Clinical Toxicology

Neurological manifestation of carbon monoxide poisoning

I.K. Hart,¹ P.G.E. Kennedy,¹ J.H. Adams² and N.E. Cunningham³

Departments of ¹Neurology and ²Neuropathology, Institute of Neurological Sciences, Southern General Hospital, Glasgow G51 4TF and ³Department of Pathology, Crosshouse Hospital, Kilmarnock, Ayrshire, UK.

Summary: The clinical signs and post-mortem findings in a case of carbon monoxide poisoning are described, and correlated with the computed tomographic (CT) scan appearances. The value of serial CT scanning as a diagnostic tool is highlighted.

Introduction

The precise diagnosis of the cause of coma in a young adult often presents considerable problems to the clinician. We describe here a case of carbon monoxide (CO) poisoning which took some time to elucidate and in whom an initial computed tomographic (CT) scan was normal. However, serial scanning proved to be particularly helpful in confirming the diagnosis.

Case history

A 24 year old male non-smoker had complained of throbbing frontal headache for two weeks, a symptom also experienced by his flatmate. He was subsequently found unrousable and had last been seen conscious 48 hours earlier. On admission to a local hospital he was in deep coma. Twelve hours later his neurological condition had not improved and he was transferred to the Institute of Neurological Sciences. On examination he was dehydrated, tachypnoeic, febrile (temperature 39°C), and had a tachycardia of 160/min. Blood pressure was 110/74 mm Hg. Tense bullae were noted over the dorsal surfaces of both feet. He was comatose, did not respond to verbal commands and his eyes were closed. He made occasional incomprehensible sounds and flexed to pain in all four limbs. There was no neck stiffness. Pupils were equal in diameter, 5 mm, and fully reactive to light. There

was early right sided papilloedema. Occasional spontaneous conjugate lateral roving eye movements were seen and doll's eye movements were absent. The gag reflex was present. Muscle tone was increased in all limbs and all deep tendon reflexes were brisk. Plantar responses were extensor bilaterally. Frequent episodes of severe extensor spasms were observed, lasting up to one minute. A decerebrate posture was adopted intermittently.

Investigations revealed serum urea of 24.3 mmol/l and creatinine 206 μ mol/l. Aspartate aminotransferase was raised at 64010 IU/l, alanine aminotransferase at 14910 IU/l, creatine kinase at 25180 IU/l and lactic dehydrogenase at 2262 IU/l. Urine testing was positive for myoglobin. Serum and urine toxicology screen was negative. On 60% O₂ by face mask PaO₂ was 180 mmHg, PaCO₂ 30 mmHg, pH 7.49 and base excess + 1. Serum electrolytes, glucose and ammonia were normal. There was a neutrophilia of 18.9×10^9 /l and a thrombocytopenia of 89×10^9 /l.

Blood, urine, and throat and nasal swabs were sterile on culture. There were no significant titres in paired serum and cerebrospinal fluid (CSF) samples for the following agents: herpes simplex, varicella zoster, cytomegalovirus, mumps, measles, influenza A and B, psittacosis, brucella, toxoplasma, leptospirae, Q fever, legionella and mycoplasma. Monospot was negative. Screen for human immunodeficiency virus, hepatitis A and B was negative.

Chest X-ray, tomoscan of chest and abdomen and initial CT head scan were normal. There was diffuse slowing of all rhythms most marked over

Correspondence: Professor P.G.E. Kennedy, Ph.D., M.D., M.R.C.P.

Accepted: 23 September 1987

the left hemisphere on electroencephalogram. CSF was sterile with normal total protein and glucose and no cells.

Initial management was designed to treat possible herpes encephalitis and Gram negative septicaemia. Intravenous acyclovir, dexamethasone, chloramphenicol and erythromycin were given and diazepam was used to control the extensor spasms. Next morning it became known that the patient had been found in a poorly ventilated room with a mains gas fire burning. This, together with the clinical findings and evidence of systemic upset, led us to suspect a diagnosis of CO poisoning despite the normal CT scan. A blood sample, taken on admission to the referring hospital and over an hour after the patient had been removed from his bedroom, revealed a carboxyhaemoglobin (COHb) level of 10% and confirmed the diagnosis.¹

On a second CT scan three days after admission there were diffuse low density areas throughout the basal ganglia and white matter (Figure 1). Ten days later the white matter lesions were more extensive. His temperature and pulse returned to normal within two days. Abnormal haematological and biochemical findings fell to within their respective normal ranges within seven days. The patient died three weeks after admission having shown no change in neurological state.

