Cognitive impairment and parkinsonism as a manifestation of delayed neuropsychological sequelae after carbon monoxide poisoning: a case report

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ABSTRACT
We report a case of delayed neuropsychological sequelae manifesting as cognitive impairment and parkinsonism in a 72-year-old woman who attempted suicide by carbon monoxide poisoning 20 years earlier.

Key words: Carbon monoxide poisoning; Cognitive dysfunction; Parkinsonian disorders

INTRODUCTION
Carbon monoxide (CO) is an odourless gas and is produced from incomplete combustion of carbon-based fuels from fires, engine exhausts, and gas burning stoves. CO binds to haemoglobin with an affinity up to 300 times greater than that of oxygen. This generates carboxyhaemoglobin that impairs mitochondrial respiration and results in tissue hypoxia. 3% to 40% of survivors develop a permanent encephalopathy known as delayed neuropsychological sequelae (DNS), which manifests as a combination of cognitive impairment, movement and psychiatric disorders. CO poisoning is a common method of suicide in Asia; 18.3% of all suicides in Hong Kong between 1997 and 2007 and 33.5% of total suicide deaths in Taiwan in 2006 are attributable to CO poisoning. Recognising DNS is important in future care and prognosis. We report a case of DNS manifesting as cognitive impairment and parkinsonism in a woman who attempted suicide by CO poisoning 20 years earlier. Multi-disciplinary treatment was used to improve cognition and function.

CASE PRESENTATION
In July 2020, a 72-year-old woman was referred to the geriatric medicine department for assessment of cognition and low mood. Three months earlier, she was admitted after a fall-related traumatic brain injury resulting in bilateral sub-dural haemorrhages and seizures. She had hypertension, hyperlipidaemia, and depression. She had undergone mastectomy for right breast cancer 20 years earlier. She needed assistance in all instrumental activities of daily living (IADLs) and most basic ADLs. She had deficits in all six of the neurocognitive domains, with severe executive dysfunction, impaired language with paucity of spontaneous speech, and impaired memory and attention for 10 years. She was apathetic with low mood. Notably, in her early 50s, she had attempted suicide by CO poisoning and required mechanical ventilation for 10 days, after which her cognitive and functional deficits developed.

Examination revealed features of parkinsonism with hypomimia, bilateral cogwheeling and lead-pipe rigidity of the upper limbs, generalised bradykinesia, and slow gait with decreased arm swing. Her abbreviated mental test score was 8/10. Her mini-mental state examination score was 22/30, with impairments in orientation and visuospatial tasks and unimpaired three-item recall. Her Geriatric Depression scale score was 11/15.

She had vitamin B12 deficiency (<111 pmol/L) [normal range, 145-637 pmol/L] and was administered vitamin B12 replacement. Test results of full blood count, renal and liver profiles, thyroid
function, and electrolytes were within normal limits. Non-contrasted computer tomography of the brain showed chronic lacunar infarcts in bilateral striato-capsular regions and patchy hypodensities in the deep white matter (Figure). T2-weighted magnetic resonance imaging (MRI) showed hyperintensities in the basal ganglia and globus pallidus, whereas coronal T1-weighted MRI showed generalised cerebral involutional changes (more pronounced in bilateral frontal lobes) and bilateral hippocampal atrophy (Figure).

Her initial diagnosis was cognitive impairment and depression and frontotemporal lobe degeneration, given the pattern of cerebral atrophy and paucity of speech. This was later revised following a psychiatry review. She was diagnosed with major depressive disorder and cognitive impairment contributed to the previous hypoxic ischaemic injury secondary to CO poisoning, given the involvement of the globus pallidus. She was started on escitalopram and intensive speech and physical training, with integrated multi-disciplinary care. In a follow-up in October 2020, she had improvement in function.

DISCUSSION

DNS is under-recognised and this leads to the lack of appropriate therapy. The development of DNS is often punctuated by an initial temporary period where the patient is seemingly lucid and asymptomatic. Its onset may be anywhere from 2 to 240 days after initial exposure. Management of DNS is largely supportive. Understanding the underlying pathological processes enables clinicians to provide better holistic care. DNS secondary to CO-mediated inhibition of aerobic respiration, hypoxia, and oxidative stress that culminates in cellular necrosis and apoptosis. Delayed symptoms are a result of demyelination secondary to polymorph cellular degranulation, myeloperoxidase release, and lipid peroxidation. These may continue to develop even years after initial insult. Hyperintensities on

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**Figure.** (a) Computed tomography of the brain showing (a) bilateral frontal atrophy, relatively disproportional to the rest of the brain, and (b) chronic lacunar infarcts in internal capsule and striato-capsular region, with lacunar in left basal ganglia. (c) T2-weighted FLAIR images showing periventricular hyperintensities and hyperintensities in the left basal ganglia and globus pallidus. (d) T2-weighted contrast magnetic resonance imaging (MRI) showing bilateral basal ganglia hyperintensities and periventricular deep white matter hyperintensities. (e) T1-weighted coronal MRI showing bilateral hippocampal atrophy with the right more pronounced than the left.
T2-weighted and FLAIR MRI sequences affecting periventricular white matter and the centrum semiovale are commonly found.\textsuperscript{5,6} The basal ganglia, thalamus, and hippocampus are also commonly affected owing to their high cell concentration and greater susceptibility to hypoxia.\textsuperscript{5,6} Globus pallidus lesions are the hallmark of CO poisoning and may be evident within 24 hours.\textsuperscript{5} Diffuse brain atrophy is present in up to 80\% of patients within 6 months of exposure.\textsuperscript{5,6}

Patients may present with a combination of movement, cognitive, and psychiatric disorders. 40\% of patients develop depression and those with cognitive impairment often demonstrate impaired executive function, attention, processing speed, and visuospatial function.\textsuperscript{7,8}

Parkinsonism is the most common movement disorder, accounting for 10\% of all movement disorders. It is caused by both cerebral white matter lesions that involve nigrostriatal tracts and preferential damage to the globus pallidus and basal ganglia.\textsuperscript{5,9}

Improvements of DNS can occur within 12 months of exposure, but DNS may be permanent in up to 25\% of cases.\textsuperscript{2} Management of DNS is largely supportive. Treatment with cholinesterase inhibitors early in the course of DNS by strengthening the hippocampal acetyl-cholinergic neuronal function and delaying neuronal death enables improvement in mini-mental state examination score and frontal lobe function.\textsuperscript{10} However, its long-term benefits are unclear and evidence is lacking.

CONCLUSION

Treatment beyond the acute stage for CO poisoning is important as long-term effects are common. Understanding the underlying pathological processes that result in mood, movement, and cognitive disorders enables provision of holistic care. DNS significantly affects quality of life and function. Treatment with cholinesterase inhibitors may be beneficial, but larger scale studies are needed to determine its long-term efficacy.

CONTRIBUTORS

All authors designed the study, acquired the data, analysed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

CONFLICTS OF INTEREST

All authors have disclosed no conflicts of interest.

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DATA AVAILABILITY

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

ETHICS APPROVAL

The patient was treated in accordance with the tenets of the Declaration of Helsinki. The patient provided written informed consent for all treatments and procedures and for publication.

REFERENCES