**Long-term outcome and relapse of anti-NMDAR encephalitis——a cohort study in western China**

**Table e-1. Comparison between male and female in patients with anti-NMDAR encephalitis.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Number of patients (percentage) | |  |
|  | Female, n (%)  128 | Male, n (%)  116 | p-value |
| **Age, median (IQR)** | 30.8 (21.7-38.0) | 24.5 (18.0-35.0) | **0.001a** |
| Ethnicity | | | **0.05b** |
| Han nationality | 128 (100) | 112 (96.5) |
| Minority | 0 (0) | 4 (3.4) |
| Location | | | **0.01c** |
| Rural | 53 (41.4) | 72 (62.1) |
| Urban | 75 (58.6) | 44 (37.9) |
| Symptoms | | |  |
| Fever | 47 (36.7) | 48 (41.4) | 0.45c |
| Headache | 42 (32.8) | 47 (40.5) | 0.21 c |
| Ataxia | 4 (3.1) | 2 (5.2) | 0.68 d |
| Limb weakness | 7 (5.5) | 6 (5.2) | 0.91c |
| Limb numbness | 2 (1.6) | 1 (0.9) | 1.0 d |
| Cognitive disorder | 79 (61.7) | 82 (70.7) | 0.24 c |
| Dizziness | 7 (5.5) | 10 (8.6) | 0.33 c |
| Disturbance of consciousness | 47 (36.7) | 53 (45.7) | 0.15 c |
| Speech disturbance | 35 (27.3) | 25 (21.6) | 0.29 c |
| Dyskinesias and movement disorders | 54 (42.2) | 44 (37.9) | 0.46 c |
| Sleep disorders | 48 (37.5) | 44 (37.9) | 0.94 c |
| **Seizures** | 91 (71.1) | 95 (81.9) | **0.04** c |
| Focal onset | 49 (38.3) | 42 (36.2) | 0.70 c |
| Generalized onset | 75 (58.6) | 80 (69.0) | 0.10 c |
| Epileptic state | 40 (31.3) | 33 (28.4) | 0.60 c |
| Psychosis | 119 (93.0) | 103 (88.8) | 0.25 c |
| Mania | 56 (43.8) | 50 (43.1) | 0.91 c |
| Depression | 13 (10.2) | 14 (12.1) | 0.63 c |
| Hallucinations | 111 (86.7) | 92 (79.3) | 0.12 c |
| Autonomic dysfunction≥1 of the following | 59 (46.1) | 59 (50.9) | 0.46 c |
| Hyperhidrosis | 55 (43.0) | 59 (50.9) | 0.22 c |
| Tachycardia | 35 (27.3) | 26 (22.4) | 0.37 c |
| Urinary retention or hesitation | 26 (20.3) | 30 (25.9) | 0.30 c |
| Hyponatremia | 22 (17.2) | 16 (13.8) | 0.46 c |
| Central hypoventilation | 18 (14.1) | 23 (19.8) | 0.22 c |
| Admission to the ICU | 18 (14.1) | 17 (14.7) | 0.89 c |
| **Tumor** | 36 (28.1) | 2 (1.7) | **0.001**d |
| Auxiliary examinations | | |  |
| **Abnormal MRI** | 46 (35.9) | 58 (50.0) | **0.02** c |
| Abnormal EEG | 101 (78.9) | 87 (75.0) | 0.47 c |
| **Abnormal CSF** | 52 (40.6) | 68 (58.6) | **0.005** c |
| Treatment | | | 0.04 d |
| No treatment | 2 (1.6) | 8 (6.9) |
| IVIg alone | 46 (35.9) | 34 (29.3) |
| IVMP alone | 11 (8.6) | 18 (15.5) |
| IVIg combined IVMP | 69 (53.9) | 56 (48.3) |
| ≥3 different immune therapies at first | 12 (9.4) | 10 (8.6) | 0.83 c |
| mRS admission, median (IQR) | 4 (4-5) | 4 (3-5) | 0.86 a |
| Length of hospital stay (days), median (IQR) | 24 (16-30) | 22 (13-30) | 0.31 a |
| Poor response to treatment at week four | 15 (11.7) | 22 (19.0) | 0.11 c |

a Mann–Whitney U test

b Fisher’s exact test.

c Pearson’s Chi-square test.

d Chi-squared tests with continuity correction. Abbreviations: ICU, intensive care unit; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; EEG, electroencephalogram. Measurement data are expressed as median (IQR) according to the non-normality of distribution.

**Table e-2. Multivariable analysis of independent predictors for long-term worse functional outcome (mRS: 3-6) in patients with NMADR encephalitis**.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | B | SE | Wald | df | P-value | OR | 95%CI |
| Disturbance of consciousness | 1.06 | 0.42 | 6.41 | 1 | 0.01 | 2.91 | 1.27-6.65 |
| Epileptic state | 0.63 | 0.40 | 2.44 | 1 | 0.12 | 1.88 | 0.85-4.12 |
| Central hypoventilation | 0.59 | 0.46 | 1.68 | 1 | 0.19 | 1.81 | 0.73-4.48 |
| Abnormal WBC (\*10^6/L) | 0.70 | 0.41 | 2.94 | 1 | 0.08 | 2.02 | 0.90-4.52 |

Abbreviations: WBC, white blood cell; OR, odd ratio, mRS, modified Rankin Scale score.

