

## Multiple Sclerosis and Peripheral Multifocal Demyelinating Neuropathies Occurring in a Same Patient

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The co-occurrence of multiple sclerosis and peripheral demyelinating neuropathy is rare. It has been disputed whether these are pathologically related or coincidental findings. We report a 36-year-old woman who presented with diplopia, right facial palsy and left-sided weakness. Brain magnetic resonance imaging showed a lesion indicative of central demyelinating disease. Nerve conduction studies revealed peripheral multifocal demyelinating neuropathies. We suggest that the central and the peripheral lesions may be continua of a demyelinating process.

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**Key Words:** Multiple sclerosis, Demyelinating neuropathy, Conduction block

Co-occurrence of multiple sclerosis (MS) and peripheral demyelinating neuropathy is rare, and there have been disputed whether these are pathogenetically related or coincidental findings.<sup>1-8</sup> We report a combination of MS and peripheral multifocal demyelinating neuropathies in a Korean patient.

### CASE REPORT

A 36-year-old woman presented in April, 2006 with one week history of sustained headache in the right temporal area associated with numbness of the right face, hearing impairment, and vertigo. Ten years before, she underwent a thyroid gland operation due to hyperthyroidism and had been under thyroid hormone replacement therapy. Four months before the admission, she underwent a Caesarean section and had been breast-feeding. She had never experienced dry mouth,

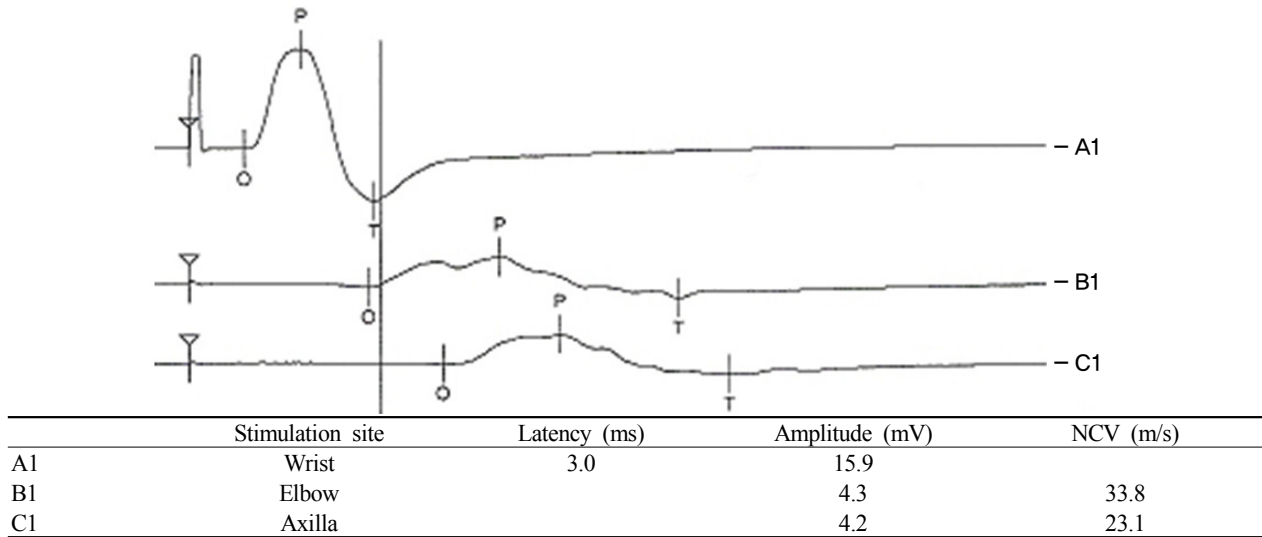
xerophthalmia, skin or oral ulcer, spontaneous abortion, or arthritis. Family history and other medical history were unrevealing. On admission, she complained of diplopia, but extraocular movement dysfunction or nystagmus were not observed. Muscle weakness of right face and palate were recorded, but dysphagia and dysarthria were not definite. Mild weakness of left extremities was recorded and deep tendon reflexes of left side were hypoactive. Pathologic reflexes or abnormality of muscular tone were not recorded. Her cerebellar function test was insignificant.

Her chest and cardiologic evaluation results were normal. Laboratory test such as complete blood cell count, erythrocyte sedimentation rate, and serologic tests including C-reactive protein, anti-GQ1b antibody, syphilis serology, human immunodeficiency virus antibody, rheumatoid factor, autoimmune markers such as antinuclear antibody, serum immunoglobulin did not show any abnormality. Her urine analysis did

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**Figure 1.** Demyelinating pattern with conduction block and temporal dispersion in motor conduction studies of left median nerve (2006.04.24, before the treatment).

