EJCRIM
European Journal
of Case Reports
in Internal Medicine

DELAYED NEUROLOGICAL SEQUELAE OF CARBON MONOXIDE INTOXICATION INITIALLY TREATED AS INFECTIOUS MENINGO ENCEPHALITIS

Xavier Jannot[1], Alpha Oumar Diallo[1], Judicaelle Didierjean[2], Jean-Edouard Terrade[1], Emmanuel Andrès[1], Marine Feuermann[1], Noel Lorenzo-Villalba[1]

[1] Service de Médecine Interne, Hôpitaux Universitaires de Strasbourg, Strasbourg, France
[2] Service de Neurologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, France

Corresponding author's e-mail: noellorenzo@gmail.com

Received: 07/02/2025
Accepted: 17/02/2025
Published: 03/03/2025

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Incolla
This article is licensed under a Commons Attribution Non-Commercial 4.0 License

How to cite this article: Jannot X, Diallo AO, Didierjean J, Terrade JE, Andrès E, Feuermann M, Lorenzo-Villalba N. Delayed neurological sequelae of carbon monoxide intoxication initially treated as infectious meningo encephalitis. *EJCRIM* 2025;**12**:doi:10.12890/2025_005235

ABSTRACT

We report the case of a 75-year-old woman admitted to the emergency department for confusion, gait disturbances and mutism associated with an inflammatory syndrome occurring 3 weeks after acute carbon monoxide intoxication. The main hypothesis upon arrival was infectious meningoencephalitis, and the patient was put on acyclovir and antibiotics in meningeal doses. After a short stay in intensive care, the patient's condition did not improve, and the revaluation of her case history and imaging studies led to the diagnosis of post-interval syndrome secondary to carbon monoxide intoxication after a 3-week asymptomatic period. Post-interval syndrome is a complication poorly known to clinicians, manifesting as neuropsychiatric disorders after carbon monoxide intoxication despite an initial period of improvement. Repeated magnetic resonance imaging, in conjunction with compatible clinical findings, allow the diagnosis to be made. No neurological improved was noted after 6 months follow-up.

KEYWORDS

Carbon monoxide intoxication, delirum, meningo-encephalitis

LEARNING POINTS

- Post-interval syndrome is little-known to clinicians and should be considered in any patient presenting with neurological disorders after a symptom-free interval following carbon monoxide intoxication.
- Repeated magnetic resonance imaging at a distance from the onset of post-interval syndrome (more than a month) helps to distinguish it from cytotoxic oedema which it may be initially confused.
- The prognosis is poor with no proven effective treatment to date.

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

INTRODUCTION

Acute confusional syndrome can represent a challenge for clinicians considering the wide spectrum of clinical aetiologies. Questioning the patient himself/herself can be complex, and the help of relatives is often of help. The clinical examination is essential for correctly orienting paraclinical examinations and advancing the diagnosis, leading ultimately to appropriate treatment[1].

Carbon monoxide poisoning is a cause of acute or subacute neurological disorders. The most frequent symptoms include nausea, headache, dyspnoea and tachycardia, but can sometimes lead to more complex neuro-psychiatric syndromes[2]. The pathological mechanism of carbon monoxide intoxication is based, on the one hand, on hypoxemia resulting from carbon monoxide's affinity for oxygen, which is 200 times greater than that of oxygen, producing carboxyhaemoglobin. Besides, carbon monoxide causes oxidative stress and systemic inflammation, independently of hypoxemia, and ultimately leads to symptoms, mainly cardiac and neurological.

Lesions and clinical repercussions depend on both the dose of carbon monoxide inhaled and the duration of exposure[3]. Diagnosis is therefore based on blood carboxyhaemoglobin levels, frequently on arterial blood gas sampling. Management is essentially based on non-invasive oxygen therapy, even including hyperbaric chamber treatment[4]. However, clinicians are less familiar with chronic impairment after appropriate management and transient improvement and refer to it as delayed neurologic sequelae in carbon monoxide intoxication (DENI).

