Turk J Phys Med Rehab 2016;1(62):79-82
DOI: 10.5606/tftrd.2016.29584

Scientific Letter / Bilimsel Mektup

Hyperreflexia in acute motor axonal neuropathy

Akut motor aksonal nöropatide hiperrefleksi

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Received / *Geliş tarihi*: September 2015 Accepted / *Kabul tarihi*: September 2015

We observed hyperreflexia in the course of the motor axonal neuropathy form of Guillain-Barré syndrome (GBS). Herein, we would like comment on a rare case.

Acute motor axonal neuropathy (AMAN) is a type of GBS accompanied by peripheral axonal involvement where acute motor paralysis, loss of reflex or hyporeflexia, insignificant sensory loss, and albumino-cytologic disproportion in cerebrospinal fluid are seen with no demyelinating findings in electromyography (EMG).[1] Commonly known as acute inflammatory demyelinating polyneuropathy (AIDP), GBS's spectrum has expanded in recent years to include variants with unusual attributes. Types such as AMAN and acute motor or sensorial axonal neuropathy have also begun to be more understood. In AMAN, there is an axonal damage with underlying inflammation of the peripheral nerves without demyelination. In the underlying etiology, *Campylobacter jejuni*, cytomegalovirus, Epstein-Barr virus, influenza, mycoplasma, coxsackie virus, and hepatitis viruses, previous surgery, delivery, or some vaccinations are shown to be related causes.[2,3] Motor conduction studies of AMAN cases show that the compound muscle action potential (CMAP) amplitudes are significantly low. The activity of motor unit potential reduced by fibrillation and positive spike potentials reflecting intensive denervation are of interest in needle EMG in these cases.[4] An autoimmune attack is thought to be occurring against GM1 ganglioside in peripheral nerves. In several studies, immunoglobulin antibodies produced against GM1, GM1b, and GD1a gangliosides were obtained from serous fluids of cases and it was suggested that these antibodies were generated against the membrane liposaccharides of *Campylobacter jejuni*, showing cross-reactivity with gangliosides in the node of Ranvier. In this scenario, rapid recovery is usually seen within weeks, despite the axonal damage.[5-7] This letter presents a female case who was diagnosed with AMAN based on fulminant progressive weakness in her arms and legs. She responded to intravenous immunoglobulin (IVIG) treatment and maintained deep tendon reflexes during follow-up.

A 46-year-old woman was consulted in our outpatient clinic due to weakness in arms and legs and difficulty in walking and doing fine works with her hands for three days. Her medical history showed bloody diarrhea 10 days ago. On neurological examination, the muscle strength was 4/5 in the upper extremity proximal, 3/5 in the distal, 4/5 in the lower extremity proximal, and 2/5 in the distal. There was no bilateral reflex in the sole skin and deep tendon reflexes were increased in all extremities. Sensorial examination findings were unremarkable. She preserved thermo-algesic and proprioceptive sensitivity. No cerebellar signs, tremor, dysmetria or dysdiadochokinesia were detected. There were no meningeal signs either. Electromyography and cerebrospinal fluid (CSF) analysis findings were normal. It was thought to be a case of acute inflammatory neuropathy based on her medical history and clinical findings. 400 mg/kg intravenous immunoglobulin treatment was administered for five days in our clinic. Significant recovery was observed in motor weakness on the 10th day of treatment. The muscle strength was 4+/5 in the upper extremity proximal, 4/5 in the distal, 4+/5 in

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Cite this article as:
Kotan D. Hyperreflexia in acute motor axonal neuropathy. Turk J Phys Med Rehab 2016;62:79-82.

the lower extremity proximal, and 4/5 in the distal. Reflexes were hyperactive and there were no reflexes in the sole skin. The following laboratory test results were normal including complete blood count, blood sedimentation rate, blood glucose, serum electrolytes, urea, creatinine, serum protein content, cholesterol, triglycerides, and liver and muscle enzymes. The CSF analysis carried out 13 days later showed normal cells with increased protein values (63 g/dL; N: 15-45 g/dL). The intracranial pressure, glucose level, and cell values in the CSF were normal. Repeated EMG on the second week showed reduced CMAP amplitudes in motor conductions with normal nerve conduction (Table 1). Sensory conduction studies of the right median, ulnar, superficial and sural were normal. Median F responses were within normal ranges. Needle EMG showed spontaneous denervation activity and discreting motor unit potential activities. Our case was considered to be consistent with AMAN. The seroimmunological study of anti-glycolipid antibodies conducted by enzyme immunoassay showed the presence of immunoglobulin G antibodies against ganglioside GM1 at a titer of >1/1,000. Neuroimaging studies (cranial, cervical, and thoracolumbar MRI scans) produced normal results. Our case in the recovery period was scheduled for follow-up visits with monthly IVIG treatment and a physical therapy program.

