

Symmetrical Femoral Neuropathy and Rhabdomyolysis Complicating Carbon Monoxide Poisoning

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Although carbon monoxide (CO) is a common cause of morbidity due to poisoning, peripheral neuropathy following CO poisoning has rarely been reported. Furthermore, rhabdomyolysis caused of CO poisoning is also uncommon. The report focuses on a patient with symmetrical femoral neuropathy and rhabdomyolysis associated with CO poisoning.

A 32-year-old male was admitted to hospital in a deep coma following CO poisoning. On admission, rhabdomyolysis was also identified (total creatinine phosphokinase, 19662 IU/L; CK-MB, 272 IU/L). After receiving hyperbaric oxygen, the patient regained consciousness; however, bilateral hip flexors and knee extensors were still weak in accordance to the manual muscle test. Lumbar spine magnetic resonance imaging (MRI) was performed and did not reveal any abnormal lesions. Nerve conduction examination and electromyography results indicated symmetrical femoral neuropathy. After taking the rehabilitation program for peripheral and central nervous system lesions, the patient achieved functional improvement in ambulation, endurance and balance. (*Chang Gung Med J 2006;29(4 Suppl):103-8*)

Key words: carbon monoxide poisoning, symmetrical peripheral neuropathy, rhabdomyolysis, hyperbaric oxygen.

Carbon monoxide (CO) is a colorless, tasteless, odorless, and non-irritating gas, and is the most common cause of death due to poisoning in both Europe and North America.⁽¹⁾ In Taiwan, CO poisoning is also a common cause of death.⁽²⁾ The clinical symptoms of CO poisoning are variable, vague, and nonspecific, including nonspecific viral illnesses, impaired cognitive function, neuropsychiatric symptoms, and delayed neurological syndrome. Previous reports of rhabdomyolysis and myonecrosis due to CO poisoning are rare.^(2,3) Peripheral neuropathy is also rarely documented after CO poisoning. The report focuses on a patient with symmetrical femoral neuropathy and rhabdomyolysis following CO poisoning.

CASE REPORT

This 32-year-old man was admitted to the rehabilitation department because of decreased muscle strength found in his bilateral lower limbs and right hand after being affected by burning coal.

The patient was healthy prior to the incident and had no history of drug abuse. He was found collapsed and unconsciousness on Nov. 6, 2003, obviously related to burning coal at his home according to a statement from his mother and a colleague. On admission, he was still unconscious, impervious to painful stimuli, and showed no spontaneous movement.

Initial laboratory data were as follow: serum

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blood urine nitrogen, 40 mg/dl; serum creatinine, 1.8 mg/dl; sodium, 142 mmol/l; potassium, 5.0 mmol/l; total creatinine phosphokinase (CK), 19662 IU/L; CK-MB, 272 IU/L; Troponin I, 1.93 ng/ml; ALT, 97 IU/L; and, AST, 566 IU/L. Leukocyte count was 25900/mm³ with 74% segmented neutrophils, 14% lymphocytes, and 12% monocytes. Other laboratory data, including urine analysis, were normal. Brain computerized tomography (CT) (Nov. 7, 2003) identified a low density in the bilateral globus pallidus and slightly swollen grey matter. These findings are compatible with CO intoxication with hypoxic-ischemic encephopathy. Under the diagnosis of CO intoxication with encephalopathy and rhabdomyolysis, the patient received hyperbaric oxygen therapy (HBO). Following therapy, the patient could respond to oral commands and regained some muscle power. However, cognitive function remained impaired. Laboratory data indicated a gradual reduction of the CK level (12772 IU/L, 11590 IU/L and 291 IU/L, respectively). Because of persisting paraplegia, right hand numbness, fecal and urine incontinence, electroencephalography (EEG) and lumbar spine MRI were performed but did not reveal any abnormal lesions. Consequently, the patient was referred to the

rehabilitation department due to paraplegia.

