Journal of Inflammation Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Oligoclonal Bands as Predictors of Disease Severity and Prognosis in Anti-NMDAR Encephalitis

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Purpose: Oligoclonal bands (OCBs) are frequently observed in anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis, though their clinical significance remains unclear. This study explored the association between OCBs and clinical manifestations, disease severity, and prognosis in patients with anti-NMDAR encephalitis, and evaluated its potential clinical significance.

Patients and Methods: This retrospective study included 85 anti-NMDAR encephalitis cases treated at the First Affiliated Hospital of Guangxi Medical University between June 2017 and January 2024. Participants were grouped into OCB-positive (n=47) and OCB-negative (n=38) groups to analyze disease severity and prognosis. Disease severity was assessed using the Clinical Assessment Scale for Autoimmune Encephalitis (CASE) and modified Rankin Scale (mRS). Prognostic stratification using discharge mRS scores categorized patients into mild-moderate group (mRS<3) and severe group (mRS≥3), with multivariable regression analysis identifying key prognostic predictors.

Results: The OCB-positive group exhibited more severe clinical manifestations, including severe seizure types, disturbance of consciousness, movement disorders, and a higher incidence of intensive care unit (ICU) admission. OCB-positive patients exhibited significantly elevated cerebrospinal fluid (CSF) protein levels and neutrophil percentage in peripheral blood. Additionally, OCB-positive patients showed markedly higher median scores on both the mRS and CASE scales than OCB-negative patients at all time points (admission to last follow-up). Multivariable regression analysis identified two prognostic factors of unfavorable outcomes in anti-NMDAR encephalitis: the presence of OCBs (OR 3.741, 95% CI 1.026–13.637; *P*=0.046) and disturbance of consciousness (OR 11.481, 95% CI 2.633–50.057; *P*=0.001). Furthermore, The receiver operating characteristic (ROC) curve analysis demonstrated that the combination of OCBs and disturbance of consciousness exhibited excellent predictive performance, with an area under the curve (AUC) of 0.873 (95% CI: 0.792–0.954).

Conclusion: OCB positivity correlates with heightened disease severity and unfavorable prognosis in anti-NMDAR encephalitis, supporting its utility as a prognostic biomarker.

Keywords: anti-NMDAR encephalitis, oligoclonal bands, predictors, disease severity, prognosis

Introduction

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis, caused by GluN1 subunit-targeting antibodies, ranks among the most prevalent forms of autoimmune encephalitides.[1] Anti-NMDAR encephalitis is characterized by multiple clinical manifestations, including seizure, cognitive impairment, psychiatric symptoms, movement disorders, autonomic dysfunction, and disturbance of consciousness.[2] Intrathecal oligoclonal bands (OCBs) synthesis is identified by the presence of immunoglobulin bands in cerebrospinal fluid (CSF) without corresponding detection in paired serum samples,[3–5] a process driven by clonally expanded B-cell populations in the central nervous system (CNS).[6] The OCBs testing offers significant advantages as it can be conducted even with a suspected anti-NMDAR encephalitis diagnosis. Approximately 50–70% of individuals suffering from anti-NMDAR encephalitis exhibit positive OCBs.[7–9] The positive OCBs indicate an immune response within the CNS. The ongoing intrathecal humoral immune response may be related to the severity and prognosis of anti-NMDAR encephalitis. Currently, there is limited research on the role of OCBs in anti-NMDAR encephalitis, and their clinical significance in anti-NMDAR encephalitis remains poorly understood.

Received: 22 April 2025
Accepted: 2 August 2025
Published: 13 August 2025

Previous studies have demonstrated that OCB-positive status may correlate with disease activity levels and serve as a prognostic factor in certain neurological disorders. For example, in autoimmune encephalitis, OCB-positive patients have been shown to exhibit significantly worse clinical outcomes than OCB-negative patients.[10] Similarly, in multiple sclerosis (MS), OCB positivity occurs more frequently in progressive disease phenotypes, suggesting a possible association between OCBs and the severity of MS.[11] In myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), patients with OCB positivity exhibit significantly higher relapse rates, highlighting the potential prognostic utility of OCBs in neuroinflammatory disorders.[12] However, despite these findings, evidence on the role of OCBs in anti-NMDAR encephalitis remains limited and inconclusive. Prior investigations were constrained by the inclusion of relatively small sample sizes and heterogeneous cohorts comprising different types of autoimmune encephalitis, which complicates the interpretation of results. Consequently, the clinical significance of OCBs in anti-NMDAR encephalitis, particularly their potential impact on disease severity and clinical outcomes, remains unclear and requires further investigation in well-defined, larger patient cohorts.

This research aimed to explore the impacts of OCBs regarding clinical features, disease severity, as well as prognosis in anti-NMDAR encephalitis by systematically comparing OCB-positive and OCB-negative patients. Additionally, this study sought to identify biomarkers that could facilitate risk stratification, guide personalized treatment strategies, and improve prognostic prediction in anti-NMDAR encephalitis.

Materials and Methods

Study Design and Participants

This retrospective cohort study enrolled a total of 136 patients diagnosed with anti-NMDAR encephalitis at the First Affiliated Hospital of Guangxi Medical University between June 2017 and January 2024. After a thorough screening process, 9 patients were excluded due to incomplete medical records. Additionally, 4 patients were excluded because they had other diseases that could affect their neurological status, thereby confounding the study results. Furthermore, 38 patients were excluded as they did not undergo OCBs testing, which was essential for the analysis, as shown in Figure 1. To assess selection bias, baseline characteristics were compared between the OCBs-tested (n=85) and untested groups (n=38). No significant differences were observed in demographics, clinical manifestations, complications, immunotherapy regimens, laboratory findings, or short-term outcomes (all P>0.05; see Supplementary Table S1).

