성공적인 회복을 보인 한랭 노출 유발 말초 신경 손상: 증례 보고

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Successful Recovery of Peripheral Polyneuropathy from Non-Freezing Cold Injury: A Case Report

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Non-freezing cold injury (NFCI) results from prolonged exposure to wet conditions at temperatures near or just above the freezing point. The clinically reported signs of NFCI are mostly sensory symptoms. In this case report, we present a young healthy woman who was presumed to have developed cold-induced peripheral polyneuropathy following whole-body exposure to cold temperatures for at least 48 hours. Our patient showed severe peripheral polyneuropathy in the lower extremities during the initial nerve conduction study and electromyography. The findings were consistent with her clinical symptoms of tingling sensation and gait disturbance. Serial electrodiagnostic studies demonstrated gradual improvement and eventually normalization. Her clinical symptoms also significantly improved over several weeks of comprehensive rehabilitation. NFCI is a rare condition, and its pathophysiology and clinical course remain unclear. Nonetheless, it shows a reversible pattern early after the injury, and early diagnosis and treatment are required.

Keywords: Peripheral nervous system diseases; Cold injury; Polyneuropathies

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Introduction

The effect of temperature on the peripheral nerve has been widely studied before. It has been confirmed that cold temperature has profound effects on the peripheral nervous system because it affects the voltage-gated ion channels, acetylcholinesterase, and the contractile apparatus of muscle [1]. Exposure to cold temperature may result in several different neuropathies. Frostbite, for example, is a local cold injury that occurs at temperature below freezing point and may further lead to tissue necrosis due to direct

cell damage or vascular impairment caused by ice crystal [2].

Besides frostbite, non-freezing cold injury (NFCI) is another type of damage in the peripheral nervous system that results from exposed to low temperatures between 0°C and 15°C for several hours or days [2]. Although NFCI is not commonly reported, it is a classic condition found among certain group of people, including soldiers [3], mountain climbers, hikers, the homeless, and those who have experienced drowning [1]. Clinically reported signs of NFCI are mostly sensory, which include pain, numbness, tingling sensation of limbs [4], cold hypersensi-

tivity, loss of thermal sensitivity, and allodynia [3]. In this case report, we present a patient who was presumed to develop peripheral polyneuropathy from NFCL.

Case Report

A 20-year-old female came to our hospital presenting a tingling sensation in her left thumb and both lower extremities. Two weeks before visiting our hospital, the patient was robbed while studying abroad in England, and suffered from a stab wound in the epigastrium. It was a snowy winter day, and the outdoor temperature was near freezing point. It was estimated that she was stunned for at least 48 hours outdoors before arriving at the emergency room. In the initial evaluation at the hospital in England, computed tomography (CT) scans showed the stab wound had reached the rectus sheath. Also, no definite features of frostbite was shown on the inspection. Fortunately, it was a superficial wound that did not expand to the muscle layer and healed well with simple suture. Although the stab wound recovered without complications, the feeling of numbness remained in the left thumb and both lower legs below the knee since she arrived at the emergency room. Magnetic resonance image (MRI) of the lumbar spine and brain CT were performed to evaluate the tingling sensation in the lower extremities and the patient's initial loss of consciousness, but there were no abnormalities.

After returning to Korea, the symptoms of gait disturbance and severe tingling sensation persisted, and the patient came to our hospital. The patient complained that she felt a sense of electric shock in the bilateral soles of her feet. Sense of vibration and proprioception at the great toes also decreased. Muscle strength of lower extremities are generally grade 4+/5, except for right ankle dorsiflexion, which shows grade 3+/5, according to the Medical Research Council scale. Muscle atrophy of bilateral distal lower extremities of the patient was observed. The patient's deep tendon reflex of bilateral biceps and knee jerk were normoactive. The initial Berg Balance Scale was 52 out of 56 with impaired one leg standing and tandem gait. She was able to walk a few steps only under supervision due to impaired dynamic standing balance.