CASE PRESENTATION

A 75-year-old woman was referred to the emergency department for a rapidly progressive deterioration in general condition associated with gait disturbances and mutism evolving over the last 3 days. Her personal medical history mainly included essential hypertension and non-insulin-dependent type 2 diabetes. No notable family history.

The patient had been in Turkey from May to November. During her stay, she suffered carbon monoxide poisoning in her home, with no initial severity criteria, which manifested as memory problems associated with confusion and hallucination, leading to hospitalization in neurology. The work-up carried out in Turkey revealed non-specific lesions on cerebral magnetic resonance imaging (MRI) (images and report unavailable), and treatment with aspirin was initiated. The patient's neurological situation improved, and she was able to return home. However, her condition deteriorated 3 weeks after intoxication, with reappearance of altered mental status associated with gait disorders, confusion and mutism, prompting her family to fly her back to France earlier.

On admission to the emergency department, her heart rate was 77 bpm, blood pressure was 133/80 mmHg, room air saturation was 96% on room air, and she was apyretic. She had a Glasgow Coma Scale (GCS) score of 10 (Y4, V2, M4). Her pupils were reactive and symmetrical with preserved reflexes. No meningeal syndrome was described but the presence of bilateral epileptoid tremor was noted, suggesting pyramidal irritation. The rest of the clinical exam was irrelevant.

Laboratory investigations revealed acute renal failure with creatinine (142 µmol/l) and glomerular filtration rate 31 ml/min, hypernatremia (152 mmol/l), mild hypokalaemia (3.3 mmol/l), normal corrected calcium, phosphatemia and magnesemia. C-reactive protein was 45 mg/l and the white blood cell cunt was elevated (14,7 $\times 10^9$). Haemoglobin, platelets, liver and coagulations test were normal. Arterial blood gases showed mild hypoxemia at 68 mmHg with pH 7.43, with no other abnormalities.

The patient's neurological condition remained unchanged despite normalization of natraemia after treatment prompted an initial cerebral computed tomography (CT) scan. This exam came back negative and was followed by cerebral MRI that was uninterpretable due to the patient's movements. The electroencephalogram (EEG) showed a bi- and triphasic pattern with slowing suggestive of aspecific encephalitis. Investigations were completed by a lumbar puncture: which revealed a protein level of 0.76 g/l and a CSF/blood glucose level ratio of 0.4, compatible with viral or bacterial meningoencephalitis, prompting the initiation of treatment with cefotaxime, amoxicillin and dexamethasone at meningitis doses in association with acyclovir. Given the fluctuating neurological condition (GCS score between 8 and 11), the patient was transferred to the intensive care unit.

A second lumbar puncture was performed 48 hours later but it was negative for Lyme disease, herpes virus and bacterial infection. Serology for syphilis and human immunodeficiency virus were negative as were anti-neuronal antibodies. The ratio of interleukin 6 to interleukin 10 was 0.02. The control EEG still showed a slowed but symmetrical pattern, with no paroxysmal elements.

A brain MRI was performed revealing mainly punctiform hypersignals in the deep sustentorial and subcortical white matter, with a few confluent patches suggesting a Fazekas II vascular origin, but which could be part of a toxic encephalopathy (very subtle lesions). Acyclovir was discontinued and the other antibiotics were continued for a total of 7 days. The patient was still confused but she was alert. She was then transferred to the internal medicine department after 5 days in intensive care.

The patient's neurological status remained the same. Regarding the aetiology of her condition, the infectious hypothesis seemed doubtful, given the MRI and lumbar puncture results. We therefore asked for the brain MRI to be re-read, and after further discussions with the neurologists, the hypothesis of post-interval syndrome following carbon monoxide intoxication seemed the most likely.

In this setting, management was strictly symptomatic with speech therapy, physiotherapy and dietary management.

