Clinical features and treatment of acute motor axonal neuropathy

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Abstract: This paper aims to investigate the clinical features and treatment of patients with acute motor axonal neuropathy (AMAN). The clinical data of 9 patients with AMAN treated in our hospital were retrospectively analyzed from prodromal infections, clinical features, neuroelectrophysiological examination, treatment and the scores of Hughes functional grading scale. Diarrhea was the most common prodromal infection, and weakness of four limbs and muscles atrophy acutely emerged. The patient's condition progressed rapidly. In these cases, therapy of immunoglobulin combined with methylprednisolone was effective. Therefore, early diagnosis and timely treating with immunoglobulin therapy are most important methods to improve the prognosis.

Keywords: Guillain-Barre syndrome; Electrophysiology; Immunotherapy

1. Introduction

Acute Motor Axonal Neuropathy (AMAN) is one of the main subtypes of Guillain-Barré Syndrome (GBS), with relatively independent immunopathological mechanisms and clinical characteristics. This study aims to analyze the clinical features of Acute Motor Axonal Neuropathy, explore its neuroelectrophysiological mechanisms, and discuss the principles of treatment, in order to provide clues for diagnosis and treatment in clinical practice.

2. clinical information

2.1. General information

This group of 9 patients were all diagnosed with Acute Motor Axonal Neuropathy (AMAN) and admitted for treatment in the Department of Neurology at Xuanwu Hospital, Capital Medical University, from February 2012 to August 2014, in accordance with the "Chinese Guidelines for the Diagnosis and Treatment of Guillain-Barré Syndrome" published in 2010; at the same time, patients with significant persistent asymmetric limb weakness, bladder or rectal dysfunction as the initial symptoms, persistent bladder or rectal dysfunction, cerebrospinal fluid mononuclear cell count >50×10⁶/L [0~8] ×10⁶/L, the presence of segmented nuclear leukocytes, and obvious sensory disturbance levels were excluded. There were 6 males and 3 females; ages ranged from 21 to 69 years old, with an average of (50.66±16.33) years old; 6 cases had an acute course, and 3 had a subacute course. Five cases had a definite history of infection 1-2 weeks before onset (2 cases of upper respiratory tract infection, 3 cases of diarrhea), and 3 cases had an unclear history of infection. All patients in this group had their first episode, with the peak time ranging from 5 days to 4 weeks, among which 5 cases had limb weakness as the initial symptom, showing weakness in both lower limbs or both upper limbs (2 cases), as well as weakness in a single lower limb (1 case); involvement of the glossopharyngeal and vagus nerves in 2 cases; peripheral sensory disturbance in 3 cases; muscle atrophy in 5 cases; physical examination revealed diminished or absent tendon reflexes, with 2 cases showing unilateral Babinski sign positivity; autonomic dysfunction in 2 cases; pain in both lower limbs in 2 cases; and respiratory muscle paralysis in 1 case.

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2.2. Auxiliary Inspection

Cerebrospinal fluid (CSF) and serological tests were performed on all 9 patients in this group after admission. Lumbar puncture for CSF examination was conducted, with pressures ranging from 80 to 160 mm H₂O \([1 \text{ mm H}_2\text{O} = 9.81 \times 10^{-3} \text{ kPa}, (80~180) \text{ mm H}_2\text{O}]\), white blood cell (WBC) count was \((0.13) \times 10^6/\text{L} \ ([0~6) \times 10^6/\text{L}]\), and protein quantification was 15 to 106 g/L \((<45 \text{ g/L})\); oligoclonal bands (OB) were weakly positive in 1 case. Both serum and CSF anti-ganglioside antibodies GM1 were negative in 3 cases.

Neuroelectrophysiological examination was conducted on all 9 patients in this group within 2 weeks after admission, testing the motor nerve conduction velocity (MNCV), distal latency (DL), and sensory nerve conduction velocity (SNCV) of the bilateral median nerves, ulnar nerves, common peroneal nerves, and tibial nerves, as well as the distal compound muscle action potential (CMAP), and the F-wave latency and occurrence rate of the ulnar and tibial nerves. The results showed that the amplitude of the compound muscle action potentials was reduced in all patients, with more than 2 distal nerve amplitudes below 80% of the lower limit of the normal value, and 3 patients exhibited sensory nerve conduction velocity and amplitude both below the normal values.

