CASE REPORT

AN UNUSUAL CASE OF MULTIFOCAL MOTOR NEUROPATHY WITH CRANIAL NERVE INVOLVEMENT AND HYPERREFLEXIA

Hande Türker, Oytun Bayrak, Levent Güngör, Murat Sarıca, Musa Onar
Ondokuzmayıs University, Faculty of Medicine,Department of Neurology, Samsun, Türkiye

ABSTRACT

Multifocal motor neuropathy is characterized by progressive, asymmetric weakness of the limbs with persistent conduction blocks (CB). Sensory loss is very rare and it also rarely presents with cranial nerve involvement and hyperreflexia. Here we described a 32-year-old woman with progressive weakness of hand muscles associated with weakness of orbicularis oculi muscles and fasciculations of tongue. The electrophysiological examination revealed persistent conduction blocks in both of the ulnar, right median and left posterior tibial nerves together with F-waves with abnormal persistence. These findings and the persistency of conduction blocks along with a response to IVIG made it likely that the diagnosis was multifocal motor neuropathy. The case seemed to be worth reporting because of her unusual clinical findings.

Keywords: Multifocal motor neuropathy, Cranial nerve involvement, Hyperreflexia

KRANİAL SİNİR TUTULUMU VE HİPERREFLEKSİ İLE GİDEN MULTİFOKAL MOTOR NÖROPATİ: OLGU SUNUMU

ÖZET

Multifokal motor nöropati (MMN), kalıcı iletim bloklarının eşlik ettiği, ilerleyici, asimetrik ekstremite güçsüzlüğüyle karakterizedir. Duysal etkilenim çok seyrek olarak görülür. MMN'nin kranial sinir tutulumu ve refleks artışı ile birlikteliği nadiren bildirilmiştir. Burada, el kaslarındaki ilerleyici güçsüzlüğe, orbikularis okuli kaslarında güçsüzlük ve dilde fasikülasyonun eşlik ettiği 32 yaşında MMN'li bir kadın hasta sunulmuştur. Elektrofizyolojik incelemede her iki ulnar, sağ median ve sol posterior tibial sinirlerde iletim blokları ve F dalgalarında persistans anormalliği saptandı. Bu bulgularla birlikte, ileti bloklarının persistansı ve tablonun İVİG'e yanıtlı olması bize multifokal motor nöropati tanısını düşündürttü. Hasta, kliniğindeki seyrek rastlanır öğeler nedeniyle rapor edilmeye değer bulundu.

Anahtar Kelimeler: Multifokal motor nöropati, Kranial sinir tutulumu, Refleks artışı

INTRODUCTION

Multifocal motor neuropathy (MMN) is characterized by slowly progressive, asymmetrical weakness of the limbs without sensory loss. The upper extremities are often affected in the first place and distal muscles are affected more than proximal muscles. On electrophysiological examination there may be evidence of demyelination and persistent conduction blocks (CB)[1-3]. Differentiation of MMN from motor neuron disease is important because MMN is a treatable disorder.

Upper motor neuron signs and cranial nerve involvement are usually absent[1] although MMN is rarely reported presenting with hyperreflexia and cranial nerve symptoms[4,5]. In this report, we describe a case of MMN with hyperreflexia and cranial nerve symptoms and we want to emphasize that the lesion distribution may be more widespread than it is considered.

