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ORIGINAL COMMUNICATION

Clinical characteristics and outcomes between children and adults with anti-N-Methyl-D-Aspartate receptor encephalitis

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Abstract Anti-N-Methyl-D-Aspartate receptor (NMDAR) encephalitis is an acute neurological disorder affecting children and adults. We aimed to compare the clinical characteristics, treatments, and outcomes between children and adults with anti-NMDAR encephalitis and to assess the probable risk factors. In this observational study, patients who tested positive for anti-NMDAR antibody in the cerebrospinal fluid were enrolled. The patients were divided into children and adults group on the basis of age (whether <16 or not). Clinical outcomes were assessed at onset, 1, 3, 6, 9, and 12 months after the patients received treatment and were scored based on whether they required hospitalization and intensive care. A total of 15 children and 14 adults were examined. The adults more likely manifested status epilepticus, central hypoventilation, and pneumonia but less likely exhibited movement disorder than the children did. All of the patients were subjected to corticosteroid treatment, 11 children and 9 adults were treated with intravenous immunoglobulin, and only the adults received plasma exchange or cyclophosphamide. The children recovered faster than the adults, especially in the first 6 months. Risk factors included age, status epilepticus, changes in consciousness, central hypoventilation, and pneumonia. Adults exhibit worse outcomes than children mostly because of status epilepticus.

Keywords Anti-NMDAR encephalitis · Children · Adults · Prognosis · Status epilepticus

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Introduction

Anti-N-Methyl-D-Aspartate receptor (NMDAR) encephalitis is an acute form of encephalitis caused by an autoimmune reaction. The major symptoms of this disease include abnormal behavior, speech dysfunction, seizure, movement disorder, decreased consciousness level, and autonomic dysfunction [1]. Symptoms can be alleviated by first-line treatments, including corticosteroid, plasma exchange, and immunoglobulin, and second-line treatments, including cyclophosphamide and rituximab [2].

Since it was first described in 2007 [3], anti-NMDAR encephalitis has been extensively investigated because of its high incidence and potential lethality [4]. Besides adults, this disease also affects children [5, 6]. The spectrum of symptoms changes on the basis of age [5], but differences in EEG, MRI, and outcomes between children and adults with anti-NMDAR encephalitis remain unclear. This study aimed to report the clinical data from 15 children and 14 adults with anti-NMDAR encephalitis, compare their outcomes, and discuss the probable risk factors.

Methods

NMDAR antibody testing

The NMDAR antibody was tested in patients' CSF and serum. Positive test was defined when the materials fulfilled both criteria: (1) specific staining against the NMDAR with substrates including rats' hippocampus and cerebellum. (2) Positive cell-based assay with HEK293 cells transfected with NR1.

Patients

Patients with acute onset of neurological or psychiatric symptoms of unknown etiology were considered eligible for this study if they presented anti-NMDAR (+) in the cerebrospinal fluid (CSF) from January 2012 to December 2015. Patients were included in the children's group if they aged less than 16 years. Written consent was obtained from all of the patients.

Clinical data collection

Symptoms, CSF, EEG, and MRI data were collected. Symptoms were divided into six categories [1]: (1) abnormal behavior or cognitive dysfunction, (2) speech dysfunction, (3) seizure, (4) movement disorder, (5) decreased consciousness level, and (6) autonomic dysfunction. A symptom observed at onset was regarded as the first symptom. The first CSF, EEG, and MRI data were considered. Therapeutic regimens were also recorded. First-line treatments were corticosteroid, intravenous immunoglobulin, and plasma exchange. Second-line treatment was cyclophosphamide.

Outcome assessments

Clinical outcomes were assessed through inpatient or outpatient service, at onset, 1, 3, 6, 9, and 12 months after the treatments were administered. The outcomes were grouped into four stages on the basis of their hospitalization or intensive care needs [7]: (1) Stage 1, recover completely; (2) Stage 2, mild psychiatric symptom or movement disorder without affecting normal life; (3) Stage 3, severe psychiatric symptom, movement disorder, or uncontrollable epileptic seizure; and (4) Stage 4, coma and status epilepticus.

Statistical analysis

Data were statistically analyzed using IBM SPSS Statistics 22. Skewness and Kurtosis coefficient were used to evaluate whether the quantitative data met a normal distribution. Data were considered as normal distribution if both Skewness and Kurtosis coefficient <1. For the data did not fit this criterion, we used Mann–Whitney test to evaluate the significance. Others were compared by t test or Fisher's exact test. The factors affecting the outcomes were assessed through Spearman analysis. Kaplan–Meier estimates of the proportion of the patients who left Stage 4 or reached Stage 2 through a 12-month follow-up were calculated.

