Check for updates

Original Article

Clinical EEG and Neuroscience
1–7
© EEG and Clinical Neuroscience Society (ECNS) 2018
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/1550059418800867
journals.sagepub.com/home/eeg
SAGE

Analysis of Relation Between Electroclinical Features and Cerebrospinal Fluid Antibody Titers in Patients With anti-NMDAR Encephalitis

Ailiang Miao[1,2]*, Mingyang Du[1]*, Lingling Wang[1,2], Jianqing Ge[1,2], Hengdong Lu[3], Haiyan Xu[4], Hongxing Liu[1], Chuanyong Yu[1], Caiyun Wu[1], Yuan Gao[1], Jintao Sun[1], Qi Shi[1], and Xiaoshan Wang[1,2]

Abstract

Purpose. This study aimed to determine the relation between electroclinical features and cerebrospinal fluid (CSF) antibody titers in patients with anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) encephalitis. *Method*. Clinical symptoms and electroencephalography (EEG) at different stages were analyzed in 51 hospitalized patients with anti-NMDAR encephalitis. *Results*. Behavioral changes were the initial symptoms in 90.9% (20/22) of female patients with high (1:10 or 1:32) CSF antibody titers. A greater number of clinical symptoms were observed in the patients with high CSF antibody titers than in those with low (1:1 or 1:3.2) CSF antibody titers (mean 3.11 $\pm$ 1.06 vs 1.62 $\pm$ 0.65, $P = .000$). The number of clinical symptoms was greater in the female patients than in the male patients (mean 3.52 $\pm$ 0.98 vs 2.69 $\pm$ 1.09, $P = .000$). At the peak stage, worse background activity (BA) in EEG recordings was observed in patients with high CSF antibody titers than in those with low CSF antibody titers (Mann-Whitney *U* test, $P = .001$). The peak-stage BA in EEG was worse in female patients than in male patients (Mann-Whitney *U* test, $P = .000$). Modified Rankin scale scores were higher in patients with high CSF antibody titers than in those with low CSF antibody titers (mean 2.62 $\pm$ 1.42 vs 0.75 $\pm$ 0.97, $P = .000$). Brush patterns and constant chewing were observed primarily in female patients with high CSF antibody titers. Epileptic discharges were located predominately in the frontal regions and were noted to vary. *Conclusion*. The electroclinical features of patients with anti-NMDAR encephalitis were associated with gender and CSF antibody titers.

Keywords

anti-*N*-methyl-D-aspartate receptor encephalitis, clinical symptoms, electroencephalogram, brush pattern, cerebrospinal fluid antibody titers

Received February 6, 2018; revised July 19, 2018; accepted August 11, 2018.

Introduction

Anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is an autoimmune disease associated with serum antibodies against functional NMDARs.[1,2] This syndrome usually develops with a sequential presentation of symptoms, including headache and fever, followed by behavioral changes and psychosis. Seizures can occur at any stage but most commonly manifest early.[3] However, current data are unclear regarding the associations between cerebrospinal fluid (CSF) antibody titers and clinical symptoms and outcome.

Electroencephalography (EEG) may be useful for diagnosing anti-NMDAR encephalitis. In addition to the extreme delta brush (EDB),[4] the EEG patterns of beta/delta power ratio and rhythmic alpha sinusoidal waves have also been observed in patients with anti-NMDAR encephalitis.[5,6] To date, no study has established whether the EEGs of female and male patients differ. Uncertainty also exists in the matter of whether patients with high CSF antibody titers have worse EEG findings than patients with low CSF antibody titers.

[1]Department of Neurology, Nanjing Brain Hospital, Nanjing Medical University, Nanjing, Jiangsu, China
[2]Department of Video-Electroencephalogram, Nanjing Brain Hospital, Nanjing Medical University, Nanjing, Jiangsu, China
[3]Department of Electroencephalogram, Nanjing Brain Hospital, Nanjing Medical University, Nanjing, Jiangsu, China
[4]Medical Records Room, Nanjing Brain Hospital, Nanjing Medical University, Nanjing, Jiangsu, China

*These authors contributed equally to this manuscript.

Corresponding Author:
Xiaoshan Wang, Department of Neurology, Nanjing Brain Hospital, Nanjing Medical University, Guang Zhou Road 264, Nanjing, Jiangsu 210029, China.
Email: xianshanwang1971@163.com
Full-color figures are available online at journals.sagepub.com/home/eeg

Our study aimed to determine the clinical and electrographic features of male and female patients with CSF antibody titers ranging from 1:1 to 1:32.