Figure 1 Tomoscan with contrast enhancement 3 days after admission, with diffuse low density areas throughout the basal ganglia and white matter.

Post-mortem examination

This was carried out under a warrant from the Procurator Fiscal of Kilmarnock. The brain was normal externally. In coronal slices of the cerebral hemisphere there were widespread abnormalities in the white matter in the form of essentially symmetrical, slightly granular, pale grey areas. The frontal, parietal, occipital and temporal lobes and the corpus callosum were affected. The abnormal tissue was well demarcated from the adjacent normal white matter, and where it approached the cerebral cortex, the subcortical arcuate fibres appeared to be spared. A further abnormality was the presence of sharply defined zones of granularity and discolouration in the medial segment of the anterior portion of each globus pallidus. The cerebellum, brain stem and spinal cord appeared normal.

Celloidin, paraffin and frozen sections were examined. The abnormal tissue in the white matter had an irregular outline but was sharply demarcated from the adjacent normal white matter (Figure 2). There was total loss of myelin, the highly cellular abnormal tissue being composed of sheets of sudanophilic lipid phagocytes and reactive astrocytes. There were also some reactive changes in blood vessels. The lesions in the globus pallidus were also sharply defined and of similar appearance to the abnormal white matter with, in addition, loss of neurones. No other abnormalities were seen. In particular, there was no evidence of diffuse hypoxic damage to the neocortex, basal nuclei, Ammon's horns or the cerebellum. There were no significant findings outside the central nervous system.

Discussion

Carbon monoxide is generated by incomplete combustion of any carbon based fuel. As a result, death from accidental CO poisoning is common causing 114 deaths in England and Wales in 1979.² The mechanism of CO toxicity is thought to be via tissue hypoxia and not by any direct cellular action.³ Hypoxia is produced in two ways. Firstly, CO is able to compete successfully with oxygen (O_2) for binding with the ferrous ion of haemoglobin (Hb) because of its superior affinity, the $CO:O_2$ affinity ratio being 210:1. Secondly, the COHb which is formed increases the affinity of Hb for O_2 thereby altering the shape of the O_2 Hb dissociation curve from sigmoid to exponential and shifting it to the left. The net effect is that for a given arterial PO_2 less O_2 is released from Hb to the tissues.

Figure 2 In this section from the frontal lobe there is extensive demyelination with an irregular edge. Celloidin section, myelin stain.

The most severe effects are seen in organs with high basal O_2 consumption. Symptoms of poisoning reflect this but are dependent on concentration of inspired CO and duration of exposure.⁴ At a blood COHb of 10% psychomotor impairment is seen, at 10–20% there is dyspnoea, at 20–30% throbbing headache, at 40% nausea, vomiting and muscle weakness, at 50–60% seizures and above 60% coma.

CO poisoning should always be considered when a comatose person is found in a confined area with poor ventilation, and the correct diagnosis confirmed by blood COHb estimation. If there is delay in transporting the patient to hospital or in obtaining a blood sample, CO levels may be low because the eliminatory half life of CO from the body is only 2–4 hours and even shorter when O_2 is given.⁵ Then diagnosis may be confirmed in retrospect by an appropriate history and a characteristic constellation of clinical signs, laboratory findings and CT scan appearances.

The cardinal manifestations of severe CO poisoning were present in our case. Neurologically these consist of generalized extra-pyramidal rigidity,

episodic decerebrate rigidity, hyperreflexia, intact pupillary responses to light, papilloedema and cutaneous bullae.⁶ The systemic complications of skeletal muscle necrosis,⁷ renal failure⁸ and blood dyscrasia⁹ were reflected by myoglobinuria, raised muscle enzyme, azotaemia, neutrophilia and thrombocytopenia.

Although our patient was in coma, the initial CT scan, carried out 16 hours after the patient's discovery, was normal. Abnormalities were only revealed on repeating the scan 3 and 10 days later. This also allowed the progression of the lesions to be followed. Sawada *et al.*¹⁰ studied the CT scan appearances of 21 patients with severe CO poisoning. Ten patients had normal admission CT scans and each made a good recovery. In the other 11 patients CT scans were abnormal and in this group outcome was significantly worse. They proposed that normal admission CT scan in severe CO poisoning was a reliable guide to favourable prognosis. Manifestly this was not the case in our patient. We suggest that serial CT scanning may be a better guide to diagnosis, and probably prognosis, since we have shown that the appearance of lesions on CT scan can be delayed.

