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Delayed cyanide induced dystonia

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Abstract

A 16 year old man ingested 1 g potassium cyanide in 1969. A few days after an apparently full recovery he developed a severe dystonia syndrome. He had a positive response to an apomorphine test and showed improvement with levodopa treatment. A 21 year follow up showed minimal neurological sequelae; CT showed bilateral putaminal lucencies. Visual and brain stem auditory evoked potentials were normal.

Cyanide is toxic because of its ready reaction with the trivalent ion of cytochrome oxidase and the widespread histotoxic hypoxia that ensues.[1] A wide range of severe but non-specific clinical signs are usually seen: impairment of consciousness, seizures, cardiac arrhythmias, hypotension, tachypnoea, and, finally, respiratory arrest secondary to dysfunction of the medullary respiratory centre.[2]

Cyanide is rapidly absorbed. Symptoms begin a few seconds after exposure and death usually occurs in less than 30 minutes. The average lethal dose for potassium cyanide is about 250 mg.[2] As cyanide poisoning is almost always lethal, delayed neurological sequelae have been only rarely described.[2–7] We report on a patient who survived cyanide poisoning and whom we have followed up for 21 years.

Case report

On 7 April 1969 a 16 year old man ingested about 1 g potassium cyanide. On admission he was comatose, his blood pressure was undetectable, and he had deep respiratory depression. His heart rate was 70 beats/min. Besides cardiopulmonary resuscitation, he received intravenous sodium thiosulphate. Three hours later his blood pressure was 100/50 mm Hg and he was fully conscious. After 24 hours he was neurologically intact and the results of a general physical examination were normal.

A few days later he developed slurred speech and involuntary athetoid movements of his right hand; these progressively became more intense, affecting his neck, trunk, and limbs. He developed a generalised dystonia with hyperextension of his lower limbs and trunk. Occasionally he showed opisthotonoid posturing. He was fully oriented but unable to speak, although able to understand. Neither the involuntary movements nor the dystonia subsided with a short trial of chlorpromazine treatment.

Twenty nine days after ingesting the cyanide he still showed opisthotonoid posturing, which became fixed with hyperextension of his lower limbs, flexion of his arms, and hyperextension of his fingers. He was unable to walk without help, and when helped he walked on tiptoes. His facial muscles were grossly hypertonic, keeping his mouth halfway open and hindering the mobility of his lips and tongue; he was therefore unable to speak. A pseudomyotonic contracture of the eyelids ensued any time he closed his eyes. On attempting to move his limbs he developed involuntary simultaneous contraction of both agonist and antagonist muscles. His mental state was normal. Apomorphine (1 mg) was given subcutaneously. Ten minutes later the dystonia of his limbs was greatly reduced, followed by noticeable improvement in the dystonias of his neck and trunk. Thirty minutes after injection facial hypertonia subsided dramatically and he was able to move his jaw and lips, to speak, and to stick out his tongue. After 90 minutes the effects of apomorphine disappeared completely.

He received a trial with progressively larger doses of levodopa as a part of an experimental drug study protocol.[6] His condition improved as the dose was increased. After 14 days, when he was taking 3000 mg, the dystonias of his limbs, trunk, and face were reduced to about a half. He was able to talk and sit up by himself. Six days later, while taking 3600 mg, he was able to walk without help. Levodopa was

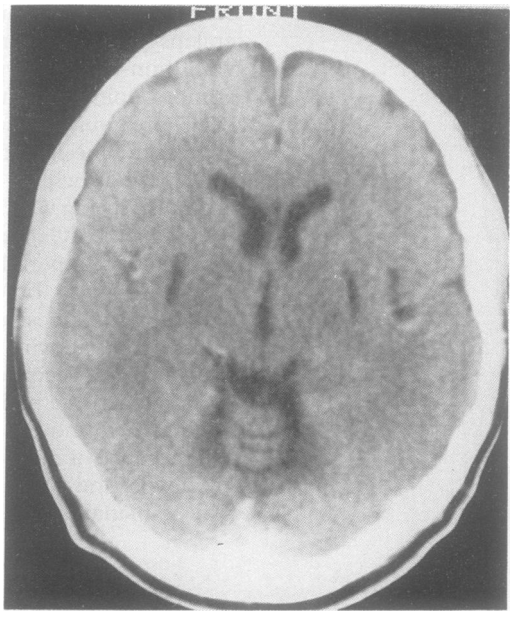

Figure High resolution brain computed tomogram performed 21 years after cyanide poisoning, showing bilateral putaminal lucencies and mild diffuse cortical atrophy.