Patients and Methods

Patients

A total of 51 patients from the Department of Neurology of Nanjing Brain Hospital were included. The inclusion criteria were as follows: (1) patients who fulfilled the anti-NMDAR encephalitis diagnostic criteria with rapid development (disease course <3 months) of one or more symptoms, including mental behavioral disorders, cognitive impairment, language impairment, consciousness disturbance, epilepsy, involuntary movement, autonomic nervous system dysfunction, or central hypoventilation and (2) patients with positive anti-NMDAR IgG in CSF with or without combined positive anti-NMDAR IgG in serum. Patients were excluded if diagnosed with other diseases, such as viral encephalitis, brain tumor, metabolic diseases, and drug poisoning.[7]

Patient Data

The following patient data were collected: age; gender; presence or absence of malignancy (teratomas and others); neurological symptoms such as seizures, psychiatric symptoms, and autonomic symptoms; high (1:10 or 1:32) or low (1:1 or 1:3.2) CSF anti-NMDAR titers; EEG or video-EEG (VEEG) data from 48 patients (no EEGs from 3 patients); magnetic resonance imaging (MRI) from 51 patients; arterial spin labeling (ASL) from 9 patients; lumbar puncture; thyroid function, prolactin (PRL), and aquaporin 4 (AQP4) test results from 1 patient; antibodies against intracellular antigens (including Hu, Ri, GAD, amphiphysin, Tr, Yo, CV2, ANNA-3, PCA-2, and Ma2) from 8 patients; and modified Rankin scale (mRS)[8] scores after 8–34 months of immunosuppressive treatment.

EEG Data

Ninety-two EEG or VEEG recordings (61 from 30 female patients, 31 from 18 male patients) were obtained from 48 patients. The EEG recordings of all patients were reviewed, and the following variables related to EEG characteristics were collected: focal slowing, epileptic discharges (EDs); and the presence or absence of brush patterns and background activity (BA), including mild diffuse polymorphic slowing (mild DPS), moderate diffuse polymorphic slowing (moderate DPS), and severe diffuse polymorphic slowing (SDPS). The initial stage was within 14 days of symptom onset, the peak stage was 14 to 60 days after symptom emergence, the improvement stage was 60 to 180 days after disease onset, and the recovery stage was 180 days after disease onset.[9,10] The EEG recordings were analyzed according to the clinical stage.

Statistics

Data input and statistical analyses were performed using the Statistical Package for Social Sciences (IBM Corporation, Armonk, NY, USA). The Mann-Whitney U test was adopted to compare EEG categorical variables at the peak stage between female and male patients and between patients with low and high CSF antibody titers. The independent-samples t test was used to compare symptoms between female and male patients, and between patients with low and high CSF antibody titers, as well as to compare outcomes between patients with low and high CSF antibody titers. The chi-squared test was used to compare imaging results between patients with low and high CSF antibody titers. $P < .05$ indicated statistical significance.

Results

Patient Characteristics

We retrospectively identified 51 patients with anti-NMDAR properties (30 females; 21 males). The ages of male patients were older than those of female patients (38.4 ± 16.7 vs 25.8 ± 11, $P = .005$). One patient with anti-NMDAR and lesions in the bilateral parietal lobe was diagnosed with astrocyte glioma through pathology. Four patients presented ovarian cysts, and 1 patient manifested pituitary microadenoma.

Antibody Titers

A total of 59 CSF antibody titers were observed for 49 patients and 64 serum antibody titers were examined in 51 patients (Table 2). The serum antibody titers were higher than the CSF antibody titers in 49 patients. Because of failed lumbar punctures, the CSF antibody titers of 2 patients (1 female and 1 male) were not collected. However, the serum antibody titers for these 2 patients were positive. The female patient presented behavioral changes, seizures, and constant oral involuntary movements. The male patient displayed behavioral changes, focal seizures, memory deficits, consciousness disturbance and EDB. A total of 45 (97.8%) CSF antibody titers from 46 patients with successfully obtained EEG recordings were detected at the initial stage or peak stage. High CSF antibody titers were observed in 75.9% (22/29) of female patients and 70% (14/20) of male patients, whereas low CSF antibody titers were noted in 24.1% of female patients and 30% of male patients. Antibodies against intracellular antigens were negative in 8 patients. In addition to temporal lesions, subcortical structures were also involved in 1 patient with anti-NMDAR. Therefore, AQP4 was also examined and found to be positive.

Clinical Symptoms and CSF Antibody Titers

Patients with high CSF antibody titers experienced more clinical symptoms than those with low CSF antibody titers (mean 3.11 ± 1.06 vs 1.62 ± 0.65, $P = .000$). Similarly, more clinical symptoms were observed in female patients than in male patients (mean 3.52 ± 0.98 vs 2.69 ± 1.09, $P = .000$). Behavioral changes were observed in 89.7% (26/29) of female patients and 50% (11/20) of male patients. Meanwhile,

Table 1. Summary of Clinical Symptoms in Patients With Different Cerebrospinal Fluid Antibody Titers.[a]