Basal ganglia lesions on CT scan in CO poisoning are well recognized.^{10,11,12} However, to our knowledge, this is the first case to be reported where CT scan appearances of diffuse damage to the subcortical white matter have been correlated with post-mortem findings. Pathological studies have suggested that lesions in the basal ganglia are early manifestations in acute CO poisoning and that more widespread lesions only develop after several days.¹²

Our case suggests that these changes can appear in close association and that the pattern of development of lesions may be different where exposure to CO is chronic.

The classical structural damage produced in the brain by CO is diffuse hypoxic injury with selectively severe involvement of the pallidum.¹³ Pallidal changes were present in our case, but there was no evidence of diffuse hypoxic damage. This may be due to the fact that exposure to CO was prolonged and that it was probably in low concentration. Other types of damage have been described including the delayed type of demyelination and generalized destruction of myelinated fibres.¹⁴ The latter, the most striking feature in the present case, appears to be a relatively uncommon type of structural damage that is not delayed but occurs as a direct effect of intoxication. This seemingly contradicts the view that CO cannot produce effects by a direct cellular action.³

Treatment of CO poisoning consists of giving high concentration O_2 by face mask or, if available,

exposure to hyperbaric O₂ in a pressure chamber.¹⁵ Fluid and electrolyte balance should be controlled carefully. More recently it has been recommended that severe cases should be given early treatment with steroids and diuretics to prevent the development of cerebral oedema.¹⁶

References

1. Volans, G.N. & Byatt, C.W. Poisoning from domestic products. *Prescribers Journal* 1986, **26**: 87–97.
2. Editorial. Carbon monoxide, an old enemy forgot. *Lancet* 1981, **ii**: 75–76.
3. Bour, H. & Ledingham, I. Carbon monoxide poisoning. Elsevier, New York, 1967.
4. Winter, P.M. & Miller, J.N. Carbon Monoxide Poisoning. *JAMA* 1976, **236**: 1502–1508.
5. Goldsmith, J.R. & Landaw, S.D. Carbon monoxide and human health. *Science* 1968, **162**: 1352–1359.
6. Garland, H. & Pearce, J. Neurological complications of carbon monoxide poisoning. *Q J Med* 1967, **144**: 445–455.
7. Finley, J., Van Beck, A. & Glover, J.L. Myonecrosis complicating carbon monoxide poisoning. *J Trauma* 1977, **17**: 536–543.
8. Loughridge, W.I., Leader, L.P. & Bowers, D.A.L. Acute renal failure due to muscle necrosis in carbon monoxide poisoning. *Lancet* 1958, **ii**: 349.
9. Stonesifer, L.D., Bone, R.C. & Hiller, F.C. Thrombotic thrombocytopenic purpura in carbon monoxide poisoning. *Arch Int Med* 1980, **140**: 104–108.
10. Sawada Y., Ohashi, N., Maemura, K. *et al.* Computerised tomography as an indication of long term outcome after acute carbon monoxide poisoning. *Lancet* 1980, **i**: 783–785.
11. Sawada, Y., Sakamoto, T., Nishide, K. *et al.* Correlation of pathological findings with computerised tomographic findings after acute carbon monoxide poisoning. *Lancet* 1983, **ii**: 1296.
12. Nardizzi, L.R. Computerized tomographic correlation of carbon monoxide poisoning. *Arch Neurol* 1979, **36**: 38–39.
13. Brierly, H.B. & Graham, D.I. Hypoxia and vascular abnormalities of the CNS. In: Adams, J.H., Corsellis, J.A.N. & Duchon, L.W. (eds) *Greenfield's Neuropathology*. Edward Arnold, London, 1984, pp 145–148.
14. La Presle, J. & Fardeau, M. The central nervous system and carbon monoxide poisoning. II. Anatomical study of brain lesions following intoxication with carbon monoxide (22 cases). *Prog Brain Res* 1967, **24**: 31–74.
15. Myers, R.A., Linberg, S.E. & Cowley, R.A. Carbon monoxide poisoning. The injury and its treatment. *JACEP* 1979, **8**: 579–585.
16. Boutros, A.R. & Hay, J.L. Management of carbon monoxide poisoning in the absence of hyperbaric oxygenation chamber. *Crit Care Med* 1976, **4**: 144–153.

Acknowledgements

We would like to thank Mr L. McLeod, Procurator Fiscal, Kilmarnock and North Ayrshire for his permission to report this case. The help of the staff of the Neuro-radiology and Medical Illustrations Departments of the Institute of Neurological Sciences is warmly appreciated.