The brain MRI re-evaluation at 3 months revealed a clear increase in the white matter hypersignals previously

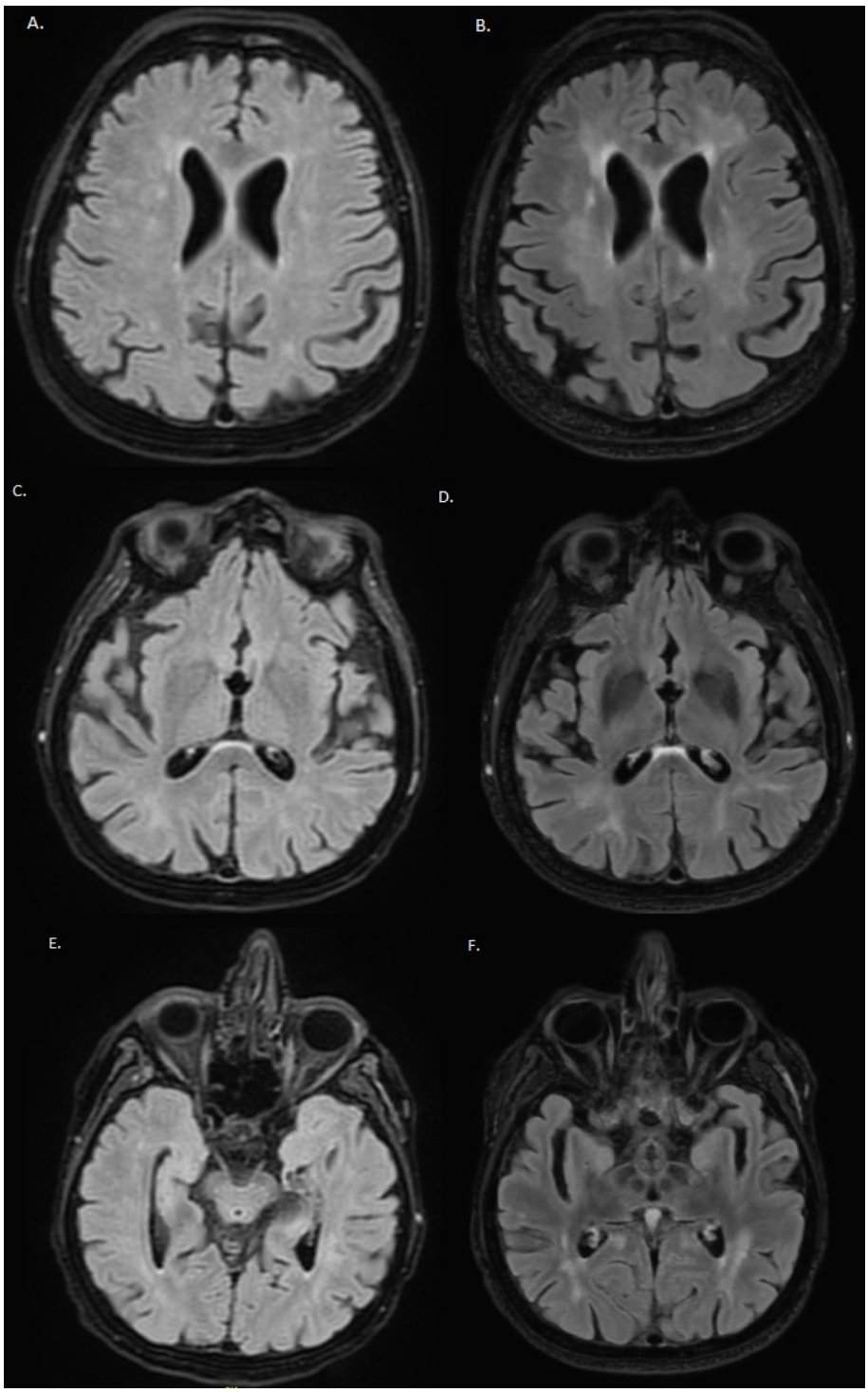


Figure 1. Comparison of initial (A, C, and E) and three-month follow-up MRI images (B, D, and F).