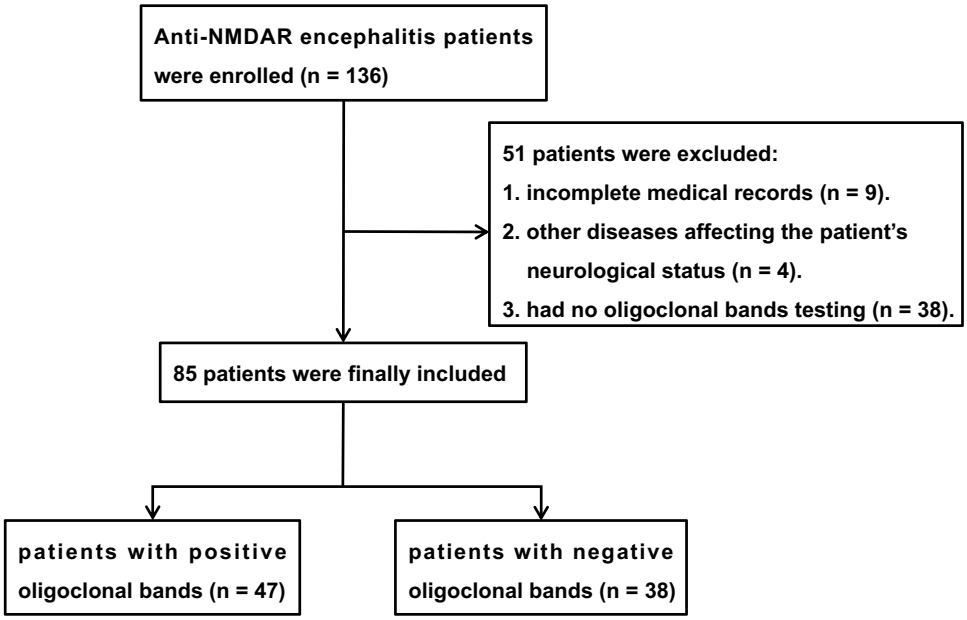

Figure 1 Flow chart of study patients.
Abbreviation: NMDAR, N-methyl-D-aspartate receptor.

Ultimately, the study enrolled 85 patients, all of whom met the 2016 diagnostic criteria for autoimmune encephalitides, including typical medical symptoms and detection of anti-NMDAR antibodies within CSF. To assess the possible influence of OCBs on disease advancement, patients were categorized into OCB-positive (n=47) and OCB-negative (n=38) groups.

This study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (2025-E0217). Written informed consent was obtained from all participants or their legal guardians. Patients data were fully anonymized and used solely for scientific analysis in strict compliance with the ethical principles of the Declaration of Helsinki.

Data Collection

Our study systematically collected essential clinical data from medical records, encompassing demographic data (such as age and gender), clinical features (including memory deterioration, cognitive impairment, speech dysfunction, mental behavior disorders, epileptic seizure, movement disorders, autonomic nervous dysfunction, and disturbance of consciousness), and comorbidities (such as urinary tract infection and pulmonary infection). Additionally, data included hospital stays, intensive care unit (ICU) admission, laboratory findings (including CSF and peripheral blood analyses), magnetic resonance imaging (MRI) results, and details of immunotherapy. The severity and prognosis of the disease were assessed using standardized tools, including the modified Rankin Scale (mRS) and Clinical Assessment Scale for Autoimmune Encephalitis (CASE), ensuring an objective evaluation of patient condition. To ensure comprehensive follow-up, all patients were monitored for at least 12 months post-discharge. For OCB analysis, CSF samples were collected at the time of the patient's first admission for anti-NMDAR encephalitis. OCB detection was performed via isoelectric focusing followed by immunoblotting. Positivity was strictly defined as the presence of one or more discrete immunoglobulin bands in the CSF that were absent in the corresponding serum sample. Qualitative results (positive/negative) were used for analysis. This thorough data collection and analysis framework allowed for a detailed comparison of OCB-positive and OCB-negative populations, aiming to elucidate OCBs' role in anti-NMDAR encephalitis.

Statistical Analysis

Statistical analysis was performed using IBM SPSS 27.0, and figures were created using GraphPad Prism 10. Continuous variables were described as mean±standard deviation (SD) for data that followed a normal distribution, or as the median with interquartile range (IQR) for data that followed a non-normal distribution. Categorical data were described as counts (percentages) [n (%)]. For comparisons, categorical variables were analyzed using the chi-square test. As for continuous variables, the independent *t*-test was utilized for normally distributed data, while the Mann–Whitney *U*-test was used for non-normally distributed data. Candidate variables with $P<0.05$ in univariate analyses were included in the multivariable regression analysis, which was then used to identify the prognostic factors for anti-NMDAR encephalitis. Additionally, the predictive performance of prognostic factors was evaluated using receiver operating characteristic (ROC) curve analysis. A P-value<0.05 was considered statistically significant.

Results

Clinical Features of Research Participants

In this research, 47 (55.3%) patients were classified as OCB-positive, and 38 (44.7%) as OCB-negative. The demographics and clinical traits of both groups were analyzed, as presented in Table 1.

