CASE REPORT

DOI: 10.4274/gulhane.galenos.2025.12989
Gulhane Med J

Successful treatment of an older patient with delayed neurological sequelae and delirium after carbon monoxide poisoning with memantine

Hatice Tuğba Yazır[1], Zehra Sarıkaya Demirbaş[1], Candeniz Avcı[2], Mehmet İlkin Naharcı[1]

[1]University of Health Sciences Türkiye, Gülhane Training and Research Hospital, Clinic of Geriatrics, Ankara, Türkiye
[2]Lüleburgaz Private Breath Hospital, Clinic of Internal Medicine, Kırklareli, Türkiye

Cite this article as: Yazır HT, Sarıkaya Demirbaş Z, Avcı C, Naharcı Mİ. Successful treatment of an older patient with delayed neurological sequelae and delirium after carbon monoxide poisoning with memantine. *Gulhane Med J.* [Epub Ahead of Print]

Date submitted:
27.02.2025
Date accepted:
10.06.2025
Epub:
24.02.2026

Corresponding Author:
Zehra Sarıkaya Demirbaş, M.D., University of Health Sciences Türkiye, Gülhane Training and Research Hospital, Clinic of Geriatrics, Ankara, Türkiye
zehra.sarikaya@windowslive.com

ORCID:
orcid.org/0000-0003-2663-4119

Keywords: CO poisoning, geriatrics, memantine, delayed neurological sequelae, delirium

ABSTRACT

Carbon monoxide (CO) poisoning can cause delayed neurological sequelae (DNS), a condition with no effective treatment. We report a 66-year-old male patient who recovered from acute CO poisoning but developed DNS and delirium one week later. He showed akinetic mutism, parkinsonism, rigidity, and cognitive impairment. Non-pharmacological approaches and donepezil were tried, but due to side effects, memantine (20 mg/day) was started. Over the course of one year, the patient showed significant improvement in neurological and functional status, with improvements in cognitive function (Mini-Mental State Examination: 26) and brain magnetic resonance imaging findings. This case suggests memantine may contribute to DNS recovery.

Introduction

Carbon monoxide (CO) poisoning is a major cause of death and illness worldwide, with an incidence and mortality rate of 137 and 4.6 per million individuals, respectively (1). Brain, heart muscles, kidneys, and skeletal muscles are among the most affected tissues (2). CO poisoning can lead to delayed neuropsychiatric sequelae (DNS), which refers to brain damage that emerges after a period ranging from a few days to six weeks following recovery from hypoxic injury (3). DNS occurs in 1-47% of individuals affected by CO poisoning. The clinical manifestations of DNS include motor dysfunction, gait abnormalities, autonomic dysfunction, seizures, and blindness (4). Currently, there is no effective treatment for DNS and the precise pathophysiological mechanisms remain to be elucidated.

This case report presents a patient who recovered from acute CO poisoning. Significant improvements in long-term neurological deficits were achieved with memantine treatment.

Case Presentation

A 66-year-old male patient was found unconscious by his relatives in a room in his house, which was heated with a coal stove and permeated by a strong smell of smoke. The patient had no history of chronic illness, regular medication use, smoking, or alcohol consumption. Upon arrival at the emergency department, his Glasgow Coma Score (GCS) was 3. Following reservoir oxygen therapy, GCS score increased to 11 (E4-M5-V2).

Analysis of the arterial blood gas sample revealed a pH of 7.35, lactate of 5.7 mmol/L, and carboxyhemoglobin level of 29.8%. Hyperbaric oxygen therapy (HBOT) was not administered because air trapping was detected in the upper lobe of the right lung on thoracic computed tomography (CT). The cranial CT findings of the patient, who had no previous cranial imaging, were normal when performed in the emergency department. He was hospitalized in the intensive care unit and high-flow normobaric 100% oxygen was administered (Figure 1a). After 12 days, the patient was discharged with normal neurological and general examination findings. Seven days after discharge, he was brought back to the hospital with complaints of inability to communicate, urinary incontinence, muscle stiffness, and inability to walk. On examination, akinetic mutism, parkinsonism, widespread trunk and extremity muscle stiffness, and a hypomimetic face were observed. Activity of daily living (ADL) score was 0 out of 6 (totally dependent), instrumental activities of daily living (IADL) score was 0 out of 5 (totally dependent), and the Mini-Mental State Examination (MMSE) score was 0 out of 30 (Table 1). Brain magnetic resonance imaging (MRI) T2-weighted images revealed diffuse hyperintensity in the bilateral hemispheric white matter, consistent with delayed leukoencephalopathy secondary to prior CO exposure. Additionally, hyperintense changes were observed in the bilateral globus pallidus regions (Figure 1b*). An electroencephalogram revealed bitemporal slowing of brain activity.

