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CASE REPORT

A Case of Severe 2,4-Dichlorophenoxyacetic Acid Poisoning Causing Diagnostic and Treatment Challenges

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Abstract: 2,4-Dichlorophenoxyacetic acid is a poisonous herbicide. Though poisoning reports from this compound are rare, there is a tendency toward increased use of it in the agrarian society of Ethiopia. We herein report a case of a young female farmer from rural Ethiopia who was admitted to a local hospital after presenting with loss of consciousness and excess oral secretions 2 hours after a suicidal ingestion of an unknown toxic agent. She was originally treated for organophosphate poisoning, and then transferred to Saint Peter's Hospital in Addis Ababa for more intensive care. There, ingestion of 2,4-D was confirmed, and she received supportive care, mechanical ventilation, and forced alkaline diuresis. Despite these interventions, she died several days later. Due to the similarity of some clinical signs with organophosphate poisoning in acute settings, there are possible missed cases of 2,4-D acid herbicide poisoning. No specific treatment is known, so a high index of suspicion for early detection, decontamination, and initiation of supportive care is crucial to improve survival after exposure. In addition, local policies on proper and controlled use of these herbicides are needed to improve awareness among users and prevent accidental and intentional exposures.

Keywords: 2,4-dichlorophenoxyacetic acid, herbicide, poisoning, Ethiopia

Introduction

2,4-Dichlorophenoxyacetic acid (2,4-D) is a poisonous herbicide widely used in Ethiopian agriculture and accounts for >70% of herbicides imported into the country.[1] 2,4-D is a highly toxic compound causing a wide spectrum of symptoms and organ involvement (heart, lungs, GI tract, muscle, endocrine system, and nerves) after oral, skin, or inhalational exposure.[2–4] It is believed that ingestion is a more relevant route of exposure,[3] and urinary excretion is the main route of elimination from the body.[3] We present a case of a young female farmer who had been admitted to the ICU at Saint Peter's Hospital in Addis Ababa after suicidal ingestion of a toxic agent had led to diagnostic challenge. As it was considered organophosphate (OP) poisoning, treatment was immediately started at the referring hospital. Later, after probing the history, it was found to be 2,4-D, and the misdiagnosis and treatment delay resulted in an unfavorable outcome.

Case Description

A 23-year-old female presented to the emergency department with loss of consciousness and excess oral secretions 2 hours after ingestion of an unspecified poison. She had no abnormal body movement, fever, diarrhea, vomiting, or sweating. She had been initially been taken to a nearby primary hospital, where she was treated for possible OP poisoning with atropine and cimetidine for 3 days, before she was transferred to Saint Peter's hospital. After thorough questioning, it was found that the patient had consumed about 30 mL of 2,4-D in a suicide attempt, precipitated by financial problems. She did not have any known history of psychiatric illness, suicidal attempts, depressive episodes, or substance abuse. No prior cardiac, renal, or metabolic disorders were noted.

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On arrival at the emergency department, the patient was unconscious. Her vitals were PR 110/min, BP 120/70 mmHg, RR 21/min, and SPO_2 96% on room air. Physical examination results were remarkable: a GCS of 6 out of 15, dilated and reactive pupils, hypertonic and hyperreflexic lower extremities, and upgoing plantar reflex. Upon initial investigation, complete blood-cell count, renal function test, liver-function test, and random blood glucose were normal. Her electrocardiogram showed sinus tachycardia, while chest X-ray was unremarkable. Arterial blood-gas analysis and serum level of the toxin could not be determined, as neither means of testing was available at the hospital.

The patient was transferred to the intensive care unit (ICU), intubated for airway protection, and started immediately on forced alkaline diuresis. Her ICU course was remarkable for the development of renal failure (creatinine 3.1 mL/dL [reference range 0.5–1.2 mg/dL], BUN 133 mg/dL [reference range 16.6–48.5 mg/dL], urinalysis 3+ hemoglobin, and many red blood cells), due to toxin-induced rhabdomyolysis (creatine phosphokinase level of 1,330 µg/L). Subsequently, the patient became hypotensive, and vasopressor support was started. Echocardiography and abdominal ultrasonography were both unremarkable. Despite these efforts, she died of circulatory collapse on the third ICU day.

Discussion

2,4-D is a widely used herbicide. There are several formulations of 2,4-D, including esters, acids, and salts.[5] It is a highly poisonous compound. The main routes of exposure care skin, inhalation, and oral ingestion. Ingestion is a more relevant route of exposure.[3] The mechanism of its toxicity is unclear, but mitochondrial injury is described. Cell-membrane damage, uncoupling of oxidative phosphorylation, and disruption of acetyl coenzyme A metabolism are found. A significant amount of muscle damage occurs, and ventricular fibrillation is the most common cause of death.[6] Urinary excretion is the main route of elimination from the body, and toxicity is markedly increased at doses that exceed the capacity of the renal anion-transport mechanism.[3,6]

