Severe adverse effects related to dermal exposure to a glyphosate-surfactant herbicide

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This is a case of severe chemical burns following prolonged accidental exposure to a glyphosate-surfactant herbicide. The patient developed local swelling, bullae and exuding wounds. Neurological impairment followed affecting finger flexion and sensation with reduced nerve conduction. Imaging revealed oedema of the soft tissue and juxta-articular osteopenia, and a causal relationship to exposure is suggested.

Keywords Skin contamination; Muscle damage; Nerve damage; Herbicide

Introduction

Herbicides containing glyphosate are extensively used in Western countries for forestry and agricultural and gardening purposes.1 The widespread uses of the product and the potential health effects have been discussed.1,2 Repeated testing for skin irritancy and toxicity has classified the product to be of “low acute toxicity”2 comparing it with baby soap and dish-washing detergent.3 However, there are case reports suggesting a caustic effect of some glyphosate formulations.4–6

A typical glyphosate-surfactant herbicide consists of glyphosate, formulated as a salt, and an added surfactant, which can vary in both nature and concentration.1 Most often, the surfactant is a polyethoxylated tallow amine (POEA).2 The surfactant dissolves the wax coating on the leaves of the plant facilitating the uptake of glyphosate.7 Experimental studies have suggested that the toxicity of POEA formulation is more profound than the toxicity of glyphosate alone, and the discussion of a possible potentiating effect is on-going.1

Case report

A 43-year-old man with a history of alcohol abuse was admitted to the emergency department (ED). He had skin corruptions on his left hand and arm, on the left side of his chest and on his left leg. Two days earlier, he had used a concentrated glyphosate-surfactant herbicide given to him by a neighbour in a half-litre plastic bottle. He diluted the herbicide with water, shook the bottle and accidentally sprayed the liquid on himself. On the next day, the affected areas began to swell, especially his arm, and on the second day, vesicles, bullae and exuding wounds appeared on his arm and hand, and also on his chest and leg. Moreover, he had touched his face with contaminated hands resulting in a periorbital oedema and redness on the left side of his head. On admission, he seemed mildly inebriated but answered and cooperated relevantly.

His hand corrosion involving an area of the palm 11 × 11 cm, extending laterally to the ulnar side, was characterized by redness, bullae and deep second-degree skin necrosis with detachment of the epidermis. A small haematoma was found in the skin of the left axillary region and right upper arm. There were a few bullae on the dorsal side of the hand as well. The arm and fingers were swollen affecting the range of motion – especially full extension of the fingers; however, total passive extension was possible without inducing pain. There was no sign of tendon or nerve damage of the hand, and the extension deficit was predicted to be due to oedema. Blood tests showed elevated infection parameters and elevated acute phase reactants: CRP, 187 (reference value, <10) mg/L; WBC, 15.7 (3.5–10.0) × 10^9/L; and platelets, 771 (165–400) × 10^9/L; and signs of muscle injury: myoglobin, 640 (<75) μg/L; and creatine kinase, 7699 (50–270) U/L. There were no signs of pressure lesions on the trunk or extremities, and the patient was not aware of any unconsciousness up to the time of admission.

Supportive therapy involving nasal oxygen, analgesics, intravenous fluids and corticosteroids was initiated. The
patient was transferred to the orthopaedic care for further wound treatment and mobilization. After the removal of the superficial necrotic skin, sensation was intact. After 3 days, the patient was discharged. The wounds seemingly healed without complications, but the patient subsequently experienced total lack of sensation on his left hand.

After 2 months, the swelling decreased considerably with a slight improvement in finger flexion. Despite hand therapy, including extension splints, the flexion contracture of the fingers became manifest. Nerve conduction studies (NCS) of the left arm performed 3 months after the exposure showed severe affection of the distal axons on the median, ulnar and radial nerves with normal or near-normal motor nerve conduction from the wrist to the elbow. Both sensory and motor nerve functions were affected. Right-side NCS was normal. Four months post-exposure, X-rays showed marked juxta-articular osteopenia (Fig. 1), and oedema of the soft tissue was found on MRI. After 7 months, these changes were more pronounced, and an NCS showed improvement in nerve conduction in both the medial and the ulnar nerves. After 9 months, the patient had regained near-normal sensation. He still had pronounced atrophy of the intrinsic muscles of the hand and loss of strength with decreased range of motion (Fig. 2); however, an NCS of the radial nerve showed improved function after 10 months. EMG showed denervation of the abductor pollicis brevis and the abductor pollicis minor. Some discrepancy between the less pronounced denervation and the significant atrophy of, especially, the muscle of the first interosseous muscle (between the thumb and the index finger) supports the fact that the damages may be due to direct injury of both nerves and muscles.