**Table e-3. Clinical data in 39 patients with relapsing anti-NMDAR encephalitis both at onset and at relapse.**

|  |  |  |
| --- | --- | --- |
|  | First event (onset) | Second event  (first relapse) |
| Initial presentations | | |
| Psychogenic (n, %) | 27 (69.2%) | 21 (53.8%) |
| Seizure (n, %) | 11 (28.2%) | 7 (17.9%) |
| Other (n, %) | 1 (2.5%) | 11 (28.2%) |
| Clinical accumulate symptoms | | |
| Fever (n, %) | 14 (35.9%) | 4 (10.2%) |
| Headache (n, %) | 12 (30.7%) | 3 (7.7%) |
| Ataxia (n, %) | 2 (5.1%) | 0 (0.0%) |
| Limb weakness (n, %) | 3 (7.7%) | 1 (2.5%) |
| Cognitive disorder (n, %) | 28 (71.8%) | 6 (15.4%) |
| Dizziness (n, %) | 2 (5.1%) | 2 (5.1%) |
| Disturbance of consciousness (n, %) | 14 (35.9%) | 2 (5.1%) |
| Speech disturbance (n, %) | 7 (17.9%) | 6 (15.4) |
| Dyskinesias and movement disorders (n, %) | 17 (43.6%) | 1 (2.5%) |
| Sleep disorders (n, %) | 15 (38.4%) | 9 (23.1%) |
| Seizures (n, %) | 28 (71.8%) | 14 (35.9%) |
| Focal onset (n, %) | 17 (43.6%) | 6 (15.4%) |
| Generalized onset (n, %) | 23 (58.9%) | 12 (30.7%) |
| Epileptic state (n, %) | 13 (33.3%) | 1 (2.5%) |
| Psychosis (n, %) | 36 (92.3%) | 24 (61.5%) |
| Mania (n, %) | 8 (20.5%) | 5 (12.8%) |
| Depression (n, %) | 7 (17.9%) | 1 (2.5%) |
| Hallucinations (n, %) | 32 (82.1%) | 22 (56.4%) |
| Autonomic dysfunction, ≥1 of the following (n, %) | 16 (41.0%) | 4 (10.2%) |
| Hyperhidrosis (n, %) | 16 (41.0%) | 3 (7.7%) |
| Tachycardia (n, %) | 9 (23.1%) | 2 (5.1%) |
| Urinary retention or hesitation (n, %) | 9 (23.1%) | 3 (7.7%) |
| Hyponatremia (n, %) | 5 (12.8%) | 0 (0%) |
| Central hypoventilation (n, %) | 3 (7.7%) | 1 (2.5%) |
| ICU admission (n, %) | 7 (17.9%) | 1 (2.5%) |
| Initial status at onset (mRS) | | |
| mRS 1 (n, %) | 0 (0%) | 2 (5.1%) |
| mRS 2 (n, %) | 2 (5.1%) | 25 (64.1%) |
| mRS 3 (n, %) | 13 (33.3%) | 8 (20.5%) |
| mRS 4 (n, %) | 12 (30.7%) | 2 (5.1%) |
| mRS 5 (n, %) | 12 (30.7%) | 2 (5.1%) |

**Table e-4. The summary of main ancillary tests results.**

|  |  |  |  |
| --- | --- | --- | --- |
| MRI lesion location at onset | Total | Male | Female |
|  | N=244 | N=116 | N=128 |
|  | Number (percentage) | | |
| Total with abnormal findings | 103 (42.21) | 58 | 46 |
| Hippocampi and Insular regions | 34 (13.93) | 16 | 18 |
| Cerebral cortex | 45 (18.44) | 20 | 25 |
| Thalamus | 7 (2.86) | 4 | 3 |
| Deep white matter | 10 (4.09) | 3 | 7 |
| Brainstem | 4 (1.64) | 1 | 3 |
| Basal ganglia | 9 (3.69) | 5 | 4 |
| Other mild atypical MRI findings**\*** (could not have a clinicopathologic significance) | |  |  |
| Meninges enhancement | 12 (4.91) | 8 | 4 |
| Enlarged temporal horns of the lateral ventricles | 3 (1.23) | 2 | 1 |
| Pituitary lesions | 2 (0.82) | 2 | 0 |
| Non-specific periventricular white matter lesions | 7 (2.87) | 6 | 1 |
| EEG | |  |  |
| Total with abnormal findings | 188 (77.04) | 87 | 101 |
| Epileptic discharges | 52 (21.31) | 24 | 28 |
| Slow activity | 178 (72.95) | 82 | 96 |
| CSF analysis | Number of patients with abnormal findings | Median (range) | |
| Intracranial open pressure (mmH2O) | 64 (26.23) | 150 (30-260) | |
| WBC (×10 6 /L) | 124 (50.82) | 9 (0-860) | |
| Protein (g/L) | 66 (27.05) | 0.29 (0.25-0.43) | |
| Glucose (mmol/L) | 0 | 3.59 (2.5-5.3) | |
| Chloride (mmol/L) | 0 | 125 (100-133) | |
| QIgG, (IgG CSF/IgG serum) | 43 (19.36) | 1.685 (0-208) | |

Abbreviations: MRI, magnetic resonance imaging; EEG, electroencephalogram; CSF, cerebrospinal fluid; WBC, white blood cell; QIgG, IgG Synthesis Rate.

**e-Figure legend 1.** **The factors predictive of survival from first relapse were verified by Cox proportional hazard analysis and present as a forest plot.** HR, hazard ratio; CI, confidence interval; ICU, intensive care unit; mRS, modified Rankin Scale; MRI, magnetic resonance imaging; EEG, electroencephalogram; CSF, cerebrospinal fluid.

**e-Figure legend 2.** **Kaplan-Meier curves show the frequency of relapse-free disease in 244 patients with anti-NMDAR encephalitis.**

The plots show that neither non-tumor (A) nor no-treatment (B) or patients with more than three different immune therapies (C) at first onset was associated with reported relapse frequency statistically.