Case Report
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Mixed acid-base abnormality in a patient with herbicide poisoning – possible insights on the mechanism of toxicity

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Abstract

2, 4-Diclorophenoxyacetic acid (2, 4-D), a herbicide, is an uncommon cause of intentional poisoning in humans. We report a patient who survived after ingestion of a fatal dose of 2, 4-D and explore possible mechanisms for the observed metabolic abnormalities. A 48-year-old male was brought following ingestion of a mixture of 2, 4-D and metribuzin (50-gm each). He presented with vomiting and altered sensorium and required intubation and mechanical ventilation. There was evidence of rhabdomyolysis, non-oliguric renal failure and multiple electrolyte abnormalities. The acid-base abnormalities were consistent with mixed respiratory alkalosis with normal anion gap metabolic acidosis. The patient was treated with supportive care and alkaline diuresis and made an uneventful recovery. The metabolic acidosis was attributed to proximal tubular dysfunction while the respiratory alkalosis with altered conscious state and normal oxygenation suggested central hyperventilation as the mechanisms for the observed metabolic abnormalities with 2, 4-D poisoning.

Keywords: 2, 4-Dichlorophenoxyacetic acid, metribuzin, herbicide, poisoning, metabolic

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1. Introduction

Herbicides are a subcategory of pesticides used to control noxious plants. Herbicide poisoning is an infrequent cause of pesticide poisoning. In humans, the toxic effects may be acute or chronic and are dependent on the duration of exposure, the type of herbicide and the quantum of exposure.

2. Case history

We report a 48-year old male (65 kg), a chronic smoker and alcohol consumer, who presented with acute toxicity following ingestion of two herbicide compounds (50-gm of 2, 4-Dichlorophenoxyacetic acid (2, 4-D) and 50-gm of metribuzin). He presented within 30-min of ingestion to a local hospital with stiffening of the limbs, vomiting and altered sensorium. Following gastric lavage at this hospital, he was referred to our hospital.

At presentation to our Emergency Department (ED), the Glasgow Coma Score (GCS) was 12/15. He was tachycardic (heart rate 146/min) and had a blood pressure (BP) of 150/90 mm Hg. His respiratory rate was 46/min with oxygen saturation (SpO_2) of 96% on room air. Pupils were normal sized and equally reacting and there were no focal neurological deficits. Rest of systemic examination was normal. Chest radiograph and non-contrast computed tomography (CT) of the brain were normal. He was transferred to the ward for observation and managed with supportive measures, including hydration with 2.5 liters of normal saline over the next 24-hours. There were no further episodes of vomiting or diarrhea following admission to hospital.

Over the next 24-h, the sensorium progressively decreased (GCS 7/15) and he was intubated for airway protection and shifted to the intensive care unit (ICU). Investigations (Table 1) following ICU admission showed multiple electrolyte abnormalities (hypocalcaemia,

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hyperphosphatemia, hypokalemia) with deranged liver enzymes, elevated serum creatinine and high creatinine phosphokinase (CPK) The initial arterial blood gas (ABG) at admission and the subsequent one taken in the ICU revealed mixed respiratory alkalosis and normal anion gap metabolic acidosis (delta ratio 0.3) with acidic urine (pH 4.7). His electrocardiograph (ECG) revealed prolonged corrected QT (QTc) interval of 540 msec.

In view of the rhabdomyolysis and renal failure, hydration was continued judiciously using chloride free fluids and the electrolyte abnormalities (hypocalcaemia, hypokalemia) were corrected. Alkaline diuresis with intravenous sodium bicarbonate was done to facilitate toxin removal. Serial monitoring of electrolytes, creatinine, CPK and urine pH was performed (Table 1). He was hemodynamically stable and continued to be weaned from ventilatory support. By day 5, the sensorium improved and the patient was extubated and transferred to the ward. Repeat ECG prior to discharge showed normalization of the QT interval.

3. Discussion

Triazines (like Atrazine, Metribuzin) and Phenoxy acid derivatives (like 2,4-D; 2,4,5 Trichlorophenoxy acid) are commonly used herbicides.[1] Metribuzin is a broadleaf herbicide of the triazine chemical family. Metribuzin acts through a mechanism that is lacking in mammalian species and hence has a low degree of toxicity in mammals.[2] 2, 4-D, a broadleaf weedicide, may be absorbed by oral, dermal and inhalational routes.[3] In animals, 2, 4 D affects ribonuclease function and uncouples oxidative phosphorylation.

In the few case reports of 2, 4-D poisoning in humans,[3–5] neurological (marked central nervous system depression, restlessness, cerebral edema)[3–5] and gastrointestinal manifestations (vomiting, abdominal pain)[3,4] were frequent. Others have reported rhabdomyolysis,[3–5] metabolic acidosis,[3,4] renal failure,[3,4] elevated transaminases[3–5] and shock.[3] Our patient had features of vomiting, rhabdomyolysis, metabolic acidosis, electrolyte abnormalities, elevated liver enzymes and acidic urine that could be explained by the ingestion of a large lethal dose (approximately 769 mg/kg) of 2,4-D. However other constituents in the mixture that the patient had ingested could have also contributed to some of the manifestations seen in this patient.

There are a few possible explanations for the observed metabolic abnormalities seen with this poisoning. First, the ABG abnormalities of a normal anion gap hyperchloremic metabolic acidosis with low urine pH, multiple electrolyte abnormalities and the absence of other perpetrators (normal saline infusion and gastrointestinal loss) suggest a proximal renal tubular injury as the cause of acidosis. A urine anion-gap would have added more light to this; however this was not done. Secondly, the concomitant respiratory alkalosis (initial CO_2 values <15 mm Hg) in the setting of altered conscious state and normal oxygenation indices would suggest central hyperventilation or cerebral irritation akin to what happens in salicylate poisoning.[3]

The management of herbicide poisoning is supportive and there are no antidotes for chlorphenoxy herbicides. Since the half-life of 2, 4-D in humans is around 18 hours, which can be prolonged up to 70 to 90 hours in the presence of acidic urine,[3] alkaline diuresis has been used to enhance elimination of the herbicide,[5] although this is

Table 1. Serial laboratory values

Investigations	ED	Ward	Intensive care unit			
	Day 1	Day 2	Day 3	Day 5	Day 8	Day 10
S. Creatinine (mg/dl)	1.06	-	1.9	1.62	1.36	0.89
Blood urea (mg/dl)	21	-	80	64	47	39
S. Creatinine phosphokinase (U/L)	-		21,116	1, 07, 962	43, 542	7236†
S. Sodium (mEq/L)	-	149	155	147	137	-
S. Chloride (mEq/L)	-	117	127	119	196	-
Urine pH	-	-	4.7*	5.47	7.29‡	-
ABG pH	-	7.59	7.61	7.5	7.52	-
ABG $PaCO_2$ (mm Hg)	-	14	12	24	28	-
S. Bicarbonate (mEq/L)	-	13.4	12.1	18.7	22.9	-
Base excess	-	-8.3	-9.3	-4.5	0	-

* Done on day 4; † done on Day 11; ‡ done on Day 7; Patient was intubated and ventilated on Day 3 and extubated on Day 7

not routinely recommended. Our patient responded to judicious management of the metabolic abnormalities along with alkaline diuresis and had a successful outcome.

Although there are a few case reports of this poisoning,[3–5] we report this case to present possible explanations for the observed metabolic abnormalities with this poisoning.

4. Conflict of Interest

None Declared

5. References

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