Clinical comparison and analysis of rapid and slow recovery in acute motor axonal neuropathy

Li Jie[1,a],Chen Dong[2,b,*],

[1]Shanghai Dianji University, Department of Mechanical Engineering, No. 300 Shuǐhuá Road, Shūyuàn Town, Pudong New Area, 200120, China,
[2]Fujian Business University, Department of Accounting, No. 19 Huangpu, Gulou District, Fuzhou City, 350000, China,
a.lijie0921@sina.com,b.dong_chen@163.com
***Corresponding Author**

Abstract: Objective: To compare and analyze the clinical and neurophysiological characteristics of rapidly and slowly recovering acute motor axonal neuropathy (AMAN) patients. Methods: Clinical data of 50 AMAN patients treated at our hospital were collected. Patients with a Hughes score of ≥3 during the peak of the illness were included in the slow recovery group, and those with a score of <3 were included in the rapid recovery group. The clinical and electrophysiological characteristics of the two groups were retrospectively analyzed and compared. Results: A total of 27 patients were included in the slow recovery group, and 23 in the rapid recovery group. The slow recovery group had a Hughes score of 4-6 at the peak of the illness, older age at onset, more frequent preceding diarrhea, involvement of the bulbar muscles, complete limb paralysis, and respiratory muscle involvement requiring mechanical ventilation. The rapid recovery group had a Hughes score of 2-4 at the peak of the illness, younger age at onset, milder clinical symptoms, milder limb paralysis, and frequent limb numbness. Electromyography characteristics of AMAN: The sensory nerve action potential (SNAP) and sensory nerve conduction velocity (SCV) were normal. The distal motor latency (DML) and motor nerve conduction velocity (MCV) of the median nerve, ulnar nerve, and tibial nerve were all within the normal range; the peroneal nerve DML was higher than the normal value ($P<0.05$), while MCV was lower than the normal value ($P<0.05$), but there was no statistically significant difference between the two groups. The compound muscle action potential (CMAP) amplitude began to decrease within the first week, and the CMAP amplitude of the median nerve, ulnar nerve, and peroneal nerve, except for the tibial nerve, was lower in the slow recovery group than in the rapid recovery group (all $P<0.05$). The F-wave latency ratio of each motor nerve in AMAN patients was reduced, and the rate of unobtainable F-waves in the upper limb ulnar nerve and lower limb tibial nerve was higher in the slow recovery group than in the rapid recovery group (all $P<0.05$). Conclusion: AMAN is characterized by pure motor nerve involvement, normal sensory nerves, axonal damage to motor nerves, and associated conduction block. The lower the motor nerve CMAP amplitude and the higher the proportion of unobtainable F-waves, the slower the recovery and the poorer the prognosis.

Keywords: Guillain-Barré Syndrome; Acute Motor Axonal Neuropathy; Compound Muscle Action Potential Amplitude; Conduction Block

1. Introduction

Acute motor axonal neuropathy (AMAN) is an important subtype of Guillain-Barré syndrome (GBS), which is an acute inflammatory peripheral neuropathy mediated by immune responses following infections. It primarily involves the degeneration of spinal nerve roots and motor fiber axons, and clinically manifests as acute or subacute onset of symmetrical flaccid quadriplegia. In severe cases, it can lead to respiratory muscle paralysis, with about 10% to 20% of patients dying from acute complications or leaving sequelae [1]. Previously, it was thought that patients with MAN had slow recovery and even residual limb functional disabilities, with poor prognosis. However, a subset of AMAN patients in clinical practice can recover rapidly.

https://doi.org/10.62852/css/2024/1

2. Materials and methods

2.1. General information

A total of 50 cases of AMAN admitted to our hospital from January 2012 to December 2018 were included, all of which met the diagnostic criteria for AMAN in the "Chinese Guidelines for the Diagnosis and Treatment of Guillain-Barré Syndrome" (2010 edition) [2]. The clinical symptoms during the peak of the illness (defined as the period when the patient's limb strength was at its worst or when mechanical ventilation was initiated) were scored using the Hughes scale [3]. All 50 AMAN patients were treated with intravenous immunoglobulin (0.4g/kg) for 5 days, and methylprednisolone pulse therapy (500mg/day) for one week. The Hughes score was reassessed after two weeks. Patients with a Hughes score ≥3 were included in the slow recovery group, and those with a Hughes score <3 were included in the rapid recovery group.

2.2. Methods

Collect basic information such as patient gender, age, and clinical symptoms. All patients underwent lumbar puncture for cerebrospinal fluid examination between 7 to 14 days after onset of the disease; the first neurophysiological examination was conducted within 5 to 10 days of the onset, measuring parameters including sensory nerve conduction velocity (SCV), sensory nerve action potential (SNAP), motor nerve conduction velocity (MCV), distal motor latency (DML), compound muscle action potential (CMAP) amplitude; and the appearance rate of F-waves. Neurophysiological results were compared with the age-matched normal values from the Electrophysiology Laboratory of Peking Union Medical College Hospital to determine if there were any abnormalities.