Results

Clinical characteristics

We examined 15 children and 14 adults. Of the total number of patients, 17 patients were followed up for 12 months. Patients who failed to be followed up by inpatient or outpatient service had complicated reasons, which were confirmed by telephone counseling subsequently: two patients or their relatives thought the residual symptoms were too mild to be outpatient; five patients choose local medical institutions for further treatment because of the distance; three patients were worried about the costs; and two patients were lost. The average ages of children and adults were 7.7 and 28.3 years, respectively. Trends in gender were not evident in the two groups (Table 1).

The patients in the two groups developed a similar spectrum of first symptoms. Most patients manifested seizure (40 % in children and 14 % in adult) or psychiatric symptoms (47 % in children and 78 % in adult) at onset. Other first symptoms included movement disorder in two children and speech dysfunction in one adult. Fever was observed in six adults in the early stage of the disease. Fever was more frequently detected in adults than in children ($P = 0.035$, Table 1).

Psychiatric behavior was the most common symptom documented in the whole follow-up period and accounted for approximately 96 %. This symptom was followed by seizure, change in consciousness, speech dysfunction, movement disorder, central hypoventilation, and status epilepticus, which were 83, 66, 45, 45, 45, and 41 % of all cases, respectively (Table 1). The occurrence of status epilepticus was significantly higher in the adults than in the children ($P = 0.025$), but the occurrence of movement disorder was significantly lower in the adults than in the children ($P = 0.025$). Central hypoventilation ($P = 0.065$) and pneumonia ($P = 0.025$) also were detected more frequently in the adults than in the children. As such, the affected adults, especially those with status epilepticus, needed a breathing machine support (Table 1; Fig. 1).

Auxiliary examinations

The CSF did not remarkably differ between the two groups, except the protein ($P = 0.035$) and glucose ($P = 0.048$) levels were higher in the adult group. Abnormal EEG results were obtained in 97 % of the cases, mostly with diffuse slowing. A typical δ brush was observed in five children and seven adults ($P = 0.462$). Spike or sharp waves were detected in eight patients ($P = 1.000$). Likewise, abnormal MRI was found in 34 % patients, including four children and six adults ($P = 0.420$), with FLAIR

Table 1 Overview of clinical data of patients based on age distribution

	Children ($n = 15$)	Adults ($n = 14$)	P
Sex (male/female)	8/7	6/8	0.715
Age	7.7 ± 3.02	28.3 ± 11.12	0.001
Onset symptom			
Seizure (yes/no)	6/9	2/12	0.215
Psychiatric behave (yes/no)	7/8	11/3	0.128
Movement disorder (yes/no)	2/13	0/14	0.483
Fever (yes/no)	1/14	6/8	0.035
Others (yes/no)	0/15	1/13	1.000
Involved symptom			
Seisure (yes/no)	12/3	12/2	1.000
Status epilepticus (yes/no)	3/12	9/5	0.025
Psychiatric behave (yes/no)	15/0	13/1	0.483
Speech dysfunction (yes/no)	8/7	5/9	0.426
Movement disorder (yes/no)	10/5	3/11	0.025
Consciousness changed (yes/no)	8/7	11/3	0.245
Central hypoventilation (yes/no)	4/11	9/5	0.066
Pneumonia (yes/no)	5/10	11/3	0.025
Lumbar puncture			
Pressure (abnormal/normal)	3/12	6/8	0.245
Cell count ($\times 10^6$/L)[a]	3.9 ± 5.21	3.8 ± 7.40	0.325
Protein (mg/L)	171.9 ± 47.49	242.5 ± 107.80	0.035
Glucose (mg/L)[a]	3.8 ± 0.73	4.5 ± 1.10	0.048
Anti-NMDA			
Cerebrospinal fluid (positive/negative)	15/0	14/0	1.000
Serum (positive/negative)	11/4	12/2	1.000
EEG			
δ Brush (yes/no)	5/10	7/7	0.462
Spike wave (yes/no)	4/11	4/10	1.000
MRI			
Total (yes/no)	4/11	6/8	0.450
White matter involved (yes/no)	2/13	4/10	0.390
Gray matter involved (yes/no)	2/13	2/12	1.000
Immunotherapy			
Starting time (days from onset)	21.5 ± 12.07	24.9 ± 17.82	0.391
Corticosteroids (yes/no)	15/0	14/0	1.000
Immunoglobulins (yes/no)	11/4	9/5	0.700
Plasma exchange (yes/no)	0/15	6/8	0.006
Second-line drugs (yes/no)	0/15	6/8	0.006
Anti-epileptic drug (single/combine)	11/1	2/10	0.001
Antipsychotic drug (single/combine)	4/6	4/4	1.000

[a] The significance of these data was calculated by Mann–Whitney test

hyperintensities in lobes, basal ganglia, or white matter (Table 1; Fig. 2).

