CASE REPORT

Subacute Acrylamide Intoxication with Severe Visual Disturbance: A Case Report

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ABSTRACT

A 35-year-old man was admitted due to somnolence and progressive sensory-motor polyneuropathy, followed by severe visual impairment in both eyes after direct skin exposure to an acrylamide monomer solution. The results of an ophthalmological examination including central critical flicker fusion frequency and the decreased amplitude of action potentials observed in the visual evoked potential studies suggested that acrylamide intoxication resulted in neuronal degeneration in the optic pathways. Additional attention should be directed to the potential effect of acrylamide on the human visual system.

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Introduction

Acrylamide is a vinyl monomer that is primarily used in the production of polyacrylamide—an ingredient of paper coatings, soil stabilisers, sedimentation, adhesives, and paints. It has also been recognised that acrylamide is formed in foodstuffs containing asparagine and reducing carbohydrates, such as fried potatoes and cereal-based products, during their thermal processing at high temperatures.¹ It is neurotoxic, and many cases of chronic acrylamide poisoning have been reported since the 1950s.^{2–4} The characteristic signs of chronic acrylamide poisoning are erythema, sensory-dominant peripheral neuropathy, excessive sweating, and ataxia. Subacute exposure at higher doses causes confusion, hallucination, slurred speech, and cognitive impairment in humans.^{2,3} Animal experiments have also shown that acute intoxication with large amounts of acrylamide induces hypotension, poor postural and motor coordination, hind limb ataxia, generalised tremulousness, behavioural changes, massive sympathetic discharges, recurrent tonic-clonic convulsions, and even death due to respiratory failure caused by laryngeal spasm and obstruction.⁵ In contrast, symptomatic visual disturbances have been rarely reported in human cases of acrylamide intoxication. Here we present the case of a patient who showed severe visual impairment in addition to

the aforementioned characteristic signs after intense acrylamide exposure.

Case presentation

A 35-year-old Japanese man began handling acrylamide monomer solutions while working in a chemical factory that produces construction material 52 days before admission. Nineteen days before admission, while pouring a 40% acrylamide monomer solution from an oil drum to a reaction chamber for polymerisation using a suction pump, he accidentally spilled the residual acrylamide monomer solution in the pump over his legs. Although he immediately removed his pants and washed his legs with water and ethanol, he received a chemical burn with erosion on the exposed skin. Thereafter, he started to feel dizzy and could not work for 8 consecutive days prior to the admission due to illness. When speaking on phone to his employer 7 days before admission, he was reported to be confused and speaking inconsistently. He was finally found collapsed and delirious in front of his house 6 days before admission and was taken to the emergency department of a psychiatric hospital. On arrival, his speech was slurred and dysarthric. He also showed difficulty in walking and could not position his arms adequately while attempting to use his hands. He subsequently became somnolent and within a few

days was unable to stand by himself. His limb weakness also progressed during this period, and he was transferred to our hospital for further investigation. On admission, he had a fever of 38.2°C, tachycardia (110 beats/min), high blood pressure (150/84 mm Hg), and excessive sweating. He was somnolent and could not speak. A neurological examination revealed bilateral isocoric pupils with a preserved light reflex. The oculoccephalic reflex was also preserved, whereas the corneal reflex in his left eye had decreased. He had dyspnea in the supine position because of his tongue sinking into the throat. He sometimes moved his arms abruptly and violently, resulting in bruising, and he could not produce any controlled arm movements. Conversely, he barely moved his legs, even in response to painful stimuli. The deep tendon reflex was absent in both limbs, and Babinski's sign was negative. He had constipation, a distended bladder, and insufficient micturition. He showed no signs of meningeal irritation. Laboratory data revealed mild inflammation, elevated serum creatine kinase levels (434 U/L), and hyperthyroidism (serum free thyroxine, 2.05 ng/dL; free triiodothyronine, 4.89 pg/dL; and thyroid-stimulating hormone, <0.005 μ U/mL). Neither cerebrospinal fluid (CSF) analysis nor brain magnetic resonance imaging (MRI) revealed any abnormalities.

He consecutively underwent intravenous immunoglobulin (400 mg/kg daily for 5 days) and high-dose methylprednisolone infusion (1000 mg of methylprednisolone daily for 5 days) therapies. During these therapies, his alertness improved, and he started to complain of a burning sensation in his legs; however, his limb weakness persisted even after the treatment. These symptoms and neurological signs persisted for 3 months until he was transferred to another hospital for rehabilitation. On hospital day 4, sensory nerve conduction studies of the right median and sural nerves showed that the amplitudes of sensory nerve action potentials for these nerves were 6 and 12 μ V, respectively (Table 1). These action potentials completely disappeared on day 15 and remained absent till day 82. Motor nerve conduction studies of the right median and tibial nerves also demonstrated a gradual decrease in the amplitude of the compound muscle action potential from hospital day 4 to day 82. These results suggested the progression of peripheral neuropathy in this patient. We concluded that this patient suffered from acute acrylamide intoxication because of the history,

Table 1. Temporal changes in the nerve conduction studies performed during the disease course.

Nerve	Parameter	Day 4	Day 15	Day 82
R Median	MCV (m/s)	48	48	45
	CMAP (mV)	6.5	5.1	1.7
	SCV (m/s)	51	NE	NE
	SNAP (μ V)	6	NE	NE
R Tibial	MCV (m/s)	30	30	NE
	CMAP (mV)	12.3	1.6	NE
R Sural	SCV (m/s)	58	NE	NE
	SNAP (μ V)	12	NE	NE

Note. CMAP = compound muscle action potential; MCV = motor conduction velocity; NE = not evoked; R = right; SCV = sensory conduction velocity; SNAP = sensory nerve action potential.

characteristic neurological findings, and lack of abnormal findings in CSF or MRI studies, suggestive of inflammation or neoplasm.