The electrodiagnostic study was performed to differentiate the cause of her sensory symptoms (Table 1). The initial sensory nerve conduction study (NCS) showed absent sensory nerve action potential on the bilateral superficial peroneal, medial and lateral plantar, and sural nerves. The initial motor NCS displayed low amplitude of compound muscle action potential (CMAP) in tibial nerve and no response of CMAP in common peroneal nerve. The initial electromyography demonstrated denervation

potential on the left extensor digitorum brevis, tibialis anterior, and right extensor digitorum brevis muscles. Reduced recruitment patterns on minimal volition in the left extensor digitorum brevis, tibialis anterior, gastrocnemius, peroneus longus, and right tibialis anterior muscles were also shown. Long duration of motor unit action potentials (MUAPs) on minimal volition in left tibialis anterior and gastrocnemius muscles was observed. Large amplitude of MUAPs on minimal volition in left gastrocnemius muscle was observed. No MUAPs was observed in the right extensor digitorum brevis muscle (Table 2). F-waves were not evoked in the bilateral common peroneal and posterior tibial nerves. There was no definite abnormality in the bilateral upper extremities (data not shown). Clinical and electrodiagnostic findings were compatible with severe sensori-motor peripheral polyneuropathy (mainly axonal injury) involving lower extremities.

Diagnostic blood work was done to exclude other causes of peripheral polyneuropathy including serum vitamin level, lupus anticoagulant antibody, anti-nuclear antibody, et cetera, and the results presented within normal limit. Our patient had no underlying disease and no specific findings on blood test results, so other causes of peripheral polyneuropathy were excluded from the diagnosis. Critical illness polyneuropathy was less likely because of the short duration of her treatment in the intensive care unit, no ventilator care, no history of sepsis, and no evidence of multiple organ or brain damage. There were no abnormalities in radiologic tests, including the MRI and CT. Based on our findings, comprehensive rehabilitation therapy including gait training, muscle strengthening exercise, and standing balance training was continued for 3 weeks after hospital admission. We prescribed a combination of gabapentin, nortriptyline, and oxcarbazepine to control the sensory symptoms. Our patient gradually improved so she was able to stand in one leg for about 10 seconds and walk heel-to-toe at the time of discharge. Muscle strength of right dorsiflexion improved from 3+/5 to 4+/5. Follow-up electrodiagnostic study was performed 6 weeks after the onset, which showed small responses in the sensory NCS; these were notable results compared to our initial results, which presented no response (Table 1). Reinnervated features of MUAPs in left tibialis anterior and bilateral gastrocnemius were shown in the follow-up study (Table 2).

Our patient continued rehabilitation therapy at the outpatient clinic for more than 4 months. She showed enough improvement to walk up the stairs by herself and could perform most activities of daily living. A year after, her balance was restored enough to do active outdoor activities such as running. The neuropathic pain was resolved significantly, so she took only 10 mg of ami-

Table 1. Result of Nerve Conduction Study

Time	Initial (2 weeks from onset)			2nd follow-up (6 weeks from onset)			3rd follow-up (17 months from onset)		
Nerve/sites	Peak latency (ms)	Amplitude (μV)	CV (m/s)	Peak latency (ms)	Amplitude (μV)	CV (m/s)	Peak latency (ms)	Amplitude (μV)	CV (m/s)
Sensory nerve conduction studies									
L sural (lower leg)									
Calf		Not evoked		4.70	7.2*	38.8	3.10	10.2	62.5
R sural (lower leg)									
Calf		Not evoked		4.35	5.3*	40.0	2.90	13.8	58.8
R superficial peroneal (ankle)									
Lateral leg		Not evoked		3.20	5.0*	48.9	2.80	6.4*	62.5
L SUP peroneal (ankle)									
Lateral leg		Not evoked		3.40	6.1*	53.8	2.70	17.0	66.6
Motor nerve conduction studies									
R common peroneal (EDB)									
Ankle		No response			No response		3.50	4.0	
Fib head		No response			No response		10.85	2.9	43.5
L common peroneal (EDB)									
Ankle		No response		4.70	0.2*		3.35	4.7	
Fib head		No response		11.30	0.2*	45.5	9.75	3.9	50.0
R tibial (knee)-AH									
Ankle	4.65	0.5*		4.50	0.9*		3.70	11.5	
Popliteal	13.20	0.3*	42.1	12.75	0.7*	44.8	12.60	7.2	41.6
L tibial (knee)-AH									
Ankle	4.85	0.4*		4.65	0.4*		4.10	8.5	
Popliteal	12.80	0.2*	57.1	12.25	0.2*	48.7	12.00	7.0	46.8