**Table 1.** Serial nerve conduction studies (NCS)

(A)

2006.04.24	Right				Left			
	Latency (ms)	Amplitude (mV)	NCV (m/s)	F-wave (ms)	Latency (ms)	Amplitude (mV)	NCV (m/s)	F-wave (ms)
Motor NCS								
Median nerve				39.2 ↑				42.8 ↑
APB-wrist	3.4	15.3			3.0	15.9		
Wrist-elbow	9.8	14.3	34.5 ↓		9.5	4.3 ↓	33.8 ↓	
Elbow-axilla	12.2	16.7	37.5 ↓		13.4	4.2 ↓	23.1 ↓	
Ulnar nerve				39.4 ↑				41.6 ↑
ADM-wrist	2.1	17.9			2.0	16.8		
Wrist-below elbow	6.9	10.2	44.8 ↓		6.8	9.7	45.8 ↓	
Wrist-above elbow	8.6	5.4 ↓	38.2 ↓		8.9	9.4	33.3 ↓	
Elbow-axilla	10.7	4.3 ↓	35.7 ↓		11.8	6.2 ↓	20.7 ↓	
Peroneal nerve				47.0				56.8 ↑
EDB-ankle	3.4	7.5			4.5	9.5		
Ankle-fibular head	10.6	5.6	44.7		11.6	6.9	44.4	
Tibial nerve				53.4 ↑				54.4 ↑
AH-ankle	4.3	26.2			4.1	31.6		
Ankle-knee	12.1	15.9	46.2		12.5	15.7	44.0	
Sensory NCS		(μV)				(μV)		
Median nerve								
Finger-wrist		18.0	45.5			24.0	45.5	
Wrist-elbow		3.4 ↓	54.3			3.8 ↓	52.8	
Elbow-axilla		29.4	54.1			28.4	51.1	
Ulnar nerve								
Finger-wrist		11.0	39.6			15.6	43.8	
Wrist-elbow		11.3 ↓	49.2			8.8 ↓	54.9	
Elbow-axilla		10.9 ↓	46.9			NP	NP	
Sural nerve		17.1	40.7			22.0	45.3	

NCV; nerve conduction velocity, APB; abductor pollicis brevis, ADM; abductor digiti minimi, EDB; extensor digitorum brevis, AH; abductor hallucis, NP; no potential.

(B) (Continued from previous page)