Treatments and outcomes

All of the patients were subjected to corticosteroid treatment ($P = 1.000$), 11 children and 9 adults were given intravenous immunoglobulin ($P = 0.700$), 6 adults were treated with plasma exchange ($P = 0.006$), and 6 adults were administered with cyclophosphamide ($P = 0.006$). The average intervals between clinical presentation and treatment were 21.5 and 24.9 days for children and adults, respectively ($P = 0.391$). Anti-epileptic and antipsychotic drugs were used on the basis of patients' symptoms. The

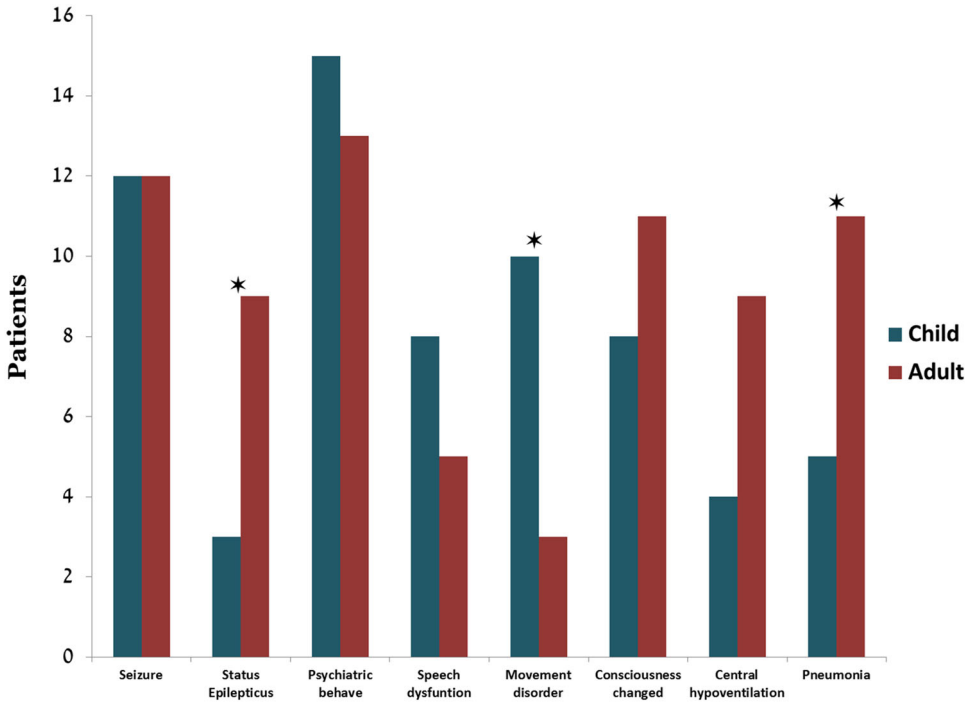

Fig. 1 Spectrum of symptoms during follow-up on the basis of age distribution. *A significant difference between children and adults ($P < 0.05$). The most common symptoms during the whole follow-up was psychiatric behavior, followed by seizure, altered consciousness, speech dysfunction, movement disorder, central hypoventilation, and status epilepticus. Adults more frequently suffered from status epilepticus and pneumonia but less frequently experienced movement disorder than children did

adults more likely received two or more anti-epileptic drugs to control seizure than the children did ($P = 0.001$, Table 1).

At baseline, four children and ten adults were in stage 4, and no patients reached stage 2. In the last follow-up, nine children and six adults reached stage 2, and no patients were still in stage 4. However, five children and seven adults were missing during follow-up. The adults were more critical at onset than the children ($P = 0.027$). And the adults also experienced difficulty in recovering from such condition in the first 3 months to a greater extent than the children. The children more likely to get clinical remission (reaching stage 2) in the 6th month ($P = 0.002$) than the adults did, but no difference was observed between the two groups in the final observation ($P = 0.466$) (Table 2; Fig. 3). The factors associated with leaving stage 4 were age ($P = 0.012$), status epilepticus ($P = 0.000$), altered consciousness ($P = 0.000$), central hypoventilation ($P = 0.000$), and pneumonia ($P = 0.002$). The factors associated with reaching stage 2 were age ($P = 0.043$), altered consciousness ($P = 0.023$), and pneumonia ($P = 0.005$) (Table 3). Further correlations with status epilepticus were detected by Spearman test, but the results revealed negative (Table 4).