Following rehabilitation, the patient's bilateral knee extensors remained weak for two months after the episode with numbness of the bilateral medial knee areas and the fifth finger of his right hand. However, the patient did not report experiencing any muscle pain or tenderness. Physical examination showed lack of symmetrical knee jerks, diminished touch and pin-pick sensation of bilateral medial knee areas and advanced atrophy over bilateral thighs. A manual muscle test identified significant weakness of bilateral hip flexors (2/5) and knee extensors (2/5). Left with the possibility of peripheral neuropathy, nerve conduction studies and electromyography were performed on Feb. 12, 2004. There was no response upon right ulnar nerve stimulation in the sensory study. In the motor study, the conduction velocity (19 m/s) of the right ulnar nerve was decreased with low amplitude (6.2 mV). The bilateral femoral nerves amplitude (right 1.1 mV; left 1.0 mV) was below normal in accordance to the testing laboratory. Furthermore, there was no response in the right ulnar nerve and bilateral femoral nerves in the F-wave study (Table 1). In the electromyography study, the bilateral vastus medialis muscles showed fibrillation

Table 1. Nerve Conduction Studies

Never stimulated	Stimulation site	Recording site	Amplitude (motor = mV Sensory = μ V)		Latency (msec)		Conduction velocity (m/sec)		F-wave latency (msec)	
			RT	LT	RT	LT	RT	LT	RT	LT
Median (m)	Wrist	APB	14.7	14.4	2.8	3.0			27.3	
	Elbow	APB	14.5	14.3	7.8	7.9	56	57		
Ulnar (m)	Wrist	ADM	11.8	15.3	3.2	2.9			NR	
	Below elbow	ADM	11.7		8.2		50			
	Above elbow	ADM	6.2	15.2	13.9	8.3	19	52		
Median (s)	Wrist	Index finger	45.5	66.9	2.3	2.6	64	63		
Ulnar (s)	Wrist	Little finger	NR	30.7	NR	2.7	NR	58		
Femoral (m)	Groin	Rectus femoris	1.1	1.0	5.1	6.0			NR	NR
Tibial (m)	Ankle	AHB	30.8	30.7	5.4	5.7				
	Popliteal fossa	AHB	29.7	30.4	14.2	14.4	45	46		
Peroneal (m)	Ankle	EDB	6.2	8.6	3.7	4.5			46.8	
	Fibular head	EDB	5.7	7.7	11.9	13.1	48	45		
Sural (s)	Calf	Posterior ankle	22.4	18.7	3.0	2.8	47	50		

Abbreviations: m: motor study; s: sensory; RT: right; LT: left; NR: no response; APB: abductor pollicis brevis; ADM: abductor digiti minimi; AHB: abductor hallucis brevis; EDB: extensor digitorum brevis.

Note: All sensory latencies are onset latencies. All sensory conduction velocities are calculated using onset latencies. The report F-wave latency represents the minimum F-wave latency.

at rest, and reduced motor unit action potential during voluntary contraction (Table 2). The observation results indicated symmetric femoral neuropathy with significant axonal loss and demyelination of the right ulnar nerve at the elbow. A Follow-up brain MRI on Feb. 13, 2004, identified diffused hyperintensities on T2-weighted images in the right global pallidus, bilateral periventricle and left parietal subcortical white matter.

After taking a rehabilitation program for peripheral and central nervous system lesions, the patient achieved functional improvement in ambulation, endurance and balance. At that time, he could walk a distance of 500-meters without any device. Furthermore, the sensory impairment of the right hand showed a near full recovery. Improvement in muscle power of the bilateral knee extensor, from 2/5 to 4/5 in the manual muscle test, was attained after continuing the rehabilitation programs when he was discharged.

DISCUSSION

Carbon monoxide created by incomplete combustion of fossil fuels swiftly diffuses across the alveolar-capillary interface, binding strongly with hemoglobin to form carboxyhemoglobin, resulting in a leftward shift of the oxyhemoglobin dissociation curve. This shift, combined with CO inhibition of cytochrome P-450-mediated cellular respiration, produces tissue hypoxia, anaerobic metabolism, and lactic acidosis.⁽⁴⁾

The nonspecific symptoms of CO poisoning are headache, lightheadedness, nausea, vomiting, malaise, visual disturbances, palpitations, and confusion.^(4,5) Principal reductions in cognitive function are impaired memory, attention, visual-spatial skills, arithmetic skills, and executive functions.⁽⁵⁾ A wide

variety of neuropsychiatric effects may occur, such as psychosis, mood disturbances, personality change, dementia, concentration deficit, apathy, disorientation, amnesia, mutism, fecal or urinary incontinence, gait disturbance, dyspraxia, glabella signs and grasp reflex.⁽⁶⁾ Myonecrosis and rhabdomyolysis due to CO poisoning have also been reported.^(2,3) Peripheral neuropathy has rarely been reported following CO poisoning.