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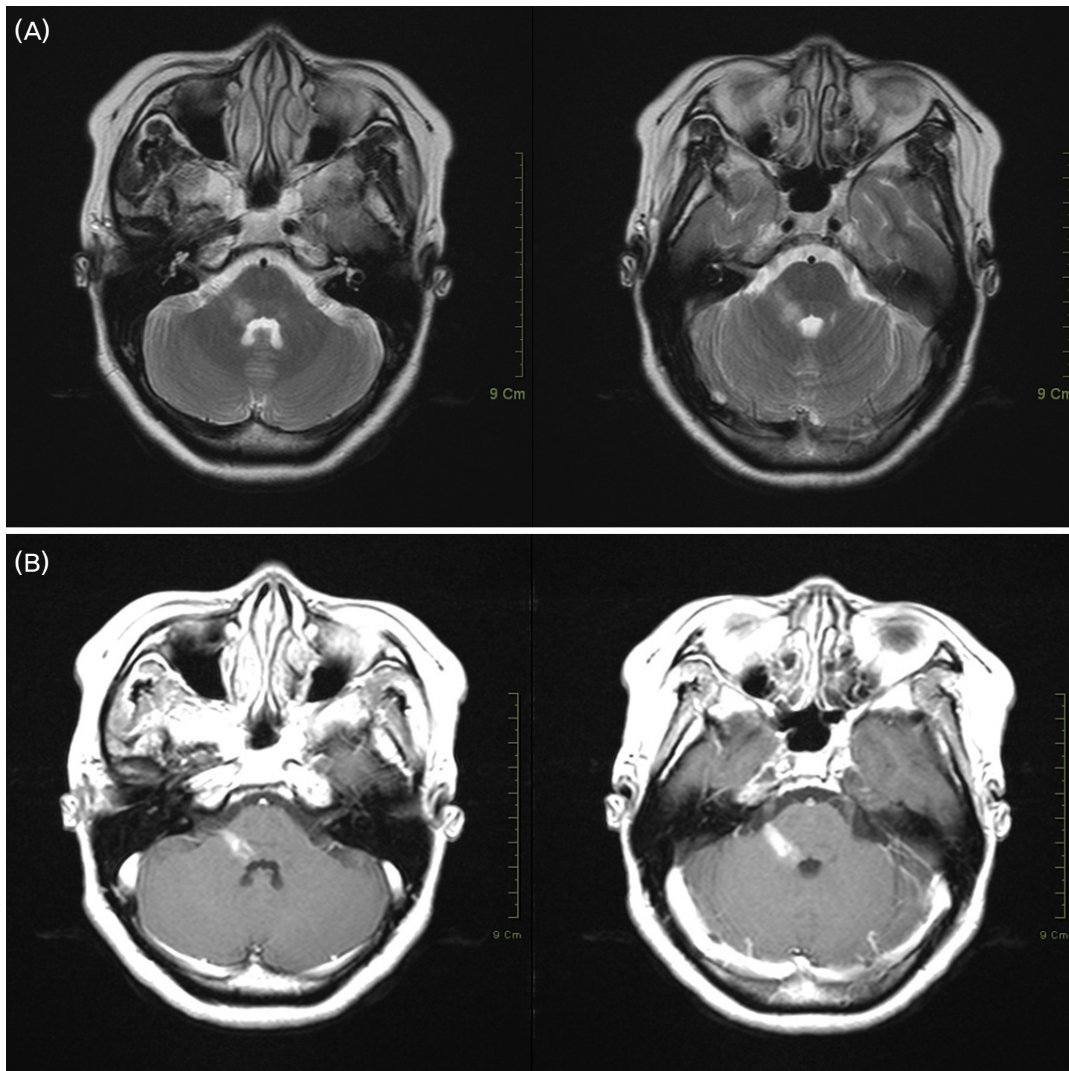
	Right				Left			
	Latency (ms)	Amplitude (mV)	NCV (m/s)	F-wave (ms)	Latency (ms)	Amplitude (mV)	NCV (m/s)	F-wave (ms)
Motor NCS								
Median nerve				38.2 ↑				36.5 ↑
APB-wrist	3.0	15.0			3.3	14.8		
Wrist-elbow	10.0	8.7	31.4 ↓		10.4	2.8 ↓	31.7 ↓	
Elbow-axilla	12.3	7.2	39.1 ↓		13.2	2.6 ↓	28.6 ↓	
Ulnar nerve				35.2 ↑				39.6 ↑
ADM-wrist	2.0	17.3			2.3	15.0		
Wrist-below elbow	6.8	10.7	43.8 ↓		6.7	8.1	45.5 ↓	
Wrist-above elbow	8.5	5.2 ↓	38.2 ↓		8.8	7.9 ↓	38.1 ↓	
Elbow-axilla	10.3	4.1 ↓	41.7 ↓		13.0	5.1 ↓	20.2 ↓	
Peroneal nerve				41.6				43.8
EDB-ankle	3.5	10.6			4.5	8.5		
Ankle-fibular head	10.7	8.4	45.8		11.0	6.7	47.7	
Tibial nerve				44.6				44.5
AH-ankle	3.8	27.0			4.7	24.5		
Ankle-knee	11.4	17.0	44.7		12.0	15.6	43.8	
Sensory NCS		(μV)				(μV)		
Median nerve								
Finger-wrist		25.0	44.4			13.0	44.4	
Wrist-elbow		7.2 ↓	55.9			5.1 ↓	58.1	
Elbow-axilla		30.0	57.1			20.0	56.3	
Ulnar nerve								
Finger-wrist		15.0	39.1			13.0	39.1	
Wrist-elbow		12.0 ↓	52.8			5.8 ↓	52.6	
Elbow-axilla		11.0 ↓	46.3			5.0 ↓	47.5	
Sural nerve		22.0	44.4			22.0	41.7	

NCV; nerve conduction velocity, APB; abductor pollicis brevis, ADM; abductor digiti minimi, EDB; extensor digitorum brevis, AH; abductor hallucis, NP; no potential.

not show hematuria or proteinuria. Cerebrospinal fluid (CSF) analysis showed a protein level of 63 mg/dL, a glucose level of 65 mg/dL, and 3 cells/mm<sup>3</sup>. An immunoglobulin G index (IgG index) was 0.564 and the CSF level of myelin basic protein (MBP) was 10 ng/mL (normal level <1 ng/mL). An oligoclonal band of CSF was not demonstrated. The motor nerve conduction velocities of both median and ulnar nerves were markedly decreased and multiple conduction blocks were recorded on left median and both ulnar nerves (Fig. 1). The F wave latencies of both median, ulnar, tibial, and left peroneal nerves were prolonged and H-reflexes were not demonstrated bilaterally. These nerve conduction studies (NCS) were indicative of multifocal demyelinating neuropathies (Table 1-A).