	Female (29)		Male (20)	
Clinical Symptoms	1:1 or 1:3.2 (7)	1:10 or 1:32 (22)	1:1 or 1:3.2 (6)	1:10 or 1:32 (14)
Behavioral changes	4 (3 onset)	22 (20 onset)	2 (1 onset)	9 (6 onset)
Seizures	5 (3 onset)	14 (2 onset)	4 (4 onset)	8 (7 onset)
No. of focal seizures	4 focal seizures	7 focal seizures	3 focal seizures	5 focal seizures
Consciousness disturbance	0	13	0	8
Cognitive impairment	2	16	0	6 (1)
Language impairment	1	7	1	2
Focal limb weakness	1 (1 onset)	0	1 (1 onset)	0
Involuntary oral movement	0	6	0	0
Total number of clinical symptoms	13	78	8	33

[a]Onset denotes number of patients with the clinical symptoms manifesting onset symptoms.

Table 2. Summary of Antibody Titers and EEG Recordings in Patients.

	Clinical Stage			
Antibody Titers[a]	<13 Days (Initial Stage)	14-60 Days (Peak Stage)	60-180 Days (Improvement Stage)	>180 Days (Recovery Stage)
CSF antibody titer	14 (14 patients)	31 (31 patients)	7 (6 patients)	7 (5 patients)
Serum antibody titer	14 (14 patients)	34 (34 patients)	7 (6 patients)	9 (5 patients)
Low CSF antibody titer	1 normal	1 normal	3 instances of mild DPS (3 patients) 1 OED	1 normal
	3 instances of mild DPS (3 patients)	9 instances of mild DPS (7 patients)		2 instances of mild DPS (2 patients)
	2 FEDs, 1 TED, 1 PED (2 patients)	1.instance of moderate DPS		1 FED
		3 FED (3 patients)		
		4 focal waves (4 patients)		
High CSF antibody titer	4 normal (4 patients)	1 normal (1 patients)	1 normal (1 patient)	2 normal (2 patients)
	3 instances of mild DPS (3 patients)	7 instances of mild DPS (7 patients)	2 instances of mild DPS (2 patients)	3 instances of mild DPS (3 patients)
	1 instance of moderate DPS	14 instances of moderate DPS (12 patients)	5 instances of moderate DPS (3 patients)	4 instances of moderate DPS (2 patients)
	1 FED	12 instances of SDPS (9 patients)	3 instances of SDPS (3 patients)	4 instances of SDPS (3 patients)
		5 brushes (5 patients)	1 brush	2 brushes (1 patient)
		1 FED (1 patient)	2 focal waves (2 patients)	3 FEDs, 1 TED (2 patients)
		3 focal waves (3 patients)		1 focal wave (1 patient)

Abbreviations: CSF, cerebrospinal fluid; Mild DPS, mild diffuse polymorphic slowing; moderate DPS, moderate diffuse polymorphic slowing; SDPS, severe diffuse polymorphic slowing; FED, frontal epileptic discharge; TED, temporal epileptic discharge; OED, occipital epileptic discharge; PED, parietal epileptic discharge.
[a]Low CSF antibody titer: 1:1 or 1:3.2; high CSF antibody titer: 1:10 or 1:32.

behavioral changes comprised the initial symptoms in 90.9% (20/22) of female patients with high CSF antibody titers. Seizures were observed in 60% (12/20) of the male patients and 65.5% (19/29) of female patients, and 61.3% (19/31) of seizures were focal seizures (Table 1). Constant chewing was noted in 7 female patients during the peak clinical state (6 patients with 1:32 CSF antibody titers, 1 patient with 1:10 CSF antibody titers, and 1 female patient with uncollected CSF antibody titers), which resulted in serious tongue and tooth injury. Bilateral facial Botox injections and intravenous anesthetics were ineffective treatments for involuntary oral movements.

EEG Findings and CSF Antibody Titers

A total of 87 EEGs and CSF antibody titers were collected from 46 patients (Table 2). During the peak stage, the BA of the patients with low CSF antibody titers showed normal or mild DPS. Moderate DPS or SDPS during the peak stage was observed in 72.4% (21/29) of patients with high CSF antibody