Peripheral neuropathy resulting from CO poisoning commonly occurs in young adults. The lower extremities are particularly vulnerable to peripheral neuropathy, and the left side is more so than the right, whereas mononeuropathy and polyneuropathy are the most common peripheral neurological deficits caused by CO poisoning.⁽⁷⁾

There are several causes in peripheral neuropathy: (1) Mononeuropathy by compression, produced by laying on a hard surface for hours or days, or petechial hemorrhages;⁽⁸⁾ (2) Metabolic polyneuropathy; (3) Vasculitis produces secondary ischemic damage in affected tissues;⁽⁹⁾ (4) Substantial subfascial edema of various muscle groups results in compartment syndrome;⁽¹⁰⁾ (5) CO by itself or hypoxia induced by CO, may be toxic to peripheral nerves.⁽⁸⁾

In this case, the nerve conduction studies of the right ulnar nerve showed demyelinating neuropathy at the elbow, and the sensory impairment of the right hand was a near total recovery after taking rehabilitation programs. Compression was suggested to be the cause of the right ulnar neuropathy.

The patient developed a femoral neuropathy while recovering from a state of depressed consciousness after a CO poisoning episode. The femoral neuropathy of this patient is symmetrical suggesting strong evidence against causation by compressive trauma or by petechial hemorrhaging into the nerves.⁽⁸⁾

Table 2 Electromyography

Muscle	Fibrillations	Fasciculations	Motor Unit Action Potentials
Right L4 Paraspinal	None	None	Normal
Right Iliopsoas.	None	None	Normal
Left Iliopsoas.	None	None	Normal
Left Vastus Medialis	2+	None	No spontaneous activity; decreased recruitment; increased duration and amplitude
Right Vastus Medialis	2+	None	No spontaneous activity; decreased recruitment; increased duration and amplitude

Additionally, no previous muscle weakness or systemic disease in this patient was present before the accident. The bilateral hip flexors and knee extensor muscle weakness combined with numbness at the bilateral medial knee area were described after CO poisoning. The medical course of femoral neuropathy in this patient was not chronic and progressive. However, the most natural course of polyneuropathy is chronic, slowly progressive, and has a distal-to-proximal gradient character.⁽¹¹⁾ Therefore, we can exclude the possibility of polyneuropathy.

Furthermore, the patient did not complain about any muscle pain, tenderness or hypoesthesia during the hospitalization process. However, burning and dysesthetic pain, sensory loss, and weakness in the distribution of multiple individual peripheral nerves are typical symptoms and signs in patients with vasculitis neuropathy.⁽¹²⁾ Most nonsystemic vasculitis neuropathy (NSVN) is a stepwise progressive, distal-predominant, asymmetric or symmetric, sensorimotor polyneuropathy.^(9,12) Nerve conduction studies in NSVN usually reveal low amplitude in sensory nerves and compound muscle nerve action potentials which are greater amplitude loss in the upper compared to lower limbs.⁽¹²⁾ In the patient, no typical symptoms and significant muscle weakness in upper and distal limbs were found. Therefore, we can also exclude the possibility of femoral neuropathy induced by nonsystemic vasculitis.

Sungur and Guven showed that CO poisoning may produce severe rhabdomyolysis.⁽²⁾ Skeletal muscle sensitivity to CO poisoning can lead to a severe and disabling myonecrosis.⁽³⁾ The mechanisms of CO-myonecrosis are as follows: (1) decreased hemoglobin carrying capacity of oxygen; (2) CO-inactivated cytochrome oxidase, which leads to an inability to meet the energy requirements necessary to maintain aerobic respiration of working muscle cells; and (3) CO interfering with the normal binding of oxygen to myoglobin, which is an essential oxygen reservoir within the muscle tissue.⁽³⁾ Substantial subfascial edema of various muscle groups resulting from myonecrosis with CO poisoning and rhabdomyolysis associated with trauma and prolonged immobilization results in compartment syndrome.^(3,10) As compartment pressure nears terminal arteriolar pressure, the nutrients cannot reach capillary beds from the circulation system, resulting in tissue ischemia.⁽¹³⁾

In this case, rhabdomyolysis was noted, however, insufficient evidence was available to support the presence of compartment syndrome associated with rhabdomyolysis. Furthermore, the myopathy of rhabdomyolysis is typically self-limiting, resulting in little residual muscle damage.⁽¹⁰⁾ After medical treatment, the CK level gradually declined and paraparesis persisted. This finding suggests evidence against causation by rhabdomyolysis.

