

# Pallidoreticular Lesion in Carbon Monoxide Intoxication by Gradient Echo: Report of a Case with Parkinsonism Features and Review of the Literature

Nai-Ching Chen<sup>1</sup>, Chun-Chung Lui<sup>2</sup>, Shu-Hua Huang<sup>3</sup>, Chi-Wei Huang<sup>1,4</sup>, Chen-Chang Lee<sup>2</sup>, Wen-Neng Chang<sup>1</sup>, Chang-Hung Chen<sup>1</sup>, Yu-Ting Lin<sup>1</sup>, Chiung-Chih Chang<sup>1,4</sup>

## Abstract-

**Purpose:** Pallidoreticular damage was defined by lesions involving both the pallidum and the substantia nigra and was only reported in four cases after CO intoxication.

**Case Report:** We report a patient with initial consciousness disturbances followed by parkinsonian features after carbon monoxide intoxication. The unique features in this patient included primary globus pallidus hemorrhage followed by delayed hemorrhage in pallidoreticular topography demonstrated by T1- and T2-weighted imaging. In the follow-up study 7 months later, the patient still presented with parkinsonism features and executive dysfunction while the pallidoreticular signal was only visible by gradient echo sequences but not the other MR conventional sequences. Hypometabolism in the frontal and basal ganglion regions were evident from 99mTc-TRODAT-1 study and partial responsiveness to levodopa in alleviating parkinsonian features was considered.

**Conclusion:** This case highlights the delayed development of pallidoreticular damages and its linkage in modulating prefrontal-subcortical neuronal circuits.

**Key words:** carbon monoxide intoxication, hemorrhage, pallidoreticular topography, parkinsonism

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## INTRODUCTION

Compared with basal ganglion hemorrhagic necrosis<sup>(1)</sup>, pallidoreticular damage involving both the pallidum and substantia nigra pars reticulata was only mentioned in four cases after carbon monoxide (CO)

intoxication<sup>(2-5)</sup>. This uncommon situation has rarely been examined solely in studies on CO intoxication. Although parkinsonian features after CO intoxication have been reported and the nigrostriatal pathway with clinical features of parkinsonism have been well studied<sup>(6)</sup>, whether there is an association between pallidoreticular injury

From the Departments of <sup>1</sup>Neurology, <sup>2</sup>Radiology and <sup>3</sup>Nuclear Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, <sup>4</sup>Department of Biological Science, National Sun Yat-Sen University, Kaohsiung, Taiwan.

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Correspondence to: Chiung-Chih Chang, MD. 123, Ta-Pei Road, Niasung, Kaohsiung County 833, Taiwan.  
E-mail: neur099@adm.cgmh.org.tw

and parkinsonism in patients after CO intoxication requires further analysis. This study describes one case with delayed pallidoreticular lesion after CO intoxication, and provides a comparison with the other four cases reported in the literature to better delineate the clinical characteristics<sup>(2-5)</sup>.

