

Delayed Neuropsychiatric Sequelae and Neuroimaging Findings as a Result of Carbon Monoxide Acute Poisoning and/or Chronic Intoxication

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Abstract

Carbon monoxide (CO) is a colorless, odorless, nonirritant gas that accounts for numerous cases of CO poisoning every year. CO intoxication is produced by a variety of sources of incomplete combustion of hydrocarbons, such as poorly functioning or indoor propane-powered heating systems, indoor burning of charcoal burning briquettes and gasoline-powered generators that are not placed in appropriate locations. The initial symptoms are nonspecific, such as: headache, dizziness, nausea, fatigue and impaired manual dexterity, but when COHb levels are between 30% and 70%, loss of consciousness ensues. Subsequently with the resolution of acute symptoms there may be a lucid interval prior to the development of delayed neurologic sequelae (DNS). Neuropsychologic abnormalities with chronic CO exposure are reported very often. In this short review of the literature we describe the neuroimaging (CT and MRI) findings, the delayed neurologic sequelae (DNS) and the neuropsychiatric findings following CO intoxication.

Abbreviations (if used)

CNS: Central nervous system
CO: Carbon monoxide
COHb: Carboxyhemoglobin
DNS: Delayed neurologic sequelae

Introduction

Numerous cases of CO poisoning are reported each year due to CO intoxication as a result of incomplete combustion of hydrocarbons, such as poorly functioning or indoor propane-powered heating systems, indoor burning of charcoal burning briquettes and gasoline-powered generators that are not placed in appropriate locations. Once CO is inhaled it binds to hemoglobin. The common denominator is the formation of carboxyhemoglobin (COHb) which leads to decreased red cell oxygen-carrying capacity and decreased release of oxygen to tissues and drives the tissue to hypoxia, especially in the arterial border zones of the brain. The initial symptoms are nonspecific when COHb is 15-30% such as: headache, dizziness, nausea, fatigue and impaired manual dexterity. Upon the development of ischemia with COHb levels between 30% and 70%, loss of consciousness ensues, that is accompanied by hypotension and eventually death. Should the patient be alive, the resolution of acute symptoms might follow and a lucid interval of 2-40 days usually follows prior to the development of delayed neurologic sequelae (DNS), as a result of diffuse demyelination in the brain. The symptoms include lethargy, behavioral changes, forgetfulness, memory loss and extrapyramidal features. Neuropsychological abnormalities with chronic CO intoxication are reported very often. The most common MRI imaging findings following CO exposure consists of white-matter lesions in the centrum semiovale and periventricular area and abnormalities in the globus pallidus [1].

Reaching to diagnosis requires clinical experience and a high index of suspicion. In these lines, the necessary elements are: clinical examination, analysis of ambient air CO and patient COHb levels. In addition, cardiological as well as neurological evaluation including brain imaging (CT and/or MRI scan) and neuropsychological testing are also required [2].

Methods

This study conducted a comprehensive review of the literature and assessed the results of 12 large cohort studies, retrospective observational studies, reviews and case reports regarding DNS and neuropsychiatric findings subsequent to recovery from CO poisoning and/or chronic intoxication, after reviewing and searching Pubmed. Development of DNS defined as any neurological symptoms or signs that newly developed within 6 weeks of discharge. The data were collected from studies conducted between 1998-2019. Also studies in Chinese language were included.

Also areas of brain tissue affected are mentioned, based on neuroimaging (CT and MRI) findings following CO exposure, after thorough estimation and assessment of 19 large cohort studies, retrospective observational studies, reviews and case reports either with or without clinical correlation, after reviewing and searching Pubmed.

We eventually considered it necessary to include differential diagnosis of globus pallidus lesions, because similar MRI findings in globus pallidus have also been reported in other toxic or metabolic causes, in many inherited disorders and specific syndromes or diseases.

Results

A) Delayed Neurologic Sequelae & Neuropsychiatric Findings After CO Poisoning and/or Chronic Intoxication

Delayed onset neuropsychiatric symptoms subsequent to recovery from CO poisoning and/or chronic intoxication have been described as DNS. The possible symptoms derived from selected papers include:

- Cognitive impairments [1,3-12] (intellectual, executive, visual-spatial and constructional functions)
- Forgetfulness - memory loss [1,4-6,12,13]
- Extrapyramidal features [1,7,8,10,11,14]
- Dementia [9]
- Lethargy [1]
- Alexia [4]
- Agraphia [4]
- Constructional and Dressing Apraxia [4]
- Disorientation [13]
- Akinetic mutism [7,10]
- Gait ataxia [10]
- Bladder& bowel incontinence [7,10]
- Depression [4-6]
- Anxiety [5,6]
- Behavior changes [1]
- Psychosis [9]
- Psychic akinesia [4]
- Emotional lability [7]

B) Neuroimaging (CT and MRI) Findings After CO Poisoning and/or Chronic Intoxication

After reviewing and searching Pubmed on CT and MRI findings in cases of CO poisoning and/or chronic intoxication, areas of brain tissue affected include:

- Globus pallidus [1,2,4,15-17,16-22]
- Basal ganglia [2,8,15-22]

