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Case Report

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Prolonged cognitive dysfunction in patient with splenial lesion of the corpus callosum caused by glufosinate ammonium poisoning

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Abstract:

Glufosinate ammonium (GLA) is widely used as a commercial herbicide in many countries. Neurotoxicity of GLA has been associated with serious neurological complications such as loss of consciousness, convulsions, and memory impairment. Late-onset memory impairment due to GLA-induced hippocampal lesions is the most distinct clinical feature in GLA poisoning. However, the lesion of the splenium of the corpus callosum (SCC) is a rare condition in GLA poisoning, so the clinical features are not well known. We report the case of a 57-year-old male patient who developed SCC damage after GLA poisoning. The patient had various late-onset neurotoxic symptoms, including prolonged overall cognitive dysfunction and psychosis-like symptoms. Emergency physicians should be aware that GLA-induced SCC lesions may be associated with various late-onset neurotoxic symptoms.

Keywords:

Cognitive dysfunction, corpus callosum, glufosinate ammonium, herbicides

Introduction

Glufosinate ammonium (GLA) is an analog of glutamate-containing amino acids and is widely used as a commercial herbicide in many countries. GLA's toxicity may be caused by glufosinate and its metabolites, as well as additives such as glutamate, ammonia, and surfactant. The acute oral toxic dose of GLA is estimated to be 320–360 mg/kg.[1] In patients with GLA poisoning, early gastrointestinal symptoms are the most common, which may be associated with the surfactant's mucosal irritant effect. Neurotoxicity of GLA can lead to serious neurological complications such as loss of consciousness, convulsions, and memory impairment. Moreover, life-threatening conditions, such as hemodynamic instability or respiratory failure, may deteriorate rapidly.[2] Among various neurological complications, late-onset memory impairment due to GLA's hippocampal lesions has been reported as the most distinct clinical feature.[2] However, the lesions of the splenium of the corpus callosum (SCC) are rare conditions in patients with GLA poisoning. The clinical manifestations associated with GLA-induced SCC lesions are still not well-known. Herein, we report a rare case of a patient with various late-onset neurotoxic symptoms due to GLA-induced SCC lesions.

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Case Report

A 57-year-old male was admitted to the emergency department (ED) with a drowsy and confused mentality. The patient was found lying in a farm shed 3 h ago, and a bottle of GLA was near him. The herbicide's commercial name was Pul-Je-Lo® (DONGBANG AGRO Corp., Seoul, Korea), which was composed of GLA of 18% and surfactant and other additives of 82%. The herbicide bottle's total capacity was 500 cc, and two-thirds were empty when he was found. However, the patient and his elderly mother could not provide accurate information about his past medical history and current condition.

At the arrival time in the ED, the patient's blood pressure was 137/76 mmHg, pulse rate was 58 beats/min, respiratory rate was 19 breaths/min, and body temperature was 37.3°C. Arterial blood gas analysis (ABGA) revealed pH: 7.31, PO_2: 79.3 mmHg, PCO_2:46.3 mmHg, and HCO_3:21.3 mmol/L. The Glasgow Coma Scale (GCS) was 14 points. There were no specific findings in physical and neurological examinations except for consciousness change. The laboratory test results showed no other abnormalities except for the ammonia level elevated to 173 μg/dL (reference, 0–75 μg/dL). The nasogastric tube was inserted, and activated charcoal was administered through it. However, after 5 h, GCS rapidly deteriorated to 7 points, and the ABGA result showed respiratory acidosis (pH: 7.17, PO_2: 57.5 mmHg, PCO_2: 82.1 mmHg, and HCO_3: 22.3 mmol/L), followed by generalized convulsions. We immediately underwent endotracheal intubation and administered lorazepam and midazolam. Furthermore, hemodialysis (HD) was performed twice during the initial 24 h to remove GLA from the blood. On day 4 of hospitalization, the patient's consciousness and respiratory failure were fully recovered, and electroencephalography was normal. Serum ammonia levels increased again but gradually decreased and normalized. Furthermore, severe toxicity did not recur [Figure 1].

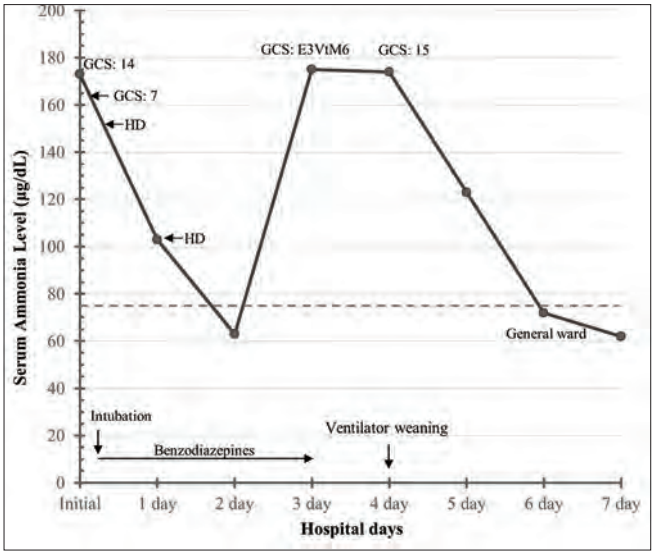

Figure 1: Serum ammonia levels (baseline, 0-75 μg/dL) and Glasgow coma scale (GCS) during treatment. HD: hemodialysis; T in GCS: Endotracheal Intubation