3. Results

3.1. Clinical features

Among the 50 AMAN patients, 27 were included in the slow recovery group, consisting of 17 males and 10 females; the average age was (51.37±12.43) years; the Hughes score during the peak of the illness ranged from 4 to 6, and the Hughes score two weeks later ranged from 3 to 6. Six cases (22.2%) had a cold within 2 weeks before the onset of the disease, and nine cases (33.3%) had diarrhea; five cases (18.5%) had a history of traumatic brain injury with subarachnoid hemorrhage or cerebral hemorrhage, and developed AMAN after the administration of monosialotetrahexosylganglioside during hospitalization; two cases (7.4%) had a history of minimally invasive surgery for lumbar spine fracture. Clinical manifestations included facial nerve palsy in nine cases (33.3%), bulbar involvement (manifested as slurred speech and coughing while drinking water, etc.) in six cases (22.2%), and sensory numbness in three cases (11.1%); among them, eight cases (29.6%) had respiratory muscle involvement requiring mechanical ventilation. There were three deaths (11.1%), all of which were associated with hyponatremia; the causes of death were cardiac arrest in one case, and respiratory failure with pulmonary infection in two cases. The rapid recovery group included 23 cases, consisting of nine males and 14 females; the average age was (42.50±15.27) years; the Hughes score during the peak of the illness ranged from 2 to 4, and the Hughes score two weeks later ranged from 1 to 2. Six cases (26.1%) had a cold before the onset of the disease, and four cases (17.4%) had diarrhea. Clinical manifestations included facial nerve palsy in three cases (13.0%), no bulbar involvement, and sensory numbness in eight cases (34.8%). Compared with the slow recovery group, the rapid recovery group had younger patients ($P<0.05$), less bulbar involvement, and more sensory numbness in the clinical manifestations (all $P<0.05$), see Table 1.

Table 1 Comparison of Clinical Characteristics between the Two Groups [(mean ± standard deviation) or number (%)]

Group	Number of Cases	Age/years	Cold History	Diarrhea History	Facial Nerve Paralysis	Bulbar Involvement	Sensory Numbness
Slow Recovery Group	27	51.37±12.43	6(22.2)	9(33.3)	9(33.3)	6(22.2)	3(11.1)

https://doi.org/10.62852/css/2024/1

Fast Recovery Group	23	42.50±15.27	6(26.2)	4(17.4)	3(13.0)	0	8(34.8)
P-value		0.038	0.409	0.420	0.215	0.032	0.011

3.2. Results of auxiliary examinations

In this group of 50 AMAN patients, 45 underwent lumbar puncture examination. The cerebrospinal fluid (CSF) test results showed that all patients exhibited the phenomenon of albuminocytological dissociation (CSF protein >0.45g/L, immunoglobulin >33.5mg/L, cell count <10 cells/μL). In the slow recovery group, the CSF protein was (1.03±0.47) g/L, and the immunoglobulin was (220.42±178.60) mg/L. In the rapid recovery group, the CSF protein was (0.98±0.68) g/L, and the immunoglobulin was (133.20±105.78) mg/L. The differences between the two groups were not statistically significant (all P>0.05).

Electromyography (EMG) test results indicate that AMAN involves only motor nerves, with sensory nerves unaffected (normal SNAP amplitude and SCV). In the slow recovery group, the SNAP values for median nerve I, median nerve III, ulnar nerve, peroneal nerve, superficial peroneal nerve, and tibial nerve were (14.98±7.01) mV, (10.78±5.54) mV, (8.90±4.63) mV, (14.85±8.67) mV, (13.76±12.21) mV, and (2.62±1.03) mV, respectively. In the rapid recovery group, the SNAP values for the aforementioned nerves were (15.62±6.56) mV, (12.78±5.71) mV, (11.13±4.50) mV, (18.61±10.73) mV, (13.43±10.50) mV, and (9.12±11.69) mV, respectively. Both groups had normal SNAP values (the normal values for SNAP of the aforementioned nerves are: >10.0 mV, >7.0 mV, >7.0 mV, >10.0 mV, >4.0 mV, >13.0 mV), and there were no statistically significant differences between the groups (all P>0.05).