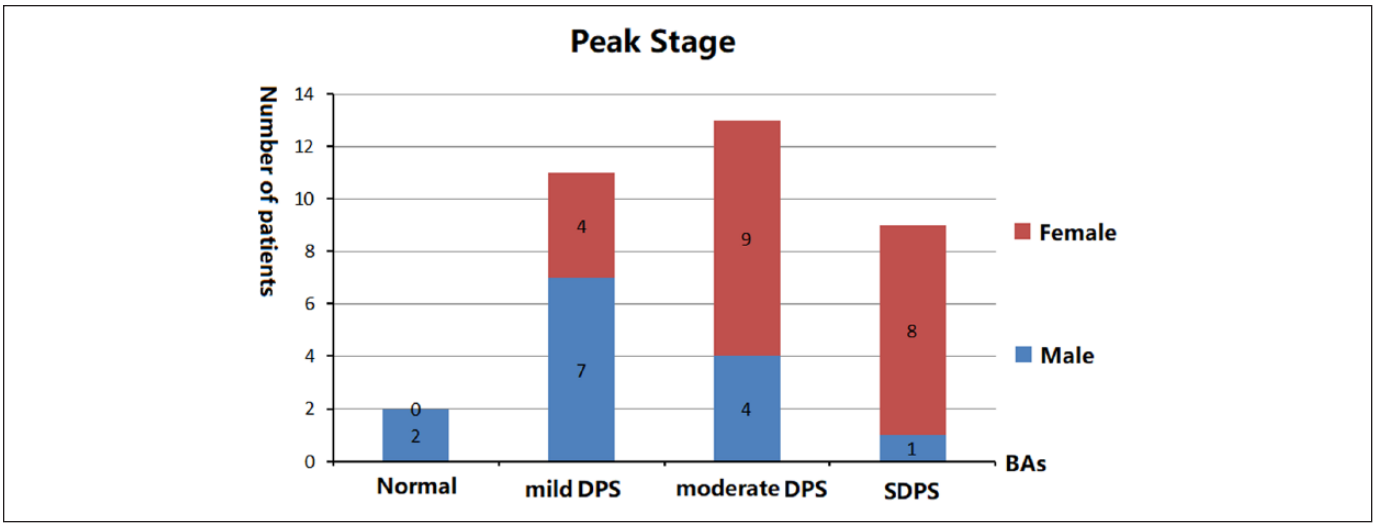

Figure 1. Peak-stage background activity was more severe in female patients than in male patients (Mann-Whitney *U* test, $P = .000$). *X*-axis: background activity (BA). *Y*-axis: number of patients. Moderate DPS, moderate diffuse polymorphic slowing; SDPS, severe diffuse polymorphic slowing; CSF, cerebrospinal fluid.

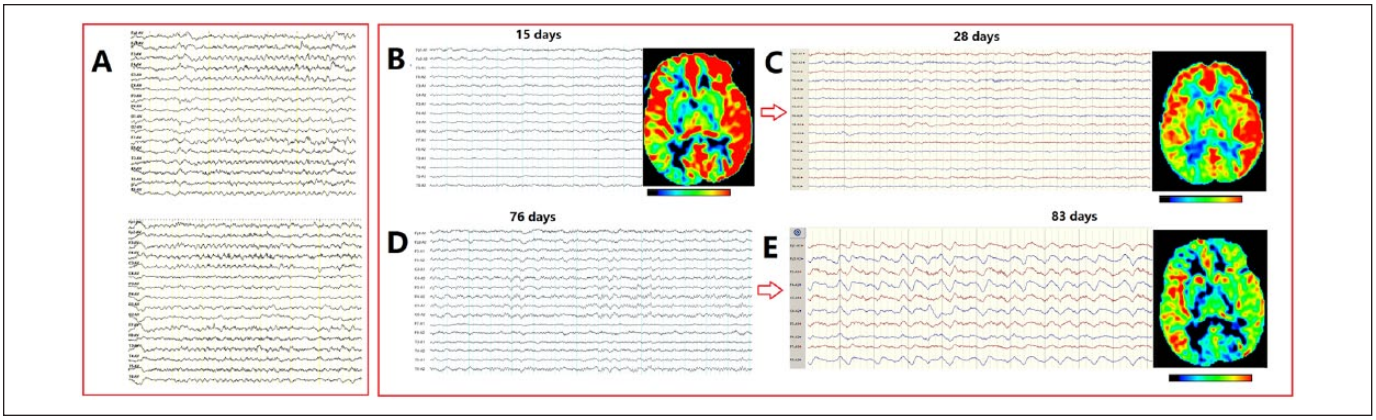

Figure 2. (A) Theta brush from 1 male patient with 1:10 CSF antibody titers. Serial EEGs (B-E) from 1 female patient with 1:10 CSF antibody titers. (B) Initial EEG (mild DPS) at 15 days after clinical onset. ASL showed that the blood flow was greater in the left cerebral cortex than in the right cerebral cortex. (C and D) Moderate DPS at 28 and 76 days after clinical onset. (E) EEG at 83 days showed SDPS and EDB, and the left cerebral cortex showed low blood flow. High-pass filter, 1 Hz; low-pass filter, 40 Hz. ASL, arterial spin labeling; DPS, diffuse polymorphic slowing; SDPS, severe diffuse polymorphic slowing; CSF, cerebrospinal fluid; EDB, extreme delta brush.

titers. The BA during the peak stage of patients with high CSF antibody titers was more severe than that of patients with low CSF antibody titers (Mann-Whitney *U* test, $P = .001$). BA at the peak stage was more severe in female patients than in male patients (Mann-Whitney *U* test, $P = .000$) (Figure 1).