In the general ward, the patient consistently exhibited anterograde amnesia and a disability of comprehension. He could not remember what he had just said. Despite repeated explanations by the medical staff and caregiver, he did not understand why he was admitted to the hospital. Besides, delirium symptoms, such as sleep disturbance, impatience, and irritability at night were accompanied. We performed brain magnetic resonance imaging (MRI) to identify structural brain injuries and conducted a computerized neurocognitive test (CNT) to evaluate cognitive function. On the brain MRI findings, diffusion-weighted images (DWI) revealed restricted diffusion with low apparent diffusion coefficient values in the SCC [Figure 2]. As a result of the CNT, high-degree impairments were observed in visual and auditory attention, short-term and working memory, and higher cognitive functions, such as inhibitory control, attention control, and executive functions. Based on the CNT result, we consulted with a psychiatrist considering the potential for a hidden psychotic disorder. The psychiatrist recommended that psychiatric treatments and further evaluations are needed for differential diagnosis. On day 11 of hospitalization, the patient was transferred to a psychiatric hospital. Three weeks later, we conducted a follow-up CNT in the outpatient department. However, there was no significant improvement in memory function and higher cognitive function. The requirement for informed consent was waived by the Institutional Review Board (IRB) Jeju National University Hospital (IRB no: 2020-06-011).

Discussion

The mechanism of neurotoxicity by GLA poisoning is still poorly understood. Previous studies have reported that neurotoxicity is associated with glufosinate and its metabolites, ammonia, and glucose hypometabolism. Glufosinate and its metabolites may bind to the

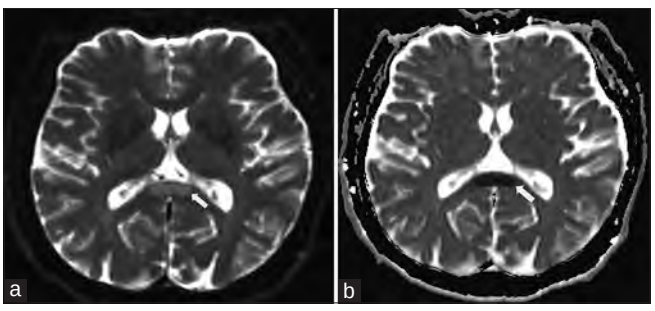

Figure 2: Axial diffusion-weighted image (a) showed a high-signal intensity lesion in the splenium of the corpus callosum (white arrow), and the apparent diffusion coefficient map (b) showed low signal intensity lesion at the same site (white arrow)

N-methyl-D-aspartate (NMDA) receptors, expressed highly in the hippocampus. Therefore, NMDA receptors can be overstimulated in GLA poisoning, which can lead to neuronal damage. This excitotoxicity mechanism is associated with glufosinate-induced convulsions, and it is also associated with memory impairment by hippocampal injury.[3,4] Furthermore, GLA irreversibly inhibits the synthesis of glutamine from ammonia by inhibiting glutamine synthetase, causing intracellular accumulation of ammonia. Hyperammonemia can cause oxidative stress on neurons, leading to cell death and tissue necrosis.[3,5] Surfactants such as polyoxyethylene alkyl ether sulfate can increase the permeability of the blood–brain barrier, thereby enhancing GLA's neurotoxicity.[6] A recent study reported decreased glucose metabolism in the lower frontal and temporal lobes on F-18 fluorodeoxyglucose positron emission tomography scan of patients with GLA poisoning. They suggested that glucose hypometabolism could lead to long-lasting memory impairment regardless of structural brain lesions.[7]

Currently, there are no specific diagnostic tests for GLA poisoning. Therefore, it is essential to identify GLA's commercial name because the composition of glufosinate and additives differs depending on the product. Treatment of GLA poisoning is mainly conservative. Early gastrointestinal decontamination and activated charcoal administration are recommended. Even if initial clinical symptoms are not remarkable, the patient should be closely monitored for at least 48 h. Because of the relatively long latency time of the GLA, life-threatening manifestations can deteriorate rapidly.[1,2] Serial ammonia measurement can help predict the development of serious toxic symptoms such as mental changes, respiratory failure, and convulsions. Therefore, physicians should pay attention to the changes in ammonia levels during treatment.[8] Even today, HD is practiced to remove GLA from the blood, but there is no clear evidence to prevent late-onset neurotoxicity. Moreover, the renal clearance of GLA is 1.6–1.8 times larger than that by HD. Therefore, HD is recommended to be limited to patients with the early phase of serious toxic symptoms or patients with renal failure.[1,5]

In this case, life-threatening manifestations developed rapidly within a few hours of admission. We immediately performed life-saving treatments, and HD was conducted twice during the initial 24 h. HD in the early phase effectively lowered serum ammonia levels, but serum ammonia levels increased again. Repeated examinations during admission showed no evidence of other conditions causing hyperammonemia, such as liver disease, renal failure, and gastrointestinal bleeding. Therefore, it was thought to be re-elevated by the GLA remaining in the blood. However, additional HD was not performed because serious toxic symptoms did not recur.