Of note, the GBS classification is of utmost importance. Since the pathogenesis of each sub-type may be independent, it sometimes requires special treatment and follows different patterns. The GBS subtypes according to the electrodiagnostic criteria are AIDP, AMAN, and acute motor and sensory axonal neuropathy (AMSAN). Among sporadic cases of GBS, about 10 to 20% are of the AMAN type. Anti-ganglioside antibodies anti-GM1, GD1a, and GD1b are found in this group.[8] Miller-Fisher syndrome, a variant of GBS, is characterized by ophthalmoplegia, ataxia, and areflexia.[1,9] The most common form of GBS is AIDP and it is easily distinguished in electrophysiological studies based on demyelination findings. Although clinically it is similar to AMAN and AIDP, a distinction can be made through nerve conduction studies. There is a significant reduction in CMAP amplitudes and an increase in the refractor

Table 1. Electrophysiological studies showing significantly reduced compound muscle action protection amplitudes at the upper and lower extremities

Electromyography	Latency [ms]	Amplitude [mV]	Conduction rate [m/s]
Right median motor			
Abductor pollicis brevis-wrist	4.3	3.3	
Abductor pollicis brevis-elbow	8.65	2.9	52.9
Abductor pollicis brevis-axilla	13.15	2.9	50.0
Left median motor			
Abductor pollicis brevis-wrist	5.3	1.3	
Abductor pollicis brevis-elbow	9.8	1.3	51.1
Abductor pollicis brevis-axilla	14.0	1.0	54.8
Right ulnar motor			
Abductor digiti minimi-wrist	4.4	0.9	
Abductor digiti minimi-elbow	10.75	0.9	49.4
Abductor digiti minimi-axilla	14.90	0.8	53.0
Left ulnar motor			
Abductor digiti minimi-wrist	2.3	1.6	
Abductor digiti minimi-elbow	8.25	1.6	52.3
Abductor digiti minimi-axilla	12.35	1.6	58.2
Right peroneal nerve			
Extensor digitorum brevis-wrist	5.7	0.6	
Extensor digitorum brevis-head of the fibula	12.8	0.4	45.4
Extensor digitorum brevis-popliteal	14.55	0.4	45.7
Sol peroneal nerve			
Extensor digitorum brevis-wrist	5.8	0.6	
Extensor digitorum brevis-head of the fibula	13.8	0.6	38.5
Extensor digitorum brevis-popliteal	14.8	0.5	41.0
Right tibial nerve			
Abductor hallucis-wrist	5.95	0.6	
Abductor hallucis-popliteal	16.2	0.6	42.0
Left tibial nerve			
Abductor hallucis-wrist	7.2	0.5	
Abductor hallucis-popliteal	17.3	0.3	41.0

period of AMAN; however, nerve and conduction rates are typically normal.[2,10] In our case, a significant reduction in CMAP as an important finding in electrophysiological studies made us to consider AMAN; thus, it was distinguished from AIDP. On the other hand, AMSAN is one of the GBS subtypes differing from AMAN with both motor and sensory nerve fibers affected. In our case, sensory nerve action potential was normal. Considering the clinical and electrophysiological findings, the existence of anti-ganglioside immunity in AMAN cases is a reliable diagnostic method.[11] In our case, the anti-GM1 immunoglobulin G isotype was positive. In addition, CSF analysis showed albuminocytologic dissociation. Therefore, we confirmed our diagnosis with laboratory findings. In their study, Kuwabara et al.[12] also reported that hyperreflexia occurred in patients with AMAN with positive anti-GM1 antibodies.

An appropriate treatment should be initiated immediately in AMAN cases.[13] We diagnosed our case based on her medical history and clinical findings and initiated IVIG treatment without a delay. In AMAN, there is an axonal damage of the peripheral nerves without inflammation and demyelination. Severe muscle weakness consistent with axonal damage in some AMAN cases displays a clinical course characterized by slow and insufficient recovery. In some cases, on the other hand, rapid and full recovery is prominent, which is different from AIDP. In such cases, it is suggested that axonal damage is mainly in the intramuscular terminal nerves and recovery is achieved with the regeneration of the most distal lesion locations.[14]

Furthermore, it should be kept in mind that a long-term follow-up is required to observe clinical recovery. In our case, monthly IVIG treatment was continued, since full recovery was not seen in motor weakness, despite a favorable response to the initial IVIG treatment. In some cases, deep tendon reflexes are maintained; they may even be quickened.[15] In our case, deep tendon reflexes were hyperactive, since the start of clinical observation. Clinical, CSF, EMG, and anti-ganglioside findings of our case and the response to IVIG treatment support the AMAN diagnosis. Other variants of GBS, such as AMAN, should be considered in all cases with acute flask paralysis. This case is important for considering that deep tendon reflexes should not be affected and may even be hyperactive at early stages of diagnosis based on clinical findings. Early recognition and treatment of GBS is also critical for the clinical improvement, long-term prognosis, and reduced mortality, and morbidity.[1] Finally, this study emphasizes that treatment should not be delayed in these cases.

In conclusion, AMAN is one of the subtypes of GBS and should be considered in the differential diagnosis of acute quadriparesis, even when there are brisk reflexes and cerebrospinal fluid examination, electrophysiological, and seroimmunological studies should be performed to confirm the diagnosis.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

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