described, corresponding today to diffuse and confluent areas of hypersignal in the subcortical, deep and periventricular frontal, parietal, occipital and temporal white matter. Damage to the splenium of the corpus callosum and atrophy of the corpus callosum, with areas of millimetric diffusion hypersignals appearing in isosignal and apparent diffusion coefficient hypersignal was also described. The hypersignals of the superior cerebellar peduncles and serrated nuclei were also noted in the fluid-attenuated inversion recovery (FLAIR) sequence, the cough being compatible with toxic leukoencephalopathy *(Fig. 1)*. No neurological improvement was noted after 6 months. The patient was transferred to a rehabilitation centre for further management.

DISCUSSION

With no other obvious cause for acute confusional syndrome after correcting hypernatremia and in the presence of inflammatory syndrome, the main hypothesis to rule out was infectious meningoencephalitis. The results of the initial lumbar puncture suggested infection prompting the initiation of antibiotic therapy. However, the patient's history of carbon monoxide intoxication had been well reported, but was not considered, probably due to the lack of knowledge of the post-interval syndrome.

Post-interval syndrome was first reported 40 years ago. The time between intoxication and onset of symptoms averaged 22.4 days (ranging from 2 to 40 days), which is perfectly

consistent with the time to aggravation experienced by our patient[5]. The main symptoms described were cognitive impairment, urinary or faecal incontinence, gait disturbance and mutism. The most frequent clinical signs were parkinsonian syndrome, retropulsion, grasping and failure to extinguish the glabellar reflex after several repetitions (Myerson's sign). Our patient's neurological condition was typical of a post-interval syndrome, albeit non-specific[5]. MRI is the preferred imaging modality, classically demonstrating confluent and relatively symmetrical involvement of the periventricular white matter and the semi-oval centre, or even the U-shaped fibres, with T2/FLAIR hypersignal, and a pathological appearance persisting in diffusion for more than 4 weeks, which may help to distinguish it from cytotoxic oedema, and narrow the differential diagnosis[6]. In our case, white matter hyperintense signals increased on follow-up brain MRI after 3 months.

The prognosis of this condition is poor, with recovery as low as 50% in a retrospective study of post-interval syndrome patients treated with hyperbaric oxygen therapy. In the absence of a control group, the probability of recovery in the absence of treatment is not known[7]. Recovery, when it occurs, is classically described within 3 to 12 months[8].

CONCLUSION

Post-interval syndrome is not well known to clinicians and should be considered in any patient presenting with neurological disorders after a symptom-free interval following carbon monoxide intoxication.

REFERENCES

1. Lee S, Howard MA 3rd, Han JH. Delirium and Delirium Prevention in the Emergency Department. *Clin Geriatr Med* 2023;**39**:535-551.
2. Reumuth G, Alharbi Z, Houschyar KS, Kim BS, Siemers F, Fuchs PC, et al. Carbon monoxide intoxication: What we know. *Burns* 2019;**45**:526-530.
3. Weaver LK. Carbon Monoxide Poisoning. *N Engl J Med* 2009;**360**:1217-1225.
4. Eichhorn L, Thudium M, Jüttner B. The Diagnosis and Treatment of Carbon Monoxide Poisoning. *Dtsch Arztebl Int* 2018;**115**:863-870.
5. Choi IS. Delayed neurologic sequelae in carbon monoxide intoxication. *Arch Neurol* 1983;**40**:433-435.
6. Geraldo AF, Silva C, Neutel D, Neto LL, Albuquerque L. Delayed leukoencephalopathy after acute carbon monoxide intoxication. *J Radiol Case Rep* 2014;**8**:1-8.
7. Hu H, Pan X, Wan Y, Zhang Q, Liang W. Factors affecting the prognosis of patients with delayed encephalopathy after acute carbon monoxide poisoning. *Am J Emerg Med* 2011;**29**:261-264.
8. Shprecher D, Mehta L. The syndrome of delayed post-hypoxic leukoencephalopathy. *NeuroRehabilitation* 2010;**26**:65-72.