

[CASE REPORT]

Decrease in Butyrylcholinesterase Accompanied by Intermediate-like Syndrome after Massive Ingestion of a Glyphosate-surfactant

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Abstract:

An 86-year-old woman intentionally drank approximately 300 mL of a glyphosate-surfactant. She was found with consciousness disturbance and experienced several vomiting episodes. On arrival, serum biochemistry revealed a decreased level of butyrylcholinesterase (B-CHE) [11 (normal range: 180-450) IU/L]. Later, her B-CHE level further decreased to single-digit values, and she became comatose with involuntary movement and an increase in muscle tone. Her consciousness level and muscle tone improved with the recovery of her B-CHE level. Physicians should be alert for the occurrence of intermediate syndrome when the B-CHE levels of patients who have consumed a massive amount of glyphosate-surfactant show a prolonged decrease.

Key words: glyphosate-surfactant, intermediate syndrome, butyrylcholinesterase

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Introduction

Glyphosate-surfactants are commonly used pesticides that are thought to be safer than paraquat. When used normally, these agents do not induce adverse effects on the development or on the reproductive or endocrine systems in humans or other animals (1).

Paraquat has not been sold since 1999, and glyphosate-surfactant can be purchased without any regulations in Japan. A hospital-based survey of clinical cases of pesticide acute poisoning revealed glyphosate-surfactant to be the most frequent cause among 137 cases (2). Acute poisoning symptoms induced by a glyphosate-surfactant include gastrointestinal symptoms, respiratory distress, hypotension, altered consciousness and renal insufficiency (3-5). However, no studies have reported the induction of a decrease in the butyrylcholinesterase (B-CHE) level or intermediate syndrome (typical symptoms of organophosphate poisoning) by glyphosate-surfactants.

We herein report the case of a patient with a transient decrease in her B-CHE level, which was accompanied by

intermediate-like syndrome, following the ingestion of a massive amount of a glyphosate-surfactant.

Case Report

An 86-year-old woman intentionally drank approximately 300 mL of a glyphosate-surfactant, which had been bought for her kitchen garden, after a quarrel with her daughter. She was found by her daughter with consciousness disturbance, having experienced several vomiting episodes. She had depression and a history of overdose. She was transported to our hospital by a physician-staffed helicopter.

Upon arrival, her vital signs were as follows: Glasgow Coma Scale (GCS), E3V3M6; blood pressure, 108/76 mmHg; pulse rate, 66 beats per minute; respiratory rate, 30 breaths per minute and saturation of peripheral oxygen with oxygen of 10 L per minute, 100%. Her pupils were 2 mm in size with prompt light reflex. The physiological findings on muscle tone, chest roentgenography and electrocardiography studies were negative. Serum biochemistry revealed a decreased level of B-CHE [11 (normal range: 180-450) IU/L] (Table). The patient underwent cathartic and activated

Table. Results of the Blood Analyses on Arrival.

Blood gas analysis: (on 10 L min ⁻¹ of oxygen)					
pH	7.406	PCO ₂	41.0 mmHg	PO ₂	75.6 mmHg
HCO ₃ ⁻	25.3 mmol/L	Base excess	1.0 mmol/L		
Cell blood count and biochemical analysis					
White blood cells	16.0×10 ³ /μL	Hemoglobin	12.1 g/dL		
Platelets	20.1×10 ⁴ /μL				
Total protein	7.4 g/dL	Butyrylcholinesterase	11 (180-450) IU/L		
Aspartate aminotransferase	20 IU/L	Alanine aminotransferase	10 IU/L		
Alkaline phosphatase	157 IU/L	γ-glutamyltransferase	10 IU/L		
Creatine phosphokinase	54 IU/L	Amylase	160 IU/L		
Blood urea nitrogen	18.6 mg/dL	Creatinine	0.66 mg/dL		
Glucose	182 mg/dL	Sodium	136 mEq/L		
Potassium	3.1 mEq/L	Chloride	102 mEq/L		
C-reactive protein	0.3 mg/dL	Fibrinogen	209 mg/dL		
Activated partial thromboplastin time	19.2 (24.9) s				
Prothrombin time	10.7 (11.7) s				
Fibrinogen degradation products	5.2 μg/mL				

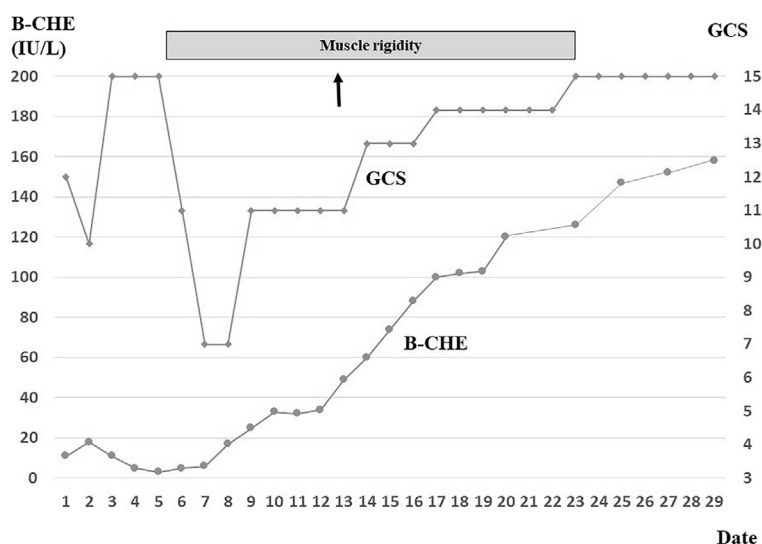


Figure. Time course of B-CHE, GCS and muscle tone. The improvement in the GCS score was correlated with the recovery of the patient's B-CHE level. The patient's muscle tone also improved after the recovery of her B-CHE level. B-CHE: butyrylcholinesterase, GCS: Glasgow Coma Scale

charcoal treatment after gastric lavage. She was admitted to our hospital, and her cardio-respiratory function was continuously monitored. Figure shows the time course in her B-CHE level, GCS and muscle tone.

