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ORIGINAL ARTICLE

# Clinical characteristics and factors associated with short-term prognosis in adult patients with autoimmune encephalitis of non-neoplastic etiology

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## Abstract

**Background** Reports that autoimmune encephalitis (AE) is associated with antibodies have increased; however, little is known about the distribution of clinical symptoms, imaging changes, and prognostic factors in patients with AE of non-neoplastic etiology. Accordingly, we evaluated the clinical characteristics and factors associated with short-term prognosis.

**Methods** From January 2016 to June 2018, 31 adult patients were diagnosed with AE of non-neoplastic etiology at Shengjing Hospital of China Medical University and their demographic and clinical characteristics were abstracted. Factors affecting disease severity and predictors of prognosis were analyzed.

**Results** Among 31 patients, 19 had anti-NMDAR, 5 had anti-GABABR, and 7 had anti-LGI1 antibody encephalitis. Status epilepticus, ataxia, and cognitive dysfunction were the most common neurological symptoms. Deep white matter (DWM) abnormalities were the most common changes observed on MRI. Logistic regression analysis indicated that conscious disturbance (odds ratio = 11.67, 95%, confidence interval 2.13–64.04; $p = 0.005$) is an independent factor associated with poor prognosis in AE.

**Conclusion** The clinical manifestations of AE are diverse; status epilepticus, ataxia, and cognitive dysfunction are most common. The DWM of the brain, rather than the limbic lobe system, was most prone to MR signal abnormalities. Conscious disturbance may be an important predictor of poor short-term prognosis in patients with AE of non-neoplastic etiology.

**Keywords** Autoimmune encephalitis · Magnetic resonance imaging · Conscious disturbance

## Introduction

Autoimmune encephalitis (AE) is a nervous system inflammatory disease mediated by autoimmune mechanisms [1]. The primary pathological mechanism is infiltration of the brain parenchyma by lymphocyte-based inflammatory cells that form sleeve-like structures around blood vessels [2]. AE can be classified as anti-intracellular antigen-related AE, anti-cell membrane surface, or anti-synaptic antigen-related AE [3]. Anti-intracellular antigen-related AE is always accompanied by tumors. Common antigens include Hu, Yo, Ri, and Ma2 [4]. Anti-cell membrane surface antigen-related and anti-synaptic antigen-related AEs are usually non-neoplastic. The known antigens include anti-*N*-methyl-D-aspartate receptor (NMDAR), leucine-rich glioma inactivation 1 protein (LGI1), gamma-aminobutyric acid B receptor (GABABR), and contact protein-like protein-2 (Caspr2) [5].

Previous studies reported typical neurological symptoms of AE, including seizures, psychiatric symptoms, and cognitive dysfunction [6]. The neurological symptoms among patients with AE are variable; sleep disorders, motor disorders, and language dysfunction are common [7]. However, associations of the specific disease course, symptomatology, and neuroimaging with the antibody type have not been clearly elucidated. Furthermore, the factors associated with severity and prognosis have not been identified.

In the present study, we analyzed the clinical characteristics and neuroimaging findings of 31 patients diagnosed with AE in our hospital to improve our understanding of this group of diseases. Moreover, we evaluated the factors affecting disease severity and short-term prognosis in patients with AE of non-neoplastic etiology.

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## Methods

Clinical data for 31 adult patients with AE were retrospectively collected at the Department of Neurology of Shengjing Hospital of China Medical University from January 2016 to June 2018. All patients were screened for the presence of autoantibodies against neuronal membrane surface antigens and synaptic antigens, including NMDAR, LGI1, GABABR, Caspr2, and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) by a cytometric bead array test of CSF or/and serum samples using standard kits (Euroimmun Medical Diagnostic Co., Ltd., Beijing, People's Republic of China). Diagnosis was based on the AE diagnostic criteria in the Position Paper published in 2016 [8]. All patients underwent MRI examinations. Other central nervous system diseases mimicking AE were excluded. Other systemic examinations, including chest CT, abdominal ultrasound, and serum tumor markers, were performed to screen for neoplasms.

MRI examinations were performed using an Achieva 3.0 Tesla scanner (Philips Healthcare, Andover, MA, USA). The standard protocol included axial T1- and T2-weighted imaging (T1WI and T2WI), fluid-attenuated inversion recovery (FLAIR) imaging, and diffusion-weighted imaging (DWI). The locations, distribution, and signal changes on MRI were recorded for all patients. The results of tests performed on blood samples, such as serum cystatin C and uric acid, were recorded. The results of other laboratory tests, including biochemical and microbiological examinations of the cerebrospinal fluid (CSF), were abstracted in all cases.