All other skin lesions had healed with scarring and alopecia (Fig. 3). A few months later, the patient died of unrelated causes.

The concentrated liquid involved in the exposure was analysed at the chemical division of the Danish Emergency Management Agency (DEMA) using ion chromatography and LC–MS. The liquid was identified as a concentrated glyphosate-surfactant formulation with the iso-propylamine salt of glyphosate as the active ingredient, with a pH of 4.5–5. The surfactant added was a mixture of polyethoxylated alkyl amines. The neighbour who supplied the liquid was subsequently contacted and stated that the content was an original and commercially prepared form of ‘Roundup® Bio’ delivered to a plant nursery where he worked.

**Discussion**

Amerio et al.⁴ described a case of a 78-year-old woman with serious chemical burns after exposure to 41% glyphosate

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**Fig. 1.** Osteopenia of the carpal bones.

**Fig. 2.** Contracture of hand muscles resulting in deformation (colour version of this figure can be found in the online version at www.informahealthcare.com/ctx).

**Fig. 3.** Chemical burn healing with alopecia (colour version of this figure can be found in the online version at www.informahealthcare.com/ctx).
with an added 15% POEA. A few hours after exposure, she developed a burning sensation and a macular rash evolving into bullae. Heras-Mendaza et al.\textsuperscript{5} described the development of an erythema multiforme-like rash following dermal exposure to glyphosate. In both cases, the elements healed without scarring in 3–4 weeks.

Two cases have described neurological symptoms following dermal exposure to glyphosate. In one case, a transfer of glyphosate mixture from the hands to the face resulted in facial swelling and locally impaired sensation.\textsuperscript{1,6} The second example involved a healthy 54-year-old man who was briefly exposed to glyphosate mixture on his arms, legs and torso. He developed a rash that healed. One month later, he developed rigidity of the extremities, and one year post-exposure, he was diagnosed with Parkinson’s disease. The authors suggested a causal relation.\textsuperscript{8}

The course of our case, that is, the development of nerve and muscular affection over several months, is unusual. It could be argued that the corrosion and damages found were caused by muscular rhabdomyolysis from overnight compression, and this hypothesis is supported by the fact that the patient had a known history of alcohol overconsumption. A thorough description of his skin lesions did not reveal obvious pressure marks, and the localization of the corrosive skin lesions apparently complied with the accidental contamination. Normal nerve conduction velocity from the wrist to above the elbow would not be expected in the case of compartment syndrome. The severe atrophy of the small muscles of the hand, even after re-innervation, also points at a local affection in the hand, as it is seen in the case of direct muscle damage together with nerve damage. The authors believe that the osteopenia seen on radiographs 4 months post-exposure is far more pronounced than would be expected from disuse alone. We suspect that it is due to nerve injury resembling complex regional pain syndrome (Sudeck’s atrophy).

The bottle analysed was collected from the patient’s residence shortly after his admission to the ED and was identified by him. Therefore, the identification of the agent is as valid as possible.

The patient did not decontaminate the skin for more than 24 hours. The long exposure time could explain the deeper than previously reported damage to nerves and muscles.

**Conclusion**

We suggest that the ability of the surfactant to enhance penetration in cases of prolonged exposure may result in the damage of skin, muscles and the coating on nerve axons. The atrophy of hand muscles could be the result of the nerve affection but may also be a direct caustic effect. We suppose that the initial elevation of myoglobin and creatine kinase levels illustrates primary muscular damage. Initially, there was no suspicion of compartment syndrome, and we do not consider this a likely mechanism.

According to data sheets for concentrated glyphosate-surfactant herbicides, skin toxicity has been tested using the OECD 404 test guidelines. The product is applied to the test animals for an exposure time of 4 hours. It is questionable whether this method is sufficient to assess the effects of exposure times longer than 4 hours and the long-term effects of prolonged exposure.

We believe that it is important to further investigate the dermal effects of prolonged exposure to a glyphosate-surfactant herbicide, especially the combined toxicological effect of the surfactant and glyphosate.

The importance of preventive measures must be emphasized, that is, appropriate handling according to the data sheets and the use of appropriate protective measures. In the case of direct skin exposure, immediate thorough washing and rinsing of the exposed area with soap and water are of the utmost importance.

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**Declaration of interest**

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

**References**