The slow recovery group's median nerve I, median nerve III, ulnar nerve, peroneal nerve, superficial peroneal nerve, and tibial nerve had sensory conduction velocities (SCV) of (54.92±8.10) m/s, (56.54±8.05) m/s, (58.31±6.42) m/s, (54.38±6.87) m/s, (56.48±6.51) m/s, and (44.93±3.08) m/s, respectively. The rapid recovery group's SCV for the aforementioned nerves were (57.95±11.05) m/s, (58.20±7.46) m/s, (56.42±5.92) m/s, (53.12±6.06) m/s, (53.36±6.02) m/s, and (47.53±6.31) m/s, respectively. Both groups had normal SCV values (the normal values for SCV are: median nerve I, median nerve III, ulnar nerve, and peroneal nerve >50 m/s, superficial peroneal nerve >45 m/s, tibial nerve >40 m/s), and there were no statistically significant differences between the groups (all P>0.05).

Among the motor nerves, the distal motor latency (DML) and motor conduction velocity (MCV) of the ulnar nerve, median nerve, and tibial nerve were normal. The peroneal nerve DML was higher than the normal value (P<0.05), while the MCV was lower than the normal value (P<0.05). However, there were no statistically significant differences between the two groups, see Tables 2 and 3.

The compound muscle action potential (CMAP) amplitude of all motor nerves was lower than the normal value, and the CMAP amplitude of the median nerve, ulnar nerve, and peroneal nerve in the slow recovery group was lower than that in the rapid recovery group (all P<0.05), see Table 4.

The F-wave latency ratio of all motor nerves was reduced, and the non-elicitation rate of F-waves in the upper limb ulnar nerve and lower limb tibial nerve in the slow recovery group was higher than that in the rapid recovery group (all P<0.05), see Table 5.

Table 2 Comparison of Distal Motor Latency (DML) between the two groups (milliseconds, mean ± standard deviation)

Group	Number of Cases	Median Nerve	Ulnar Nerve	Peroneal Nerve	Tibial Nerve
Slow Recovery Group	27	3.96±0.72	2.95±0.58	5.05±1.34	5.04±1.15
Fast Recovery Group	23	3.63±0.77	3.07±0.94	4.97±1.54	4.73±0.96
P-value		>0.05	>0.05	>0.05	>0.05

https://doi.org/10.62852/css/2024/1

Table 3: Comparison of Motor Conduction Velocity (MCV) between the two groups (meters per second, mean ± standard deviation)

Group	Number of Cases	Median Nerve	Ulnar Nerve	Peroneal Nerve	Tibial Nerve
Slow Recovery Group	27	51.56±5.67	55.81±7.40	43.57±8.61	45.02±5.60
Fast Recovery Group	23	53.32±7.61	52.26±8.96	42.64±5.38	42.62±5.44
P-value		>0.05	>0.05	>0.05	>0.05

Table 4-1: Comparison of Distal Compound Muscle Action Potential (CMAP) Amplitudes between the two groups (millivolts, mean ± standard deviation)

Group	Number of Cases	Median Nerve	Ulnar Nerve	Peroneal Nerve	Tibial Nerve
Slow Recovery Group	27	1.64±2.16	1.87±2.51	1.52±1.54	2.42±2.81
Fast Recovery Group	23	4.18±4.05	3.45±3.26	2.33±2.12	3.21±2.87
P-value		0.000	0.032	0.047	0.093

Table 4-2: Comparison of Proximal Compound Muscle Action Potential (CMAP) Amplitudes between the two groups (millivolts, mean ± standard deviation)

Group	Number of Cases	Median Nerve	Ulnar Nerve	Peroneal Nerve	Tibial Nerve
Slow Recovery Group	27	1.31±1.71	1.65±2.48	1.23±1.22	1.93±2.34
Fast Recovery Group	23	3.68±3.74	2.83±3.07	1.96±1.83	1.99±1.84
P-value		0.000	0.048	0.05	0.337

Table 5: Comparison of F-Wave Non-Elicitation Rates between the two groups (number of cases, percentage)

Group	Number of Cases	Median Nerve	Ulnar Nerve	Tibial Nerve
Slow Recovery Group	27	11(40.7)	12(44.4)	17(63.0)
Fast Recovery Group	23	7(30.4)	4(17.4)	6(26.1)
P-value		0.647	0.006	0.021

4. Discussion

AMAN is a motor neuron axonal disorder characterized by Wallerian-like degeneration, uneven thickening and thinning, and axonal disruption, with myelin sheaths largely intact; it primarily affects the anterior roots of spinal nerves and peripheral motor nerve fibers [4]. The results of this study suggest that the slow recovery group had a Hughes score of 4-6 at the peak of the illness, were older in age, more commonly had diarrhea as a preceding infection, and presented with bulbar involvement, complete limb paralysis, and potential respiratory muscle involvement requiring mechanical ventilation. The rapid recovery group had a Hughes score of 2-4 at the peak of the illness, were younger in age, had milder clinical symptoms, milder limb paralysis, and often accompanied by limb numbness. Research indicates that the speed of recovery in AMAN depends on the proportion of reversible conduction block and axonal degeneration. At the onset of the disease, IgG deposits first on the axolemma of the Ranvier nodes, macrophages infiltrate the peraxonal space, and then form membrane attack complexes that activate complement, blocking sodium channels at the Ranvier nodes, leading to inactivation of sodium channels and impaired nerve impulse conduction [5,6].

