




CASE REPORT

Delayed neuropsychiatric sequelae with improvement of decreased cerebral bold flow by single-photon emission computed tomography during hyperbaric oxygen therapy: A case report with a 10-year follow-up

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Abstract

Background: Delayed neuropsychiatric sequelae (DNS) occurs in 10%–30% of acute carbon monoxide poisoning cases. Patients with this condition present higher brain dysfunction. Hyperbaric oxygen (HBO) therapy was reportedly an effective treatment for DNS in the acute phase. Favorable predictive factors affecting the prognosis of patients with DNS after HBO therapy include younger age and longer interictal periods. However, the relationship between these factors and neuroimaging findings remains unclear.

Case Presentation: The patient was a 59-year-old man with DNS, who developed major depressive disorder and attempted suicide with charcoal briquettes. He was diagnosed with carbon monoxide poisoning and underwent acute HBO therapy. After a 1-month lucid period, the patient developed intermittent carbon monoxide poisoning with cognitive dysfunction, following which HBO therapy was re-initiated. Following treatment, the patient returned to work for 10 years. Frontal lobe hypoperfusion, measured by single-photon emission computed tomography and cognitive impairment, improved with HBO therapy. However, magnetic resonance imaging revealed brain volume atrophy over time.

Conclusion: This study reported a case of DNS that completely resolved within a 10-year follow-up period. Cerebral blood flow reduction, mainly in the frontal lobe, improved along with cognitive recovery during HBO therapy. Despite gradually progressive brain atrophy over the past decade, no noted deficits in cerebral blood flow were observed in the frontal lobes. These findings suggest that improvement in cerebral blood flow during HBO therapy and its retention may be factors associated with a favorable prognosis in patients with DNS.

KEYWORDS

carbon monoxide poisoning, cognitive impairment, delayed neuropsychiatric sequelae, hyperbaric oxygen therapy, recovery

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BACKGROUND

Suicide is a serious global public health concern. According to the World Health Organization, more than 700,000 people commit suicide annually.¹ In 2019, over 20,000 suicides occurred in Japan, 70% of which involved men.² Suicides caused by burning of charcoal are common in East Asia.³ In 2019, the use of charcoal briquettes was

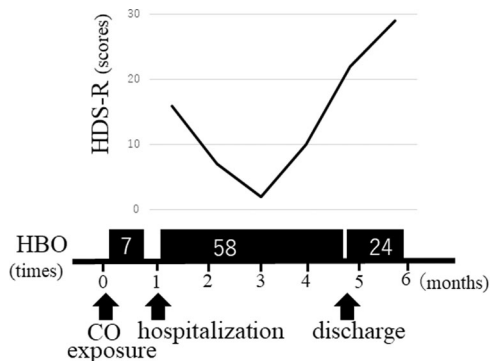


FIGURE 1 Progress chart from carbon monoxide (CO) exposure to the end of hyperbaric oxygen therapy (HBO). HDSR, Hasegawa Dementia Scale-Revised.

the third (8.7%) most common method of suicide among Japanese men, following hanging and jumping.⁴

Delayed neuropsychiatric sequelae (DNS) occurs in 10%–30% of cases of acute carbon monoxide (CO) poisoning. Patients with this condition present with higher brain dysfunction, such as disorientation and memory loss.⁵ Hyperbaric oxygen (HBO) therapy is reportedly an effective treatment for DNS in the acute phase.^{6–8}

Predictive factors for favorable prognosis following HBO therapy include younger age, longer interictal periods, and independence in performing activities of daily living during intermittent CO poisoning.⁹ However, the relationship between these factors and neuroimaging findings remains unclear.