One theta brush (Figure 2A) and 6 EDBs were observed in 7 patients (6 patients with high CSF antibody titers; 1 male patient with undetermined CSF antibody titers) (Table 2). Brush patterns were primarily located in the unilateral or bilateral frontotemporal regions at their respective peak stages (Figure 2A and E) and were a better marker for disease severity than epileptic seizures. EDs were observed in 9 patients, and were predominately located in the frontal regions (Table 2, Figure 3). The EDs in 4 patients were variable (Figure 3C-H).

Imaging

A total of 62.8% (32/51) of patients showed normal MRIs. Brain lesions were observed in 37.2 patients (19/51). On MRI, hyperintensities involving the frontal cortex, temporal cortex, and parietal cortex were noted in 15.8% (3/19), 84.2% (16/19) and 36.8% (7/19) of patients, respectively. ASL showed changes in the brain blood flow in all patients (9/9; 4 patients showed normal MRI, and 5 patients featured abnormal MRI). ASL was more sensitive than MRI for detecting brain lesions. From 6 to 33 days after clinical onset, ASL showed high blood flow in the frontal, temporal, and parietal cortices (Figure 2B) that subsequently disappeared (Figure 2E). There were no statistically significant differences in the imaging of patients with anti-NMDAR between low CSF antibody titers and high CSF antibody titers ($P > .05$).

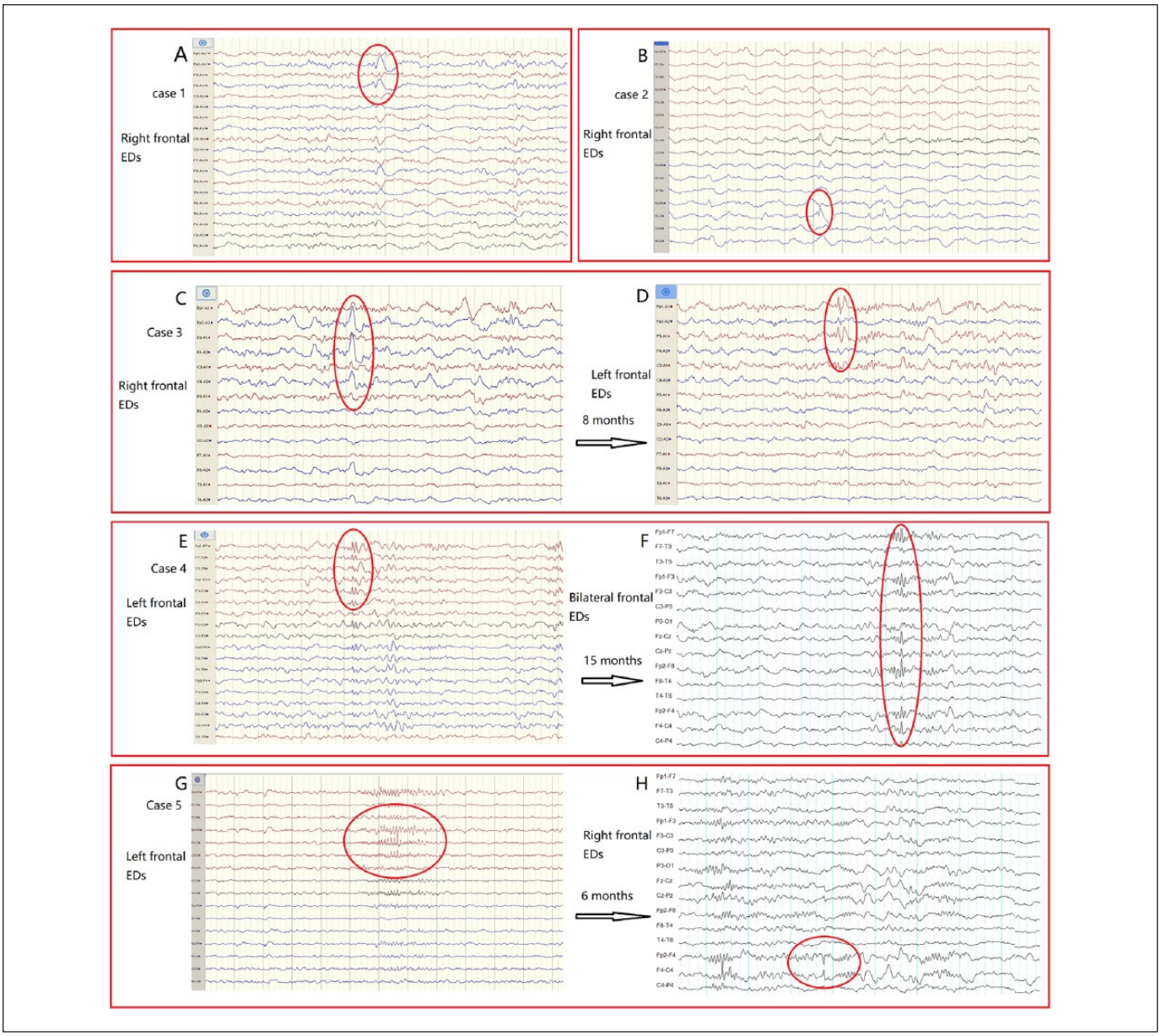

Figure 3. Epileptic discharges (EDs, red circles) in the frontal regions of 5 patients. After 8 months, the right frontal sharp wave in case 3 evolved into left frontal EDs. ED variability was also observed in cases 4 and 5. High-pass filter, 1 Hz; low-pass filter, 40 Hz.