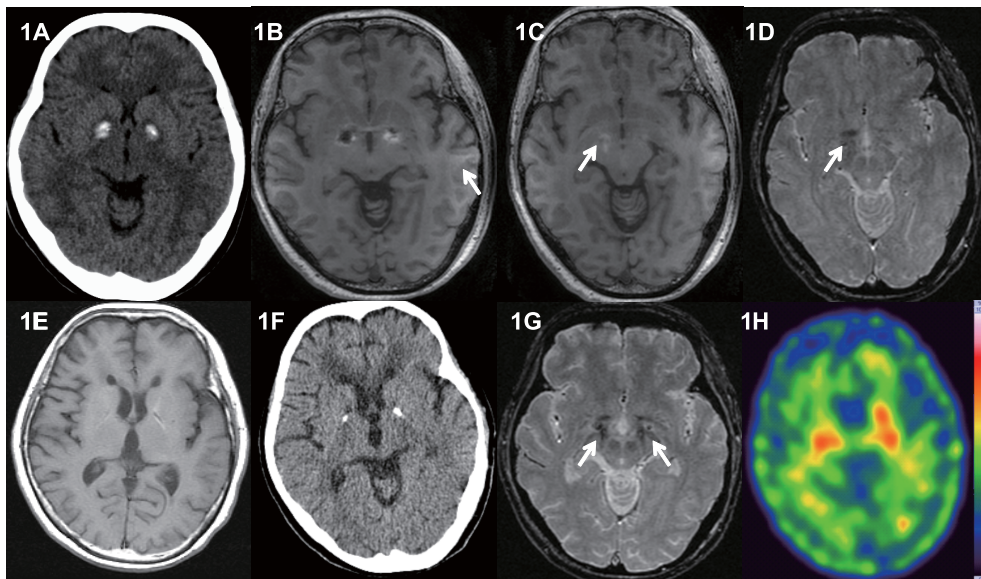
## CASE REPORT

A 57-year-old woman was found unconscious after attempting charcoal burning suicide and was sent to the emergency department immediately. The initial blood carboxyhemoglobin level was 19.3% (reference < 2%) and blood pressure was 130/90 mmHg. Brain computed tomography (CT) performed immediately revealed bilateral globus pallidus hyperdense lesions with CT number of 71 Hounsfield units, consistent with hemorrhage (Figure 1A). Except equivocal hypodense lesions found in the periventricular regions, no signal changes were

detected by brain CT.

After admission, the patient received 10 sessions of hyperbaric oxygen therapy, with 2.5 atm for 120 minutes at each session<sup>(7)</sup>. After 16 days, the patient was still in a state of decreased arousal, and her mini-mental state examination (MMSE) score was 3. Severe akinesia and cogwheel rigidity was found. There was no resting tremor, dystonia or myoclonic jerk during the extrapyramidal system examination.

Twenty-eight days after CO intoxication, she was still not able to answer questions using complete sentences, although she could communicate by saying simple phrases or sentences. The brain magnetic resonance imaging (MRI) showed relatively low signal intensity lesions with high signal intensity rim in the bilateral globus pallidus T1-weighted images (Figure 1B). Besides, faint high signal intensity over right substantia nigra was noted in this T1-weighted images (Figure 1C). Mild low signal intensity lesions was detected in right



**Figure 1.** (1A) Brain computed tomography showed bilateral basal ganglion hyperdense lesions after one day of carbon monoxide (CO) intoxication. (1B) Axial T1 weighted MRI at the level of the basal ganglion. A low signal intensity core with high signal intensity rims over the globus pallidus after 28 days of CO intoxication. (1C) Axial T1 weighted MRI of the midbrain with high signal intensity lesions on the right side (arrows) after 28 days of CO intoxication. (1D) Gradient echo of the midbrain with low signal intensity in right substantia nigra after 28 days of CO intoxication. (1E) Axial T1 weighted MRI at the level of the basal ganglion. Faint low signal intensity in the globus pallidus on T1WI after 7 months of CO intoxication. (1F) Brain computed tomography showed decreased volume of bilateral basal ganglion hyperdense lesions after 7 months of CO intoxication. (1G) Gradient echo of the midbrain with low signal intensities bilaterally (arrows) after 7 months of CO intoxication. (1H) Decreased TRODAT binding ratio in the basal ganglia after 7 months of CO intoxication.

substantia nigra in gradient echo of the midbrain (Figure 1D, arrow).

We started levodopa treatment, initiated at 50 mg three times a day for one month and a maintenance dosage of 100 mg three times a day for six months, for her parkinsonian features. Evaluation 7 months after CO intoxication showed improvement in rigidity and aspon-taneity after medication but she still had problems with festinating and small-step gait. The cognitive impairment was still impaired with a follow-up MMSE score of 20, digit forward 8 (reference:  $8.3 \pm 0.9$ ), digital backward 4 (reference:  $5.5 \pm 1.6$ ), design fluency 3 (reference:  $11.1 \pm 3.4$ ), verbal fluency in animal category 4 (reference:  $21.8 \pm 4.2$ ) in one minute and Stroop Interference test<sup>(8)</sup> 27 (reference:  $53.5 \pm 10.4$ ). A follow-up brain MRI 7 months after CO intoxication showed low signal intensity in the globus pallidus on T1WI (Figure 1E) with hyperdense lesions by CT (Figure 1F) (95 Hounsfield units). Low signal intensity in the sub-stantia nigra was detected only by gradient echo sequences (Figure 1G, arrows), without changes by T1WI or T2WI. The single photon emission computed tomography showed decreased <sup>99m</sup>Tc-TRODAT-1bind-

ing ratio bilaterally (right: 1.8, left: 1.41, references  $2.25 \pm 0.2$ ) (Figure 1H).

### CO intoxication patients with pallidoreticular pattern in the literature

Table 1 shows the four cases reporting pallidoreticu-lar lesions after CO intoxication after a review of the lit-erature.