On regaining consciousness, the patient reported a loss of vision. His visual acuity in both eyes was limited only to the perception of light, and the visual evoked potential (VEP) recordings revealed that light-emitting diode stimuli with goggles on either eye did not provoke any activity on hospital day 27 (Figure 1A). However, on day 78, his best-corrected visual acuity allowed for counting fingers at a

Figure 1. Changes in the visual evoked potential (VEP) over time. In both eyes, light-emitting diode stimuli delivered using goggles yielded no significant action potential in the VEP recording on hospital day 27 (A), whereas the stimuli evoked N75, P100, and N145 potentials at 61.6, 82.8, and 111.6 ms, respectively, on day 78 (B).

distance of 30 cm with the right eye and was 0.01 in the left eye. The central critical flicker fusion frequency could not be measured in the right eye and was 15.3 Hz in the left eye. Ophthalmoscopy showed mild pallor of the optic disc in both eyes. VEP recordings at that time yielded N75 and P100 potentials with latencies of 62 and 83 ms, respectively, even though their amplitudes were still low (Figure 1B). Accordingly, these results indicated a neurological impairment in the optic pathways.

Discussion

Here we described a case of acrylamide intoxication with severe visual disturbance in addition to ataxia, somnolence, and profound sensorimotor neuropathy. We confirmed that visual impairment was due to neuronal degeneration in the optic pathways on the basis of an ophthalmological examination including central critical flicker fusion frequency and the decreased amplitude of action potentials observed in VEP studies.

To the best of our knowledge, there is only one reported on two patients with acrylamide intoxication showing symptomatic visual disturbance.⁶ These patients were chronically exposed to acrylamide monomer during the process of its polymerisation in road tunnelling for 12 weeks, although detailed information was not available regarding the amount of acrylamide exposure.⁶

Other reports have also suggested that acrylamide can affect the visual pathways. Goffeng et al. examined visual evoked responses in tunnel workers who were exposed to acrylamide-contaminated water during grouting work and demonstrated prolonged latency in the onset of the occipital potential (N75), suggesting that acrylamide may affect the myelin sheaths of optic nerves.⁷ Furthermore, it has been reported that acrylamide may affect both myelin sheaths and axons in the visual pathway of some mammals. Godin et al. observed abnormal pupillary light reflex, progressive retinal degeneration, changes in optic nerve discs, and pathological axonal damage of optic nerve neurons in one of seven cows exposed to acrylamide-polluted drinking water.⁸ Merigan et al. showed that chronic oral dosing of 10 mg/kg/day acrylamide (330–470 mg/kg in total) to produce marked ataxia induced a decreased amplitude and delayed latency of the visual evoked response in

macaque monkeys.⁹ They also documented axonal swelling with neurofilament accumulation in the distal optic tract and lateral geniculate nucleus of these animals, suggesting that acrylamide may cause distal axonal damage in the optic tract.¹⁰ These pathological changes were rarely observed in the superior colliculus in this report. In contrast, O'Shaughnessy and Losos observed the swollen and intensely argentophilic axonal changes in the optic layer of the superior colliculus in rats with subacute acrylamide poisoning at higher doses (25 or 50 mg/kg/day for 10 days).¹¹ They also demonstrated that chronic acrylamide exposure at lower doses (8 or 12 mg/kg, 5 days/week for 13 weeks) resulted in no morphological change in the optic pathways. These findings indicate that different time courses and amounts of acrylamide poisoning yield distinct patterns of pathology in the optic pathways. Our patient was directly exposed to a highly concentrated acrylamide monomer solution adequate to produce skin erosion. This implies that a relatively high dose of acrylamide penetrated into the body and was sufficient for axonal degeneration in the optic pathways. This may explain the difference between the VEP findings in our patient and those reported by Goffeng et al.⁷

Interestingly, the amplitude of VEP recovered from day 27 to day 78, whereas the amplitude of action potentials in peripheral nerve conduction studies continued to decrease during this period in both the sensory and motor nerves. This observation suggests a difference in the susceptibility to acrylamide between the optic pathways and peripheral nervous system (PNS). Given that the optic pathways share some features with central nervous system (CNS) pathways, such as oligodendrocytes as myelinating cells, the difference in vulnerability to acrylamide between CNS and PNS may be responsible for the recovery in VEP findings. Igisu et al. implicated similar discrepancies between CNS and PNS in the progression of symptoms caused by acrylamide poisoning.³ In their report, three of five patients who consumed acrylamide-contaminated water initially showed mental symptoms that abated in approximately 2–4 weeks. In contrast, none of these patients exhibited sensory disturbance or diminished tendon reflexes initially, but both of these conditions appeared after several weeks and persisted for 2–4 months.³ He et al. also reported

initial cerebellar involvement in 3 of 71 workers exposed to acrylamide, with the subsequent onset of polyneuropathy.¹²

In conclusion, we present a case of human acrylamide poisoning involving severe visual disturbance and document the temporal change in VEP findings. The frequency of visual disturbance in acrylamide poisoning remains to be evaluated because this is a single case report. We recommend that the possible clinical effects of acrylamide on the visual system should be carefully considered in human cases of acrylamide intoxication.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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