Clinical severity and outcomes were scored at the time of patient admission and 1 month after discharge, using a modified Rankin Scale (mRS), by a neurologist with mRS expertise: mRS scores of 0–2 were considered mild or good in terms of functional independence, whereas scores of 3–6 indicated severe or poor outcomes [9]. Each patient's level of consciousness was assessed using the Glasgow Coma Score (GCS) that is based on their eye-opening response, verbal-behavioral response, and motor response. A GCS of 15 was considered normal, and a GCS below 8 indicated a coma [10].

## Statistical analysis

Student's *t* tests were used to evaluate continuous variables; these data are expressed as means ± SD. For discrete variables, Fisher's exact test was used, and data are reported as counts and percentages. Binary logistic regression analysis was performed to identify factors predictive of outcomes 1 month after the discharge of patients with AE; a forward stepwise variable selection method was used to calculate odds ratios (ORs) and corresponding 95% confidence intervals (CIs). Statistical analyses were performed using IBM SPSS Statistics 17; $p < 0.05$ was considered statistically significant.

## Results

### Demographic profile

Our study enrolled 31 patients with positive antibodies associated with AE (males, 10; mean age, 44.9 ± 20.9 years). Among these, 25 (80.6%) patients had acute onset of symptoms; their mean time from onset to diagnosis was 21.4 ± 18.7 days. Fever (80.6%), headache (67.7%), cough (61.3%), and vomiting (54.9%) were the most common prodromal symptoms. Nineteen patients had anti-NMDAR antibody encephalitis (12 female and 7 male), 7 had anti-LGI 1 antibody encephalitis (4 female and 3 male), and 5 had anti-GABABR antibody encephalitis (4 female and 1 male) (Table 1).

### Spectrum of neurological symptoms based on antibody type

Anti-NMDAR antibody encephalitis was the most common AE type in our case series; among these 19 patients, 11 had status epilepticus (57.9%), 10 (52.6%) had psychiatric symptoms, and 8 had ataxia, dyskinesia, dysarthria, and cognitive dysfunction (42.1%). Other neurological symptoms, such as conscious disturbance, sensory disturbance, and hallucination, were also common in these patients. Seven patients with anti-LGI1 antibody encephalitis were diagnosed in our study; 6 (85.7%) had cognitive dysfunctions and 4 had dysarthria (57.1%). Dyskinesia, ataxia, and sensory disturbance were also common neurological symptoms in patients with anti-LGI1 antibody encephalitis. Five patients were diagnosed with anti-GABABR antibody encephalitis; among these, 4 (80.0%) had ataxia, and in 3 patients (60.0%) dyskinesia, conscious disturbance, and cognitive dysfunction were found (Fig. 1).

### Spectrum of MRI lesions by type of antibody

All patients underwent MRI examinations. The mean time from onset of symptoms to examination was 17.5 ± 15.6 days, and 22 patients (70.9%) had abnormal signal changes. Thirteen patients (41.9%) were re-examined by MRI within 30 days of ending treatment and improvement was observed in all patients. Deep white matter (DWM) lesions on MRI were the most common abnormal imaging finding in our patients, and these lesions were most frequent in anti-NMDAR antibody encephalitis (Fig. 2). After DWM lesions, frontal and

**Table 1** Demographic, clinical, and laboratory data in patients with autoimmune encephalitis of non-neoplastic etiology