Based on these findings, the diagnosis of DNS and delirium after CO intoxication was considered. Non-pharmacological approaches were implemented. Plans for exercises to be performed at home were created by a physiotherapist. After one week, his diffuse rigidity had slightly lessened. His efforts to form sentences increased, and he began to recognize his relatives and indicate his need to urinate. At this visit, donepezil treatment was attempted for prolonged delirium; however, due to the development of insomnia and hallucination side effects, the medication was switched to memantine at a dose of 20 mg/day (Figure 1a). One month later, his rigidity decreased, he began to walk without assistance, and was able to eat by himself (Table 1). At the end of one year, ADL and IADL were independent (Figure 1a). Considering further detailed cognitive tests, the

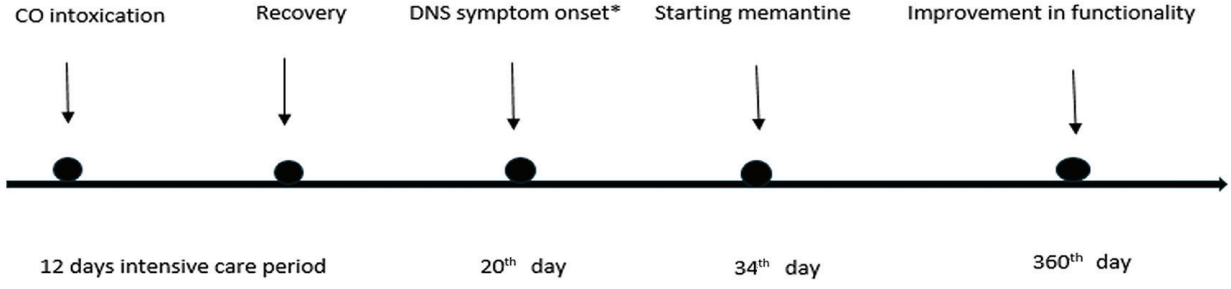

Figure 1a. The patient's course after acute CO poisoning
CO: Carbon monoxide, *DNS: Delayed neurological sequelae

Table 1. Detailed cognitive and functional evaluation on the day the patient presented with DNS symptoms and at the follow-ups

Time after exposure (days)	20	30	40	50	100	180	360
ADL (0-6)	0	0	1	2	6	6	6
IADL (0-8)	0	0	0	0	1	4	8
MMSE (0-30)	0	1	3	5	14	20	26
Clock drawing test (0-6)	0	0	0	2	2	4	5
Word fluency semantics*	-	-	-	-	-	6	14
Trail making test -A*	-	-	-	-	-	188	147
Trail making test -B*	-	-	-	-	-	Not completed	Not completed
Immediate recall short story*	-	-	-	-	-	3	5

*: These tests could not be performed on days 20, 30, 40, 50, and 100 due to the patient's developing cognitive dysfunction.
DNS: Delayed neurological sequelae, ADL: Activities of daily living, IADL: Instrumental activities of daily living, MMSE: Mini-Mental State Examination