The children recovered faster but received no plasma exchange and cyclophosphamide. As such, we verified whether plasma exchange or cyclophosphamide affected adults' outcomes. After analyzing the remitted frequency with Kaplan–Meier curves, we concluded that plasma exchange or cyclophosphamide can influence the outcomes, including the time to leave stage 4 ($P_{\text{plasma}} = 0.475$, $P_{\text{cyclophosphamide}} = 0.857$) and reach stage 2 ($P_{\text{plasma}} = 0.364$, $P_{\text{cyclophosphamide}} = 0.911$) (Fig. 4).

Discussions

A multi-institutional study, including clinical data from 577 patients with anti-NMDAR encephalitis, indicated that symptoms' presentation varies between children and adults. Adults are more likely to experience memory deficit and central hypoventilation but less likely to manifest speech disorder, movement disorder, cerebellar ataxia, and hemiparesis than children do. Most patients develop seizure during observation [5], but they do not present significant changes between children and adults. In our study, the clinical presentations were similar to those described in the previous study. The main difference was that our study compared the frequency of status epilepticus between children and adults. The higher ratio of status epilepticus in adults than in children possibly explained why more adults suffered from central hypoventilation [8] or pneumonia [9] than children did.

The overall auxiliary examination presented no remarkable change. This finding indicated that EEG and MRI findings were poorly low specific. Delta brush is a well-characterized EEG change in patients with anti-NMDAR encephalitis [10], particularly those with accompanying status epilepticus [11]. Nevertheless, other studies have concluded that a significantly higher beta/delta