Notable disparities were identified between OCB-positive and OCB-negative patients, such as disturbance of consciousness, movement disorders, ICU admission, and the time to second-line immunotherapy initiation. Specifically, OCB-positive patients demonstrated a markedly increased probability of experiencing disturbance of consciousness compared with OCB-negative patients (61.7% vs 23.7%, $P<0.001$). Similarly, a higher incidence of movement disorders was observed among the OCB-positive patients (78.7% vs 50.0%, $P=0.005$). Additionally, ICU admissions were markedly elevated in OCB-positive individuals (36.2% vs 10.5%, $P=0.006$), indicating greater disease severity in this group. Furthermore, the median time to second-line immunotherapy initiation was shorter in OCB-positive patients at 24 days (IQR: 17.0, 35.0) compared to 32.5

Table 1 Demographic Details and Clinical Features of Anti-NMDAR Encephalitis Between OCB-Positive and OCB-Negative Groups

	Total (n=85)	OCB+ (n=47)	OCB− (n=38)	*P* value
Gender, n (%)				0.286
Male	39 (45.9)	24 (51.1)	15 (39.5)	
Female	46 (54.1)	23 (48.9)	23 (60.5)	
Age, median (IQR), years	19 (15, 30)	22 (15, 39.5)	16 (14, 27)	0.089
Clinical manifestations, n (%)				
Prodromal symptoms	35 (41.2)	22 (46.8)	13 (34.2)	0.241
Memory deterioration	24 (28.2)	15 (31.9)	9 (23.7)	0.402
Cognitive impairment	58 (68.2)	34 (72.3)	24 (63.2)	0.366
Speech dysfunction	50 (58.8)	32 (68.1)	18 (47.4)	0.054
Mental behavior disorder	75 (88.2)	44 (93.6)	31 (81.6)	0.087
Epileptic seizure	61 (71.8)	37 (78.7)	24 (63.2)	0.113
Severity of seizure				0.011
No seizure	24 (28.2)	10 (21.3)	14 (36.8)	
Controlled seizure	40 (47.1)	20 (42.6)	20 (52.6)	
Drug-resistant epilepsy	11 (12.9)	9 (19.2)	2 (5.3)	
Status epilepticus	10 (11.8)	8 (17.0)	2 (5.3)	
Disturbance of consciousness	38 (44.7)	29 (61.7)	9 (23.7)	<0.001
Severity of disturbance of consciousness				0.022
No disturbance of consciousness	41 (48.2)	18 (38.3)	23 (60.5)	
Somnolence	31 (36.5)	19 (40.4)	12 (31.6)	
Stupor	4 (4.7)	2 (4.3)	2 (5.3)	
Coma	9 (10.6)	8 (17)	1 (2.6)	
Movement disorders	56 (65.9)	37 (78.7)	19 (50)	0.005
Autonomic nervous dysfunction	40 (47.1)	25 (53.2)	15 (39.5)	0.208
Complications, n (%)				
Pulmonary infection	43 (50.6)	16 (34)	27 (71.1)	0.160
Urinary tract infection	9 (10.6)	2 (4.3)	7 (18.4)	0.151
Hospital stays, median (IQR), days	15 (10, 23)	16 (9.5, 23)	14 (11, 19)	0.490
ICU admission, n (%)	21 (24.7)	17 (36.2)	4 (10.5)	0.006
Tumor, n (%)	5 (5.9)	4 (8.5)	1 (2.6)	0.252
Relapse, n (%)	11 (12.9)	9 (19.1)	2 (5.3)	0.058
Immunotherapy				
Time to first line immunotherapy initiation, median (IQR), days	15 (9, 29.5)	16 (9.5, 27)	13.5 (8, 32)	0.677
Time to second line immunotherapy initiation, median (IQR), days	30 (18, 48.5)	24 (17, 35)	32.5 (24.5, 62.5)	0.032

Abbreviations: NMDAR, N-methyl-D-aspartate receptor; OCB+, positive oligoclonal bands; OCB−, negative oligoclonal bands; IQR, interquartile range; ICU, intensive care unit.

days (IQR: 24.5, 62.5) in OCB-negative patients (P=0.032), suggesting a more aggressive disease course requiring earlier escalation of treatment in the OCB-positive cohort.

Figure 2A illustrates the classification of seizure severity in OCB-positive and OCB-negative patients. OCB-positive patients exhibited a significantly higher prevalence of severe seizure type, including drug-resistant epilepsy and status epilepticus, compared to OCB-negative individuals (*P*=0.011).

Figure 2B showed significant differences in the phenotypic disturbance of consciousness between the two groups, including somnolence, stupor, and coma. Notably, compared to OCB-negative individuals, OCB-positive patients exhibited a significantly higher prevalence of disturbance of consciousness, particularly coma (*P*=0.022).

No significant distinctions were identified in gender, age, prodromal symptoms, memory deterioration, cognitive impairment, speech dysfunction, mental behavior disorder, autonomic nervous dysfunction, urinary tract infection,