İletişim Bilgileri:
Hande Türker
e-mail: drhande@ttnet.net.tr
Ondokuzmayıs University, Faculty of Medicine, Department of Neurology, Samsun, Türkiye

CASE REPORT

A 32-year-old woman was admitted to our department because of the progressive weakness of her hand muscles. Her complaints had started in her left hand, one year before her admittance and had progressed to involve her right hand 4 months later. Two prior electromyograms, the first 10 months and the second 5 months prior to admission, were reported as carpal tunnel syndrome and C8-T1 root involvement. She had

had surgery on her left hand but her symptoms continued to progress. Her cervical computerized tomography (CT) revealed only a C5-6 posterior central bulging. On neurological examination the orbicularis oculi muscles were bilaterally weak and there were fasciculations on her tongue. The muscle strength of the thenar abductors and hypothenar abductors were 2/5, wrist extensors, elbow extensors and elbow flexors were 4/5, wrist flexors were 3/5, and arm abductors were 3/5 bilaterally (According to MRC). She had a claw finger deformity of the second digit of her left hand (Fig. 1). The strength of the ankle dorsal-flexors, plantar-flexors, knee extensors and knee flexors were 5/5 bilaterally and hip flexors were 4/5 on the left, 5/5 on the right side. Her deep tendon reflexes were increased. The sensory examinations were normal. Plantar responses were flexor.

She did not have any other systemic diseases or history of usage of any drugs. Laboratory examinations including blood count, renal and liver function tests, thyroid function tests and erythrocyte sedimentation rate were all within normal limits. Antiganglioside antibodies (anti GM1 Ab) were negative.

Electrophysiological studies:

The electrophysiological studies including nerve conduction studies (NCs) and needle electromyography (EMG) were performed on Nihon Kohden Neuropack 8 at our neurophysiology laboratory. The patient's skin temperature was kept between 31-32ºC.

Nerve conduction studies:

Median, ulnar, peroneal and posterior tibial motor NCs including F-waves were performed bilaterally. NCs were performed comprising the stimulation of the Erb's point and the popliteal fossa for median and ulnar nerves and peroneal and posterior tibial nerves respectively. For compound muscle action potentials (CMAPs), we measured the latency, amplitude and motor conduction velocity (CV). We also measured amplitude reduction and percentage of prolongation of duration on proximal versus distal stimulation. The American Association of Electrodiagnostic Medicine has proposed the criteria for the definition of definite and probable CB as follows: a) Definite CB: Presence of at least 50% or 60% reduction of proximal versus distal CMAP amplitude in the nerves of the upper and lower extremities with minimal temporal dispersion (less than 30 % increase in CMAP duration). b) Probable CB: presence of either at least 40% or 50% reduction of proximal versus distal CMAP amplitude with minimal dispersion (less than 30 % increase in CMAP duration) or at least 50% or 60% reduction of amplitude with moderate dispersion (31-60 % increase in CMAP duration)[6].

Median, ulnar and sural sensory nerve action potentials (SNAPs) were obtained antidromically, recording from digit III for median and from digit V for ulnar nerves.

