Case Report

Toxic Epidermal Necrolysis and Acute Kidney Injury due to Glyphosate Ingestion

J. Indirakshi, A. Sunnesh[1], M. Aruna[2], M. Hari Krishna Reddy[1], Anil C. V. Kumar[1], V. Sarat Chandra[1], B. Sangeetha[1], D. T. Katyarmal[2], R. Ram[1], V. Siva Kumar[1]

Departments of Dermatology, [1]Nephrology and [2]Medicine, SVIMS, Andhra Pradesh, Tirupati, India

Abstract

The literature, particularly from India, is scarce on the renal effects of glyphosate poisoning. Glyphosate causes toxicity not only after its ingestion but also after dermal exposure by inhalation route and on eye exposure. We present a patient report of glyphosate consumption which resulted in toxic epidermal necrolysis – the first report after glyphosate consumption and acute kidney injury.

Keywords: Acute kidney injury, glyphosate, hemodialysis, toxic epidermal necrolysis

Introduction

Commercial glyphosate-based formulations range from 41% or more concentration of glyphosate to 1% glyphosate formulations. The formulations comprised an aqueous mixture of the isopropylamine salt of glyphosate, a surfactant, and various minor components. Polyoxyethylene amine is commonly used as a surfactant.[1] The molecular weight of glyphosate is 169.073 g/mol. Glyphosate causes toxicity not only after its ingestion but also after dermal exposure by inhalation route and on eye exposure. We present a patient report of glyphosate consumption which resulted in toxic epidermal necrolysis – the first report after glyphosate consumption and acute kidney injury.

Case Report

A 30-year-old gentleman has consumed glyphosate (Hexagor 71%) with an intention to self-harm. He consumed 15 mL. At a primary health center, gastric lavage was done within an hour. On the same day evening, he developed body pains, oliguria, and generalized erythema. The skin lesions later evolved into multiple discrete, closely set sterile pustules on flexures such as elbows, axillae, and nape of the neck. There was erythematous maculopapular rash on the lower abdomen and upper thigh. The mucosae were normal. Within a day, he developed anuria and pulmonary edema. The skin lesions also progressed to widespread large bullous lesions on limbs and trunk. There were bleeding lip and oral ulcers, redness, and watering of eyes and scrotal moist erosion. The Nicolsky sign was positive. At admission, the blood pressure was 130/80 mm Hg. The patient had normotension during an entire hospital stay. The investigation were serum creatinine: 10.1 mg/dL, blood urea: 201 mg/dL, serum sodium: 135 mEq/L, serum potassium: 6.2 mEq/L, hemoglobin: 13.2 g/dL, total leukocyte count: 6800/mm^3 and platelet count: 60,000/mm^3, total bilirubin: 0.7 mg/dL, serum glutamic oxaloacetic transaminase: 77 U/L, serum glutamic-pyruvic transaminase: 46 U/L, serum alkaline phosphatase: 75 U/L, serum creatinine phosphokinase: 215 IU/L, serum lactate dehydrogenase: 2579 U/L, serum cholinesterase: 1589 U/mL, serum pH: 7.2, serum bicarbonate 11.5 mmol/L and urine examination: albumin: 2+, pus cells: 1–2/hpf, and red blood cells: 0–1/hpf and tubular cast present. Ultrasound abdomen revealed right kidney: 10.2 cm × 3.4 cm and left kidney: 10.4 cm × 3.2 cm. A 4 mm punch biopsy from the right forearm revealed stratified squamous epithelium with spongiosis and exocytosis, vacuolar alterations of basal keratinocytes, and there was moderate perivascular mononuclear infiltration in the papillary dermis. It was consistent with toxic epidermal necrolysis [Figure 1]. He was initiated hemodialysis and received eight sessions of hemodialysis before the urine output improved. The skin

Address for correspondence: Prof. R. Ram,
Department of Nephrology, SVIMS, Andhra Pradesh, Tirupati, India.
E-mail: ram_5_1999@yahoo.com

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lesions have disappeared over 3 weeks with the formation of new skin layers. He was discharged on day 24 after the consumption with normal serum creatinine and blood urea. At a follow-up consultation after 3 months, the serum creatinine and blood urea were 1.0 and 24 mg/dL, respectively.