CASE PRESENTATION

A 59-year-old man undergoing a major depressive episode used charcoal briquettes in X year. The following day, the patient was transported to the emergency department and was diagnosed with CO poisoning with loss of consciousness. HBO therapy was administered seven times within 2 weeks, and the patient was discharged thereafter as no depressive symptoms were observed. Two weeks after discharge, the patient presented with memory

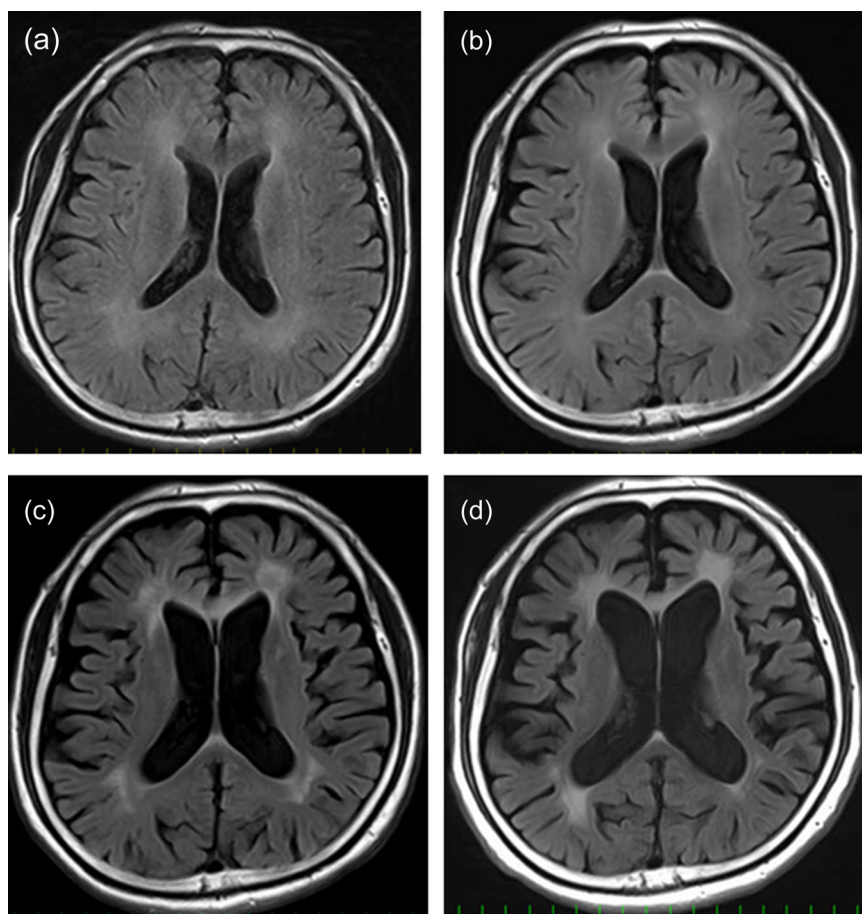


FIGURE 2 Brain magnetic resonance images in an axial section at the body of the lateral ventricle using a fluid attenuated inversion recovery sequence: (a) at the 13th hyperbaric oxygen (HBO) therapy session, (b) at the 72nd HBO therapy session, (c) 2 years after HBO therapy, and (d) 8 years after HBO therapy.

impairment and difficulty in bathing. He was admitted to our hospital 1 month after CO exposure and was diagnosed with intermittent CO poisoning. He had a Hasegawa Dementia Scale-Revised (HDS-R) (a brief cognitive scale¹⁰) score of 16 points (the cut-off point for dementia is 21/20). HBO therapy was resumed but his cognitive function declined further (HDS-R score 2 points). Eventually, he developed akinetic mutism. After the 30th HBO therapy session, his cognitive function recovered slightly (HDS-R score 9 points), but he gradually became agitated and violent, therefore drug therapy was initiated. Valproic acid (800 mg/day), risperidone (1 mg/day), and quetiapine (50 mg/day) were prescribed, resulting in the alleviation of the patient's agitation. After the 65th HBO therapy session, his HDS-R score increased to 22 points, and the patient was discharged after 99 days of hospitalization. HBO therapy was continued in the outpatient setting. After the 89th HBO therapy session, the HDS-R score increased to 29 points (out of 30), and HBO therapy was terminated (Figure 1). The patient continued to take valproic acid only from X + 1 years after discharge.