Lumbar Puncture Examination and Thyroid Function Results

The lumbar puncture pressure ranged from 65 to 280 (mean 161.7 ± 66.2) mm H_2O. The white blood cell count in the CSF ranged from 0 to 741 × 10^6/L, with a median of 12 × 10^6/L. The CSF protein level ranged from 0.1 to 1.49 g/L (mean 0.56 ± 0.3).

Regarding thyroid function, T3 levels decreased in 61% of patients (25/41) and ranged from 0.77 to 1.38 mmol/L. Thyroglobulin levels also decreased in 33.3% of patients (10/30) and ranged from 0.04 to 3.17 ng/mL. Anti-thyroglobulin antibody increased in 20.7% of patients (6/29) and ranged from 134.3 to 474 IU/mL. Increased levels of thyroid peroxidase antibody were detected in 24.1% of patients (7/29), ranging from 42 IU/mL to 560.4 IU/mL. Increased levels of serum PRL were detected in 86.7% (13/15) of patients with seizures, ranging from 32.41 to 211.5 ng/mL.

Outcome

After 8 to 34 months of immunotherapy, 4 patients were lost to follow-up. We successfully followed up 41 patients (6 female patients with low CSF antibody titers, 17 female patients with high CSF antibody titers, 6 male patients with low CSF antibody titers, and 12 male patients with high CSF antibody titers),

and 3 of 41 patients with high CSF antibody titers died of severe lung infections. The mRS scores were higher in the 29 patients with high CSF antibody titers than in the 12 patients with low CSF antibody titers (mean 2.62 ± 1.42 vs 0.75 ± 0.97, $P = .000$).

Discussion

Patients with anti-NMDAR encephalitis presented with abnormal behavior, seizures, speech dysfunction, dyskinesia, memory deficits, autonomic instability, and decreased consciousness levels.[4,7,11] The serum antibody titers were higher than the CSF antibody titers. There were more patients with high CSF antibody titers than with low CSF antibody titers.

Behavioral changes were the major symptom in patients with anti-NMDAR encephalitis, and 90.9% (20/22) of female patients with high CSF antibody titers manifested behavioral changes as their initial symptoms (Table 1). In an observational cohort study, 87% of patients exhibited 4 or more categories of symptoms by the end of the first month.[12] Our study investigated whether clinical symptoms are associated with sex and CSF antibody titers in anti-NMDAR encephalitis. A greater number of clinical symptoms were noted in patients with high CSF antibody titers than in those with low CSF antibody titers (mean 3.11 ± 1.06 vs 1.62 ± 0.65, $P = .000$). Meanwhile, the peak-stage BA was worse in patients with high CSF antibody titers than in those with low CSF antibody titers (Mann-Whitney U test, $P = .001$). The clinical symptoms were more severe in female patients than in male patients (mean 3.52 ± 0.98 vs 2.69 ± 1.09, $P = .000$). Meanwhile, female patients showed worse peak-stage BA than male patients (Mann-Whitney U test, $P = .000$) (Figure 1). Constant chewing (see video in the Supplemental Material, available with the online version of the article) during the peak stage (6 patients with high CSF antibody titers and 1 patient with undetermined CSF antibody titers) was unlikely to be caused by temporal or frontal seizures because no EDs were observed in the EEG recordings, and antiepileptic drugs (AEDs) were ineffective. Constant chewing may be a useful marker of the peak period of the disease. Similar to faciobrachial tonic seizures, which indicate leucine-rich glioma-inactivated protein encephalitis,[13] involuntary oral movements are associated with anti-NMDAR encephalitis. Orofacial dyskinesia with chewing and tongue biting resulted in traumatic injuries to the lips and tongue.[14] mRS scores were worse in patients with EDB patterns than in those wihtout.[4] In the present study, mRS scores were higher in patients with high CSF antibody titers than in those with low CSF antibody titers. This result suggests a worse prognosis in patients with high CSF antibody titers than in those with low CSF antibody titers.

