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Rhabdomyolysis Secondary to Lamotrigine Toxicity: A Case Report and Literature Review

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Abstract

Lamotrigine, an anticonvulsant and mood-stabilizing medication, is used for managing seizure disorders and bipolar disorder. However, it can cause side effects ranging from mild hypersensitivity reactions to severe reactions such as Stevens-Johnson syndrome. In overdose cases, lamotrigine primarily affects the central nervous system and cardiovascular system, leading to seizures and cardiac conduction abnormalities. This report describes a rare case of rhabdomyolysis in a 36-year-old female who intentionally overdosed on lamotrigine. This patient, with a history of seizures, anxiety, and depression, presented with nausea, abdominal pain, and elevated myoglobin and creatine kinase levels. She was treated with normal saline and improved over four days. This case highlights the need for awareness of unusual complications such as rhabdomyolysis in lamotrigine toxicity and the importance of prompt management. Further research is needed to understand the pathophysiology behind these rare effects.

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1. Introduction

Lamotrigine is an anticonvulsant and mood-stabilizing medication frequently prescribed for managing seizure disorders, including epilepsy, as well as bipolar disorder (1). This medication is generally well-tolerated; however, common side effects include hypersensitivity reactions, fatigue, dizziness, nausea, and vomiting (5). Serious adverse effects may also develop such as the potential for dangerous skin reactions, including life-threatening reactions such as Stevens-Johnson syndrome, which necessitates hospitalization (1).

In cases of overdose, lamotrigine toxicity primarily impacts the central nervous system (CNS) and the cardiovascular system (1). Clinically, this can manifest as seizures, altered mental status, and QT prolongation, often leading to life-threatening arrhythmias (1). The range of symptoms and severity is determined by the dose ingested and the presence of other ingested substances (1).

This report details a unique case involving a 36-year-old female who developed rhabdomyolysis as a result of an intentional lamotrigine overdose. Rhabdomyolysis, which is characterized by muscle breakdown and the release of intracellular contents into the bloodstream, is a rare complication of lamotrigine toxicity. Few case reports have documented this finding, emphasizing the need for further investigation into this unusual presentation of lamotrigine toxicity. This case highlights the importance of awareness of diverse and potentially life-threatening effects of lamotrigine toxicity, thus contributing to a broader understanding of its safety profile.

2. Case Presentation

A 36-year-old female with a past medical history significant for seizures, for which she was taking lamotrigine, multiple suicide attempts, anxiety, and depression, presented to the emergency department following a suicide attempt with an intentional overdose of lamotrigine one day prior. According to the patient, she was on no other medications. She reported experiencing auditory hallucinations instructing her to harm herself for an extended period. She had recently been under significant stress and felt unable to suppress the voices any longer, leading her to ingest approximately half of the pills in her lamotrigine bottle. After the ingestion, she regretted her actions and vomited within a few hours. Since then, she had experienced nausea and abdominal pain, preventing her from eating for several days. Additionally, she reported headaches, dizziness, chest pain, and shortness of breath. She denied any recent seizures as well as drug or alcohol use.

Upon arrival at the emergency department, her initial laboratory results were significant for an anion gap of 24, bicarbonate (HCO3) of 13, creatinine of 1.01 mg/dL, and urine drug screen positive for THC. Other notable lab results included an acetaminophen level of <10, ethanol level of <0.01, salicylate level of <2.5, myoglobin of 336, creatine kinase (CK) of 1597, and troponin of 20. The patient was started on normal saline for the management of rhabdomyolysis.

Over the course of four days, as she clinically improved, her laboratory results demonstrated a decreasing trend in myoglobin, CK, and creatinine levels. Her anion gap metabolic acidosis secondary to the drug overdose also resolved. While awaiting her lamotrigine level, she was started on lacosamide for seizure management. Due to ongoing hallucinations and suicidal ideation, she was discharged to an inpatient psychiatry unit. At the time of discharge, her myoglobin level was 51.6, CK level was 1035, creatinine was 0.56 mg/dL, and blood urea nitrogen (BUN) was 10.

3. Discussion

Lamotrigine overdose is relatively uncommon but has been increasing in frequency recently. Still, lamotrigine overdoses constitute a small percentage of total antiepileptic drug overdoses. The majority of cases primarily involve adults, with a smaller percentage occurring in pediatric patients.

Most patients who overdose on lamotrigine experience mild or no symptoms of toxicity. However, those who consume significantly large doses have been documented to experience severe CNS depression, seizures, cardiac conduction delays, and even death. A systematic review by Alyahya et al. found that the lowest seizure-associated serum concentrations were 3.8 mg/L for pediatric patients and 25.6 mg/L for adult patients (1). Furthermore, their findings suggested that children may be more susceptible to CNS toxicity, whereas cardiovascular toxicities primarily affect adult patients. The presence of other drugs may also influence the presentation of lamotrigine toxicity. For example, another case report describing rhabdomyolysis from lamotrigine

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toxicity involved acute ingestion of ethanol as well (4).

The mechanism of lamotrigine toxicity is incompletely understood. Lamotrigine primarily exerts its toxic effects by blocking voltage-gated sodium and voltage-activated calcium channels (1). This disrupts normal neuronal conduction, leading to altered neuronal excitability. Specifically, at high concentrations, this can result in excessive inhibition or altered neuronal signaling, contributing to the development of cardiac conduction abnormalities, seizures, and CNS depression. Lamotrigine toxicity can also result in serotonin syndrome, as it can inhibit the reuptake of serotonin. Seizures and serotonin syndrome may then lead to laboratory findings of rhabdomyolysis. However, isolated rhabdomyolysis resulting from lamotrigine overdose is rare, with only one other case reported (5). While the pathogenic mechanism of rhabdomyolysis caused by lamotrigine toxicity is unclear, genetic predispositions may play a role (5).

Management of lamotrigine overdose is primarily determined by the presentation. When patients present early after toxic ingestion, measures can be employed to prevent further absorption, such as activated charcoal and gastric lavage (1). Sodium bicarbonate may be used when cardiotoxicity due to sodium channel blockade is evident. As lamotrigine is lipophilic, lipid emulsion has also been suggested as a potential treatment strategy for cardiotoxicity if a patient is refractory to alkalinization (3). Seizures should be managed promptly with benzodiazepines as first-line agents and barbiturates and propofol as second-line agents (1). In this case, the patient presented only with mild rhabdomyolysis as a result of lamotrigine overdose and was managed entirely with IV fluids.

4. Conclusion

While lamotrigine overdose remains relatively rare compared to other antiepileptic drug overdoses, its incidence appears to be increasing. The clinical presentation of lamotrigine toxicity varies, with most cases presenting with mild symptoms but severe outcomes such as CNS depression, seizures, and cardiac conduction abnormalities can occur in those ingesting much larger doses. Children may be particularly vulnerable to toxic CNS effects, whereas adults are more likely to develop cardiotoxic effects. The underlying mechanisms of toxicity, including the inhibition of sodium and calcium channels, contribute to the complex nature of toxicity. Effective management strategies, tailored to presenting symptoms, are crucial for optimizing patient outcomes. Early intervention with measures such as activated charcoal and sodium bicarbonate can be lifesaving, while prompt treatment of seizures with appropriate medications is also essential. Providers must also ensure that the medication is held when there is suspicion of lamotrigine-induced rhabdomyolysis. Further research is needed to understand the pathophysiology behind the rare consequence of rhabdomyolysis after lamotrigine overdose.

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