Pattern reversal visual-evoked potentials (VEP) and brainstem auditory-evoked potentials (BAEP) fell within normal ranges.

On hospital day 1, T2-weighted and fluid-attenuated inversion recovery magnetic resonance imaging (MRI) studies revealed an increased signal intensity in the right cerebellopontine angle with gadolinium-enhancement (Fig. 2). This lesion showed high signal intensity on diffusion MRI and apparent diffusion coefficient maps. She did not receive any treatment because her husband wanted her to be treated by oriental medicine. Five days later, she was admitted again because of left-sided numbness and ataxia with aggravated dizziness. A follow-up MRI did not reveal any newly developed lesion. She was diagnosed as



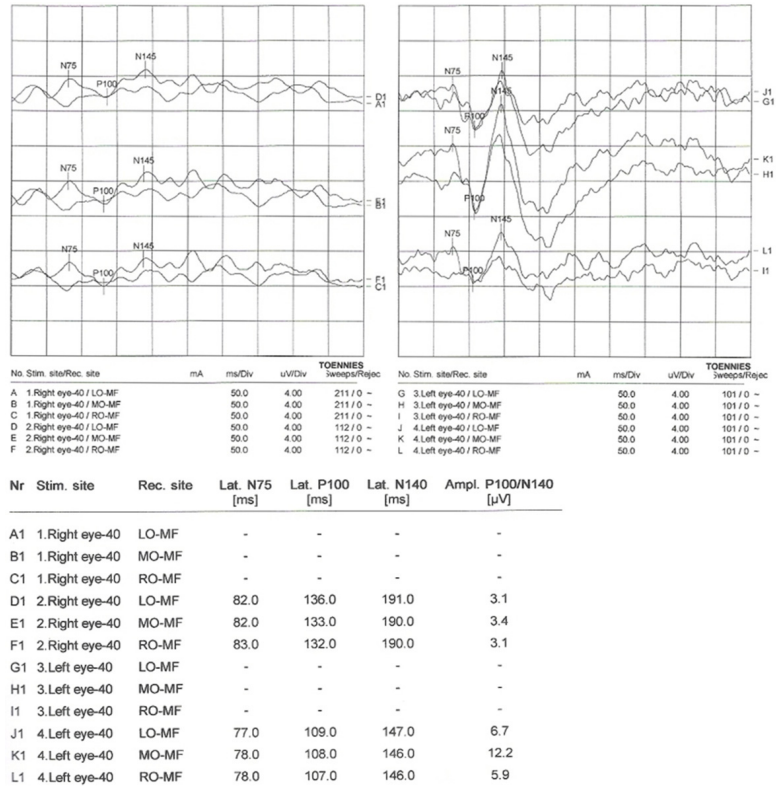
**Figure 2.** Brain MRI on first admission, (A) T2-weighted image showed a region of increased signal intensity in right cerebellopontine angle and (B) in gadolinium-enhanced image this lesion showed gadolinium-enhancement.

having multifocal demyelinating neuropathies and probable demyelinating disorder of central nervous system (CNS). Intravenous immunoglobulin (0.4 g/kg per day) was administered for 5 days. On the fourth day of immunoglobulin treatment, most of left sided-weakness and ataxia disappeared. After 15 days, the NCS showed decreased F-wave latencies of all tested nerves compared with those of previous study (Table 1-B). For about 3 months after discharge, her gait disturbance and ataxia were resolved, but numbness of right extremities appeared transiently.

In August, 2006, she was admitted for the third

time because of decreased visual acuity and color vision of right eye (0.2 OD; 1.0 OS). The swinging flashlight test showed the Marcus-Gunn pupillary sign on right eye. Other cranial nerves, motor, and sensory examinations were unrevealing. Reflexes of four extremities were hyperactive. On ophthalmoscopic examination, blurred margin of right optic disc was recorded. VEP showed prolonged P100 latency on right eye indicative of a prechiasmatic conduction defect of right visual pathway (Fig 3-A). Orbit MRI showed a gadolinium enhanced lesion on a prechiasmatic area of right optic nerve and a region of

