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Case Study

Levetiracetam-Induced Acute Hypersensitivity Reaction in a Previously Undiagnosed Epilepsy Elderly Woman: A Case Report

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Abstract

Background and Objective: Levetiracetam is one of the most commonly used antiseizure drugs. The objective of this paper was to draw attention to levetiracetam-associated hypersensitivity reaction which is not commonly reported. **Materials and Methods:** This case reports a 71-year-old woman, previously undiagnosed with epilepsy, who presented with a history of frequent seizures. Upon the neurology team's recommendation, a 1500 mg intravenous levetiracetam infusion was initiated. **Results:** Upon the intravenous administration of levetiracetam, the patient developed an acute hypersensitivity reaction, marked by respiratory compromise and angioedema. Two days post-intervention, the patient was successfully extubated and she was discharged home. **Conclusion:** This adverse reaction, though rare, emphasizes the need for cautious introduction and monitoring of newer antiseizure medications (ASMs).

Key words: Levetiracetam, hypersensitivity reaction, angioedema, antiseizure medications, elderly patient

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Levetiracetam (LEV) represents the most commonly used ASM worldwide^{1,2}. It has the advantage of being highly tolerable with a good pharmacokinetic profile compared to the 1st generation ASMs³. The LEV acts via binding to SV2A which is a component of synaptic vesicles. Although the exact result of this binding isn't well understood, it may enhance GABA release, decrease glutamate activity⁴, modulate Calcium (Ca^{2+}) and glutamatergic pathway⁵.

The LEV is almost completely absorbed orally and although its half-life is 6-8 hrs, its antiseizure action lasts for up to 30 hrs⁶. It is mainly excreted by the kidney and only 2% is eliminated by the cytochrome pathway, readjustment of its dose in renal failure patients is a must⁷.

No reported LEV-serious adverse events; the reported adverse reaction includes vestibule-cerebellar dysfunction⁶, report neuropsychiatric adverse events (NPAAE) in 20-30% of cases⁸, among these NPAAE; the irritability is the most frequent one and it seems to be dose-related⁹. A few reports indicated hypersensitivity reactions associated with levetiracetam use¹⁰⁻¹².

Hypersensitivity reactions to antiseizure medications (ASMs) present a challenging clinical scenario, often manifesting unpredictably. This case spotlights an elderly woman, initially undiagnosed with epilepsy, who encountered an acute hypersensitivity reaction following levetiracetam administration.

As ASM hypersensitivity reactions range from mild skin rashes to severe complications, understanding the underlying mechanisms is crucial¹³. Recent research suggests that Major Histocompatibility Complex (MHC)-dependent clonal T-cell proliferation plays a role in ASM-related hypersensitivity¹⁴. Despite newer ASMs generally considered safe, this case underscores the need for cautious adoption.

CASE PRESENTATION

A 71-year-old woman presented to the emergency department, King Abdulaziz Specialist Hospital, Sakaka, Saudi Arabia, on 14/07/2023 following a series of seizures. Initial investigations revealed no abnormalities, prompting further examination. During the transition to the ward, the patient experienced another seizure, subsequently aborted with intravenous diazepam.

Upon the neurology team's recommendation, a 1500 mg intravenous levetiracetam infusion was initiated. Shortly afterward, the patient exhibited signs of an acute



Fig. 1: Diffuse symmetrical edema over the upper and lower lips of the patient

hypersensitivity reaction, including shortness of breath, swelling of the lips and a drop in oxygen saturation to below 88% (Fig. 1). Prompt intervention with intravenous diphenhydramine and hydrocortisone was initiated. The patient was transferred to the Intensive Care Unit (ICU), necessitating norepinephrine, midazolam and propofol administration. A loading dose of phenytoin (20 mg/kg) was also given.

Two days post-intervention, the patient was successfully extubated and she was discharged home one week later on 23/07/2023.

DISCUSSION

There is a wide range of cutaneous side effects that have been associated with anticonvulsant drugs. These adverse effects include severe hypersensitivity syndromes as well as moderate rashes^{15,16}. This case aligns with the spectrum of ASM hypersensitivity reactions, accentuating the potential for severe manifestations. Respiratory compromise and angioedema, observed in this patient, underscore the gravity of such reactions¹³. Angioedema is a rare adverse event that has the potential to be lethal. It is characterized by the sudden swelling of the pharynx, face, mouth and tongue¹⁷. A severe impairment of the respiratory system and edema of the limbs or the digestive tract may also accompany angioedema.

Cross-sensitivity, while infrequent, remains a pertinent consideration. The patient's response to levetiracetam raises questions about possible interactions between newer and older ASMs, necessitating a nuanced approach in clinical decision-making¹⁷. Understanding the immunologic mechanisms behind drug reactions is paramount¹⁴. The unique presentation of this case, marked by rapid onset and severity, emphasizes the role of immediate interventions such as antihistamines and corticosteroids¹³.

This scenario echoes recent reports indicating an increasing incidence of hypersensitivity reactions to newer ASMs. As such, clinicians should exercise prudence when introducing these drugs, opting for slow titration and vigilant monitoring, especially in patients with prior ASM hypersensitivity^{14,18}. At present, only five anticonvulsants-lamotrigine, gabapentin, pregabalin, brivaracetam and lacosamide-have accumulated sufficient evidence to warrant a labeled warning for angioedema¹⁹. This is despite the fact that isolated reports of angioedema have been documented for the majority of anticonvulsants in the FAERS system²⁰.

CONCLUSION

This case report highlights the rare occurrence of levetiracetam-induced acute hypersensitivity reactions and emphasizes the necessity for careful monitoring and consideration of alternative treatments in patients with prior ASM hypersensitivity.

SIGNIFICANCE STATEMENT

Levetiracetam (LEV) represents the most commonly used ASM worldwide with good tolerability and a good pharmacokinetic profile compared to the 1st generation anti-seizure drug. No available reports of LEV-serious adverse events. A few reports indicated hypersensitivity reactions associated with levetiracetam use. This case spotlights an elderly woman, initially undiagnosed with epilepsy, who encountered an acute hypersensitivity reaction following levetiracetam administration. This report draws attention to the possibility of levetiracetam-induced acute hypersensitivity reactions necessitating careful patient monitoring and consideration of alternative treatment in patients known ASM hypersensitivity.

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