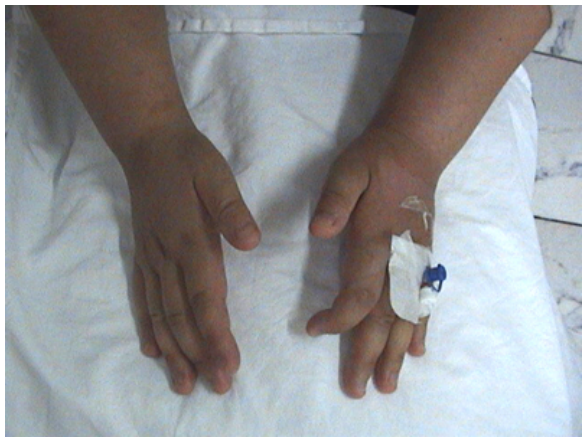

Fig. 1: Claw finger deformity of left hand

Table I and II show the results of the NCs. The median, ulnar and sural SNAPs were all in normal limits bilaterally. On the left side the amplitudes of the median and ulnar CMAPs were reduced and CMAPs could not be recorded at the Erb's point although the stimulus was supramaximal (0.1-0.2 ms duration at 50 mA) and the recordings were repeated. There was an amplitude reduction of 64 % in the ulnar nerve at the axilla and prolongation of duration was lower than 30 %. The distal latency of the ulnar CMAP was normal and the latency of the median CMAP was prolonged. Ulnar CV was normal. Persistences of F-waves of the ulnar and median nerves were reduced. The latency and the amplitude of the peroneal CMAP were normal but persistence of F-waves was again reduced. The latency and the amplitude of the posterior tibial CMAP and the persistence of F-waves were normal. Peroneal and posterior tibial CVs were normal. There was a reduction of CMAP amplitude of the posterior tibial nerve by 74 % at the popliteal fossa. According to the consensus criteria for the diagnosis of partial conduction block, the tibial nerve may only have probable partial conduction block and amplitude reduction should be over 50 percent when there is minimal temporal dispersion (duration increased by 30% or less). Our patient's NCs of posterior tibial nerve fulfilled this condition.

Table I: Motor nerve conduction studies of the patient

Side	Nerve	Recording	Latency	N	Amplitude (mv-μV)	N (mv-μV)	Duration	NCV (m/s)	N	F min. latency	*N*
Left*	**Ulnar**	**ADM**	2.7	<3.2	**4**	>6.0	5.5	54.3	>50.6	**26**	*<28*
		wrist								**4/16**	
		elbow	6.8	<7.0	**4**		5.1	76.9			
		above elbow	8.0	<10.3	**3.9**		4.5	76			
	DPCB	axilla	9.7		**1.4**		6.4				
	DPCB	erb	**No**	**CMAP**	**at erb**						
Right*	**Ulnar**	**ADM**	**3.5**	<3.2	**4.2**	>6.0	7.0	50.5	>50.6	**35**	*<28*
		wrist								**6/16**	
		elbow	**7.5**	<7.0	**3.4**		6.3	59.1			
	DPCB	above elbow	9.3	<10.3	**1.4**		6.2	>80			
	DPCB	axilla	10.2		**1.2**		6.9				
	DPCB	erb	**No**	**CMAP**	**at erb**						
Left*	**Median**	**APB**	**4.8**	<3.6	**0.7**	>6.0	4.3	57	>47.3	**28**	*<27.7*
		wrist								**7/16**	
		elbow	**8.3**	<7.8	**0.7**		4.6	61			
		axilla	11.1		**0.7**		5.0				
		erb	**No**	**CMAP**	**at erb**						
Right*	**Median**	**APB**	**4.1**	<3.6	**1**	>6.0	4.6	**31**	>47.3	**29.6**	*<27.7*
		wrist									
		elbow	**10.2**	<7.8	**1**		4.6	90			
		axilla	11.5		**1**		5.0	38			
	DPCB	erb	13.0		**0.5**		4.5				
Left	Peroneal	EDB	4.2	<5.1	3	>2	5.7	53	>41	**42.9**	*<63.4*
		ankle								**4/16**	
		cap. fib.	10.2		3		6.6	90			
		poplitea	10.9		3		6.9				
Right	Peroneal	EDB	3.4	<5.1	4	>2	5.8	42	<41	42	*<63.4*
		ankle									
		cap. fib.	9.5		4		6.7	90			
		poplitea	10.2		4		7.0				
Left*	**Post.tibial**	**AHL**	4.2	<5.0	13.7	>3	6.6	57.8	>38	48.8	*<55.6*
		ankle									
	PPCB	poplitea	10.0		**3.5**		6.9				
Right	Post.tibial	AHL	3.6	<5.0	6.7	>3	6.1	40.2	>38	46	*<55.6*
		ankle									
		poplitea	*12.3*		*4.8*		*4.8*				

