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A Suspected Case of Levetiracetam Induced Rhabdomyolysis

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Background:

A seizure is a paroxysmal alteration of neurologic function caused by the excessive, hypersynchronous discharge of neurons in the brain.[1] An epileptic seizure is a seizure caused by abnormal neuronal firing which distinguishes it from a nonepileptic event, such as a psychogenic seizure.[1] Epilepsy is the condition of recurrent, unprovoked seizures, and has numerous causes, each signifying underlying brain dysfunction.[2]

Antiepileptic drugs (AEDs) are the main treatment method for epilepsy patients, and it was reported that approximately two-thirds of epileptic seizures were controlled by AEDs.[3] Common AEDs including carbamazepine (CBZ) and sodium valproate (VPA) have been shown to have positive therapeutic outcomes in addition to being a low-cost treatment for patients. However, serious adverse reactions related to these drugs include Stevens-Johnson syndrome, menstrual disturbances, and memory deterioration, thus negatively affecting the tolerance and compliance of patients undergoing these treatment regimens.[4]

Levetiracetam (LEV) is a novel AED that has been approved as an adjunctive therapy for adults with focal epilepsy since 1999 in the US. LEV is a well-tolerated medication treatment for long-term therapy without significant effects on the immune system.[5] Common adverse effects include nausea, gastrointestinal distress, dizziness, irritability, and aggressive behavior. In recent years, LEV has been reported to have extremely rare side effects including eosinophilic pneumonia, rhabdomyolysis, thrombocytopenia, elevated kinase and reduced sperm quality.[6-9]

This report examines the presentation, treatment, and outcome of a patient who was diagnosed with a case of suspected levetiracetam-induced rhabdomyolysis in rural South Dakota.

Case Report:

A 55-year-old male patient with a past medical history of hypertension, hyperlipidemia, and a remote seizure episode presented to a rural emergency department via EMS for active convulsing and unresponsiveness. During transport, he received fentanyl 100mcg IV and midazolam 10mg IV and on arrival to the emergency department received lorazepam 2mg IV, diphenhydramine 50mg IV, and haloperidol 10mg IV. Convulsions ceased for approximately 10 minutes after IV medications were given and a head computed tomography (CT) was obtained revealing no acute intracranial anomalies. The toxicology screen

was negative. Creatinine kinase (CK) was 391. Convulsions restarted after imaging. The patient was sedated with propofol for intubation and loaded with levetiracetam 4g IV and fosphenytoin 20mg/kg IV.

The patient was transported to a tertiary care facility by flight. He was admitted to the intensive care unit for monitoring and ordered to have levetiracetam 2g IV every 12 hours and fosphenytoin 100mg IV every 8 hours. Magnetic resonance imaging (MRI) of the head showed no masses. electroencephalogram (EEG) monitoring while intubated demonstrated no evidence of recurrent or subclinical seizures. He was extubated on hospital day 2 and transferred to the acute unit.

During his hospital course, CK increased daily so IV fluids were started (Figure 1). Home medications included a statin, PCSK9 inhibitor on bi-monthly injections, and a daily baby aspirin. The statin was held on day 2 but CK continued to rise peaking at 13,385 on day 6. Levetiracetam was stopped and switched to lacosamide on day 6 after which the CK began to regress. Renal function and electrolytes were monitored closely with no development of acute kidney injury. Liver enzymes did elevate during the hospital stay likely due to rhabdomyolysis. Following a decline in CK, the patient was discharged on valproic acid with instructions for follow-up.

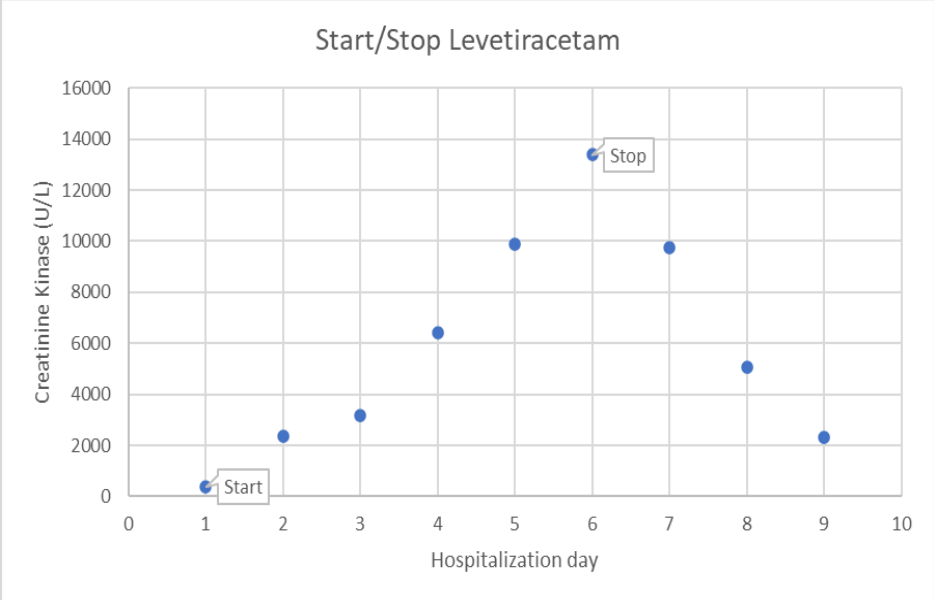

Figure 1: Trend creatinine kinase by hospitalization day.

Discussion:

Rhabdomyolysis is a condition characterized by muscle tissue necrosis resulting in the release of intracellular enzymes into circulation. The diagnosis is made when creatinine kinase reaches a level greater than 1,000 U/L or five times the upper limit of normal.[10] Patient presentation varies from asymptomatic to myalgias, weakness, and myoglobinuria. Complications include seizures, respiratory failure, acute kidney injury due to acute tubular necrosis, and electrolyte disturbances.[10] Treatment includes aggressive fluid replacement using crystalloid solution and monitoring electrolyte disturbances.[10] The patient presented above remained asymptomatic during his hospital course without any complications.

Over the past decade, only fourteen cases have been reported.[11] Levetiracetam was approved in the 1990s as a second-generation antiepileptic for the treatment of partial and generalized seizures.[12] It is a well-tolerated drug that promotes neurotransmitter binding to synaptic vesicle 2A protein.[11]

Statin drugs are known causes of rhabdomyolysis[10], however, this patient showed a temporal increase in CK with the use of levetiracetam even while his statin drug was held and no evidence of recurrent seizure activity on EEG monitoring while in the hospital. Other common causes of rhabdomyolysis include crush injuries, physical exertion, malignant hyperthermia, hypothermia, electrolyte disturbances, autoimmune diseases, and genetic conditions[11] none of which apply to this patient.

Conclusion:

This case outlines suspected levetiracetam-induced rhabdomyolysis, a potentially life-threatening adverse effect. A temporal connection was made between the use of the drug and changes in CK. The patient was treated appropriately with timely recognition, discontinuation of levetiracetam, and supportive cares. The patient did not suffer any complications as a result of the rhabdomyolysis.

Conflict of interest:

None

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