortical lesions in patient 1; (E, F) In patient 2, bilateral cortical and juxtacortical lesions in the frontal lobe aside the cerebral flax are seen on axial T2-FLAIR imaging (asterisk, atypical for ADEM), twisting Gd enhancement is observed; (G, H) Bilateral frontal cortical and juxtacortical lesions aside the cerebral flax with twisting enhancement observed in patient 12; (I, J) Diffuse swelling of the right temporal, parietal and occipital cortex on axial T2-FLAIR imaging with corresponding leptomeningeal enhancement observed in patient 5; (K) Right temporal cortex lesion in patient 3; (L) Swelling of the left tempo-parietal cortex in patient 13; (M, N) Increased metabolism in the left frontal cortex by FDG-PET in patient 6; (O, P) Temporal lobe lesions in patient 14 and 16.

MRI, magnetic resonance imaging; MOG-ab, myelin oligodendrocyte glycoprotein antibody; Gd, gadolinium; FLAIR, fluid-attenuated inversion recovery; ADEM, acute disseminated encephalomyelitis; FDG-PET, [18F] fluorodeoxyglucose positron emission tomography.