| No. | Gender | Age | Ab | Neurological symptoms | MRI | CSF laboratory test | | | GCS | Immunotherapy | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | WBC (normal 0–$5 \times 10^6$/L) | Protein (normal 0.15–0.45 g/L) | Glucose (normal 2.5–4.5 mmol/L) | | Steroids | IVIG |
| 1 | F | 30 | NMDAR | Psychiatric symptoms, focal seizure, ataxia, dyskinesia, conscious disturbance, dysarthria | Right DWM | 74 | 0.45 | 1.8 | 9 | Yes | No |
| 2 | F | 16 | NMDAR | Psychiatric symptoms, ataxia, dyskinesia, cognitive dysfunction, dysarthria, sensory disturbance | Bilateral temporal and insular lobes, bilateral DWMs | 20 | 0.96 | 2.6 | 11 | Yes | No |
| 3 | F | 25 | NMDAR | Status epilepticus | Bilateral frontal and parietal lobes, DWMs and left occipital lobe | 36 | 0.35 | 3.44 | 15 | Yes | No |
| 4 | M | 15 | NMDAR | Focal seizure, dysarthria | – | 47 | 0.32 | 3.02 | 15 | Yes | No |
| 5 | F | 65 | GABABR | Psychiatric symptoms, ataxia, conscious disturbance | – | 11 | 0.42 | 3.53 | 11 | Yes | Yes |
| 6 | F | 49 | NMDAR | Psychiatric symptoms, ataxia, cognitive dysfunction | Bilateral DWMs | 4 | 0.36 | 3.97 | 13 | Yes | No |
| 7 | M | 59 | LGI1 | Focal seizure, ataxia, dyskinesia, cognitive dysfunction, conscious disturbance, sensory disturbance | Right temporal lobe | 1 | 0.44 | 3.25 | 7 | Yes | Yes |
| 8 | F | 64 | GABABR | Status epilepticus, ataxia, dyskinesia, cognitive dysfunction, conscious disturbance, sensory disturbance | Bilateral basal ganglias and DWMs | 6 | 0.39 | 4.22 | 4 | Yes | No |
| 9 | M | 18 | NMDAR | Status epilepticus, ataxia, dyskinesia, conscious disturbance, sensory disturbance | Right parietal and temporal lobe, left cerebellum | 44 | 0.31 | 3.54 | 11 | No | Yes |
| 10 | M | 57 | NMDAR | Cognitive dysfunction | Bilateral temporal lobes | 43 | 0.30 | 3.19 | 15 | | |
| 11 | F | 51 | NMDAR | Status epilepticus, cognitive dysfunction | – | 2 | 0.42 | 3.33 | 14 | Yes | No |
| 12 | F | 62 | NMDAR | Status epilepticus, cognitive dysfunction, dysarthria | – | 41 | 0.46 | 3.69 | 14 | | |
| 13 | F | 14 | NMDAR | Psychiatric symptoms, status epilepticus, cognitive dysfunction, dysarthria | Right DWM | 18 | 0.19 | 3 | 14 | Yes | No |
| 14 | F | 30 | NMDAR | Psychiatric symptoms, status epilepticus, dyskinesia, conscious disturbance, cognitive dysfunction, dysarthria, sensory disturbance, sleep disorders, ataxia | – | 21 | 0.17 | 3.66 | 10 | Yes | Yes |
| 15 | M | 32 | NMDAR | Psychiatric symptoms, status epilepticus, dyskinesia, conscious disturbance, dysarthria, ataxia, hallucination | Right frontal lobe | 44 | 0.22 | 4.07 | 3 | Yes | No |
| 16 | M | 63 | LGI1 | Status epilepticus, ataxia, conscious disturbance, cognitive dysfunction, dysarthria, dyskinesia, sensory disturbance | Bilateral basal ganglias | 2 | 0.25 | 4.1 | 14 | Yes | No |
| 17 | F | 51 | NMDAR | Psychiatric symptoms, status epilepticus, ataxia, dysarthria, conscious disturbance, hallucination | – | 1014 | 0.27 | 3.8 | 10 | Yes | Yes |
| 18 | F | 60 | GABABR | Psychiatric symptoms, focal seizure, cognitive dysfunction, dysarthria | Bilateral hippocampus, temporal, parietal lobes, basal ganglias and DWMs | 9 | 0.21 | 5.5 | 12 | Yes | No |
| 19 | F | 63 | LGI1 | Focal seizure, cognitive dysfunction, dysarthria | Left insular lobe and DWM | 4 | 0.74 | 3.8 | 13 | Yes | Yes |
| 20 | F | 69 | LGI1 | Psychiatric symptoms, cognitive dysfunction, dysarthria | Bilateral DWMs | 5 | 0.21 | 5.7 | 15 | Yes | No |
| 21 | M | 60 | LGI1 | Status epilepticus, cognitive dysfunction, hallucination | Bilateral frontal, temporal, parietal lobes and DWMs | 3 | 0.70 | 3.41 | 15 | Yes | No |
| 22 | F | 18 | NMDAR | Psychiatric symptoms, cognitive dysfunction, hallucination | Left insular lobe and hippocampus | 508 | 1.18 | 3.9 | 15 | Yes | No |