3. Results

After a definitive diagnosis, 3 patients in this group were treated with methylprednisolone 1g/day for continuous pulse therapy for 3 to 5 days, followed by a gradual reduction in dosage, and 3 patients received intravenous immunoglobulin 0.40g/(kg·day) for continuous treatment for 5 days; vitamin B1 \([0.10\text{g intramuscular injection (once a day) for 2 weeks}]\) and mecobalamin \([0.50\text{mg intramuscular injection (once a day) for 2 weeks}]\) were used as adjuvant therapies to nourish the nerves and support symptomatic treatment. The efficacy of the treatment was evaluated after 2 weeks based on the Hughes score [normal (0 points), mild symptoms and signs (1 point), able to walk independently (2 points), able to walk 5 meters with assistance (3 points), bedridden (4 points), requiring ventilator assistance (5 points), and death (6 points)] for all cases in this group. Patients with a score of ≥3 points had a poor prognosis, and those with a score of <3 points had a good prognosis. The Hughes score of the 9 patients in this group was \([3.00 (1.50, 3.00)]\) before treatment, and \([1 (1, 2)]\) after 2 weeks of treatment. The difference between pre- and post-treatment was statistically significant according to the rank sum test for non-normal distribution (SPSS 20.0 statistical software) \((Z=-2.296, P=0.022)\), among which 6 patients had reached a good level of neurological function deficit.

4. Analysis and Discussion

Guillain-Barré Syndrome (GBS) commonly presents as Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), and Acute Motor and Sensory Axonal Neuropathy (AMSAN), with Miller Fisher Syndrome (MFS) being less common. The clinical features of AMAN include severe illness, rapid onset of paralysis in all four limbs, potential involvement of respiratory muscles and cranial nerves, early onset of muscle atrophy, high rate of disability, and poor prognosis. Electrophysiological examination shows normal motor peripheral nerve conduction function, reduced distal compound muscle action potential amplitude, normal sensory peripheral nerve, and pathologically presents as axonal degeneration of motor peripheral nerves. Guillain-Barré Syndrome is a post-infectious disease, with about two-thirds of patients having symptoms of respiratory or gastrointestinal system infection before the onset of GBS. Studies have confirmed that AMAN is an immune disease secondary to Campylobacter jejuni enteritis. The pathogenesis is triggered by Campylobacter jejuni infection, which induces humoral immunity or autoimmune responses, leading to neurological dysfunction and GBS symptoms. At the same time, lipooligosaccharides on the outer membrane of Campylobacter jejuni can induce the production of anti-GM1 and anti-GD1a antibodies in peripheral nerves. Interaction with gangliosides and binding to the axolemma at the nodes of Ranvier leads to complement activation, followed by the formation of membrane attack complexes and the disappearance of voltage-gated sodium channels (VGSC), resulting in the detachment of myelin sheath next to the Ranvier nodes and nerve conduction blockage. Subsequently, macrophages clear the damaged axons, causing varying degrees of damage to motor nerve axons. Data show
that anti-ganglioside antibodies (GM1, GM1b, GD1a, and GalNAC-GD1a) can be detected in the serum of patients with AMAN. In this group, 5 patients had a history of diarrhea and upper respiratory tract infection before the onset of the disease, and 3 had an unclear history of infection, but 3 cases of anti-GM1 antibody tests were all negative. Although anti-ganglioside antibodies are involved in the pathogenesis of GBS, and some patients with AMAN have positive reactions to serum anti-GM1 and anti-GD1a-IgG antibodies, the role of this immunological indicator in diagnosis has not been determined. Generally speaking, the lower the titer of specific antibodies, the lower the negative predictive value of the test, so a negative result does not rule out the possibility of AMAN. In addition, the positive predictive value of the aforementioned anti-ganglioside antibodies has very limited clinical significance, as patients with multifocal motor neuropathy, Miller Fisher Syndrome, amyotrophic lateral sclerosis, and other diseases can also have positive reactions.

Patients with Acute Motor Axonal Neuropathy (AMAN) have a short duration from onset to hospital admission, with a progression phase that can last from a few days to 4 weeks, often reaching the peak of the condition early on. During the course of the disease, it almost exclusively affects motor nerves, with symptoms being relatively symmetrical. Sensory symptoms or signs are rare, and clinical involvement of cranial nerves is uncommon, with autonomic nerve involvement being rare and symptoms being mild, and occasional pain symptoms are observed. All 9 patients in this group exhibited progressive weakness in the upper and lower limbs (sometimes presenting only with lower limb weakness), with reduced or absent tendon reflexes, consistent with the clinical manifestations in the diagnostic criteria for Guillain-Barré Syndrome (GBS).

Electrophysiological manifestations of AMAN are characterized by axonal polyneuropathy without sensory deficits, but about 10% of patients have sensory symptoms, among which 3 cases had subjective peripheral sensory disturbances, possibly due to primary axonal degeneration leading to mild loss of peripheral myelin sheath. AMAN, as a polyneuropathy involving both motor and sensory axons, results in severe sensory deficits and reduced or absent sensory action potentials. Cranial nerve deficits in AMAN are less common than in Acute Inflammatory Demyelinating Polyneuropathy (AIDP), but autonomic dysfunction and pain symptoms and signs do exist. In this group, 2 cases had dysphagia due to damage to the posterior group of cranial nerves, and 2 cases had autonomic nerve damage and pain symptoms. The causes of pain in AMAN patients are diverse. In GBS patients, the density of peripheral nerve fibers in the distal limbs is reduced, which is related to the incidence or severity of pain but not to autonomic dysfunction. Generally speaking, the progression of AMAN is faster than that of AIDP, and the recovery period is longer due to axonal degeneration. Five patients in this group exhibited limb atrophy, which occurred between 20 days and 10 months after onset, with slow recovery; however, some patients can rapidly recover from severe limb weakness.