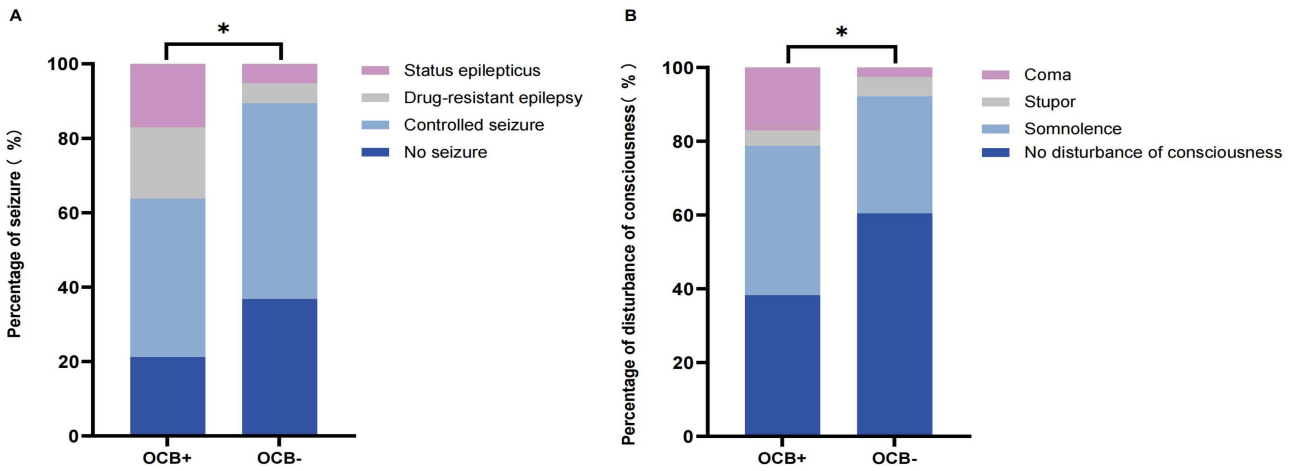

Figure 2 Comparison of the percentage of the severity of seizures (**A**) and distribution of consciousness (**B**) between OCB-positive and OCB-negative groups. *$p < 0.05$.
Abbreviations: OCB+, positive oligoclonal bands; OCB−, negative oligoclonal bands.

pulmonary infection, hospital stays, tumor presence, relapse, or time to first line immunotherapy between two groups (P>0.05).

Auxiliary Examination Results

The abnormal MRI, CSF findings, peripheral blood findings and NMDAR antibody titer of both groups were analyzed, as illustrated in Table 2.

Table 2 Auxiliary Examination Results of Anti-NMDAR Encephalitis Between OCB-Positive and OCB-Negative Groups

	Total (n=85)	OCB+ (n=47)	OCB− (n=38)	*P* value
Abnormal MRI, n (%)	38 (44.7)	26 (55.3)	12 (31.6)	0.029
CSF findings				
Q_{Alb}, median (IQR)	3.8 (2.8, 5.6)	3.8 (2.9, 5.6)	3.5 (2.8, 4.7)	0.396
z	10 (2.0, 41.5)	12 (2.5, 60.0)	8 (0.0, 14.0)	0.061
CSF protein, median (IQR), mg/L	306.6 (214.2, 452.1)	349.6 (264.9, 497.7)	242.6 (196.2, 403.4)	0.022
CSF albumin, median (IQR), mg/L	145.2 (116.3, 225.1)	160.0 (118.8, 236.7)	142.7 (116.6, 194.7)	0.545
CSF LDH, median (IQR), U/L	18.0 (14.0, 23.5)	19.0 (14.5, 25.0)	17.5 (13.0, 21.0)	0.177
Peripheral blood findings				
Serum IgG, median (IQR), g/L	12.2 (10.0, 16.1)	12.0 (10.0, 16.2)	12.4 (10.1, 14.7)	0.954
Serum albumin, mean (SD), g/L	40.8 (4.7)	40.3 (5.0)	41.4 (4.3)	0.300
Neutrophil percentage, median (IQR), %	73.8 (61.7, 80.8)	77.9 (66.9, 83.9)	66.5 (54.5, 76.2)	0.004
Lymphocyte percentage, median (IQR), %	19.1 (12.2, 28.4)	14.6 (11.0, 22.6)	22.7 (14.4, 32.9)	0.004
NMDAR antibody titer (n, %)				
CSF NMDAR antibody titers				0.104
Titers≤1:32	64 (75.3)	37 (78.7)	27 (71.1)	
1:32<titers≤1:100	10 (11.8)	7 (14.9)	3 (7.9)	
Titers>1:100	11 (12.9)	3 (6.4)	8 (21.1)	
Serum NMDAR antibody titers				0.437
Titers≤1:32	70 (82.4)	38 (80.9)	32 (84.2)	
1:32<titers≤1:100	13 (15.3)	7 (14.9)	6 (15.8)	
Titers>1:100	2 (2.4)	2 (4.3)	0 (0.0)	

Abbreviations: NMDAR, N-methyl-D-aspartate receptor; OCB+, positive oligoclonal bands; OCB−, negative oligoclonal bands; MRI, magnetic resonance imaging; IQR, interquartile range; Q_{Alb}, albumin-CSF/serum-quotient; CSF, cerebrospinal fluid; SD, standard deviation.

https://doi.org/10.2147/JIR.S535684

OCB-positive patients demonstrated an increased prevalence of abnormal MRI findings compared to the OCB-negative group (55.3% vs 31.6%, P=0.029). Regarding CSF findings, the median CSF protein levels increase in the OCB-positive group (349.6 mg/L; IQR: 264.9, 497.7), whereas the OCB-negative group was lower (242.6 mg/L; IQR: 196.2, 403.4) (P=0.022). Regarding peripheral blood findings, the OCB-positive group showed a higher median neutrophil percentage (77.9%; IQR: 66.9, 83.9) than the OCB-negative group (66.5%; IQR: 54.5, 76.2) (P=0.004). Conversely, the median lymphocyte percentage was lower in the OCB-positive group (14.6%; IQR: 11.0, 22.6) than in the OCB-negative group (22.7%; IQR: 14.4, 32.9) (P=0.004).

The analysis revealed no notable variations in Q_{Alb}, CSF cell count, CSF albumin, CSF LDH, CSF NMDAR antibody titers, serum NMDAR antibody titers, serum IgG, or serum albumin when comparing the two groups (P>0.05).

Comparison of Disease Severity and Prognosis Between OCB-Positive and OCB-Negative Groups

The mRS and CASE scores were used to evaluate disease severity and prognosis in both groups.

In terms of mRS scores, at admission, OCB-positive patients showed notably elevated median mRS scores (4; IQR: 3, 5) relative to OCB-negative patients (3; IQR: 2, 3), with statistical significance (P<0.001). This trend persisted at discharge, where the OCB-positive patients' median mRS score (3; IQR: 2, 4) still surpassed that of the OCB-negative patients (2; IQR: 1, 2) (P<0.001). At 12 months post-discharge, the OCB-positive patients maintained a higher median mRS score (1; IQR: 0, 1) than the OCB-negative patients (0; IQR: 0, 1) (P=0.006). Remarkably, during the last follow-up, the OCB-positive patients continued to exhibit elevated median mRS scores (0; IQR: 0, 1) relative to the OCB-negative patients (0; IQR: 0, 0) (P=0.021), as shown in Figure 3A.