Table II: Sensory nerve conduction studies of the patient

Side	Nerve	Recording	Latency	N	Amplitude (mv-μV)	N (Mv-μV)	Distance (cm)	NCV (m/s)	*N*
Left	Ulnar 5th finger	Sensory	2.7	<3.6	65 μV	>10.0	12	44	*>39*
Left	Median 3rd finger	Sensory	3.2	<3.5	90 μV	>16.0	14	43	*>40*
Right	Ulnar 5th finger	Sensory	2.7	<3.6	87 μV	>11.0	12	43	*>40*
Right	Median 3rd finger	Sensory	3.4	<3.5	52 μV	>10.0	14	40	*>40*
Left	Sural	Sensory	3.0	<4	20	>9	14	46	*>32*
Right	*Sural*	*Sensory*	*2.9*	*<4*	*22*	*>9*	*14*	*47*	*>32*

Footnotes: Abbreviations for both tables
APB: Abductor pollicis brevis NCV: Nerve conduction velocity EDB: Extensor digitorum brevis
ADM: Abductor digiti minimi Min. latency: Minimal latency AHL: Adductor hallucis longus
N: Normal value (According to our lab. normals in the same age group) cap.fib: Caputulum fibulum
mv: milivolt DPCB: Definite partial conduction block PPCB: Probable partial conduction block
* Pathologic values are written in bold

The latency of the right ulnar CMAP was prolonged, the amplitudes were reduced and an amplitude reduction of 58 % was found at the axilla (Fig. 2). The persistence of F-waves was reduced. The latency of the median CMAP was prolonged, the amplitudes and the CV were reduced and an amplitude reduction of 50 % was found at the Erb's point. The minimal F-wave latency was prolonged. The latencies, amplitudes and CVs of the peroneal and posterior tibial nerves together with the minimal latencies and the persistence of F-waves were normal.

Needle EMG:

Tibialis anterior, extensor digitorum communis, first dorsal interosseous, deltoid, biceps brachii, genioglossus and lingual muscles were examined on the left side whereas deltoid, extensor digitorum communis, first dorsal interosseous, orbicularis oculi and sternocleidomastoid muscles were examined on the right. All extremity muscles that were examined, except tibialis anterior, showed a severe neurogenic involvement with reduced recruitment of polyphasic, large amplitude, long duration motor unit potentials with a moderate number of fibrillation and fasciculation potentials and positive sharp waves at rest. We found a moderate neurogenic involvement of orbicularis oculi, sternocleidomastoid and lingual muscles.

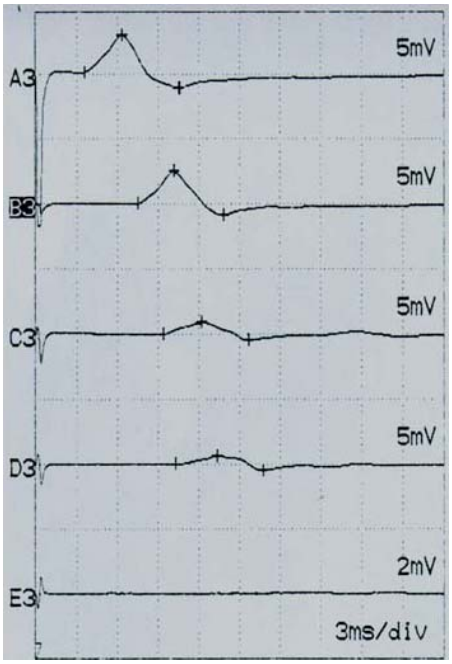

Fig. 2: Motor nerve conduction study of right ulnar nerve. There is definite conduction block at the axillary and Erb stimulation points

The asymmetrical onset of weakness of distal hand muscles in a young patient together with the conduction blocks in proximal segments in NCs made the diagnosis of MMN very likely although there was cranial nerve involvement and hyperreflexia. The patient was given 0.4g/kg/day intravenous immunoglobulins (IVIG) for 7 days. Three weeks after the administration of IVIG, conduction block in the left ulnar nerve quite improved although improvement of muscle weakness was slight (the muscle strength of the thenar abductors and hypothenar abductors became 3/5, wrist extensors, elbow extensors and elbow flexors were 4/5, wrist flexors were 3/5, and arm abductors were 4/5 bilaterally, according to MRC, in the follow-up examination). We planned to continue IVIG administration once a month for a year and the patient was admitted to the physical rehabilitation program.