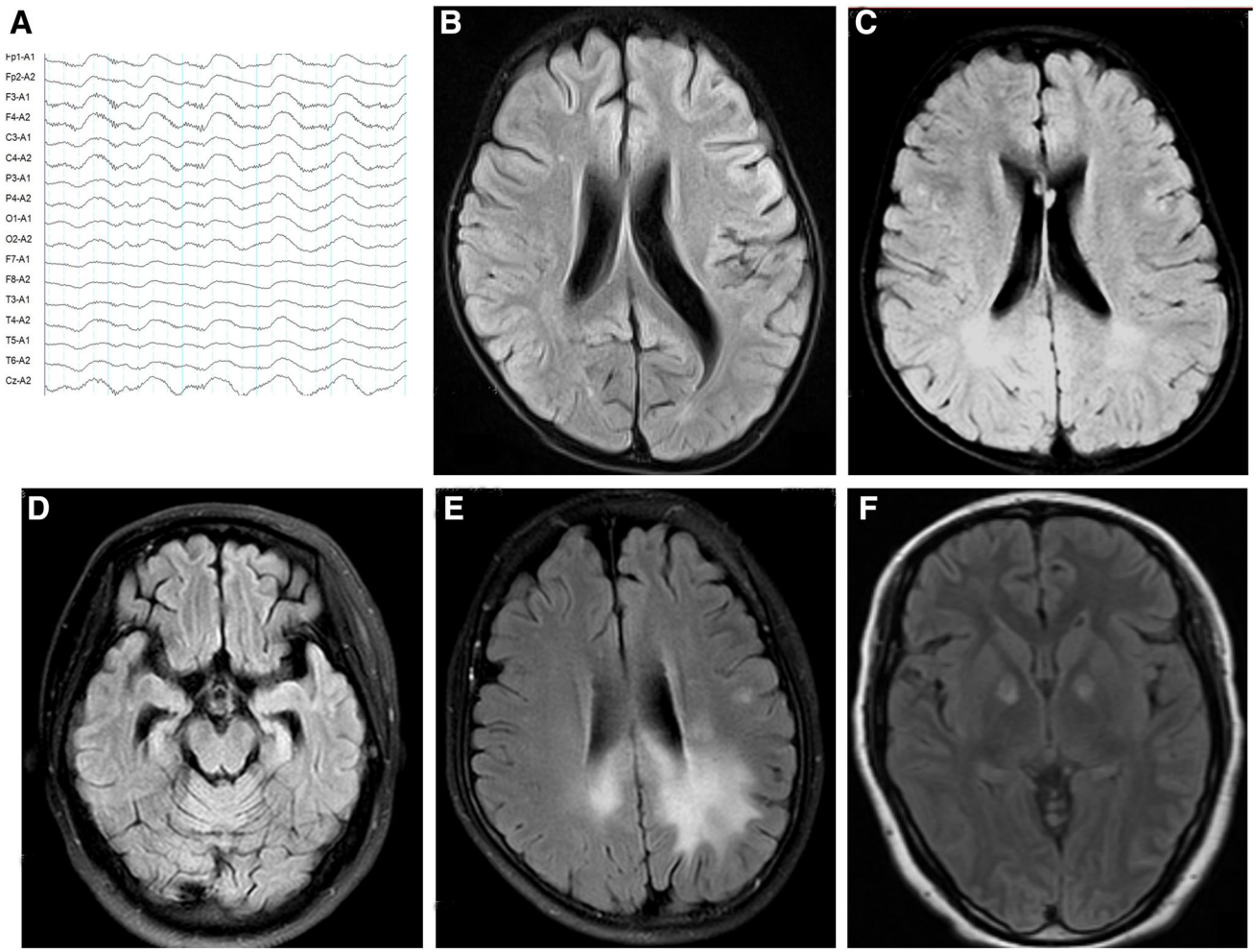

Fig. 2 EEG and MRI data of patients with anti-NMDAR encephalitis. **a**, **d** EEG and MRI data from a 26-year-old female patient with slurred speech and seizure. EEG presented a gradually descending δ brush. MRI presented an atrophy of bilateral hippocampus. **b**, **c** MRI data from a 5-year-old female patient with movement disorder. A long focal T2 abnormality in the left middle frontal gyrus was observed (**b**) but disappeared after the patient was treated with corticosteroid and immunoglobulin (**c**). **e** MRI data from a 34-year-old female patient with memory dysfunction and calculation. Diffuse abnormality was presented in the white matter of the left parietal lobe. **f** MRI data from a 27-year-old female patient with status epilepticus and teratoma. Symmetrical masses were presented in the bilateral pallidum

Table 2 The outcomes between two groups based on followed-up month

Months	Stay in stage 4			Reach stage 2		
	Children	Adult	*P*	Children	Adult	*P*
0	4 (26.7 %)	10 (71.4 %)	0.027	0 (0 %)	0 (0 %)	1.000
1	1 (6.7 %)	8 (57.1 %)	0.005	5 (33.3 %)	3 (21.4 %)	0.682
3	0 (0 %)	4 (28.6 %)	0.042	10 (66.7 %)	3 (21.4 %)	0.025
6	0 (0 %)	1 (10.0 %)	0.483	14 (93.3 %)	5 (50.0 %)	0.002
9	0 (0 %)	0 (0 %)	1.000	12 (92.3 %)	6 (85.7 %)	0.060
12	0 (0 %)	0 (0 %)	1.000	9 (90.0 %)	6 (85.7 %)	0.466

power ratio is more powerful than delta brush alone in distinguishing anti-NMDAR encephalitis from other forms of encephalitis [12]. Occasionally abnormal MRI findings have been reported. However, these findings lack specificity because hippocampus, white matter, basal ganglia, and even spinal cord can be involved [6, 13, 14].

Previous studies preferred the use of modified Rankin score (mRS) to evaluate the outcomes of patients with anti-

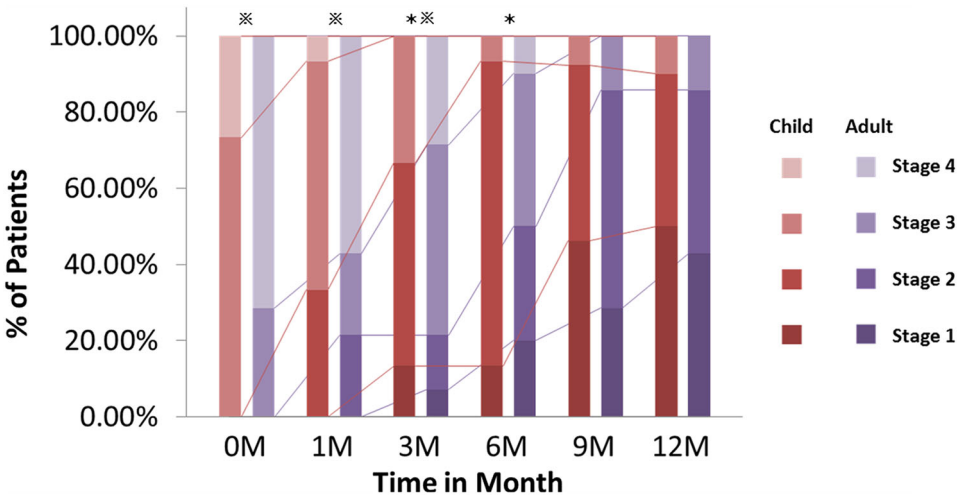

Fig. 3 Outcomes of children and adults during follow-up. ※A significant difference was observed in the ratio of children and adults who stayed in stage 4. ∗A significant difference was found in the ratio of children and adults who reached stage 2