- Cerebral white matter [2,5,6,14,16,19,23,24]
- Cerebral cortex-cortical atrophy [2,4,14,15,18,19]
- Centrum semiovale [1,3,14,18]
- Periventricular area [1,3,18]
- Hippocampal area - Hippocampal atrophy [4-6,19,23,24]
- Cerebellum - atrophy of cerebellar hemispheres [15,19]
- Corpus callosum [15,19]
- Subcortical involvement [7,14,18]
- Amygdala [19]
- Midbrain [19]
- Insula [19]
- Thalamus [18,21]
- Red nucleus (nucleus ruber) [17,18]

The vast majority of symmetric globus pallidus lesions are secondary to hypoxic, toxic or metabolic processes. Differential diagnosis is needed, because similar MRI findings in globus pallidus have also been reported in [25-28]:

- Hypoxic-Ischemic Encephalopathy
- Post opioid toxic encephalopathy
- Hyperalimantation (Manganese deposition)
- Chronic hypothyroidism (Punctate calcification)
- Inherited Disorders (Neurofibromatosis type 1, Leigh disease, Fahr disease, Wilson disease, Hallervorden-Spatz syndrome, Neurodegeneration with brain iron accumulation, Maple syrup urine disease, Methylmalonicacidemia, Mitochondrial cytopathy)
- Kernicterus
- Cyanide poisoning
- Methanol intoxication
- Hepatocerebral degeneration
- Progressive supranuclear palsy
- Influenza
- Hemolytic uremic syndrome
- Sickle cell disease
- Head trauma
- Wasp sting encephalopathy

Discussion

Delayed onset neurologic sequelae (DNS) subsequent to recovery from CO poisoning and/or chronic intoxication may include a vast variety of clinical features and symptoms. Also subsequent neuropsychiatric findings are reported very often. The salient features of DNS are: cognitive impairment, memory loss and extrapyramidal signs, while anxiety and depression are the most common neuropsychiatric symptoms. Reaching to diagnosis requires clinical experience and a high index of suspicion, because the initial symptoms are nonspecific. Besides clinical examination (cardiological and neurological evaluation included), analysis of ambient air CO and patient COHb levels should be performed upon admission, in the acute phase of CO intoxication. In addition, brain imaging (CT and/or MRI scan) and neuropsychological testing are also of primary importance, providing objective evidence about patient's clinical condition in both acute and late phase of CO intoxication.

Psychometric tests usually used are: MMSE (Mini-Mental Status Examination), SLUMS (Saint Louis University Mental Status), HAM-D (Hamilton Depression Rating Scale) and FAB (Frontal Assessment Battery). In patients with unexplained memory loss and/or cognitive impairment, especially if it is accompanied with extrapyramidal signs and anxiety or depression, the likelihood of chronic CO intoxication should not be underestimated. A careful history taking is of great importance, while physicians should be informed about the delayed neuropsychiatric sequelae following CO intoxication after a lucid interval of 2-40 days.

Brain imaging (CT and/or MRI) is very useful in order to depict the presence and extent of the underlying pathology. The most common neuroimaging findings following CO exposure consists of white-matter lesions in the centrum semiovale, in the periventricular area and more often in the basal ganglia. Although the vast majority of symmetric globus pallidus lesions are secondary to hypoxic, toxic or metabolic processes, differential diagnosis is needed, because similar MRI findings in globus pallidus have also been reported in many other disorders. Difficulty in differential diagnosis arises, when there is coexistence of other underlying pathologies of central nervous system (CNS), which could implicate the same brain areas, such as: multiple sclerosis, stroke, angiitis, etc. Under these circumstances, it could be difficult to estimate accurately the extent of the intoxicated brain tissue. Especially differential diagnosis could require an expert radiologist evaluation besides specific blood test panel, in order to exclude the other aforementioned causes of globus pallidus lesions [19-33].

Conclusion

Carbon monoxide acute poisoning and/or chronic intoxication is produced by a variety of sources of incomplete combustion of hydrocarbons. The nonspecific initial symptoms of headache, dizziness, nausea, fatigue and impaired manual dexterity, requires clinical experience and a high index of suspicion.

In patients with unexplained memory loss and/or cognitive impairment, especially if it is accompanied with extrapyramidal signs and anxiety or depression, the likelihood of chronic CO intoxication should not be underestimated. A careful history taking is of great importance, while physicians should be informed about the delayed neuropsychiatric sequelae following CO intoxication.

Brain imaging and neuropsychological testing are very useful in order to depict the presence and extent of the underlying pathology, in both acute and late phase of CO intoxication. Doctors and nursing staff need to be familiar with the performance and the evaluation of the results of these tests in everyday clinical practice.

When there is comorbidity of other underlying CNS diseases, it could be difficult performing a differential diagnosis and precise estimation of the extent of the intoxicated brain tissue. In such cases, an expert radiologist evaluation besides specific blood test panel is required.

In addition, people must be informed about the potential dangers arisen after incomplete combustion of hydrocarbons, such as poorly functioning or indoor propane-powered heating systems and/or gasoline-powered generators that are not placed in appropriate locations. Informative brochures should be included in all above machineries, as well as specific instructions should be given for the public, which will emphasize the necessity of preventive measures to diminish the hazardous effects of CO intoxication.

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