EDB has received clinical attention ever since Schmitt et al[4] proposed its potential as a characteristic EEG change in anti-NMDAR encephalitis. The EDB pattern without an electrographic evolution or a response to benzodiazepine suggests that EDB itself is an interictal and not an ictal pattern.[4] Furthermore, the patients' recovery without AEDs also implies that EDB is unlikely to be ictal in nature.[4] EDB likely represents a cortical dysfunction rather than a seizure. EDB continues to be a useful marker of disease activity and a tool for monitoring treatment response and relapses, through EDB resolution with clinical improvement.[4] In this study, the brush pattern was observed in only 14.6% (7/48) of the patients. The EDB occurrence rate in this study was lower than the 30% to 33.3% rate reported.[4,12] There are several possible explanations for this difference: (*a*) The brush pattern was observed primarily in patients with high CSF antibody titers, particularly among female patients. (*b*) The occurrence rate of brush patterns among Chinese patients is not very high.[15] The typical EDB patterns in premature infants can be found in any region of the head but are less common in the frontal region than at other sites.[16] Schmitt et al[4] showed that EDB is usually symmetric and synchronous and is typically observed broadly across all head regions. In contrast, we detected a brush pattern in the unilateral or bilateral frontotemporal regions at the respective peak stages (Figure 2A and E). Foff et al[5] recently reported that a particular electrographic characteristic, namely, the beta/delta power ratio, is significantly higher in patients with anti-NMDAR encephalitis than in those with non-NMDAR encephalitis in their EEGs on presentation. This difference may be helpful for distinguishing anti-NMDAR encephalitis from non-NMDAR encephalitis.[5] Rhythmic alpha sinusoidal waves, which presents as subclinical seizures, may be another electrographic pattern that indicates anti-NMDAR encephalitis.[6]

Acute autoimmune seizure is a common symptom of anti-NMDAR encephalitis. Seizures were observed in 60% (12/20) of male patients and 65.5% (19/29) of female patients (Table 1). Moreover, 61.3% (19/31) of the seizures were focal (Table 1). Seizures were observed as the onset symptom in 33.3% (17/51) of patients. In addition, 2 patients suffered from status epilepticus. EDs in this study were observed in only 18.75% (9/48) of cases and were found in the frontal regions (Figure 3). Similarly, a previous study showed that only a very low percentage of patients presented with EDs on EEG.[4] This result could have several explanations: (*a*) The epileptic seizures in some patients were easily controlled; therefore, EDs could not be recorded during EEG detection. (*b*) Epilepsy and involuntary movements occurred concomitantly, or, in some cases, the epilepsy-like attack observed in clinical practice was actually involuntary movement. Therefore, the detection rate of EDs on EEG was low. Distinguishing between epilepsy and involuntary movement by clinical presentation alone is occasionally difficult in patients with anti-NMDAR encephalitis, especially in those with consciousness disturbances. Therefore, EEG monitoring is valuable in such cases.[15] Approximately one-third of epilepsy cases are intractable with AED therapy.[17] Accumulating evidence supports an autoimmune basis for AED-resistant epilepsy. ED variability may contribute to AED-resistant epilepsy.[18-23]

In previous studies, MRI was abnormal in 66.6% to 69.6% of patients.[4,12] In this study, brain lesions were observed in 37.2% (19/51) of patients. However, ASL revealed changes in the brain blood flow in all patients (9/9). ASL was more sensitive than MRI for detecting brain lesions in patients with anti-NMDAR encephalitis. There were no statistically significant differences in the images from patients with anti-NMDAR between low CSF antibody titer and high CSF antibody titer ($P > .05$). More samples may be needed to illustrate the problem.

Conclusion

Behavioral changes comprised the major symptoms in patients with anti-NMDAR encephalitis. The number of symptom categories was higher in patients with high CSF antibody titers than in those with low CSF antibody titers. The peak-stage BA was more severe in patients with high CSF antibody titers than in those with low CSF antibody titers. Meanwhile, the female patients showed worse peak-stage BA than the male patients. The prognosis was also worse in patients with high CSF antibody titers than in those with low CSF antibody titers. Brush patterns and constant chewing were primarily observed in female patients with high CSF antibody titers. EDs were predominately located in the frontal regions and were noted to be variable. ASL was more sensitive than MRI for detecting brain lesions in patients with anti-NMDAR encephalitis.

Author Contributions

Ailiang Miao: drafting/revising the manuscript. Mingyang Du: acquisition of EEG and revising the manuscript. Jianqing Ge, Lingling Wang and Hedong Lu: acquisition of EEG. Xiaoshan Wang: study concept or design and study supervision. Haiyan Xu, Hongxing Liu, Chuanyong Yu, Caiyun Wu, Yuan Gao, Jintao Sun and Qi Shi: clinical work. Their contributions helped us to acquire clinical data and EEG successfully.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The work was supported by the Young Scientists Fund of the National Natural Science Foundation of China (Grant No. 81501126, http://npd.nsfc.gov.cn/), the National Natural Science Foundation of China (Grant No. 81471324, http://npd.nsfc.gov.cn/), Science and Development Foundation of Nanjing Medical University (2014NJMU050), Young Medical Key Talents Foundation of Jiangsu Province (Grant No. QNRC2016053), Training Project for Young Talents of Nanjing Brain Hospital.