(A) VEP at the time when visual symptoms of right eye happened



(B) After 8 months, follow-up VEP

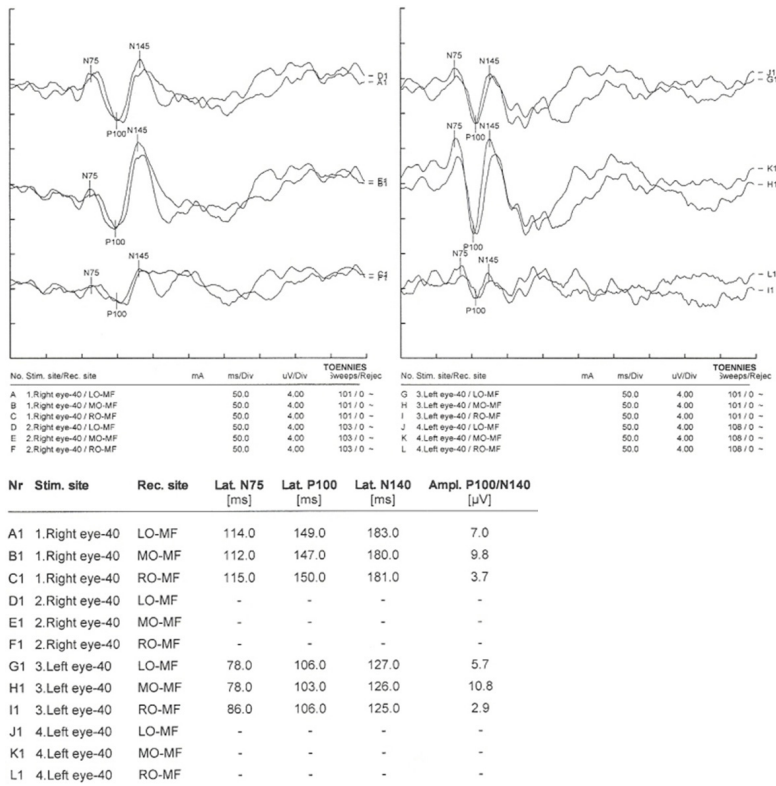


Figure 3. Pattern-reversal visual evoked potentials test shows prolonged P100 latency of right eye.



**Figure 4.** Brain MRI on third admission, (A) T2-weighted image shows a region of high signal intensity on left lateral medulla, and (B) Fat-suppression image shows a gadolinium-enhanced lesion in a prechiasmatic area of right optic nerve.

abnormally high signal intensity on left lateral medulla, which corresponded with right sided- numbness (Fig 4). A follow-up CSF analysis showed a protein level of 59 mg/dL, a glucose level of 58 mg/dL, and 0 cells/mm<sup>3</sup>. An IgG index was 0.568 and MBP level was 2.2 ng/mL. An oligoclonal band of CSF was not demonstrated. Thus, she was diagnosed as having right optic neuritis and MS and intravenous high dose steroid pulse therapy (1000 mg/day) was done for 5 days, with gradual tapering with oral prednisolone (1 mg/kg). Her visual acuity of right eye showed marked improvement in 2 weeks after steroid pulse therapy.

## DISCUSSION

MS is a chronic disorder characterized by recurrent and relapsing lesions occurring in the brain, optic nerves, and the spinal cord.<sup>9</sup> The specific pathologic finding of MS is central demyelination which does not extend beyond the root entry zones of the cranial and spinal nerves.<sup>9</sup> As several cases of MS combined with peripheral demyelinating neuropathy have been reported, questions have been arising whether MS lesions should not extend beyond the root entry zones.<sup>1-8</sup> Pollock et al. found demyelination of peripheral nerves in sural nerve biopsy of 10 patients with MS and suggested that the peripheral myelin might be involved

in MS.<sup>8</sup> Furthermore, Mendell et al. detected white matter lesions indistinguishable from those seen in MS in 16 patients with inflammatory demyelinating polyradiculoneuropathy.<sup>10</sup>

In our case, weakness and ataxia of left extremities, weakness and hypoesthesia of right face, and vertigo developed as initial manifestations which were followed by transient numbness of right extremities. Four months later, right optic neuritis suddenly developed. Thus, the series of manifestations appear to be compatible with temporal dissemination of demyelination process. Her serial brain MRI showed spatially disseminated demyelinating lesions. She was diagnosed as having MS on the basis of current diagnostic criteria.<sup>11</sup> On the first admission, her neurologic examination showed mild weakness and hyporeflexia of left extremities and the NCS revealed peripheral multifocal demyelinating neuropathies without past history of peripheral nervous system lesion. Without pathological study, it is difficult to confirm whether the two disorders occurred coincidentally or occurred as different manifestations of the same demyelinating process. MS is rare in Korea as compared to western countries. Demyelinating neuropathy is also an uncommon disorder. The clinical course of the patient as well as the co-occurrence of two rare diseases suggest that the central and the peripheral demyelination might be different manifestations of a broad spectrum of the same immunopathologic dysfunction.

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