**Table 1** (continued)

| No. | Gender | Age | Ab | Neurological symptoms | MRI | CSF laboratory test | | | GCS | Immunotherapy | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | WBC (normal 0–$5 \times 10^6$/L) | Protein (normal 0.15–0.45 g/L) | Glucose (normal 2.5–4.5 mmol/L) | | Steroids | IVIG |
| 23 | F | 67 | LGI1 | Cognitive dysfunction, dyskinesia, ataxia, dysarthria, hallucination, sensory disturbance | Left hippocampus, bilateral basal ganglias and DWMs | 10 | 0.46 | 3.6 | 9 | Yes | Yes |
| 24 | M | 57 | GABABR | Psychiatric symptoms, status epilepticus, ataxia, cognitive dysfunction, conscious disturbance, sensory disturbance | – | 19 | 0.61 | 3.07 | 12 | Yes | No |
| 25 | M | 14 | NMDAR | Psychiatric symptoms, status epilepticus | – | 5 | 0.2 | 3.31 | 15 | Yes | Yes |
| 26 | F | 77 | GABABR | Focal seizure, ataxia, dyskinesia, dysarthria, sensory disturbance | Left DWM | 8 | 0.48 | 2.66 | 12 | Yes | Yes |
| 27 | F | 62 | NMDAR | Psychiatric symptoms, ataxia, dyskinesia, dysarthria, sensory disturbance, sleep disorders | Bilateral basal ganglias and DWMs | 32 | 0.58 | 2.67 | 9 | Yes | Yes |
| 28 | F | 18 | NMDAR | Focal seizure | – | 98 | 0.53 | 3.85 | 15 | Yes | Yes |
| 29 | F | 16 | NMDAR | Status epilepticus, ataxia, dysarthria, cognitive dysfunction, sensory disturbance | Right temporal lobe, basal ganglia and DWM, left frontal lobe | 126 | 0.42 | 2.31 | 15 | Yes | No |
| 30 | M | 48 | NMDAR | Status epilepticus | Bilateral frontal, parietal lobes and DWMS | 85 | 0.65 | 3.11 | 15 | Yes | No |
| 31 | F | 62 | LGI1 | Sleep disorders | Right temporal lobe and basal ganglia, bilateral frontal lobes and DWMs | 3 | 0.36 | 3.54 | 15 | Yes | Yes |

*Ab* antibody, *MRI* magnetic resonance imaging, *IV* intravenous, *IVIG* intravenous immunoglobulin, *NMDAR* N-methyl-D-aspartate receptor, *LGI1* leucine-rich glioma-inactivated 1 protein, *GABABR* gamma-aminobutyric acid B receptor, *CSF* cerebrospinal fluid, *WBC* white blood cell, *DWM* deep white matter, *GCS* Glasgow Coma Score

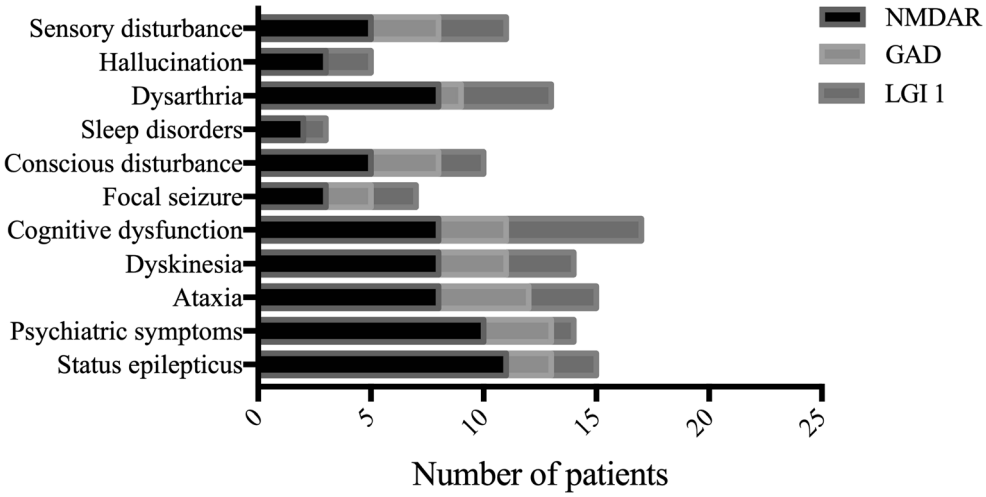


**Fig. 1** Frequency of neurological symptoms by antibody type

temporal lobes were the most commonly involved lobes in patients with anti-NMDAR antibody encephalitis, followed by lesions of the parietal lobes and basal ganglia. In patients with anti-LGI1 antibody encephalitis, lesions were more common in basal ganglia and temporal lobes than in other brain regions, except for DWM lesions. The basal ganglia were often involved in anti-GABABR antibody encephalitis. Strong signals in T2WI and FLAIR imaging as well as low signals in T1WI were observed in all patients, and strong DWI signal changes were observed in 7 patients.