Table 3 Spearman analysis of factors associated with outcomes

	Leave stage 4			Reach stage 2		
	Median time/month	|ρ|	*P*	Median time/month	|ρ|	*P*
Age (child/adult)	0 vs 2	0.477	0.012	3 vs 7.5	0.407	0.043
Sex (male/female)	0 vs 0	0.005	0.979	3 vs 4.5	0.114	0.587
Seisure (yes/no)	0 vs 0	0.207	0.299	3 vs 4.5	0.070	0.740
Status epilepticus (yes/no)	3 vs 0	0.815	0.000	9 vs 3	0.368	0.070
Psychiatric behave (yes/no)	No data	–	–	No data	–	–
Speech dysfunction (yes/no)	1 vs 0	0.134	0.506	6 vs 3	0.125	0.578
Movement disorder (yes/no)	0 vs 0	0.508	0.774	6 vs 3	0.217	0.298
Consciousness changed (yes/no)	1 vs 0	0.654	0.000	6 vs 3	0.454	0.023
Central hypoventilation (yes/no)	3 vs 0	0.653	0.000	6 vs 3	0.208	0.319
Pneumonia (yes/no)	1 vs 0	0.558	0.002	6 vs 3	0.548	0.005

NMDAR encephalitis [2, 15, 16]. Nevertheless, this scale fails to cover all stages of anti-NMDAR encephalitis and to indicate the specific treatment needed by patients. For instance, patients with mRS 5 may be in coma or status epilepticus and require life support in intensive care unit (ICU) or they exhibit severe psychiatric behavior and need care in a psychiatric department. Similarly, patients with mild movement disorder and needing outpatient care may be scored from 1 to 3. Thus, stages 1–4 were used to evaluate patients' outcomes on the basis of treatment status: in ICU, inpatient, or outpatient. The percentages of patients staying in stage 4 (mostly needing care in ICU) and reaching stage 2 (mostly needing outpatient care) were used to compare the outcomes between children and adults.

A previous study compared 14 children and 63 adults and found that children recover faster than adults do, which were similar to our results [2]. Our results also revealed that the number of adults in stage 4 was higher than that of children at onset. This phenomenon might have resulted from the higher percentage of adults with status epilepticus. The children recovered faster, especially in the first 6 months of follow-up, regardless of the percentage of patients leaving stage 4 or reaching stage 2. The adults exhibited a similar outcome in the 12th month partly because some patients underwent a short follow-up.

Quantity studies have focused on decisions regarding the type, time from disease onset to immunotherapy, and instance to facilitate a second-line immunotherapy [2, 5, 15]. Decisions are typically based on symptoms, therapeutic responses, doctors' experiences, or patients' preferences. As such, optimum treatments are not easily determined. In our study, only adults received plasma exchange or cyclophosphamide partly because of the severity of the symptoms in adults' initial episodes. Consequently, the relationship between drug use and

Table 4 The correlation with SE by Spearman test

	Child				Adult				Total			
	SE	NSE	|ρ|	*P*	SE	NSE	|ρ|	*P*	SE	NSE	|ρ|	*P*
Protein level in CSF (mg/L)	184.0 ± 67.12	168.6 ± 44.44	0.303	0.293	216.6 ± 92.31	283.9 ± 128.31	0.254	0.403	207.7 ± 84.25	204.6 ± 93.57	0.111	0.580
MRI (positive/negative)	1/2	3/9	0.075	0.789	3/6	3/2	0.258	0.373	4/8	6/11	0.020	0.917
Anti-NMDA antibody in serum (positive/negative)	3/0	8/4	0.302	0.275	7/2	5/0	0.304	0.290	5/7	13/4	0.353	0.060

SE status epilepticus, *NSE* non-status epilepticus, *CSF* cerebrospinal fluid

outcomes in the two groups was also difficult to evaluate. However, after comparing the outcomes between adults treated and untreated with plasma exchange or cyclophosphamide through a Kaplan–Meier curve, we observed that the total rate of recovery in 12 months might not significantly differ. Combining with our Kaplan–Meier survival curve and previous study [5], which indicated that both the first- and second-line immunotherapy result in improvement of patients with anti-NMDAR encephalitis, it's considered that both plasma exchange and cyclophosphamide therapy might not result in worse outcomes for adults. As a result, other factors, like elder, status epilepticus, consciousness changed, central hypoventilation, and pneumonia, were seen as more crucial for outcomes.

The risk factors of poor outcomes have altered the treatment approach. A study indicated that no need for admission to an intensive care unit predicts a good outcome [5], but data are insufficient and thus impeded the analysis of factors determining whether these patients require intensive care. Patients with severe and life-threatening illnesses, such as intractable status epilepticus and severe pneumonia, are admitted to ICU. After assessing the factors through Spearman analysis, we found that probable risk factors included status epilepticus, altered consciousness, pneumonia, central hypoventilation, and age ≥16 years. However, adult patients aged ≥16 years were more likely accompanied with four other risk factors than children (Table 1), thus discussing how to deal with patients' age was nonsensical. Moreover, patients with status epilepticus were more likely to accompany with decreasing levels of consciousness and pneumonia [17, 18], as a result, how to terminal status epilepticus was particularly important for adults with anti-NMDAR encephalitis.