Recent investigations have identified mechanisms of CO-mediated toxicity. O'Donnell et al. showed that CO-induced tissue hypoxia amplifies impairment of oxidative metabolism so that susceptible cells, such as those in the central nervous system (CNS) and myocardium, are unable to meet the energy requirements necessary to sustain cellular integrity.⁽⁵⁾ Thom demonstrated that CO exposure leads to reversible demyelination of CNS lipids resulting from lipid peroxygenation.⁽¹⁴⁾ Additionally, one hypothesis proposes that tissue hypoxia due to CO poisoning results in reoxygenation injury to the CNS.⁽⁴⁾ Hyperoxygenation helps to generate partially reduced oxygen species, oxidize essential proteins and nucleic acids, which then lead to typical reperfusion injury.⁽¹⁵⁾ Furthermore, nitric oxide freed from platelets during CO exposure has been linked to CNS damage.⁽¹⁶⁾ Demyelination is the pathological finding of clinically affected peripheral nerves in cases of CO intoxication.^(7,17) However, the actual pathogenesis of peripheral neuropathy remains unknown.

In this case, nerve conduction studies and electromyography indicated symmetric femoral neuropathy with significant axonal loss. The resulting observation differs from those previously reported. In an animal model study, most sheep exposed to 1% CO for more than 150 min developed some axonal damage in peri-ventricular white matter.⁽¹⁸⁾ In another animal model study, prolonged exposure to a lower concentration of CO caused reactive and degenerative axonal changes in cats.⁽¹⁹⁾ Therefore, the nature and extent of nerve damage may be related to time exposed to CO.

The standard treatment for CO poisoning is administration of 100% oxygen.^(4,20) Oxygen should be administered until the carboxyhemoglobin level is restored.⁽⁴⁾ The possible indications for HBO include altered mental status and neurological signs, cardiovascular dysfunction, pulmonary edema, severe acidosis or unconsciousness.⁽⁴⁾ Preserving adenosine

triphosphate (ATP) levels in tissue exposed to CO is the principal potential benefit of HBO treatment.⁽²⁰⁾

The primary poor prognostic factors are as follows: old age; long exposure to CO; delayed treatment; unconscious status upon hospital admission; prolonged coma; low Glasgow coma scores; metabolic acidosis; high lactate levels; hyperamylasaemia; high serum aspartate aminotransferase levels; electrocardiographic abnormalities; and, globus pallidus or white matter lesions in early brain computed tomography.⁽⁵⁾

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一氧化碳中毒所致對稱性股神經病變及橫紋肌溶解症

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一氧化碳是氣體中毒中常見的原因，但是起因於一氧化碳中毒所導致的周邊神經病變是很少被提及的。而且，起因於一氧化碳中毒所導致的橫紋肌溶解症的案例在文獻中也是很少被談論的。此病例報告即在討論一位因一氧化碳中毒而導致對稱性股神經病變及橫紋肌溶解症的案例。一位 32 歲的男性，因一氧化碳中毒導致深度昏迷而住院。在住院當時，因出現極高的肌胺酸酐值 (total creatinine phosphokinase, 19662 IU/L; CK-MB, 272 IU/L) 而被診斷為橫紋肌溶解症。病人在接受數次療程的高壓氧治療後，其意識逐漸改善，但雙側臀部的屈曲肌群及膝部的伸展肌群仍虛弱無力。腰部的磁振影像並未顯示有任何的異常。神經傳導及肌電圖的檢查顯示有對稱性的股神經病變。病人經積極的復健治療之後，其在行走、平衡及肌耐力方面的功能，均有明顯的改善。(長庚醫誌 2006;29(4 Suppl):103-8)

關鍵詞：一氧化碳中毒，對稱性股神經病變，橫紋肌溶解症，高壓氧。

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