ms, millisecond; μV, microvolt; CV, conduction velocity; m/s, meter per second; mV, millivolt; EDB, extensor digitorum brevis; AH, abductor hallucis.

*Decreased amplitude of sensory nerve action potential or compound muscle action potential.

Table 2. Result of Needle Electromyography

Muscle	Initial (2 weeks from onset)					2nd follow-up (6 weeks from onset)				
	IA	Fib	PSW	MUAP	Recruitment	IA	Fib	PSW	MUAP	Recruitment
Lt. L4-S1 PSP	NL	None	None			NL	None	None		
Both GMax			NT			NL	None	None	NL	Full
Both GMed			NT			NL	None	None	NL	Full
Rt. VM			NT			NL	None	None	NL	Full
Rt. TA	NL	None	None	NL	Reduced	NL	None	None	NL	Full
Rt. PL			NT			NL	None	None	NL	Full
Rt. TP			NT			NL	None	None	NL	Full
Rt. GCM (medial)			NT			NL	None	3+	Poly	Reduced
Rt. EHL			NT			NL	None	3+	NL	Reduced
Rt. EDB	Increased	3+	3+	No MUAP					NT	
Lt. VM	NL	None	None	NL	Full	NL	None	None	NL	Full
Lt. TA	Increased	1+	None	Long	Reduced	NL	None	None	Large	Full
Lt. PL	Increased	None	None	None	Full	NL	None	None	NL	Full
Lt. TP			NT			NL	None	None	NL	Full
Lt. GCM (medial)	Increased	None	None	Large, Long	Full	NL	None	1+	Poly	Full
Lt. EHL			NT			NL	None	None	NL	Full
Lt. EDB	Increased	3+	1+	NL	Reduced				NT	

IA, insertional activity; Fib, fibrillation; PSW, positive sharp wave; MUAP, motor unit action potential; Lt., left; Rt., right; PSP, paraspinalis; NL, normal; NT, not tested; GMax, gluteus maximus; GMed, gluteus medius; VM, vastus medialis; TA, tibialis anterior; PL, peroneus longus; TP, tibialis posterior; GCM, gastrocnemius; Poly, polyphasic; EHL, extensor hallucis longus; EDB, extensor digitorum brevis.

triptyline at night. At 17 months after the onset, the electrodiagnostic study presented nearly complete recovery (Table 1).

Discussion

This case report highlights a case of peripheral polyneuropathy as a clinical manifestation of NFCI. Initial electrodiagnostic study demonstrated severe sensori-motor peripheral polyneuropathy (mainly axonal injury) in the lower extremities. Sensory and motor responses were absent except for small response in tibial nerves. Follow-up electrodiagnostic study was conducted at 6 weeks and 17 months after the event. The patient's recovery was first shown in the sensory NCS, which was gradually reflected in the results of the motor NCS. At 17 months after the onset, sensory and motor NCS results nearly returned to normal range. Along with the improvement of these electrodiagnostic results, clinical symptoms were also successfully recovered during 1 to 2 years.

The mechanisms for NFCI have not yet been established. However, there have been several studies on the physiology of these injuries. In a previous study examining rats, the authors concluded that the mechanisms of cold injuries are mainly ischemic, and include slugging of blood, a symptom caused by decreased velocity due to vasoconstriction and vascular injury [5], and formation of reactive oxygen species with repeated cold ex-

posure [6]. In another study examining rabbits' hind limbs, the author reported more pronounced nerve damage in large myelinated nerve fibers than in unmyelinated fibers as a consequence of NFCI [7].