## Factors associated with severity and short-term prognosis in patients with AE of non-neoplastic etiology

To determine the factors related to the severity of AE, we compared clinical characteristics and laboratory results by mRS scores category at admission. We found that an acute onset of symptoms ($p = 0.013$), psychiatric symptoms ($p = 0.008$), ataxia ($p < 0.001$), dyskinesia ($p < 0.001$), conscious disturbance ($p < 0.001$), dysarthria ($p = 0.016$), and sensory disturbance ($p < 0.001$) were more frequent in severe cases than in mild cases. Additionally, low serum uric acid levels ($p = 0.025$) and lower GCS ($p < 0.001$) may be associated more severe AE (Table 2).

One month after discharge, 18 patients had good outcomes and 13 patients had poor outcomes. Psychiatric symptoms ($p = 0.022$), ataxia ($p = 0.017$), conscious disturbance ($p = 0.022$), high levels of serum cystatin C, and low GCS were associated with poor short-term outcomes in patients with AE. A binary logistic regression analysis indicated that conscious disturbance (OR = 11.67, 95% CI 2.13–64.04; $p = 0.005$) was independently associated with poor short-term prognosis (Table 3).

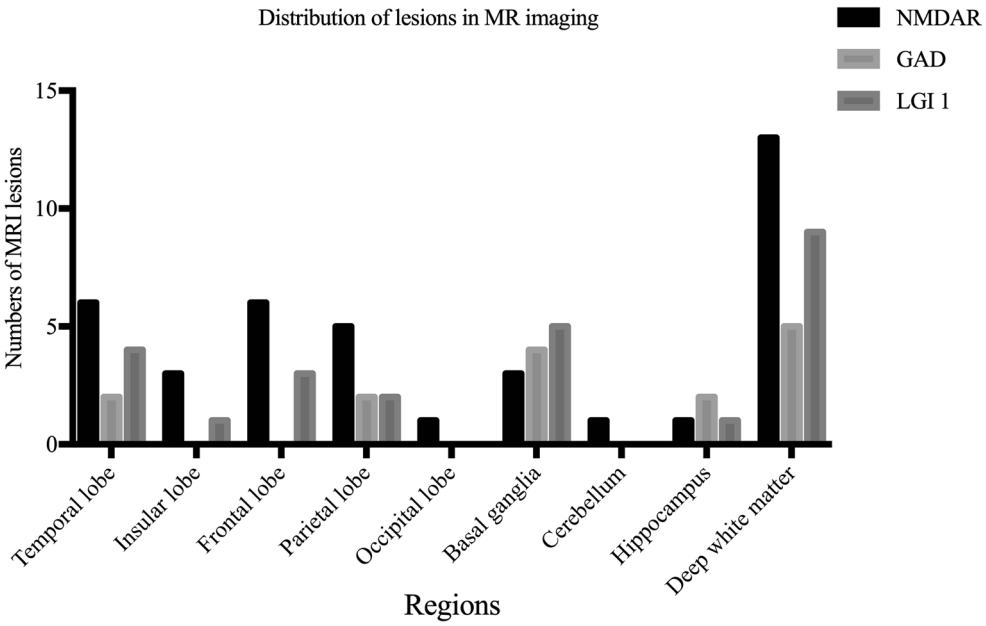


**Fig. 2** Distribution of MRI lesions location by antibody type

**Table 2** Demographic, clinical, and laboratory data associated with severity and outcomes of patients with AE of non-neoplastic etiology