Few studies have reported the treatment and outcome of patients with anti-NMDAR encephalitis and status epilepticus [11, 19–28] (Table 5). Combined with our data, we found that almost every patient received second-line immunotherapy, but these patients still required a long time to recover. Furthermore, two patients suffered from remissions after they were subjected to vagus nerve stimulation [21] or epileptic focus removal [23]. The selection of anti-epileptic drugs is vague, and guidelines are incomplete. In conclusion, treatments should be further validated to obtain additional evidence.

There were some limitations in this study. First, we only included 15 children and 14 adults for statistic calculation, which might be limited to some extent. On this account, we used Skewness and Kurtosis coefficient to evaluate whether the quantitative data met a normal distribution, and Mann–Whitney test was used if the data did not fit this criterion. Based on the existing data, we believed Spearman analysis might be more suitable to

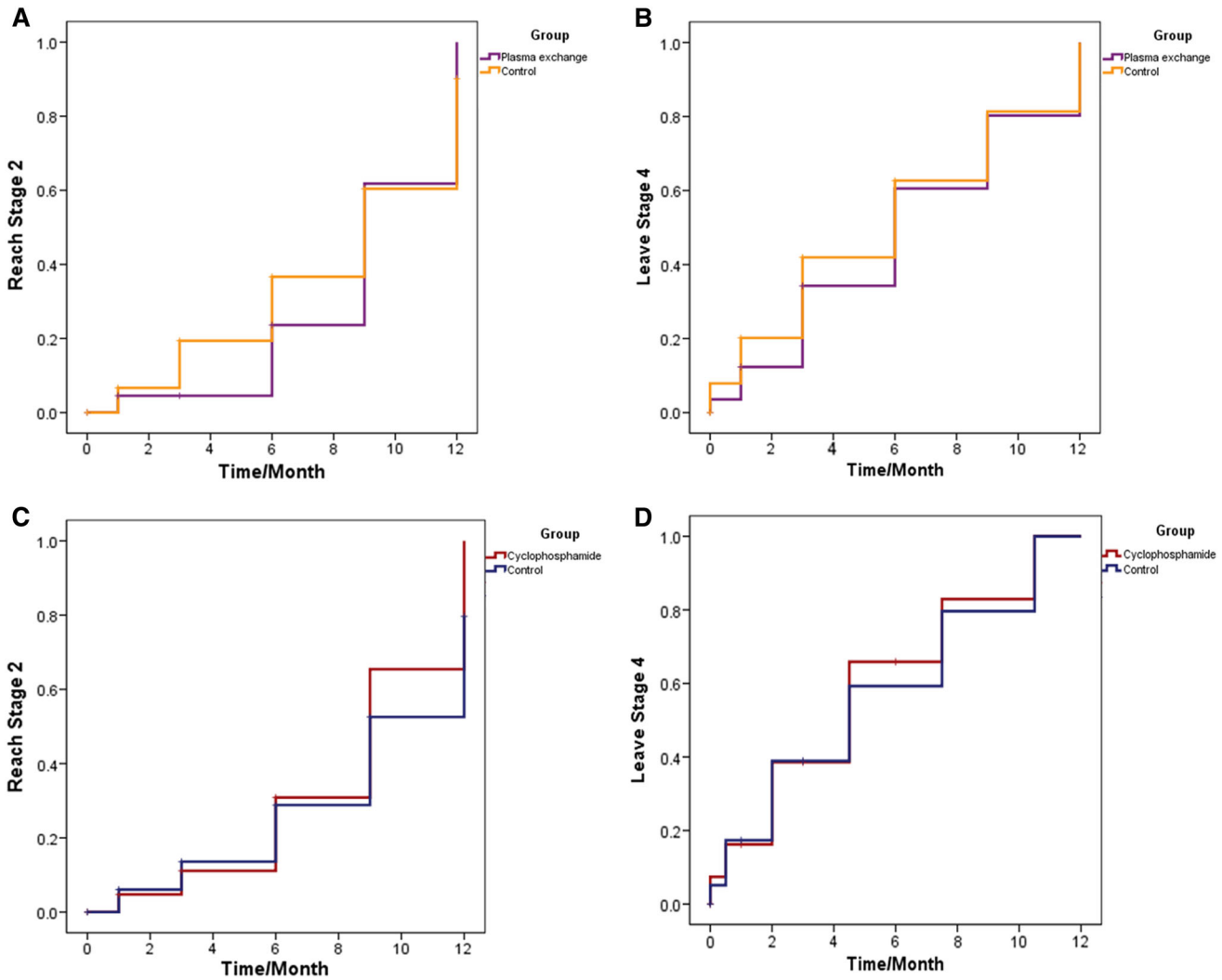

Fig. 4 Assessment of the effect of plasma exchange and cyclophosphamide for adults with anti-NMDAR encephalitis through Kaplan–Meier curve. **a** Kaplan–Meier cumulative estimates of the rate of patients reaching stage 2 with or without plasma exchange ($P = 0.364$). **b** Kaplan–Meier cumulative estimates of the rate of patients leaving stage 4 with or without plasma exchange ($P = 0.475$). **c** Kaplan–Meier cumulative estimates of the rate of patients reaching stage 2 with or without cyclophosphamide ($P = 0.911$). **d** Kaplan–Meier cumulative estimates of the rate of patients leaving stage 4 with or without cyclophosphamide ($P = 0.857$)

evaluation of the correlations between factors and outcomes, as is a nonparametric measure of rank correlation [29]. Second, the result of outcomes between children and adult had its limits, as 12 patients failed to be followed up through inpatient or outpatient service at last, but there was a trend towards positive correlation between adults and worse outcomes, especially in the first 6 months. Third, our study failed to establish the efficacy of each individual treatment, as decisions are typically based on clinical status, therapeutic responses, doctors' experiences, or patients' preferences. According to our Kaplan–Meier survival curve and previous study [5], it's assumed that treatment might not play crucial roles for outcomes in this study, and further randomized trials are needed to verify.

Conclusions