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withdrawn after 38 days of treatment; his recovery continued thereafter. Besides mild sequelae, he thereafter led a normal life and managed a small company.

Neurological examination after 21 years showed the persistence of a mild dystonia and athetoid involuntary movements of both hands. Pattern reversal visual and brain stem auditory evoked potentials were performed at this evaluation, following the guidelines of the American EEG Society. P100 latencies were 102 ms and 101 ms after stimulation of the right and left eye. Absolute latencies of auditory evoked potentias for waves I, II, III, IV, and V as well as interpeak latencies I–III and III–V were normal bilaterally. A high resolution CT in April 1990 showed symmetrical hypodensities at both putamina and a mild diffuse cortical atrophy (figure).

Discussion

Only a few cases of delayed neurological sequelae after cyanide poisoning have been reported, all of them showing remarkably consistent findings—namely, severe dysarthria, an extrapyramidal syndrome, and bilateral lesions of the basal ganglia,[2-7] which was exactly the case in our patient. In all reported cases, as in ours, the important involvement of facial musculature as well as the mildness of tremor in those who presented with Parkinsonism is noteworthy. Review of the published reports on cyanide poisoning show that a dystonia syndrome can be produced independently by putaminal or pallidal lesions, whereas for Parkinsonism both structures need to be affected.[2-4 6 7]

Cyanide, carbon monoxide, and manganese intoxication are clinically very similar, possibly because these three toxins disrupt the mechanism of cellular respiration. Manganese concentrate in mitochrondria,[8] carbon monoxide binds to haemoglobin and cytochromes, inhibiting the electron transport respiratory chain, and cyanide inhibits cytochrome oxidase. They also share selectivity for the basal ganglia.[2 3 4 6-11] Uitti *et al* emphasised the sparing of the horn of Ammon in their case of cyanide poisoning, as opposed to the customary involvement of this structure found after hypoxia—ischaemia, suggesting that the neurological sequelae are probably not related to the usually associated shock or respiratory depression.[2]

Parkinsonism or a dystonia syndrome can be elicited by any of these three toxins. Uitti *et al* found cell loss on the reticular zone of substantia nigra in cyanide poisoning with preservation of pigmented neurons on the compact zone, the affected area in idiopathic Parkinson's disease.[2] Therefore, Parkinsonism might be due to postsynaptic mechanisms. Rosenberg *et al* performed PET with 6-fluorodopa in their case. They found decreased dopaminergic activity not only in relation to focal putaminal lesions shown by MRI, but also diffusely at the nucleus, a pattern similar to that found in idiopathic Parkinson's disease.[6] Thus presynaptic mechanisms, caused by structural or functional damage of nigrostriatal pathways, might also contribute to the extrapyramidal syndrome in cyanide poisoning. The positive effect of apomorphine in our patient was transient, completely disappearing in 90 minutes, making clear that the clinical improvement was due to this drug. Levodopa also seemed to improve our patient's condition. Although a coincidental spontaneous recovery cannot be ruled out completely, the apomorphine positive test favours a true beneficial effect of levodopa.

Our patient, as well as those previously reported on, had an interval between intoxication and the development of extrapyramidal symptoms, another similarity with carbon monoxide and manganese intoxication.[7 8] He also showed a trend towards recovery after a few months, as happened in the cases of Finelli[4] and of Messing *et al*.[3] Although the improvement could be related to neuronal plasticity, a true anatomical restoration seems a more likely explanation.

Pathoanatomical studies in acute cyanide poisoning show demyelination as its most consistent change.[10] Swelling, vacuolation, and lysis of cell processes in the white matter have also been described.[10] In the case of Uitti *et al* there was no anatomical evidence of such demyelination after 19 months; no such evidence was found in radiological studies performed in our patient or in reported cases.[2-4 6] We believe that demyelination, as well as some of the axonal changes, constitute at least partially, reversible lesions.

Although there is no pathoanatomical or clinical indication of damage to brain stem or visual pathways in cyanide poisoning (except for the reticular zone of the substantia nigra), brain stem auditory and visual evoked potentials have not been analysed previously; we found them normal, confirming neurophysiologically the integrity of the brain stem.

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