Only a few studies reported a clinical manifestation of NFCI with electrodiagnostic findings. In a previous study of 31 soldiers with persistent cold intolerance 3 to 4 years after cold injury, authors have presented findings compatible with a demyelinating large-fiber neuropathy on NCS [8]. On the other hand, Vale et al. [4] revealed evidence of small fiber pathology and normal result of large fiber NCS from a study of 42 patient with chronic pain following NFCI. Jørum and Opstad [3] studied the 4-year follow-up on NFCI. Of the 26 soldiers, 16 soldiers complained of numbness in feet and cold hypersensitivity with significant changes in function of both large and small nerve fibers. 16 showed sensory neuropathy in initial NCS. During the 4-year follow-up, most of the soldiers improved clinical symptoms over time and recovered from large and small fiber neuropathy except for 7 soldiers who developed chronic symptoms of cold allodynia and hypersensitivity.

Løseth et al. [9] reported that a 29-year-old female who has suffered from accidental hypothermia developed pronounced axonal sensori-motor polyneuropathy, but with almost sparing of the tibial nerves. In small nerve fiber testing, the results showed normal. Sensory and motor amplitudes improved in the fol-

low-up NCS during first 5 years, but did not normalize. The improvement of her clinical symptoms in the first 1 to 2 years was similar to that of our patient. However, she had the sequelae of persisting weakness, atrophy of her hand muscles. These were different from the findings of our case patient, who did not show any sequelae and showed normalized results in the follow-up electrodiagnostic test. In Løseth et al. [9]'s case, the upper extremities were more severely damaged. This distinction may be due to the difference in injury mechanisms. In addition, the upper limbs were soaked in the water and the lower limbs were located outside of the water.

Collier et al. [1] presented a similar case. A 6-year-old girl fell through an ice-covered stock pond. After resuscitating from the accident, she had clinical and electrophysiological findings consistent with cold-induced axonal peripheral polyneuropathy in the bilateral upper and lower extremities. Signs of re-innervation were seen after 28 weeks. A year after the accident, small sensory and motor responses in the NCS were obtained. Although electrodiagnostic study remained abnormal, her clinical outcome was excellent.

Although NFCI is a rare condition in a patient with a history of prolonged cold exposure, if the patient shows any symptoms suggestive of peripheral polyneuropathy, it is important to be aware that cold injury can induce peripheral polyneuropathy. In previous literatures, cold-induced polyneuropathy was reversible, and its clinical symptoms improved over time. Thus, serial electrodiagnostic study may support early diagnosis for better outcomes and detect changes in the patient's nerve functions.

In our study, patient showed severe peripheral polyneuropathy in the bilateral lower extremities during initial electrodiagnostic study. Compared to other cases, she recovered rapidly. These differences can be attributed to heterogeneous factors including temperature, exposure time and frequency to cold temperature, and location at the time of incident. We conducted serial electrodiagnostic study to confirm the large fiber function, but unfortunately did not conduct test for small fiber function. Therefore, further studies are needed to elucidate the clear relationship between the patient's recovery and the test results of electrodiagnostic study, and clarify which areas are vulnerable to cold temperature, where the upper or lower limbs are affected, where mainly invaded fibers are large or small, and whether the nerve damage type is axonal or demyelinated. In Korea, only 1 case was reported in which a 22-year-old man presented severe peripheral neuropathy in a electrodiagnostic study 4 months after accidental exposure to cold temperature [10]. However, in the previous case report, serial follow-up had not been done and only initial data was available. Our case reported a series of electrodiagnostic

studies from acute period to recovery period with clinical improvement. And it is the first report to perform a serial follow-up electrodiagnostic study to present severe peripheral polyneuropathy due to NFCI in Korea.

In summary, NFCI is not common. When dealing with patients with distal symmetric neuropathic symptoms and polyneuropathy after prolonged exposure to cold temperature, we should consider the possibility of peripheral polyneuropathy from NFCI among several differential diagnoses.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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