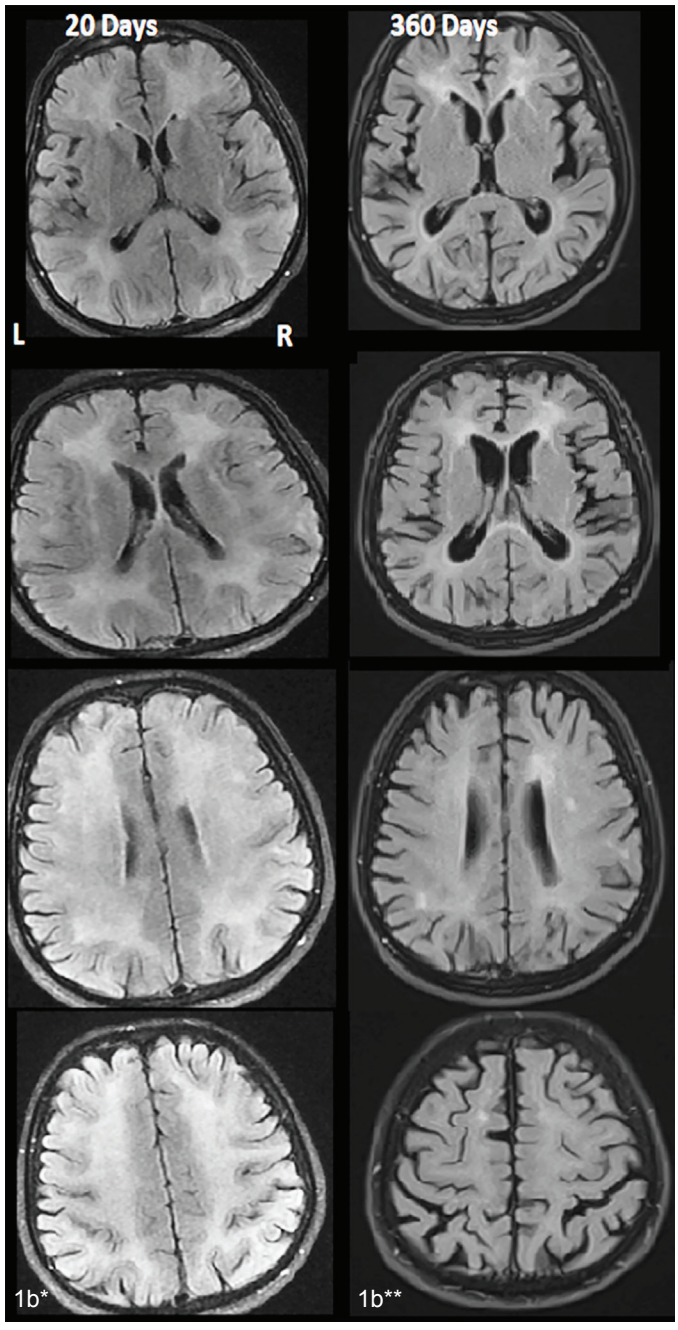

Figure 1b. Bilateral globus pallidus lesions, periventricular and deep white matter hyperintensities were seen on MRI 20 days after the first event (Figure 1b*) and regressed after 1 year (Figure 1b**)

L: Left, R: Right, MRI: Magnetic resonance imaging

MMSE scores increased to 26 points after one year (Table 1). He was able to continue his work as a farmer and maintain his daily life. Follow-up brain MRI findings after one year showed that the diffuse hyperintensities had decreased (Figure 1b¨).

Discussion

We showed for the first time that memantine hydrochloride treatment administered when DNS symptoms developed in an older adult following a recovery period after CO intoxication alleviated the neurological disorder and improved clinical status.

White matter demyelination is observed in the pathology of DNS, a rare complication that develops following a recovery period after CO intoxication. The mechanisms underlying this pathology are not well understood. Perivascular changes caused by N-methyl-D-aspartate activation and neuronal nitric oxide synthase overactivity, along with post-CO poisoning inflammation, sequester and activate neutrophils (5). Memantine may reduce this activated inflammatory response through its anti-inflammatory, neuroprotective, and hemodynamic effects mediated by glutamate receptor blockade (6). Experimental studies that found that memantine alleviated edema and infarction in rats with focal cerebral ischemia and reperfusion injury support this mechanism (7). To our knowledge, there is only one middle-aged case of DNS in which memantine was given (8).

DNS symptoms might be preventable or treatable. HBOT is considered a promising method for the prevention and treatment of DNS; however, there is no consensus on its effectiveness (9). In our case, HBOT could not be performed because of the risk of lung barotrauma. Other experimental treatments, including anti-inflammatory and immunomodulatory drugs, such as immunoglobulin, interferon, glatiramer acetate, and steroids, have been studied in clinical trials, but their success has been limited (10). The exact mechanism of CO toxicity remains unclear; however, because oxidative stress, neuronal injury, and ischemia-reperfusion-related damage contribute to the development of delayed symptoms, antioxidant therapies may offer a promising alternative treatment strategy (11,12).

As a result, successful clinical recovery from DNS in an older adult whom we monitored with detailed cognitive and functional tests and MRI during a long follow-up period, could be attributable to memantine treatment. Further clinical studies on this beneficial effect are required.

Conclusion

Our findings suggest that memantine treatment may have contributed to the significant neurological and functional improvement observed in an elderly patient with DNS following CO poisoning. While spontaneous recovery cannot be completely ruled out, the rapid improvement in cognitive and motor functions, as well as radiological findings, highlights the potential role of memantine in the management of DNS.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of this case report.

Footnotes

Authorship Contributions

Concept: H.T.Y., Z.S.D., M.İ.N., Design: H.T.Y., Z.S.D., M.İ.N., Data Collection or Processing: H.T.Y., Z.S.D., C.A., Analysis or Interpretation: H.T.Y., Z.S.D., C.A., M.İ.N., Literature Search: H.T.Y., C.A., Writing: H.T.Y., Z.S.D., M.İ.N.

Conflict of Interest: All the authors declare that they have no conflicts of interest regarding this study.

Financial Disclosure: The authors did not and will not receive any funding for this study.

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