## DISCUSSION

In contrast with the other four cases<sup>(2-5)</sup> showing pal-lidoreticular lesions following CO intoxication, the unique features in our case were the initial globus pal-lidus hemorrhage with calcification over globus pallidus in the follow up image. The pallidoreticular lesions was only detectable by gradient echo 7 months after the intoxication. In clinical features comparisons, 3 in 4 patients<sup>(2-5)</sup> with pallidoreticular damage developed parkinsonism features such as akinesia and rigidity. Both globus pallidus and pallidoreticular lesions modulated the presynaptic dopaminergic dysfunction<sup>(9)</sup> in our patient as shown by the decreased TRODAT binding

**Table 1.** Case review of carbon monoxide intoxication with pallidoreticular lesions

Year Reference	Clinical presentation	First PR signal interval from CO intoxication	Neuroimaging findings in substantia nigra	Responses to levodopa	Follow-up periods
1998 Kawanami <i>et al.</i> <sup>(2)</sup>	Severe akinesia, parkinsonism without tremor or rigidity of the limbs	1 year	T1WI: NA; T2WI: high	NA	NA
2002 Gandini <i>et al.</i> <sup>(3)</sup>	Only mild cognitive deficits, parkinsonism not mentioned	5 months	T1WI: NA ; T2WI: high	NA	12 months
2005 Kinoshita <i>et al.</i> <sup>(4)</sup>	Memory disturbance, dysarthria, urinary incontinence, and parkinsonism including rigidity and gait disturbance	12 days	DWI: high; ADC: low	NA	2 months
2008 Adam <i>et al.</i> <sup>(5)</sup>	Mild rigidity and persisting apathy, compulsive behavior	At autopsy	NA	Good	10 years
2011 Our case	Parkinsonism with akinesia, rigidity, aspon-taneity and apathy, cognitive impairment	7 months	T1WI isosignal; T2WI isosignal; gradient echo low	Partial	One year

NA = Not available; DWI = diffusion weighted image; ADC = apparent diffusion coefficient; T1WI = T1 weighted imaging; T2WI = T2 weighted imaging; PR = pallidoreticular lesions; CO = carbon monoxide

ratio. The study by Choi et al<sup>(10)</sup> suggested no clinical benefit of levodopa in treating CO patients with parkinsonism while good clinical response to levodopa was suggested by Adam et al<sup>(5)</sup>. The parkinsonian features might contribute majorly by globus pallidus lesions in our case since the patient still showed parkinsonian features after levodopa treatment.

Our case demonstrated evolutionary changes in the substantia nigra signals by repeated gradient echo sequencings. The signals appeared in the delayed phase might be metallic deposition, dystrophic calcification after tissue necrosis or increase iron deposition<sup>(11)</sup>. In comparison with the conventional T1- or T2-weighted MRI, the gradient echo sequencing showed higher sensitivity in detecting lesions appeared in the substantia nigra. Only three cases with pallidoreticular lesions from the CO intoxication literature performed neuroimaging survey (Table 1), with the detected time intervals of the pallidoreticular lesions from 12 days to one year after CO intoxication. The pathology of the pallidoreticular lesion reported by Adam et al<sup>(5)</sup> with severe neuronal loss and gliosis over bilateral pallidus and substantia nigra while the possible mechanisms purposed suggesting that substantia nigra was iron rich regions which might show selective tissue vulnerability because the high affinity of CO to heme molecules<sup>(2-5)</sup>.

Among these patients with CO intoxication and pallidoreticular pattern<sup>(2-5)</sup>, only 2 patients described having neuropsychiatric dysfunction. The case by Gandini et al<sup>(3)</sup> had mild cognitive impairment but the detailed neuropsychiatric evaluation was not available. The case described by Adam et al<sup>(5)</sup> showed compulsive behaviors and apathy in addition to impaired semantic and phonemic verbal fluency. The behavior and cognitive problems in the case by Adam et al<sup>(5)</sup> and ours might be attributed to interruption of loops connecting the prefrontal cortex and the basal ganglia<sup>(12)</sup>.

In conclusion, pallidal, pallidoreticular as well as prefrontal lobe damages all contributed to the parkinsonian features and behavior changes in patients with CO intoxication. Use of gradient echo might help in the detection of the delayed pallidoreticular lesions compared with conventional sequences.

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