| | Modified Rankin Scale pre-treatment | | | Modified Rankin Scale post-treatment | | |
|---|---|---|---|---|---|---|
| | ≤ 2 (*n* = 17) | > 2 (*n* = 14) | *p* | ≤ 2 (*n* = 18) | > 2 (*n* = 13) | *p* |
| Age (years, mean ± SD) | 42.7 ± 23.0 | 47.6 ± 18.5 | 0.528 | 43.4 ± 23.2 | 46.7 ± 18.5 | 0.669 |
| Onset to diagnosis (days, mean ± SD) | 22.2 ± 20.6 | 20.4 ± 16.8 | 0.793 | 26.3 ± 20.4 | 15.4 ± 15.1 | 0.106 |
| Sex, number of men [*n* (%)] | 7 (41.2) | 4 (28.6) | 0.465 | 6 (33.3) | 5 (38.5) | 0.768 |
| Acute symptoms onset [*n* (%)] | 11 (64.7) | 14 (100.0) | 0.013 | 13 (72.2) | 12 (92.3) | 0.162 |
| Fever [*n* (%)] | 7 (41.2) | 7 (50.0) | 0.623 | 8 (44.4) | 6 (46.2) | 0.925 |
| Respiratory tract infection [*n* (%)] | 0 | 3 (21.4) | 0.045 | 1 (5.6) | 2 (15.4) | 0.361 |
| Vomiting [*n* (%)] | 3 (17.6) | 2 (14.3) | 0.800 | 2 (11.1) | 3 (23.1) | 0.371 |
| Headache [*n* (%)] | 7 (41.2) | 4 (28.6) | 0.465 | 7 (38.9) | 4 (30.8) | 0.641 |
| Psychiatric symptoms [*n* (%)] | 4 (23.5) | 10 (71.4) | 0.008 | 5 (27.8) | 9 (69.2) | 0.022 |
| Focal seizure [*n* (%)] | 4 (23.5) | 3 (21.4) | 0.889 | 5 (27.8) | 2 (15.4) | 0.415 |
| Status epilepticus [*n* (%)] | 9 (52.9) | 6 (42.9) | 0.576 | 10 (55.6) | 5 (38.5) | 0.347 |
| Ataxia [*n* (%)] | 3 (17.6) | 13 (92.9) | < 0.001 | 6 (33.3) | 10 (76.9) | 0.017 |
| Dyskinesia [*n* (%)] | 2 (11.8) | 11 (78.6) | < 0.001 | 6 (33.3) | 7 (53.8) | 0.253 |
| Cognitive dysfunction [*n* (%)] | 10 (58.8) | 7 (50.0) | 0.623 | 10 (55.6) | 7 (53.8) | 0.925 |
| Conscious disturbance [*n* (%)] | 2 (11.8) | 11 (78.6) | < 0.001 | 4 (22.2) | 9 (69.2) | 0.009 |
| Sleep disorders [*n* (%)] | 2 (11.8) | 3 (21.4) | 0.467 | 4 (22.2) | 1 (7.7) | 0.278 |
| Dysarthria [*n* (%)] | 6 (35.3) | 11 (78.6) | 0.016 | 8 (44.4) | 9 (69.2) | 0.171 |
| Hallucination [*n* (%)] | 1 (5.9) | 3 (21.4) | 0.199 | 1 (5.6) | 3 (23.1) | 0.151 |
| Sensory disturbance [*n* (%)] | 3 (17.6) | 11 (78.6) | 0.001 | 6 (33.3) | 7 (53.8) | 0.119 |
| Intracranial hypertension [*n* (%)] | 5 (29.4) | 6 (42.9) | 0.436 | 5 (27.8) | 6 (46.2) | 0.291 |
| WBC ($10^6$/L, CSF) | 61.8 ± 120.9 | 92.3 ± 266.1 | 0.675 | 32.8 ± 37.9 | 127.4 ± 286.9 | 0.188 |
| Protein (g/L, CSF) | 0.5 ± 0.2 | 0.4 ± 0.2 | 0.307 | 0.4 ± 0.2 | 0.5 ± 0.3 | 0.341 |
| Glucose (mmol/L, CSF) | 3.5 ± 0.8 | 3.4 ± 0.7 | 0.720 | 3.6 ± 0.9 | 3.4 ± 0.7 | 0.552 |
| Serum uric acid (μmol/L) | 229.7 ± 79.3 | 169.4 ± 59.1 | 0.025 | 266.4 ± 76.5 | 173.4 ± 67.2 | 0.052 |
| Serum cystatin C (μg/L) | 0.9 ± 0.2 | 1.0 ± 0.3 | 0.148 | 0.8 ± 0.2 | 1.0 ± 0.3 | 0.042 |
| GCS | 14.4 ± 1.1 | 9.5 ± 3.1 | < 0.001 | 13.4 ± 2.9 | 10.7 ± 3.3 | 0.023 |
| Apnea [*n* (%)] | 3 (17.6) | 7 (50.0) | 0.055 | 5 (27.8) | 5 (38.5) | 0.530 |
| NMDAR [*n* (%)] | 11 (64.7) | 8 (57.1) | 0.667 | 12 (66.7) | 7 (53.8) | 0.470 |
| IVIG [*n* (%)] | | | | 8 (44.4) | 4 (30.8) | 0.296 |