After ingestion it causes a wide spectrum of symptoms and organ involvement (heart, lungs, GI tract, muscle, endocrine system, and nerves).[2–4] Due its corrosive effect in the gastrointestinal tract, nausea, vomiting, abdominal pain, throat pain, and diarrhea are common. Occasionally, gastrointestinal hemorrhage can occur early.[6,7,9] Through inhibition of voltage-gated chloride channels in skeletal muscles, it causes myotoxicity, resulting in muscle spasms, muscle weakness, and rhabdomyolysis with elevated creatine phosphokinase levels.[6,8] Direct myocardial toxicity results in tachycardia and hypotension.[9] Direct central nervous system effects result in hallucinations, ataxia, miosis, fasciculation, paralysis, convulsions, and coma.[9] Hepatitis and renal failure have also been reported.[6] Respiratory failure occurs in some patients due to hypoventilation from CNS depression and respiratory muscle weakness. Skin exposure produces skin irritation, and systemic symptoms have been reported after substantial exposure.[6,9] Massive rhabdomyolysis, metabolic acidosis, respiratory failure, refractory hypotension, and coma are markers of severe toxicity.[4]

In an acute setting, 2,4-D compounds can mimic OP and carbamate poisoning.[4] OPs and carbamates are compounds primarily used as pesticides, and they are potentially toxic to humans. The mechanism of toxicity is through inhibition of the acetylcholinesterase enzyme in the central and autonomic nervous systems and the neuromuscular junction. Acetylcholinesterase inhibition results in excess accumulation of acetylcholine at nerve terminals, which plays an important role during toxicity from excessive nicotinic and muscarinic neurostimulation.[10] The typical toxidrome in OP poisoning is salivation, lacrimation, urination, defecation, gastric cramps, and emesis symptoms that occur within minutes to hours. Central muscarinic effects result in confusion, coma, and convulsions. The nicotinic effects results in fasciculation, muscle weakness, tachycardia, and hypertension.[11]

Other than 2,4-D poisoning, such compounds as organochlorines, fungicides, mushrooms, and opioids can mimic OP poisoning. Seizure and pulmonary edema from organochlorines, as well as miosis, vomiting, coma, bradycardia, and hypotension caused by opioids, can mimic OPs.[4] Due to the similarities of clinical signs during acute toxicity, the differentiation between OPs and 2,4-D is difficult. However, as in our case, the presence of myotoxicity with elevated creatine phosphokinase and neurotoxicity are suggestive of 2,4-D poisoning.[4] Since the management of poisoning from the aforementioned compounds is different and time-dependent, early identification of the specific type of toxic agent has detrimental effects on the patients' outcome. In the case of OP and carbamate poisoning, management includes decontamination, supportive care, antimuscarinic therapy, and oximes.[10]

All patients with 2,4-D poisoning should receive immediate supportive care, which includes airway management and ventilatory support if indicated, decontamination with activated charcoal and sorbitol in appropriate conditions, gastric lavage after recent large ingestion, and routine resuscitation with crystalloids. In the presence of hypotension that is not responsive to fluid management, vasopressors are indicated. Correct electrolyte abnormalities and acidosis.[6,12,13] The role of urinary alkalization has been reported in cases of severe 2,4-D poisonings. 2,4-D is a weak acid, and urinary alkalization promotes ionization of the phenoxy acid, decreases reabsorption from the renal tubles, and results in enhanced elimination.[10,16,17]

In Ethiopia, where agrarian communities are predominant, the practice of using herbicides like 2,4- D as part of routine agricultural activity is increasing. Most herbicides available in Ethiopia are imported by public enterprises and then distributed by governmental and private organizations. Even though the Ministry of Agriculture, alongside other policy-makers, have developed product regulations, data suggest significant gaps in implementation.[14] Among the salt preparations, 2,4-dimethylamine salt, a solution of dimethylammonium salt of 2,4-D, is a widely used herbicide in Ethiopia. 2,4-D is a rare cause of poisoning, yet its utilization is increasing among agrarian societies in Ethiopia. Its use as an ingestible poison is increasing. There have been reported cases of 2,4-D poisoning from tertiary hospitals across Ethiopia.[15] Considering its rarity, misclassification and mistreatment of 2,4-D poisoning as OP or carbamate poisoning is quite common. These misclassifications results in underreporting and delayed diagnosis, which lead to poor outcomes. As such, it is imperative to take a thorough history for early identification of the poison and to initiate early supportive management and forced urinary alkalization, which may hasten elimination of this compound from the body before absorption and resulting in multisystem complications and even death.[16,17] Bottle packing, proper labeling, and secure storage and distribution of herbicides containing 2,4-D is also essential.

Conclusion

Misclassifying and mistreating 2,4-D poisoning in an acute setting is common. Therefore, health-care providers need to maintain a high index of suspicion for early detection, decontamination, and initiation of supportive care to improve survival after exposure. In an effort to reduce misdiagnosis and mistreatment of 2,4-D poisoning in an acute setting, it is very important to emphasize improving the knowledge about the presenting symptoms and complications of 2,4-D poisoning among medical staff members and availing basic toxicology tests. Since 2,4-D is highly poisonous and associated with substantial mortality among exposed individuals, preventing toxicity from it is essential. Local policies on proper and controlled use of this herbicide are needed to improve awareness among users, mainly in agrarian societies, so as to prevent accidental and intentional exposure. Creating public awareness about possible toxicity and techniques of personal protection are the first steps in preventing adverse effects.

Ethics Approval and Consent for Publication

Written informed consent was obtained from the patient's family for publication of this case. Approval from the Ethics Committee of Saint Peter's Hospital was not required to publish this case report.

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Disclosure

The authors report no conflicts of interest in this work.

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