In terms of CASE scores, at admission, OCB-positive patients showed notably elevated median CASE scores (10; IQR: 6, 15) relative to OCB-negative patients (4.5; IQR: 3, 7) (P<0.001). This trend continued at discharge, with the OCB-positive group having higher scores (5; IQR: 3, 10) than the OCB-negative group (2; IQR: 1, 3) (P<0.001). At 12 months post-discharge, OCB-positive patients still had higher median CASE scores (1; IQR: 0, 1) relative to the OCB-negative patients (0; IQR: 0, 1) (P=0.002). At the last follow-up, the OCB-positive patients continued to show elevated median CASE scores (0; IQR: 0, 1) than the OCB-negative patients (0; IQR: 0, 0) (P=0.03), as shown in Figure 3B.

Comparison of Clinical Characteristics in Anti-NMDAR Encephalitis Patients with Different Short-Term Prognosis

Based on the mRS scores at discharge, the 85 patients were stratified into mild-moderate (mRS<3; n=45) and severe (mRS≥3; n=40) groups. Table 3 compares the clinical manifestations of the two groups.

The results revealed statistically significant differences between the two groups in age, disturbance of consciousness, movement disorders, pulmonary infection, urinary tract infection, OCBs, CSF protein levels, neutrophil percentage, and lymphocyte percentage (P<0.05).

A significantly increased median age was observed in the severe group (22; IQR: 15, 43) compared to the mild-moderate group (17; IQR: 14, 26) (P=0.037). The severe group demonstrated a higher prevalence of disturbance of consciousness (80.0% vs 13.3%, P<0.001), movement disorders (85.0% vs 48.9%, P<0.001), pulmonary infection (70.0% vs 33.3%, P<0.001), and urinary tract infection (20.0% vs 2.2%, P=0.008) than those in the mild-moderate group. Additionally, compared to the mild-moderate group, the severe group exhibited a higher prevalence of oligoclonal bands (77.5% vs 35.6%, P<0.001). Regarding CSF findings, the median protein level was notably elevated in the severe group (342.9 mg/L; IQR: 262.9, 474.1) compared to the mild-moderate group (244.2 mg/L; IQR: 196.2, 449.2) (P=0.034). In terms of peripheral blood findings, the severe group showed a higher median neutrophil percentage (77.7%; IQR: 66.1, 86.0) than the mild-moderate group (68.9%; IQR: 58.4, 78.7) (P=0.021). Conversely, the median lymphocyte percentage was lower in the severe group (14.4%; IQR: 10.5, 24.1) in contrast to the mild-moderate group (20.0%; IQR: 13.9, 32.4) (P=0.017).

No substantial differences were evident in gender, prodromal symptoms, memory deterioration, cognitive impairment, speech dysfunction, mental behavior disorder, epileptic seizure, autonomic nervous dysfunction, tumor, relapse,