Cerebrospinal fluid (CSF) showing an increase in protein quantification with normal cell count, known as the protein-cell dissociation phenomenon, is a characteristic sign of Guillain-Barré Syndrome (GBS), but it is only seen in 64% of patients, so it is not a necessary condition for diagnosis. In this group, 4 cases exhibited the protein-cell dissociation phenomenon, with CSF cell counts below 50×10⁶/L, which can rule out the possibility of other diseases, such as leptomeningeal malignancies, lymphoma, cytomegalovirus polyradiculitis, human immunodeficiency virus (HIV) polyneuropathy, and poliomyelitis, etc. Nerve conduction tests can serve as an auxiliary diagnostic condition for GBS to differentiate between axonal and demyelinating subtypes. In this group, nerve conduction tests showed a decrease in motor potential amplitude (more than 80% below the normal lower limit), without demyelinating characteristics, and normal sensory nerve conduction velocity. Patients with AMAN may also exhibit transient conduction block or slowed conduction velocity, which recovers rapidly as the disease progresses, known as reversible conduction failure, possibly related to the damage of the Ranvier node conduction function by antiganglioside antibodies. In this group, electromyography of 3 patients suggested a slight decrease in sensory conduction velocity, but the main issue was axonal damage, while in acute motor-sensory axonal neuropathy, the sensory action potential is significantly reduced or absent. Therefore, sensory nerve examination helps to differentiate AMAN from acute motor-sensory axonal neuropathy. AMAN should be distinguished from multifocal motor neuropathy, myasthenia gravis (MG), polymyositis (PM), dermatomyositis, poliomyelitis, hypermagnesemia, porphyria, botulism, lead poisoning, or
organophosphate poisoning, among other diseases. Nerve conduction tests help differentiate polyneuropathy, myopathy, anterior horn cell lesions (poliomyelitis), and neuromuscular junction diseases. Currently, there is no consensus on whether AMAN should be treated with the same methods as acute inflammatory demyelinating polyneuropathy, but numerous clinical trials have confirmed that intravenous immunoglobulin and plasmapheresis are effective for GBS. Immunoglobulin is generally started within 2 weeks of onset, at a dose of 0.40g/(kg·day), for 5 consecutive days of treatment; plasmapheresis is divided into 5 sessions, completed within 2 weeks, with a total exchange volume of about 5 times the plasma volume. All 9 cases in this group were given symptomatic supportive treatment with mecobalamin and vitamin B₁, 3 cases were given immunoglobulin, and 3 cases were given methylprednisolone pulse therapy, among which 1 case showed stable and improved symptoms after combined treatment with immunoglobulin and methylprednisolone. Both plasmapheresis and intravenous immunoglobulin have multifaceted immunomodulatory effects; immunoglobulin can inhibit immune cell activation by binding to Fc receptors, allowing antiganglioside antibodies to bind to their neural targets or to locally activated complement [14]. The IgG-Fc glycosylation in the serum of GBS patients is related to the severity of the disease, thereby affecting the immunomodulatory effect of immunoglobulin; plasmapheresis can clear neurotoxic antibodies, complement factors, and other humoral inflammatory mediators [13]. The results of a small clinical study suggest that the clinical outcome of AMAN patients treated with plasmapheresis is better than that of immunoglobulin treatment [15], but the choice of treatment depends on patient or socioeconomic factors, such as the need for special equipment and high cost of plasmapheresis, making it difficult to widely apply. Moreover, plasmapheresis is difficult to implement in pediatric patients due to the large volume of blood exchange, which can cause cardiovascular autonomic dysfunction and requires enhanced nursing care. Clinical evidence shows that the therapeutic effect of immunoglobulin combined with methylprednisolone is not higher than that of immunoglobulin monotherapy, only achieving short-term effects [13]. AMAN patients often leave behind neurological deficits that severely affect their daily living activities and quality of life, such as muscle atrophy, inability to walk without assistance, and other functional impairments; neurological function improvement generally occurs in the first year after onset, and further improvement may still occur. Common neurological deficits mainly manifest as decreased muscle strength, sensory abnormalities, fatigue, or pain, and physical training has a good effect on the recovery of neurological function.

5. Conclusion

Acute Motor Axonal Neuropathy (AMAN) is the main subtype of Guillain-Barré Syndrome (GBS) in East Asian and South American populations. Although the immunopathological mechanisms of AMAN are currently understood and non-specific immunotherapy is effective for most patients, further research is still needed. This is essential for a better understanding of the disease, optimizing medical care for patients, and is crucial for the prevention or treatment of disease-related complications.

6. References