Neuroimaging results are shown in Figures 2-5. Magnetic resonance imaging (MRI) revealed deep white matter hyperintensities around the anterior and posterior horns of the lateral ventricles during HBO therapy (Figure 2a,b). At 2 and 8 years after discharge, MRI showed a gradual spread of deep white matter hyperintensity and overall brain atrophy (Figure 2c,d). No changes

were observed in basal ganglia, including globus pallidus (Figure 3). In contrast, single-photon emission computed tomography (SPECT) showed improvement in the extensive frontal hypoperfusion (Figure 4a,b) and in the basal ganglia, hippocampus, and periventricular areas of the lateral ventricles (Figure 5a,b) during HBO therapy. At 8 and 9 years after discharge, SPECT showed decreased blood flow, mainly in the frontoparietal lobe. However, it was not as extensive as the baseline image (Figure 4c,d). There was no apparent re-decrease in blood flow in the basal ganglia or other areas (Figure 5c,d).

The patient returned to work as an engineer 3 months after his discharge in X year and became a director in X + 3 years, then retired at the age of 65 years, but was rehired by the same employer. In X + 8 years, the patient had an HDS-R score of 30 points (full score), a frontal assessment battery score of 15 points (frontal lobe dysfunction cutoff point of 12), and a full intelligence quotient (IQ), measured using the Wechsler Adult Intelligence Scale-III, of 107 (verbal IQ 104, performance IQ 109). These scores indicated no cognitive dysfunction. Additionally, no apparent decline in WAIS-3rd index scores (verbal comprehension 102 points, perceptual organization 110 points, working memory 113 points, processing speed 113 points) was observed. Treatment with valproic acid was stopped in X + 9 years. From then until X + 10 years, treatment was terminated, as the patient was able to work without medication.

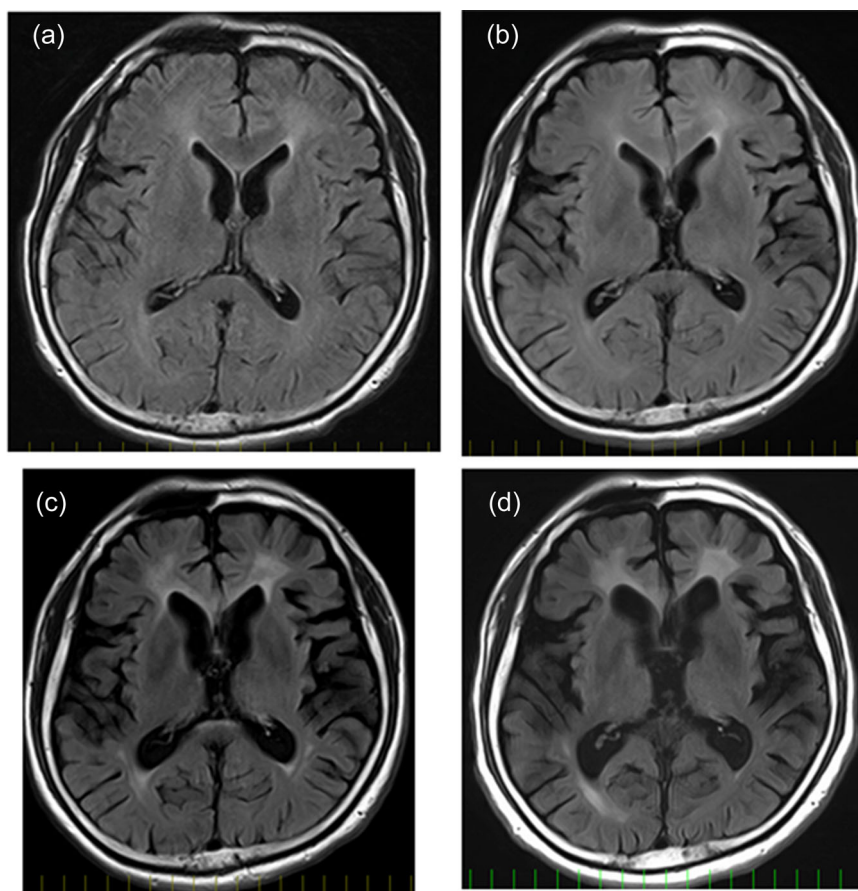


FIGURE 3 Brain magnetic resonance images in an axial section at the basal ganglia using a fluid attenuated inversion recovery sequence: (a) at the 13th hyperbaric oxygen (HBO) therapy session, (b) at the 72nd HBO therapy session, (c) 2 years after HBO therapy, and (d) 8 years after HBO therapy.