DISCUSSION

The clinical diagnosis of MMN is based on the presence of chronic and progressive asymmetrical limb weakness with a multineuropathic distribution pattern affecting the muscles of at least two different motor nerves and lasting for at least two months. There is also minimal or no sensory loss. Absence of upper motor neuron involvement is almost a rule[7]. Our case had distal, progressive weakness in her hand muscles with an asymmetrical onset for approximately one year. Her neurological examination revealed muscle weakness in the distribution of more than two different motor nerves besides hyperreflexia and cranial nerve involvement. Axelsson and Liedholm reported a similar case to ours, diagnosed as MMN with cranial nerve symptoms: an old man with a slight atrophy in the hands and right-sided hypoglossal palsy[4]. They suspected motor neuron disease at first, but the electrophysiological studies revealed bilateral ulnar CBs indicative of MMN. They treated the patient with IVIG. Leon et al reported a case of MMN with an abnormal blink reflex[8]. Their findings allowed them to suggest that the distribution of involvement pattern in MMN seemed to be more widespread than generally considered.

Oshima et al. investigated patients with hyperreflexia who exhibited paralysis with CB. To determine whether hyperreflexia corresponded to corticospinal tract dysfunction, they evaluated central motor conduction time with magnetic stimulation in these patients. Their findings indicated that corticospinal tract was at least functionally involved in some patients with MMN showing hyperreflexia[5].

Our patient was negative for anti Gm1 Ab. Although other antiganglioside antibodies such as antiGD1b were not sought for, a diagnosis of MMN does not require that every patient should have these antibodies. About one half of MMN patients lack elevated levels of these antibodies and many others have only modest elevations, to a degree often seen in other neurological and even non-neurological disorders[9].

The electrophysiological examination of our patient revealed CBs in proximal segments with reduction in the persistence of the F-waves. However, in our patient, the amplitudes of the median CMAPs were significantly reduced. This progression could have resulted because of distal conduction failure leading to axonal degeneration. Similar cases in which initially reduced CMAPs were found without major indication of demyelination were reported. The authors of these reports concluded that the conduction blocks could have resulted from immune mediated conduction failure at the nodes of Ranvier without underlying demyelination in the cases[10-12]. There are also patients of MMN in whom CB may decrease or even disappear after several years of the disease because of a progressive reduction of the distal CMAP amplitude, which may reflect either secondary axonal degeneration or the appearance of previously unrecognized very distal CB[13]. Our patient may also have a similar situation.

Motor conduction velocities are usually normal or slightly reduced outside areas of CB and are sometimes normal even at the level of segments of CB or adjacent segments confirming the predominantly focal nature of the demyelination[13]. This situation also takes place in our case and it is noteworthy that it did not happen because of the technical artifacts.

The clinical presentation of our case and electrophysiological findings as CBs in both ulnar nerves, right median and left posterior tibial nerves with reduction in the persistence of the F-waves together with the response to IVIG therapy were thought to be consistent with MMN. In our patient the progression of the disease took a year. Such acute or subacute progression is unusual but cases similar to ours were also reported[11]. There are 9 cases reported in the literature as acute multifocal motor neuropathy (AMMN) and the

pathophysiological mechanisms of AMMN probably overlap with those of chronic MMN[11].