Supplemental Material

Supplemental material for this article is available online.

References

1. Dalmau J, Tüzün E, Wu HY, et al. Paraneoplastic anti-*N*-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. *Ann Neurol*. 2007;61:25-36.
2. Prüss H, Dalmau J, Harms L, et al. Retrospective analysis of NMDA receptor antibodies in encephalitis of unknown origin. *Neurology*. 2010;75:1735-1739.
3. Rosenfeld MR, Titulaer MJ, Dalmau J. Paraneoplastic syndromes and autoimmune encephalitis: five new things. *Neurol Clin Pract*. 2012;2:215-223.
4. Schmitt SE, Pargeon K, Frechette ES, Hirsch LJ, Dalmau J, Friedman D. Extreme delta brush: a unique EEG pattern in adults with anti-NMDA receptor encephalitis. *Neurology*. 2012;79:1094-1100.
5. Foff EP, Taplinger D, Suski J, Lopes MB, Quigg M. EEG findings may serve as a potential biomarker for anti-NMDA receptor encephalitis. *Clin EEG Neurosci*. 2017;48:48-53.
6. Miao A, Wang X. Ictal rhythmic alpha sinusoidal waves in three cases of anti-NMDAR encephalitis [published online November 30, 2017]. *Clin EEG Neurosci*. doi:10.1177/1550059417745185
7. Graus F, Titulaer MJ, Balu R, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol*. 2016;15:391-404.
8. Titulaer MJ, McCracken L, Gabilondo I, et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. *Lancet Neurol*. 2013;12:157-165.
9. Gitiaux C, Simonnet H, Eisermann M, et al. Early electro-clinical features may contribute to diagnosis of the anti-NMDA receptor encephalitis in children. *Clin Neurophysiol*. 2013;124:2354-2361.
10. Nosadini M, Boniver C, Zuliani L, et al. Longitudinal electroencephalographic (EEG) findings in pediatric anti-***N***-methyl-D-aspartate (anti-NMDA) receptor encephalitis: the Padua experience. *J Child Neurol*. 2015;30:238-245.
11. Viaccoz A, Desestret V, Ducray F, et al. Clinical specificities of adult male patients with NMDA receptor antibodies encephalitis. *Neurology*. 2014;82:556-563.
12. Veciana M, Becerra JL, Fossas P, et al; Epilepsy Group of the SCN. EEG extreme delta brush: an ictal pattern in patients with anti-NMDA receptor encephalitis. *Epilepsy Behav*. 2015;49:280-285.
13. Irani SR, Michell AW, Lang B, et al. Faciobrachial dystonic seizures precede Lgi1 antibody limbic encephalitis. *Ann Neurol*. 2011;69:892-900.
14. Florance NR, Davis RL, Lam C, et al. Anti-*N*-methyl-D-aspartate receptor (NMDAR) encephalitis in children and adolescents. *Ann Neurol*. 2009;66:11-18.
15. Zhang Y, Liu G, Jiang MD, Li LP, Su YY. Analysis of electroencephalogram characteristics of anti-NMDA receptor encephalitis patients in China. *Clin Neurophysiol*. 2017;128:1227-1233.
16. Clancy RR, Bergqvist AGC, Dlugos DJ. Neonatal electroencephalography. In: Ebersole JS, Pedley TA, eds. *Current Practice of Clinical Electroencephalography*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003:160-234.
17. Kwan P, Schachter SC, Brodie MJ. Drug-resistant epilepsy. *N Engl J Med*. 2011;365:919-926.
18. Quek AM, Britton JW, McKeon A, et al. Autoimmune epilepsy: clinical characteristics and response to immunotherapy. *Arch Neurol*. 2012;69:582-593.
19. Barajas RF, Collins DE, Cha S, Geschwind MD. Adult-onset drug-refractory seizure disorder associated with anti-voltage-gated potassium-channel antibody. *Epilepsia*. 2010;51:473-477.
20. Majoie HJ, de Baets M, Renier W, Lang B, Vincent A. Antibodies to voltage-gated potassium and calcium channels in epilepsy. *Epilepsy Res*. 2006;71:135-141.
21. Liimatainen S, Peltola M, Sabater L, et al. Clinical significance of glutamic acid decarboxylase antibodies in patients with epilepsy. *Epilepsia*. 2010;51:760-767.
22. Peltola J, Kulmala P, Isojärvi J, et al. Autoantibodies to glutamic acid decarboxylase in patients with therapy-resistant epilepsy. *Neurology*. 2000;55:46-50.
23. Bien CG. Value of autoantibodies for prediction of treatment response in patients with autoimmune epilepsy: review of the literature and suggestions for clinical management. *Epilepsia*. 2013;54(suppl 2):48-55.