Figures in parentheses are percentages, unless indicated otherwise

*AE* autoimmune encephalitis, *IVIG* intravenous immunoglobulin, *WBC* white blood cell, *GCS* Glasgow Coma Score

## Discussion

In 2007, Dalmau et al. detected anti-NMDAR antibodies on the surface of neurons in the hippocampus and prefrontal lobe of patients and first proposed the concept of anti-NMDAR encephalitis, which has since attracted wide research interest [11]. Recent research has implicated several additional antibodies in the pathogenesis of AE. AE is thought to account for about 20% of all adult encephalitis [12].

In this study, we retrospectively analyzed 31 patients with AE: 19 patients with anti-NMDAR encephalitis, 7 patients with anti-LGI1 encephalitis, and 5 patients with anti-GABABR encephalitis. Anti-NMDAR encephalitis accounts for 61.3% of our cases of AE and was the most common type of AE, consistent with previous results [13]. The incidence of AE in women is evidently higher than that in men in our study. Fever, headache, cough, and vomiting were the most common prodromal symptoms in our patients.

NMDAR is an ionic glutamate receptor composed of NR1, NR2, NR3, and other subunits. It is expressed primarily in the frontal cortex and hippocampus, is involved in regulating synaptic remodeling and synaptic transmission, and is closely related to advanced neurological functions, such as learning and memory [14]. The clinical manifestations of anti-NMDAR antibody encephalitis can include headache, fever, and other precursor symptoms. During the early course of the disease, patients can have delirium, anxiety, emotional instability, and other psychiatric symptoms as well as speech disorders, seizures, and other neurological symptoms [15]. Dyskinesia, autonomic neurological symptoms, and

**Table 3** Logistic regression analysis of parameters associated with poor outcomes of patients with AE of non-neoplastic etiology

| | OR | 95% CI | *p* |
|---|---|---|---|
| Ataxia | 5.63 | 0.38–82.95 | 0.208 |
| Conscious disturbance | 11.67 | 2.13–64.04 | 0.005 |
| Psychiatric symptoms | 2.91 | 0.37–22.66 | 0.307 |
| Serum cystatin C | 2.02 | 0.29–209.46 | 0.131 |
| GCS | 1.04 | 0.68–1.58 | 0.865 |

*AE* autoimmune encephalitis, *GCS* Glasgow Coma Score

conscious disturbance may develop in later stages [13]. In our study, 57.9% of patients had status epilepticus, which was the most common neurological symptom. This was consistent with the results of a previous study in which seizures occurred in 76% of patients, and 45% of these patients had generalized tonic-clonic seizures [16]. Studies have also shown that 61.5% of adult male patients and 14% of adult female patients have seizures as their first symptom [17].

LGI1 is a secretory protein encoded by the epilepsy-related gene *lgi1*, which is expressed primarily in the hippocampus and temporal cortex [18]. The onset of LGI1-related AE is usually after 50 years of age, with an average age of 60 years, and males account for 65% of patients [19]. In addition to the typical symptoms of AE, such as memory loss, seizures, and mental disorders, faciobrachial dystonic seizures are a characteristic clinical symptom in LGI-1-related AE [20]. However, among the seven patients in our study, cognitive impairment was the most common neurological symptom. This difference may be explained by our focus on cognitive function tests for patients with AE. Arino et al. also reported a high frequency of anti-LGI1 encephalitis-related cognitive impairment, [21]. The major forms of cognitive impairment were acute or subacute onset of memory and orientation impairment. Memory impairment primarily affected short-term memory and often occurred after seizures [18].

GABABR is an important inhibitory receptor of the central nervous system that is expressed primarily in the cerebral cortex, hippocampus, and cerebellum [22]. The clinical manifestations of GABABR-related AE are cognitive dysfunction, mental and behavioral abnormalities, seizures, and other symptoms [23]. Among the five GABABR-related AE cases in our study, ataxia was observed in four cases. Because GABABR is abundantly expressed in the cerebellum, ataxia may be more common in GABABR-related AE than in other types of AE. Hoftberger et al. also reported that ataxia is common in patients with GABABR-related AE [24].