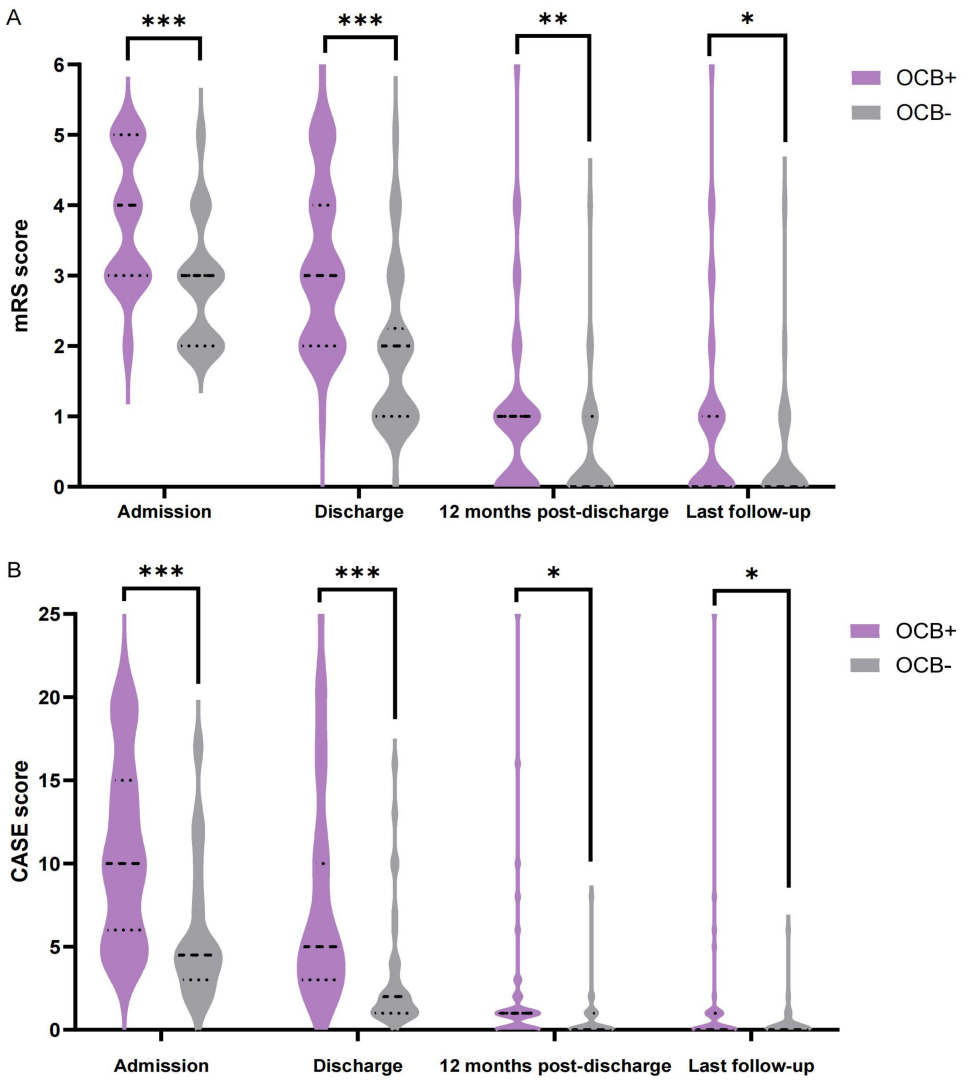

Figure 3 Comparison of mRS (**A**) and CASE (**B**) scores between OCB-negative and OCB-positive patients with anti-NMDAR encephalitis at admission, discharge, 12 months post-discharge, and last follow-up. *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$.
Abbreviations: mRS, modified Rankin Scale; CASE, Clinical Assessment Scale for Autoimmune Encephalitis; OCB+, positive oligoclonal bands; OCB–, negative oligoclonal bands.

abnormal MRI, Q_{Alb}, CSF cell count, CSF albumin, CSF LDH, serum IgG, serum albumin, or immunotherapy between the two groups ($P>0.05$).

Prognostic Factors for Short-Term Outcomes in Anti-NMDAR Encephalitis Patients

In the univariate analysis, factors showing statistical significance ($P<0.05$) were subsequently subjected to multivariable regression analysis to identify prognostic factors of poor short-term outcomes in anti-NMDAR encephalitis. Notably, OCBs (OR: 3.741, 95% CI: 1.026–13.637; $P=0.046$) and disturbance of consciousness (OR: 11.481, 95% CI: 2.633–50.057; $P=0.001$) were regarded as prognostic factors of poor short-term outcomes, as shown in Table 4.

The predictive value of OCBs and disturbances of consciousness for short-term outcomes in anti-NMDAR encephalitis was evaluated through ROC curves, with the area under the curve (AUC) being 0.873 (95% CI: 0.792–0.954), as illustrated in Figure 4, indicating strong predictive accuracy for these factors.

https://doi.org/10.2147/JIR.S535684

Table 3 Comparison of Clinical Data in Anti-NMDAR Encephalitis with Different Levels of Severity Upon Discharge

	Total (n=85)	mRS≥3 (n=40)	mRS<3 (n=45)	*P* value
Gender, n (%)				0.305
Male	39 (45.9)	16 (40.0)	23 (51.1)	
Female	46 (54.1)	24 (60.0)	22 (48.9)	
Age, median (IQR), years	19 (15, 30.5)	22 (15, 43)	17 (14, 26)	0.037
Clinical manifestations, n (%)				
Prodromal symptoms	35 (41.2)	20 (50.0)	15 (33.3)	0.119
Memory deterioration	24 (28.2)	12 (30.0)	12 (26.7)	0.733
Cognitive impairment	58 (68.2)	26 (65.0)	32 (71.1)	0.546
Speech dysfunction	50 (58.8)	27 (67.5)	23 (51.1)	0.125
Mental behavior disorder	75 (88.2)	38 (95.0)	37 (82.2)	0.068
Epileptic seizure	61 (71.8)	31 (77.5)	30 (66.7)	0.268
Disturbance of consciousness	38 (44.7)	32 (80.0)	6 (13.3)	<0.001
Movement disorders	56 (65.9)	34 (85.0)	22 (48.9)	<0.001
Autonomic nervous dysfunction	40 (47.1)	22 (55.0)	18 (40.0)	0.167
Complications, n (%)				
Pulmonary infection	43 (50.6)	28 (70.0)	15 (33.3)	<0.001
Urinary tract infection	9 (10.6)	8 (20.0)	1 (2.2)	0.008
Tumor, n (%)	5 (5.9)	4 (10.0)	1 (2.2)	0.128
Relapse, n (%)	11 (12.9)	6 (15.0)	5 (11.1)	0.594
Auxiliary examination				
Abnormal MRI, n (%)	38 (44.7)	21 (52.5)	17 (37.8)	0.173
CSF findings				
Oligoclonal bands, n (%)	47 (55.3)	31 (77.5)	16 (35.6)	<0.001
Q_{Alb}, median (IQR)	3.8 (2.8, 5.6)	4.0 (2.9, 5.6)	3.5 (2.7, 5.7)	0.374
CSF cell count, median (IQR), $\times 10^6$/L	10 (2.0, 41.5)	10.0 (3.0, 62.5)	10 (0.0, 26.0)	0.373
CSF protein, median (IQR), mg/L	306.6 (214.2, 452.1)	342.9 (262.9, 474.1)	244.2 (196.2, 449.2)	0.034
CSF albumin, median (IQR), mg/L	145.2 (116.3, 225.1)	154.4 (123.3, 211.1)	142.7 (116.0, 234.0)	0.546
CSF LDH, median (IQR), U/L	18.0 (14.0, 23.5)	18.5 (14.5, 24.5)	18.0 (13.0, 22.0)	0.346
Peripheral blood findings				
Serum IgG, median (IQR), g/L	12.2 (10.0, 16.1)	12.2 (9.9, 21.0)	12.3 (10.1, 13.9)	0.431
Serum albumin, mean (SD), g/L	40.8 (4.7)	39.8 (5.4)	41.7 (3.8)	0.057
Neutrophil percentage, median (IQR), %	73.8 (61.7, 80.8)	77.7 (66.1, 86.0)	68.9 (58.4, 78.7)	0.021
Lymphocyte percentage, median (IQR), %	19.1 (12.2, 28.4)	14.4 (10.5, 24.1)	20.0 (13.9, 32.4)	0.017
Immunotherapy				
Time to first line immunotherapy initiation, median (IQR), days	15.0 (9.0, 29.5)	16.0 (9.5, 29.5)	12.0 (9.0, 28.0)	0.768
Time to second line immunotherapy initiation, median (IQR), days	30.0 (18.0, 48.5)	28.0 (18.5, 48.5)	30.0 (17.0, 46.0)	0.666

Abbreviations: NMDAR, N-methyl-D-aspartate receptor; mRS, modified Rankin Scale; IQR, interquartile range; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; Q_{Alb}, albumin-CSF/serum-quotient; SD, standard deviation.