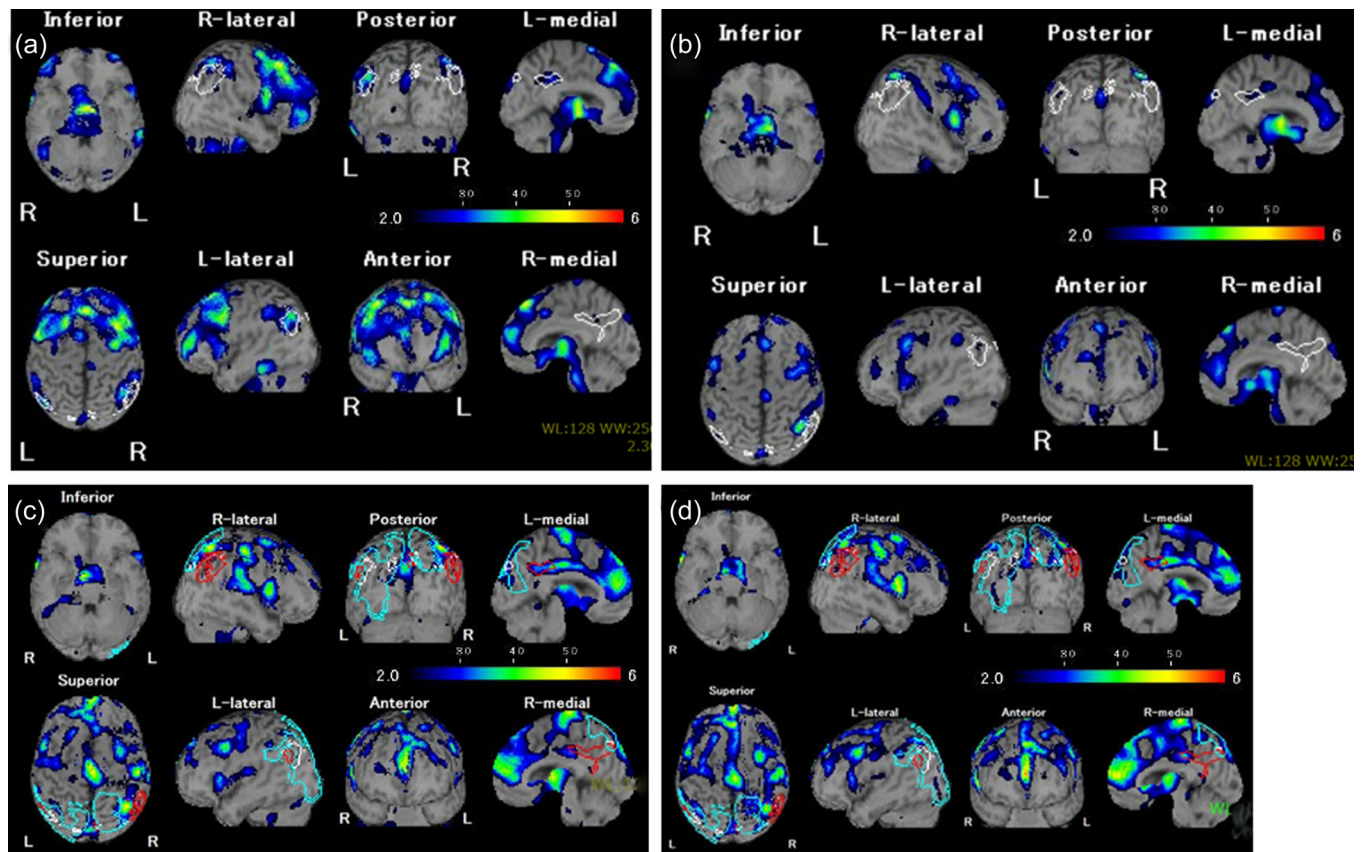


FIGURE 4 Brain single photon emission computed tomography using technetium-99m-ethyl cysteinate dimer: (a) at the 32nd hyperbaric oxygen (HBO) therapy session, (b) at the 74th HBO therapy session, (c) 8 years after HBO therapy, and (d) 9 years after HBO therapy.