The differential diagnosis of MMN from motor neuron disease is important because MMN is a treatable disorder. There may still be some patients in whom the differential diagnosis of MMN from motor neuron disease is quite hard. The literature contains some examples of these patients. Parry et al reported 5 cases of MMN who had muscle atrophy, cramps and fasciculations with preserved reflexes. Although the clinical picture of these cases led to an initial diagnosis of motor neuron disease, nerve conduction studies revealed multifocal CBs predominantly involving proximal nerve segments[14]. Kaji et al reported 2 patients with MMN whose clinical signs included atrophy of the tongue and limb muscles closely resembling that of motor neuron disease and nerve conduction studies revealed multifocal CBs without sensory abnormalities[15]. However the classical motor neuron disease presents with needle EMG findings, which cannot be seen in MMN. The most important of these findings are the reinnervation motor unit action potentials seen together with chronic denervated motor unit action potentials and this provides evidence for a continuous degeneration and regeneration pattern of involvement[16]. Our patient lacked these EMG findings. Her age and sex, the neurological examination findings and the clinical progression which were related with a multineuropathic distribution pattern together with the response to IVIG therapy were not found consistent with motor neuron disease. Nevertheless, it can still be debated that the definite diagnosis of our patient may become more clear in the upcoming follow-ups. We emphasize that in patients with distal, progressive asymmetrical weakness, MMN should be kept in mind even if they have cranial nerve involvement and hyperreflexia. A detailed electrophysiological examination should also be performed for detection of CBs in proximal segments of the nerves, especially at the upper extremities.

REFERENCES

1. Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders. 2nd ed. Philadelphia: Elsevier, 2005: 389-420.

2. Biessels GJ, Franssen H, van den Berg LH, et al. Multifocal motor neuropathy. J Neurol 1997; 244:143-152.

3. Nobile- Orazio E. Multifocal motor neuropathy. J Neuroroimmunol 2000; 115:4-18.

4. Axelsson G, Liedholm LJ. Multifocal motor neuropathy-unusual cause of hypoglossal palsy. Lakartidningen 2002; 99:1448-1450.

5. Oshima Y, Mitsui T, Yoshino H, et al. Central motor conduction in patients with anti-ganglioside antibody associated neuropathy syndromes and hyperreflexia. J Neurol Neurosurg Psychiatry 2002; 73: 568-573.

6. Olney RK. Consensus criteria for the diagnosis of partial conduction block. Muscle Nerve 1999; 22: 225-229.

7. Nobile-Orazio E, Cappellari A, Meucci N, et al. Multifocal motor neuropathy: clinical and immunological features and response to IVIG in relation to the presence and degree of motor conduction block. J Neurol Neurosurg Psychiatry 2002; 72:761-766.

8. Leon-S FE, Pradilla G, Chavez AM, DeLeon MA, Rueda OL, Bayona J. Contralateral early blink reflex in multifocal motor neuropathy. Electromyogr Clin Neurophysiol 1998; 38:419-422.

9. Parry GJ. Antiganglioside antibodies do not necessarily play a role in multifocal motor neuropathy. Muscle Nerve 1994; 17:97-99.

10. Caposso M, Caporale CM, Pomilio F, Gandolfi P, Lugaresi A, Uncini A. Acute motor conduction block neuropathy. Another Guillian- Barre syndrome variant. Neurology 2003; 61: 617-622.

11. Lefaucheur JP, Gregson NA, Gray I, von Raison F, Bertocchi M, Creange A. A variant of multifocal motor neuropathy with acute, generalized presentation and persistent conduction blocks. J Neurol Neurosurg Psychiatry 2003; 74: 1555-1561.

12. Rajabally YA, Strens LHA, Abbott RJ. Acute motor conduction block neuropathy followed by axonal degeneration and poor recovery. Neurology 2006; 2: 287-288.

13. Orazio EN, Terenghi F. Other dysimmune neuropathies. peripheral neuropathy. American Academy of Neurology Continuum. 2003; 9:70-76.

14. Parry GJ, Clarke S. Multifocal acquired demyelinating neuropathy masquerading as motor neuron disease. Muscle and Nerve. 1988; 11: 103-107.

15. Kaji R, Shibasaki H, Kimura J. Multifocal demyelinating motor neuropathy: cranial nerve involvement and immunoglobulin therapy. Neurology 1992; 42: 506-509.

16. Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders. 2nd ed. Philadelphia: Elsevier, 2005: 423-437.