On the second day, she complained of pain with delirium, but her physical and laboratory findings showed no remarkable changes. On the third day, she became alert and was able to drink water. Her peripheral oxygen improved to the normal range under room air. On the fourth and fifth days, her B-CHE levels further decreased to single-digit values; however, she was asymptomatic. On the sixth day, she developed consciousness disturbance and involuntary movement with an increase in muscle tone. Urgent head magnetic resonance imaging and electroencephalography showed negative findings. She temporarily showed apnea with re-

duced peripheral oxygen but obtained spontaneous respiration. On the seventh day, she became comatose. On the ninth day, her GCS score improved, but she displayed catalepsy-like movement. On the 13th day, she showed convulsions, which were treated by levetiracetam.

Her consciousness level and muscle tone improved according to the recovery of her B-CHE level. Her symptoms improved further the next day, and she was eventually able to feed herself and walk. As the patient's condition was complicated by depression, she was transported to a psychiatric hospital.

Discussion

This is the first case of glyphosate-surfactant poisoning to

be accompanied by a transient decrease in the B-CHE level and intermediate-like syndrome. There have been no clinical reports describing cases in which the ingestion of a large amount of glyphosate-surfactant resulted in a severe and prolonged decrease in a patient's B-CHE level. Accordingly, we were unable to clarify whether or not this severe effect on the B-CHE level after the ingestion of a large amount of glyphosate-surfactant occurs in all humans.

In normal use, glyphosate-surfactant does not alter the levels of B-CHE (6). However, in some species, glyphosate-surfactant can reduce the level of acetylcholinesterase (A-CHE) in erythrocytes, brain and muscle (7). Glyphosate-surfactant can also reduce the level of B-CHE in massive doses (8). B-CHE can act as a backup for acetylcholinesterase and as a scavenger for poisons that might inhibit acetylcholinesterase activity (9). In organophosphate-induced neurotoxicity, A-CHE and/or B-CHE inhibition was found to be correlated with the occurrence of intermediate syndrome (10). In addition, Yilmaz et al. prospectively performed therapeutic plasma exchange for patients who developed intermediate syndrome during follow-up for organophosphate intoxication (11). As a result, a statistically significant increase was detected in the plasma B-CHE levels of patients after therapeutic plasma exchange. Thirteen of 17 patients showed clinical improvement and were discharged after therapeutic plasma exchange. These results suggested that low levels of B-CHE have the potential to induce intermediate syndrome. Accordingly, the ingestion of a massive amount of glyphosate-surfactant may reduce the level of B-CHE, even in humans, which has the potential to induce intermediate syndrome, similarly to organophosphate poisoning.

Conclusion

Physicians should pay attention to the occurrence of intermediate syndrome when the B-CHE levels of patients who have ingested a massive amount of a glyphosate-surfactant are decreased for a prolonged period of time.

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References

- Williams GM, Kroes R, Munro IC. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. *Regul Toxicol Pharmacol* **31**: 117-165, 2000.
- Nagami H, Maejima F, Nishigaki Y, Natsukawa S. Hospital-based survey of clinical cases of pesticide poisoning in Japan 2010-2012. *Jpn Asso Rural Med* **64**: 14-22, 2015.
- Roberts DM, Buckley NA, Mohamed F, et al. A prospective observational study of the clinical toxicology of glyphosate-containing herbicides in adults with acute self-poisoning. *Clin Toxicol (Phila)* **48**: 129-136, 2010.
- Chen YJ, Wu ML, Deng JF, Yang CC. The epidemiology of glyphosate-surfactant herbicide poisoning in Taiwan, 1986-2007: a poison center study. *Clin Toxicol (Phila)* **47**: 670-677, 2009.
- Lee HL, Chen KW, Chi CH, Huang JJ, Tsai LM. Clinical presentations and prognostic factors of a glyphosate-surfactant herbicide intoxication: a review of 131 cases. *Acad Emerg Med* **7**: 906-910, 2000.
- Kwiatkowska M, Paweł J, Bukowska B. Glyphosate and its formulations--toxicity, occupational and environmental exposure. *Med Pr* **64**: 717-729, 2013 (in Polish).
- Larsen KE, Lifschitz AL, Lanusse CE, Virkel GL. The herbicide glyphosate is a weak inhibitor of acetylcholinesterase in rats. *Environ Toxicol Pharmacol* **45**: 41-44, 2016.
- Lajmanovich RC, Attademo AM, Peltzer PM, Junges CM, Cabagna MC. Toxicity of four herbicide formulations with glyphosate on *Rhinella arenarum* (anura: bufonidae) tadpoles: B-esterases and glutathione S-transferase inhibitors. *Arch Environ Contam Toxicol* **60**: 681-689, 2011.
- Masson P, Lockridge O. Butyrylcholinesterase for protection from organophosphorus poisons: catalytic complexities and hysteretic behavior. *Arch Biochem Biophys* **494**: 107-120, 2010.
- Çolak Ş, Erdoğan MÖ, Baydin A, Afacan MA, Kati C, Duran L. Epidemiology of organophosphate intoxication and predictors of intermediate syndrome. *Turk J Med Sci* **44**: 279-282, 2014.
- Yilmaz M, Sebe A, Ay MO, Gumusay U, Topal M, Atli M, Icme F, Satar S. Effectiveness of therapeutic plasma exchange in patients with intermediate syndrome due to organophosphate intoxication. *Am J Emerg Med* **31**: 953-957, 2013.

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