DISCUSSION

This was the first case report of a patient with DNS who underwent long-term follow-up after being treated with HBO therapy. Cognitive function tests and neuroimaging modalities were used to assess the patient throughout the follow-up period. He developed DNS with akinetic mutism. However, he recovered with HBO therapy, and good cognitive function was maintained for 10 years after discharge. Gradual progressive brain volume atrophy and white matter hyperintensities were detected on MRI, whereas SPECT showed preserved cerebral blood flow, which was restored during HBO therapy.

CO poisoning causes cerebral nerve damage, which manifests as high signals and edema, mainly in the bilateral globus pallidus and white matter,¹¹ on T2 weighted images. In a 9-month prospective study, white matter lesions observed in the acute phase extended to the subcortical areas.¹² In addition, patients with DNS exhibited significantly lower gray matter volumes than those without for up to 9 months after CO intoxication, suggesting severe cerebral nerve damage.¹² SPECT revealed severe frontal hypoperfusion and a decrease in severity was observed during the 6th month of follow-up without HBO therapy.¹³ Few reports have described neuroimaging changes after HBO therapy. Lin et al. described the neuroimaging findings of a patient with DNS before

and after HBO therapy.¹⁴ At 6 weeks after HBO therapy, MRI scans showed an improvement in hyperintense lesions in deep white matter. Meanwhile, SPECT showed improved hypoperfusion in the cerebral blood flow, consistent with the present case. The long-term effects of HBO therapy after cerebral ischemia include improved cognitive function in rats.¹⁵ In the present case, the SPECT results reflected improved cognitive function. One of the therapeutic mechanisms of HBO therapy for cerebral ischemia is to increase cerebral blood flow by inducing cerebral angiogenesis,¹⁶ which may be why cerebral blood flow and cognitive function were preserved despite the noticeable frontal lobe atrophy observed. However, further prospective observational studies with neuroimaging are needed.

The optimal number of HBO therapy sessions for DNS remains unknown. However, additional sessions of HBO therapy for acute CO poisoning were considered sufficient to prevent subsequent poisoning.^{7,17} In the present case, the patient received 89 sessions of HBO therapy, and his cognitive function continued to improve. Similarly, Monji et al.¹⁸ reported two cases of DNS wherein the patients received more than 100 HBO therapy sessions while cognitive function was measured in the frontal lobe. The restoration of cognitive function is possibly related to the optimal number of HBO therapy sessions for patients with DNS.