https://doi.org/10.62852/css/2024/1

If the immune response ceases, the lesion manifests as a reversible conduction block, which is associated with rapidly recovering AMAN; if the immune response intensifies further, forming membrane attack complexes, calcium enters the axon, the cytoskeleton degrades, mitochondria are destroyed, cells swell, chromatin dissolves, ultimately leading to axonal damage and Wallerian-like degeneration, which is associated with slowly recovering AMAN and may leave residual limb functional disabilities [7,8].

A significant reduction in CMAP amplitude is a typical manifestation of axonal damage; the lower the CMAP amplitude, the more severe the condition of AMAN patients and the longer the recovery time. The results of this study suggest that the CMAP amplitude of AMAN patients begins to decrease within the first week, and except for the tibial nerve, the CMAP amplitudes of the median nerve, ulnar nerve, and peroneal nerve in the slow recovery group are all lower than those in the rapid recovery group (all $P<0.05$). Uncini et al. [11] showed that there are two patterns of CMAP amplitude recovery in AMAN patients: one is that the CMAP amplitude remains at a low level, which is closely related to severe degeneration and loss of motor nerve root axons; the other is a rapid increase in CMAP amplitude, where the reduction in CMAP amplitude is due to mild axonal dysfunction caused by reversible conduction block in motor nerves [12].

5. Results

In terms of electrophysiological examination, the motor conduction velocity (MCV) and distal motor latency (DML) of patients in both groups were within the normal range, but the DML of the peroneal nerve in the slow recovery group was higher than the normal value, and the MCV was lower than the normal value. Additionally, the compound muscle action potential (CMAP) amplitudes in the slow recovery group were generally lower than those in the rapid recovery group, indicating more severe axonal damage. The reduced F-wave elicitation rate also indicated more severe axonal damage in the slow recovery group.

6. References

[1] Satoshi Kuwabara. Guillain-Barré syndrome[J]. Curr Neurol Neurosci Rep, 2007, 7: 57-62.
[2] Chinese Medical Association Neurology Branch Neuromuscular Disease Group. Guidelines for the diagnosis and treatment of Guillain-Barré syndrome in China[J]. Chinese Journal of Neurology, 2010, 43: 583-586.
[3] Hughes RA, Hadden RD, Gregson NA, et al. Pathogenesis of Guillain-Barré syndrome[J]. J Neuroimmunol, 1999, 100: 74-97.
[4] Kaida K, Ariga T, Yu RK. Antiganglioside antibodies and their pathophysiological effects on Guillain-Barré syndrome and related disorders - a review[J]. Glycobiology, 2009, 19: 676-692.
[5] Susuki K, Rasband MN, Tohyama K, et al. Anti-GM1 antibodies cause complement-mediated disruption of sodium channel clusters in peripheral motor nerve fibers[J]. J Neurosci, 2007, 27: 3956-3967.
[6] Susuki K, Yuki N, Schafer DP, et al. Dysfunction of nodes of Ranvier: A mechanism for anti-ganglioside antibody-mediated neuropathies[J]. Exp Neurol, 2012, 233: 534-542.
[7] Kokubun N, Nishibayashi M, Uncini A, et al. Conduction block in acute motor axonal neuropathy[J]. Brain, 2010, 133: 2897-2908.
[8] Uncini A, Capasso M. Acute motor conduction block neuropathy followed by axonal degeneration and poor recovery[J]. Neurology, 2006, 67: 543.
[9] Hiraga A, Mori M, Ogawara K, et al. Recovery patterns and long-term prognosis for axonal Guillain-Barré syndrome[J]. J Neurol Neurosurg Psychiatry, 2005, 76: 719-722.
[10] Peedicayil S, Jose J, Gafoor VA, et al. Reversible conduction failure in acute motor axonal neuropathy[J]. Ann Indian Acad Neurol, 2014, 17: 142-143.
[11] Li Lin, Zhang Ru Shu. Analysis of electrophysiological and pathological characteristics of Han Chinese patients with Charcot-Marie-Tooth disease type X1[J]. Neural Injury and Functional Reconstruction, 2019, 14: 128-131.
[12] Uncini A, Manzoli C, Capasso M. Acute motor conduction block neuropathy at acute multifocal; motor neuropathy: an attempt at a nosological systematization[J]. Muscle Nerve, 2010, 41: 283-285.

https://doi.org/10.62852/css/2024/1