Most previous studies of GLA poisoning have reported late-onset memory impairment due to GLA-induced hippocampal lesions.[1-3,5,8] Furthermore, several reports of GLA-induced SCC lesions presented that there were no neurological complications other than reversible memory impairment.[6,9] However, our patient developed not only memory impairment, but also prolonged overall cognitive dysfunction. These are rare clinical manifestations that are distinct from previous reports. Various diseases, toxic substances, and trauma can cause SCC lesions. The MRI-documented SCC lesions may be associated with various symptoms, including delirium, ataxia, convulsions, hallucinations, and may even be asymptomatic. However, the exact causal relationship between SCC lesions and clinical symptoms is still not well-understood.[10] This case presents that GLA-induced SCC lesions may cause not only memory impairment but also prolonged overall cognitive dysfunction. However, there was a diagnostic limitation in that other MRI sequences could not be identified. Besides, we were unable to perform a follow-up DWI to confirm the change in the SCC lesions. The patient's symptoms were atypical enough to require an assessment of the likelihood of a psychotic disorder. The patient's CNT result also suggested a potential psychotic disorder. CNT is a standardized tool for quantitative assessment of overall cognitive function, including high cognitive function, and is useful as a screening test for psychotic disorders.[11] However, subsequent CNT results showed that the patient's overall cognitive impairment did not significantly improve despite psychiatric treatment.

Conclusion

This case report illustrates that GLA-induced SCC lesions can lead to prolonged overall cognitive dysfunction. Furthermore, symptoms associated with GLA-induced SCC lesions may be atypical enough to require an assessment of the likelihood of a psychotic disorder. CNT is a useful tool for quantitatively assessing overall cognitive dysfunction, including memory impairment in a patient with GLA poisoning. Emergency physicians should be aware that GLA-induced SCC lesions may be associated with various late-onset neurotoxic symptoms.

Author contribution statement
HJL and JHK conceived and designed, wrote the paper. All authors have confirmed and approved the content of the final manuscript.

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Conflicts of interest
None declared.

Patient Consent
The requirement for informed consent was waived by the Institutional Review Board (IRB) Jeju National University Hospital (IRB no: 2020-06-011).

References

1. Hirose Y, Kobayashi M, Koyama K, Kohda Y, Tanaka T, Honda H, *et al*. A toxicokinetic analysis in a patient with acute glufosinate poisoning. Hum Exp Toxicol 1999;18:305-8.
2. Mao YC, Hung DZ, Wu ML, Tsai WJ, Wang LM, Ger J, *et al*. Acute human glufosinate-containing herbicide poisoning. Clin Toxicol (Phila) 2012;50:396-402.
3. Kim HH, Min YG. Anterograde amnesia after acute glufosinate ammonium intoxication. Acute Crit Care 2018;33:110-3.
4. Lantz SR, Mack CM, Wallace K, Key EF, Shafer TJ, Casida JE. Glufosinate binds N-methyl-D-aspartate receptors and increases neuronal network activity *in vitro*. Neurotoxicology 2014;45:38-47.
5. Mao YC, Wang JD, Hung DZ, Deng JF, Yang CC. Hyperammonemia following glufosinate-containing herbicide poisoning: A potential marker of severe neurotoxicity. Clin Toxicol (Phila) 2011;49:48-52.
6. Kim TY, Park DW, Park CK, Lee YJ, Lee SR. Reversible splenial lesion in the corpus callosum on MRI after ingestion of a herbicide containing glufosinate ammonium: A case report. J Korean Soc Radiol 2014;70:399-402.
7. Park S, Kim JI, Cho NJ, Oh SW, Park J, Yoo ID, *et al*. Decreased glucose utilization contributes to memory impairment in patients with glufosinate ammonium intoxication. J Clin Med 2020;9:1213.
8. Moon JM, Chun BJ. Serial ammonia measurement in patients poisoned with glufosinate ammonium herbicide. Hum Exp Toxicol 2016;35:554-61.
9. Jeong TO, Yoon JC, Lee JB, Jin YH, Hwang SB. Reversible splenial lesion syndrome (resles) following glufosinate ammonium poisoning. J Neuroimaging 2015;25:1050-2.
10. Doherty MJ, Jayadev S, Watson NF, Konchada RS, Hallam DK. Clinical implications of splenium magnetic resonance imaging signal changes. Arch Neurol 2005;62:433-7.
11. Gur RC, Ragland JD, Moberg PJ, Bilker WB, Kohler C, Siegel SJ, *et al*. Computerized neurocognitive scanning: II. The profile of schizophrenia. Neuropsychopharmacology 2001;25:777-88.