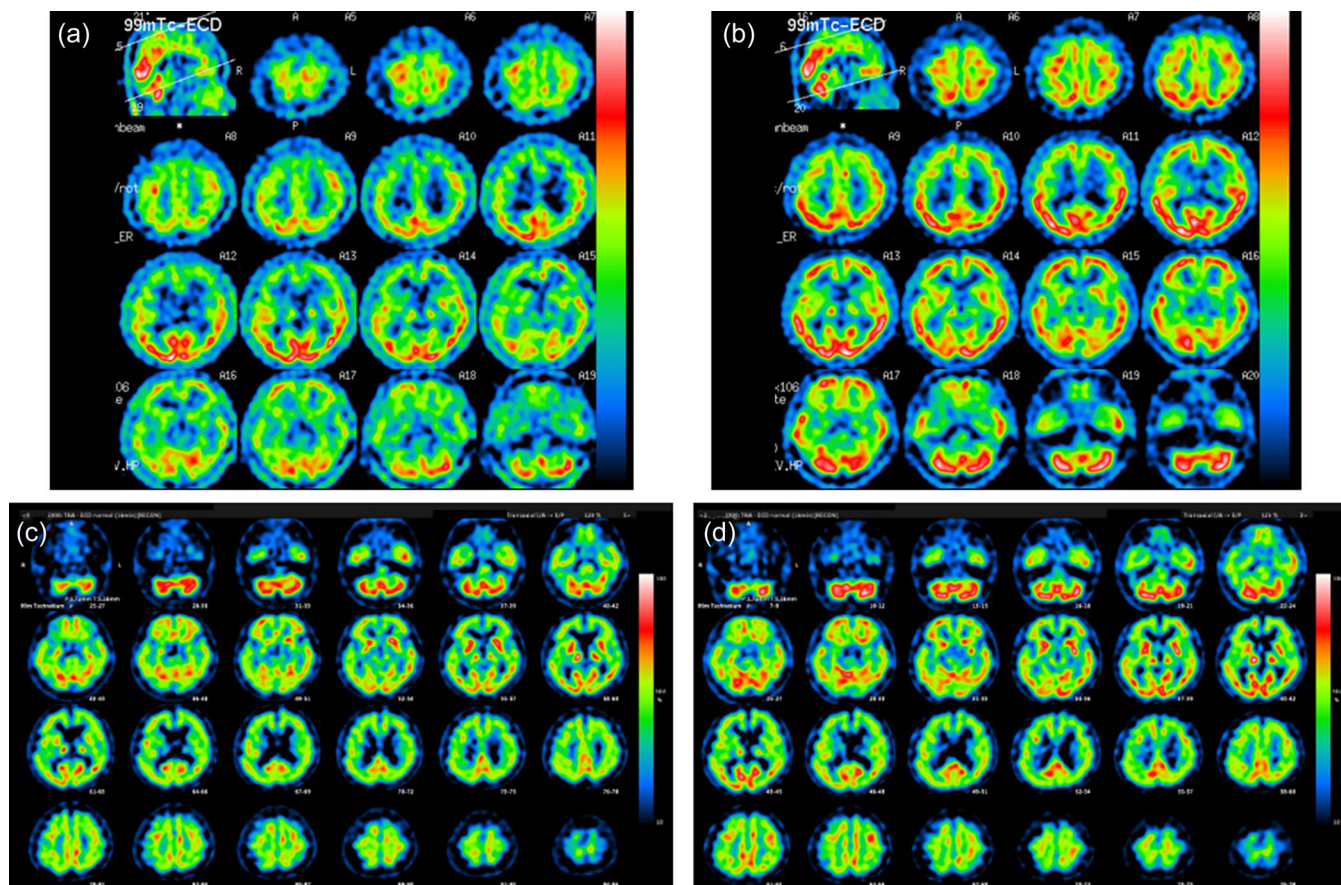


FIGURE 5 Brain single photon emission computed tomography using technetium-99m-ethyl cysteinate dimer: (a) at the 32nd hyperbaric oxygen (HBO) therapy session, (b) at the 74th HBO therapy session, (c) 8 years after HBO therapy, and (d) 9 years after HBO therapy.

Our report had some limitations. First, voxel-based analysis of gray matter volume was not measured. Second, MRI and SPECT machines have changed significantly during the 10-year study period, and the variation in neuroimaging machines through this period may have affected imaging results.

CONCLUSION

In conclusion, this study reported a patient with DNS that completely resolved within a 10-year follow-up period. The cerebral blood flow reduction, mainly in the frontal lobe during the acute phase, improved with HBO therapy, and this was accompanied by the patient's cognitive recovery. Furthermore, gradually progressive brain atrophy was observed over the past decade. However, the cerebral blood flow in the frontal lobe remained normal. These findings suggest that improving and retaining cerebral blood flow during HBO therapy had a protective effect on brain function. Thus, improvement in cerebral blood flow during HBO therapy and its retention are possible factors associated with a favorable prognosis in patients with DNS.

AUTHOR CONTRIBUTIONS

Kosuke Hagiwara wrote the original draft. Toshio Matsubara and Shin Nakagawa assisted in writing the paper. All authors contributed to and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

N/A.

ETHICS APPROVAL STATEMENT

Written consent from the patient was obtained for the reporting of this case.

PATIENT CONSENT STATEMENT

Written consent from the patient was obtained for the reporting of this case.



CLINICAL TRIAL REGISTRATION

N/A.

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