Cranial MRI is of limited value for diagnosing AE, because most imaging changes are not specific to AE. In our study, 70.9% of AE cases had abnormal MR signal changes, which was higher than that reported by Heine et al. [25]. The most common signal changes in MRI were in DWM. Lesions in the frontal lobe, temporal lobe, and parietal lobe were common in patients with anti-NMDAR encephalitis. In patients with anti-LGI1 encephalitis and anti-GABABR encephalitis, we found that the basal ganglia and temporal lobe were most commonly involved. Typical imaging changes of lesions were strong signals in T2WI and FLAIR imaging and low signals in T1WI, and, in some patients, strong DWI signals.

Few observational clinical studies have evaluated which factors determine the severity and prognosis of AE, and their findings were inconsistent. Liao et al. found that the time interval from symptom onset to hospital admission and urinary incontinence/retention were associated with poor outcomes based on a follow-up study of 70 patients with onconeural antibody-associated disorders. However, their logistic regression analysis revealed that only urinary incontinence/retention was independently associated with poor prognosis [26]. We found that various psychiatric symptoms and neurological symptoms, such as ataxia, dyskinesia, conscious disturbance, dysarthria, and sensory disturbance, may be associated with the severity, of AE. Other factors, such as acute symptom onset, low GCS, and low serum uric acid, may also be associated with severity. Furthermore, we found that psychiatric symptoms, conscious disturbance, low GCS, and high serum cystatin C may be related to poor short-term prognosis. Multivariate logistic regression analysis showed that conscious disturbance was independently related to poor short-term prognosis in AE. This finding was consistent with the results of Aungsumart et al., who evaluated 31 cases of anti-NMDAR encephalitis and also found that an abnormal level of consciousness was associated with an unfavorable outcome [27]. Additionally, in our study, the mRS scores of older patients were higher than those of younger patients at onset and at 1 month after hospital discharge. The poor short-term prognosis of older patients was consistent with previous reports [28]. We found that abnormal changes in MRI were more common in the elderly; however, the exact mechanism of imaging abnormalities was not yet clear and there was a lack of specificity in patients with AE. Further studies may need to confirm our results. The first-line treatment for AE includes intravenous glucocorticoid therapy, immunoglobulin, and plasma exchange [29]. Early combination therapy has been reported to provide better efficacy [30]. In our study, 17 patients were treated with glucocorticoid therapy alone (intravenous infusion of methylprednisolone [1000, 500, 250, 120 mg/day for 3 days each]), 5 patients were treated with intravenous immunoglobulin alone (0.4 g/kg/day for 5 days), and 9 patients were treated with combination therapy. However, at follow-up 1 month after discharge, we found that 41.9% of the patients did not exhibit improvement; this finding is inconsistent with most previous research results. Possible explanations for this discrepancy include a difference in case-mix severity of the studied cases or the short length of follow-up. T. Iizuka et al. reported four cases of anti-NMDAR

encephalitis [13], who all had good prognosis, but the time required for their recovery was approximately 4–7 years. Sai et al. drew the same conclusion; after 4 months to 2 years of follow-up, most patients had a good prognosis [31]. To ensure a high follow-up rate, we evaluated the prognosis of patients at only 1 month after discharge. This is a likely explanation for the poor early prognosis we observed in more than 40% of patients.

Despite collecting detailed clinical and imaging data of patients, our research has some limitations. Firstly, the diagnostic methods employed to exclude neoplastic diseases related to AE were relatively simple, and their sensitivity and specificity may be lower than that of PET/CT. Secondly, most of our patients lacked EEG examination to identify the type of seizure they manifested during hospitalization. In the future, we will strive to improve EEG examinations. Finally, to ensure a high follow-up rate, we only followed patients for 1 month after discharge. This follow-up time was too short to adequately describe long-term prognosis.

## Conclusion

Our results show that status epilepticus, ataxia, and cognitive dysfunction were more common than other neurological symptoms in AE. The DWM of the brain, rather than the limbic lobe system, was prone to abnormal signal changes on MRI. Conscious disturbance may be an important predictor of poor short-term prognosis in patients with AE of non-neoplastic etiology.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that there is no conflict of interest.

**Ethical standards** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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