Table 4 Multivariable Regression Analysis: Predictors of Anti-NMDAR Encephalitis Patients' Short-Term Prognosis

	B	SE	OR (95% CI)	*P* value
Oligoclonal bands	1.319	0.660	3.741 (1.026–13.637)	0.046
Disturbance of consciousness	2.441	0.751	11.481 (2.633–50.057)	0.001
Movement disorders	0.852	0.722	2.345 (0.570–9.648)	0.237
CSF protein	0.001	0.001	1.001 (0.998–1.003)	0.594
Neutrophil percentage	0.033	0.085	1.034 (0.876–1.220)	0.693
Lymphocyte percentage	0.051	0.102	1.052 (0.861–1.285)	0.619
Pulmonary infection	0.593	0.736	1.809 (0.428–7.651)	0.421
Urinary tract infection	0.339	1.221	1.403 (0.128–15.374)	0.781
Age	0.010	0.024	1.010 (0.963–1.059)	0.677

Abbreviations: NMDAR, N-methyl-D-aspartate receptor; CSF, cerebrospinal fluid; B, beta coefficient; SE, standard error; OR, odds ratio; CI, confidence interval.

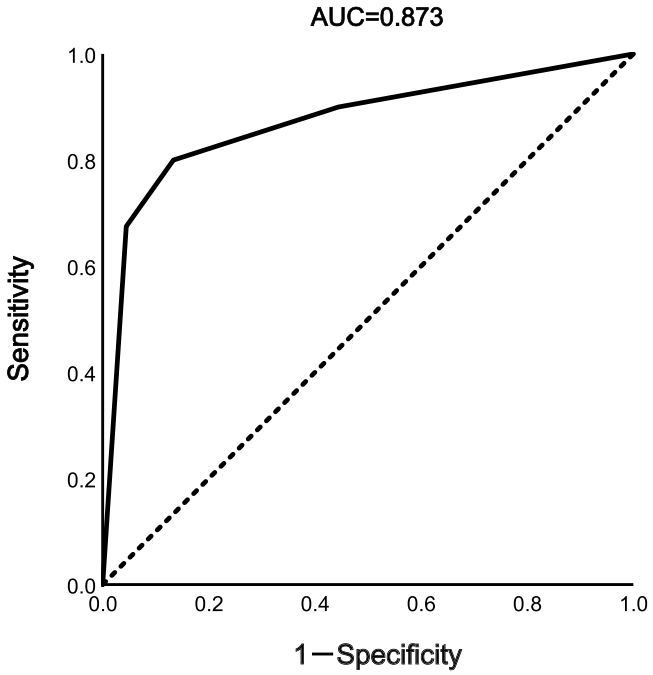

Figure 4 Receiver operating characteristic (ROC) curve for predicting the value of oligoclonal bands and disturbances of consciousness in evaluating the prognosis of anti-NMDAR encephalitis.
Abbreviation: AUC, area under the curve.

Discussion

Anti-NMDAR encephalitis is the most prevalent among autoimmune encephalitides, which are potentially life-threatening.[13,14] Early evaluation of disease status and prognosis, combined with timely therapeutic interventions, can help minimize disability and enhance outcomes.[15,16] Nevertheless, specific prognostic biomarkers to measure disease severity and predict outcomes in anti-NMDAR encephalitis are still lacking.[17] OCBs are regarded as markers of chronic immune activation within the CNS and are commonly detected in some chronic inflammatory diseases.[18,19] Notably, the presence of OCBs has been reported as a prognostic indicator in several neurological disorders, including autoimmune encephalitis, MS, and radiologically isolated syndrome (RIS).[10,20–22] These findings indicate that OCBs may contribute to the pathogenesis and progression of anti-NMDAR encephalitis, offering potential as an indicator for evaluating disease severity and forecasting clinical outcomes.

Positive OCBs have been reported in 50–70% among anti-NMDAR encephalitis patients.[7–9,23] In this research, 47 (55.3%) patients exhibited positive OCBs, aligning with prior research findings. Our investigation demonstrated a significant correlation between OCBs and CSF protein levels, with OCB-positive patients showing markedly higher CSF protein concentrations compared to their OCB-negative counterparts. This observation can be attributed to the fact that the presence of OCBs is linked to increased blood-brain barrier (BBB) permeability,[24] which may lead to elevated CSF protein levels.[25] In anti-NMDAR encephalitis, NMDA receptor activation mediates the disruption of BBB permeability through the Rho/ROCK signaling pathway.[26] The detection of OCBs in the CSF is mainly due to this enhanced BBB permeability,[24] which facilitates the transudation of plasma proteins into the CSF compartment. Moreover, our research revealed that OCB-positive patients exhibited elevated neutrophil percentage and a lower lymphocyte percentage in peripheral blood compared to OCB-negative patients, likely reflecting a more heightened neuroinflammatory state in the OCB-positive group. Prior research has demonstrated that the severity of anti-NMDAR encephalitis correlates positively with neutrophil counts and negatively with lymphocyte counts.[27] These results indicate that OCBs may act as an indicator of neuroinflammation and BBB disruption, potentially clarifying their link to poorer clinical outcomes in anti-NMDAR encephalitis. Together, these results underscore the involvement of OCBs in the pathophysiology of the disease, linking immune dysregulation, BBB impairment, and disease severity.