Discussion

The experimental studies suggest that the toxicity of the surfactant, polyoxyethylene amine, is greater than the toxicity of glyphosate alone and commercial formulations alone. Ingestion of >85 mL of the concentrated formulation is likely to cause significant toxicity in adults.[1]

In plants, glyphosate disrupts the shikimic acid pathway. It results in the death of the plant in 4–20 days.[2] The mechanism of toxicity of glyphosate in mammals is thought to be uncoupling of oxidative phosphorylation.[1]

Based on animal studies, it was found that only 30% is absorbed from gastrointestinal tract. The peak plasma concentrations of glyphosate are attained at 1–2 h. The initial concentration is mainly in small intestine, colon, kidney, and bone.[1] The major quantity of glyphosate is excreted unchanged in the urine.[1] The data in humans are limited, but a similar pattern is observed.[1] Gastrointestinal corrosive effects and dysphagia are common. Respiratory distress, impaired consciousness, pulmonary edema, cardiogenic shock, and arrhythmias might appear. Bradycardia and ventricular arrhythmias are often present preterminally.

Cardiovascular collapse is a major cause of death after glyphosate exposure,[3] and patients respond poorly to conventional fluid and vasopressor therapy.[3]

Skin exposure resulted in several different manifestations. Skin contact with glyphosate had caused irritation[4] and contact dermatitis. Chemical burns that later led to the appearance of erythematous macules that developed into bullae within 24 h were reported.[5] Facial swelling, paresthesia and periorbital edema, and a generalized pompholyx were all reported.[6] Our patient had ingested the glyphosate. It is possible, and ours is the first report of toxic epidermal necrolysis after consumption of glyphosate.

Acute kidney injury and hepatic impairment are usually due to reduced organ perfusion due to hypovolemia and cardiogenic shock, although a direct toxic effect of glyphosate or surfactant may also contribute.[1]

The clinical features attributed to surfactant toxicity include vomiting, diarrhea, hemolysis, hypotension, altered mental status, and pulmonary edema.[7] The clinical features such as metabolic acidosis, central nervous system depression, and nephrotoxicity may be primarily attributed to the glyphosate itself.[7]

Management is symptomatic and supportive. Gastric lavage may be considered if a life-threatening amount of a concentrated glyphosate formulation has been ingested within 1 h. Activated charcoal may adsorb the surfactant component of glyphosate.[8] Decontamination with activated charcoal

Figure 1: Toxic epidermal necrolysis.

should be undertaken in those with a protected airway and who present early.

Early invasive monitoring, early ventilatory and hemodynamic support, and maintenance of euvolemia are of paramount importance. Hypotension secondary to fluid loss should be treated with crystalloids, colloids, and blood products. Inotropes may also be employed. Metabolic acidosis should be treated quickly with sodium bicarbonate infusion.

Hemodialysis has not been preferred in patients with glyphosate intoxication for the reason hemodialysis could not remove the surfactant, which may be partially responsible for the toxicity,[3] due to its large molecular size. However, hemodialysis does remove glyphosate.[8] Hemodialysis may improve acidosis and hyperkalemia. The literature search revealed that in Lee's series,[9] three patients were commenced on hemodialysis for acute kidney injury. All of these patients died. In Stella's series,[8] both patients initiated on renal support died. There were only a few published reports of successful hemodialysis in patients who ingested glyphosate. In one patient, the daily hemodialysis was instituted for the treatment of prerenal failure consequent to a massive loss of gastrointestinal fluid 3 days after ingestion.[10] In another report, two patients exhibited unresponsive hemodynamic states despite aggressive treatment. Both patients progressed to an anuric state. Hemodialysis was conducted due to hyperkalemia in one patient and due to metabolic acidosis in the second patient. The authors could not entirely dismiss that the hypovolemia was secondary to gastrointestinal fluid loss as the cause of their hypotension.[7]

There was evidence of utility of hemoperfusion in herbicide, like glyphosate poisoning[11] hemoperfusion could serve as the preferred method to enhance toxin elimination irrespective of protein-binding and molecular size. There was experimental evidence to suggest that the final reduction rates of a few ingested surfactants were higher for hemoperfusion than for hemodialysis.[12]

Our patient had neither gastrointestinal cause nor hypotension due to any other reasons to account for acute kidney injury.

We did not perform a renal biopsy for there was no indication. The timing of rise and fall of serum creatinine and presence of tubular cast points toward a possibility of acute tubular necrosis. Our patient recovered completely from acute kidney injury highlighting a possible role of hemodialysis in the management of glyphosate poisoning. We could not perform serum glyphosate levels.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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