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Seizure as the main presenting manifestation of three patients with acute glufosinate-ammonium poisoning

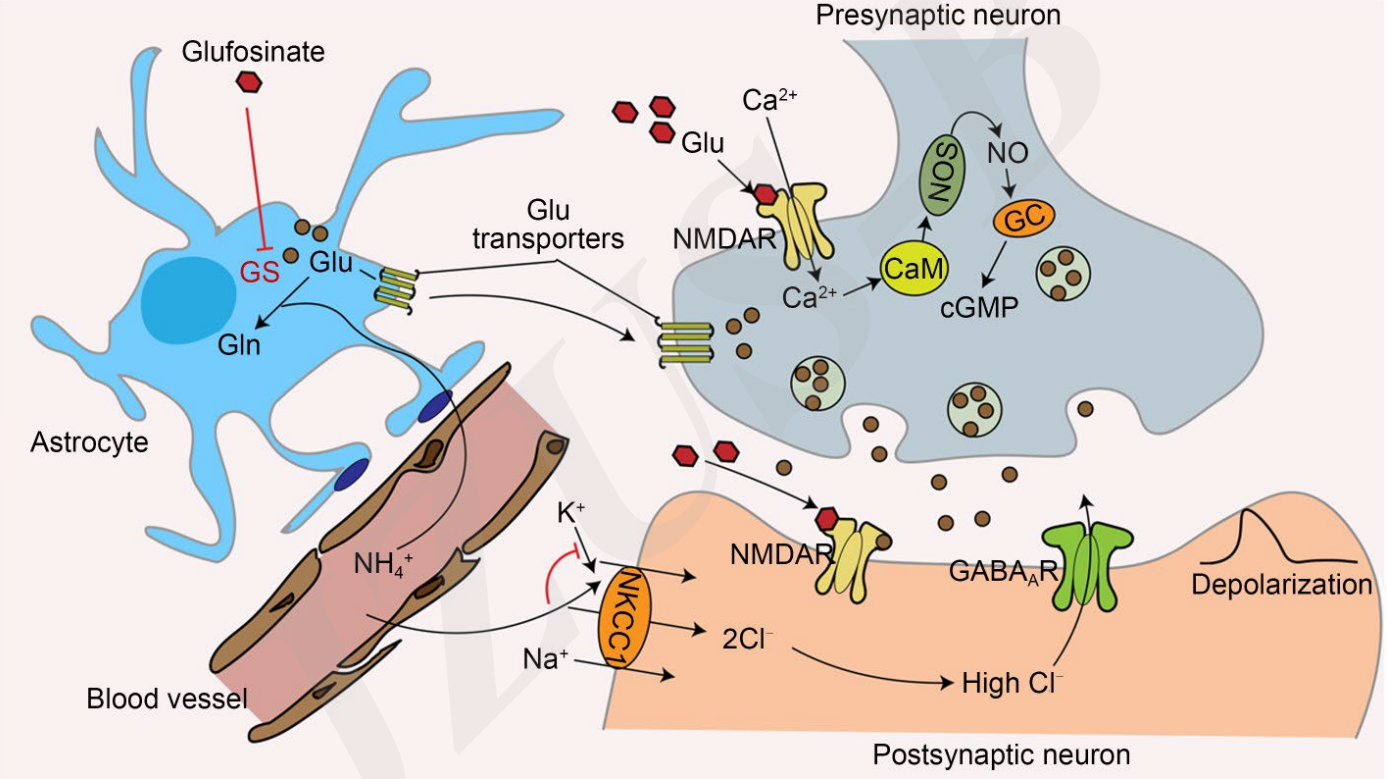
Key words: Glufosinate-ammonium, Seizure, Herbicide poisoning, Head CT

Innovation points

In this paper, we describe three patients in our hospital who presented neurological symptoms after glufosinate-ammonium herbicide poisoning. And we discuss prediction and examination methods for neurotoxicity in glufosinate-ammonium herbicide poisoning patients.

Innovation points

Mechanism of neurotoxicity after glufosinate-ammonium poisoning.



Glufosinate-ammonium and its metabolites can not only bind to NMDAR，but also activate NMDAR by increasing Glu content. The elevated blood ammonia can also further activate NMDAR, and damage inhibitory neurotransmission in cerebral cortex by over-activating NKCC1. GC: guanosine cyclase, Glu: glutamate, Gln: glutamine, GS: glutamine synthetase, NMDAR: N-methyl-D-aspartate receptor, NKCC1: Na+-K+-2Cl− cotransporter isoform 1, NOS: nitric oxide synthase, NO: nitric oxide, cGMP: cyclic guanosine monophosphate, GABAAR: γ-aminobutyric acid receptor.

Innovation points

Mechanism of neurotoxicity after glufosinate-ammonium poisoning.

(1) Previous studies have shown that glufosinate and its metabolites bind to the NMDA receptors that are highly expressed in the hippocampus.
(2) After the destruction of the Glu-Gln cycle, Glu levels increase. Then the Glu binds to the NMDA receptor, which produces neuroexcitatory toxicity.
(3) When blood ammonia levels rise, the gaseous form, NH3, readily crosses the blood-brain barrier. At the same time, NH_4^+ can enter the brain via Na^+-K^+-$2Cl^-$ cotransporter isoform 1 (NKCC1), which competitively impairs the potassium buffering of astrocytes and increases extracellular potassium concentration, resulting in neurological dysfunction and seizures. Meanwhile, excessive NH_4^+ and K^+ depolarize the neuronal γ-aminobutyric (GABA) reversal potential (EGABA) by driving the overactivation of NKCC1. Eventually, the inhibitory neurotransmission in the cortex is impaired.
(4) Blood ammonia can increase Ca^{2+} influx and trigger Glu release. At the same time, Ca^{2+} binds to calmodulin and activates nitric oxide synthase (NOS), resulting in increased formation of nitric oxide (NO). Nitric oxide synthase activates guanosine cyclase (GC), increases cyclic guanosine monophosphate (cGMP) content, promotes NMDA receptor activation, and produces excitotoxicity.