Furthermore, our study indicated that OCB-positive patients displayed a more common incidence of abnormal MRI findings than OCB-negative patients. This observation aligns with findings in other neuroinflammatory conditions, such as MS, one research found that OCB positivity has been linked to increased cortical lesions and intrathecal inflammation.[28] Another study showed that among MS patients, OCB positivity was linked to the number of periventricular lesions.[29] The presence of OCBs may indicate a chronic inflammatory state in the CSF,[30,31] potentially contributing to an increased incidence of cortical lesions and more severe clinical manifestations in OCB-positive groups. These findings are consistent with our observations that OCB-positive patients showed a greater tendency to display severe clinical manifestations in anti-NMDAR encephalitis, including severe seizure type, disturbance of consciousness, and movement disorders. Our results align with prior research indicating that OCB positivity is associated with more severe clinical features in autoimmune encephalitis.[10,20] Prior studies have shown that OCBs detected at disease onset in anti-NMDAR encephalitis patients are connected to a more severe disease course, resulting in ICU admission, severe seizure type, and worse clinical outcomes.[32] Our results further underscore this connection, revealing that OCB-positive patients had an elevated risk of ICU admission. In addition to this observed association with severe seizure types, the implications of refractory epilepsy are particularly important. Studies report that a subset of anti-NMDAR encephalitis patients develop seizures poorly responsive to first-line immunotherapy or antiepileptic drugs, often necessitating second-line immunotherapies or prolonged ICU support,[33,34] these patients frequently experience prolonged disease courses, delayed recovery, and greater long-term disability. Collectively, these observations imply that the presence of OCBs may assist in recognizing individuals at increased risk of severe disease manifestations, including refractory epilepsy, thereby underscoring the potential role of OCBs in informing early clinical decisions and interventions aimed at mitigating poor outcomes.

A significant finding is that anti-NMDAR encephalitis patients with positive OCBs showed increased disease severity and worse outcomes, demonstrated by elevated mRS and CASE scores at admission, discharge, 12 months post-discharge, and last follow-up assessments. These findings highlight that OCB-positive patients consistently demonstrated more severe initial symptoms, slower recovery, and poorer functional outcomes compared to their OCB-negative counterparts. This analysis reveals that OCB positivity is related to heightened inflammatory responses and greater central nervous system involvement, which contribute to poorer clinical outcomes.

In this research, the OCB-positive patients exhibited a significantly higher mRS score at discharge than OCB-negative patients ($P<0.001$). To further investigate predictors of short-term prognosis in anti-NMDAR encephalitis, we performed multivariable regression analysis. Based on disease severity, patients were stratified into two groups: a mild-moderate group (mRS<3) and a severe group (mRS≥3).

The results of our multivariable regression analysis indicated that the presence of OCBs and disturbance of consciousness were independent risk factors for unfavorable prognosis in anti-NMDAR encephalitis patients. ROC analysis demonstrated that the AUC values for OCBs and disturbance of consciousness in predicting prognosis were 0.873, indicating its good reference value. These results suggest that OCBs and disturbances of consciousness were identified as potential indicators of poor prognosis, highlighting their potential clinical utility in risk stratification and guiding treatment decisions for anti-NMDAR encephalitis patients. Previous researches have demonstrated that the presence of OCBs may be related to increased disease severity and worse outcomes in some neurological disorders. For instance, in autoimmune encephalitis, OCB positivity was markedly related to a reduced likelihood of achieving good clinical outcomes relative to those who were OCB-negative.[10] In patients with MOGAD, those who were OCB-positive faced a greater risk of relapse, especially within the first year.[35] In individuals with MS, the presence of OCBs in the CSF was correlated with a higher risk of poor prognosis.[36–38] OCBs indicate a sustained intrathecal humoral immune response, reflect clonal B-cell expansion within the CNS.[39] Thus, the presence of OCBs in anti-NMDAR encephalitis may arise from sustained and prolonged antigen exposure within the CNS, driving a persistent immunological response. This ongoing immune activation exacerbates neuroinflammation, leading to increased BBB permeability, neuronal injury, and cortical dysfunction, ultimately contributing to more severe neurological deficits. Consequently, in anti-NMDAR encephalitis, OCBs could serve as an early biomarker of disease severity, aiding clinicians in identifying patients who may require more intensive therapeutic interventions and closer monitoring.

Limitations

There are certain limitations that need to be addressed in our study. Firstly, the retrospective design employed may introduce selection bias. Therefore, further validation of the findings through larger-scale prospective cohort studies is necessary. Secondly, the underlying mechanism linking OCBs to the severity of anti-NMDAR encephalitis remains unclear, requiring future research to clarify it.

Conclusion

In conclusion, our results suggest that the detection of OCBs in CSF is linked to more severe clinical symptoms, a more aggressive disease progression, and poorer prognostic outcomes in anti-NMDAR encephalitis patients. OCB-positive patients showed an increased likelihood of severe symptoms, ICU admission, and worse functional outcomes. These findings highlight the potential value of OCBs as a biomarker for assessing disease severity and predicting prognosis in anti-NMDAR encephalitis.

Acknowledgments

The authors would like to thank the participants and their families.

Funding

This study was supported by the National Natural Science Foundation of China (82060236, 82460254) and the Natural Science Foundation of Guangxi Province (CN) (2023GXNSFAA026247).

Disclosure

The authors report no conflicts of interest in this work.

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