Adults are more likely to experience fever at onset accompanied with status epilepticus, altered consciousness, and pneumonia during the course of disease than children with anti-NMDAR encephalitis do. The overall auxiliary examination presents no remarkable change between two

Table 5 Detail of cases with status epilepticus and anti-NMDA receptor encephalitis

Sex	Age	Type of SE	Therapy		Time/condition to recover	References
			Immunoregulation	AEDs		
Female	21M	Convulsive	Glucocorticoid, Immunoglobulin, Rituximab	Lorazepam, Levetiracetam, Phenobarbital, Phenytoin	5 Months	[20]
Male	34Y	Non-convulsive	Glucocorticoid, Immunoglobulin	Lorazepam, Phenytoin, Valproate, Topiramate	4 Months	[11]
Female	28Y	Non-convulsive	Glucocorticoid, Immunoglobulin, Rituximab, Cyclophosphamide, Surgery	Thiopental, Levetiracetam, Phenytoin, Phenobarbital, Lamotrigine	18 Months	[19]
Male	46Y	Convulsive, non-convulsive	Glucocorticoid, Immunoglobulin, Vagus nerve stimulation	Phenytoin, Levetiracetam, Midazolam, Propofol, Phenobarbital, Topiramate, Valproate	After vagus nerve stimulation	[21]
Female	48Y	Non-convulsive	Glucocorticoid, Immunoglobulin, Plasma exchange, Rituximab, Cyclophosphamide	Midazolam, Propofol	7 Months	[22]
Male	7Y	Convulsive	Glucocorticoid, Immunoglobulin, Plasma exchange, Rituximab	Midazolam, Propofol, Phenobarbital, Valproate, Thiopental, Levetiracetam, Vigabatrin, Carbamazepine, Lamotrigine	After epileptic focus removed	[23]
Male	30Y	Convulsive	Glucocorticoid, Immunoglobulin, Plasma exchange, Azathioprine	Midazolam, Propofol, Diazepam, Valproate	12 Months	[24]
Male	17Y	Convulsive	Glucocorticoid, Immunoglobulin	Phenytoin, Phenobarbital, Valproate, Thiopental, Midazolam	12 Months	[25]
Male	63Y	Convulsive	Glucocorticoid, Immunoglobulin	Phenytoin, Valproate, Levetiracetam	36 Months	[26]
Female	21Y	Convulsive	Glucocorticoid, Immunoglobulin	Phenytoin, Phenytoin, Levetiracetam, Diazepam	18 Months	[26]
Female	9Y	Non-convulsive	Glucocorticoid, Immunoglobulin, Rituximab	Lorazepam, Levetiracetam, Fosphenytoin, Phenobarbital	12 Months	[27]
Female	19Y	Non-convulsive	Immunoglobulin, Plasma exchange, Rituximab	Lorazepam, Propofol, Diazepam, Phenytoin, Levetiracetam, Valproate, Oxcarbazepine	10 Months	[28]

groups. Moreover, our study detects a probable poor prognosis of adult, especially in the first 6 months, and highlights promptly that manner of status epilepticus is essential to maximize adults' living quality.

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Compliance with ethical standards

Conflicts of interest None.

Ethical standards This study was conducted in compliance with the ethical standards.

Informed consent Written consents were obtained from the patients.

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