Case Report

Creatine phosphokinase elevation exacerbated by levetiracetam therapy

Julia E. Isaacson a, Dongwhoon J. Choe b, Michael J. Doherty c,⁎

a Dartmouth College, Department of Psychological & Brain Sciences, Maynard Street, Hanover, NH 03755, USA
b University of Washington, School of Public Health, 1959 NE Pacific Street, Seattle, WA 98195, USA
c Swedish Epilepsy Center, 550 17th Avenue, Seattle, WA 98122, USA

Abstract

Article history:
Received 17 September 2014
Received in revised form 26 September 2014
Accepted 29 September 2014
Available online 22 October 2014

Keywords:
Epilepsy
Toxicity
Rhabdomyolysis
Renal
Sarcolemma
Muscle

1. Introduction

Levetiracetam (LEV) is used to treat generalized and partial seizures of various etiologies. Three case reports document LEV-associated renal compromise [1–3]. Rhabdomyolysis postconvulsive seizure may limit kidney excretion of muscle breakdown products like creatine phosphokinase (CPK). In this case report, CPK elevations postseizure were beyond what might otherwise be expected for mild rhabdomyolysis. Possible mechanisms of protracted CPK elevation with LEV therapies are briefly discussed.

2. Case study

A 19-year-old right-handed male presented following a complex partial seizure with secondary generalization in the setting of stress and sleep deprivation. A second convulsive event lasting 2 min occurred in the emergency room. The patient was given 2 mg IV lorazepam, 2000 mg IV LEV, and 1200 mg oxcarbazepine (OXC), and no further seizures occurred. The patient was maintained on LEV extended release 500 mg daily. The patient had not used LEV therapies prior to this hospital admission.

Epilepsy etiology was due to a right frontal arteriovenous malformation (AVM) located in the left leg primary motor cortex (Fig. 1). The AVM had previously been treated with gamma knife radiosurgery (20 Gy at 50% isodose to encompass a volume of 1.2 mL). Outpatient anticonvulsant medications for this patient prior to the present hospitalization included OXC 600 mg in the morning and 900 mg in the afternoon or evening and lorazepam 0.5 mg prn for breakthrough seizures. Of note, this patient is an avid weight lifter and very muscular (Fig. 2). Although an avid weight lifter, the patient denied using supplemental agents for muscle bulking such as anabolic steroids or protein powders.

Seizures postradiation manifested most commonly as nocturnal convulsions. They occurred rarely in the daytime, and if they did, a warning of lightheadedness, dizziness, and a lost sense of balance would progress to bilateral muscle cramping, tonic–clonic movements, tongue biting, and postictal confusion.

This admission was complicated by a rapid rise in CPK and mild renal compromise, a new finding for the patient (Fig. 3). A nephrology consultant did not suspect acute tubular necrosis or other abnormalities. Maximum creatinine was 2.17 mg/dL and had normalized prior to CPK maximum. The patient’s CPK levels were slow to resolve despite appropriate IV hydration. During the entire period of CPK elevation, the patient’s urine remained clear/yellow; trace hematuria was noted only on day two. His day nine serum myoglobin was 228 ng/mL (normal range: 10–92 ng/mL). An initial serum myoglobin level was not checked.

With a marked drop of CPK on day 5 (CPK: 2736), the patient was discharged on LEV and OXC combination therapy (Fig. 3). However, blood work postdischarge showed CPK levels again in the 29,000 range, suggesting that the day five CPK measurement was a lab error.
Levetiracetam was discontinued on day eight; day nine blood work showed a halving of CPK levels from 29,136 to 14,918 and a normal level of creatinine. Creatine phosphokinase levels continued to decline rapidly after LEV discontinuation, with normalization occurring nearly a month later after resumption of a normal exercise regimen.

3. Discussion

Two convulsive seizures and subsequent LEV therapy led to a dramatic increase in CPK in this muscular male. Although this could indicate a delayed rhabdomyolysis, the classic findings including marked elevations in myoglobin/myoglobinuria, decreased urine output, and muscle pain were not evident. Additionally, following muscular injury, rhabdomyolysis-related CPK elevations typically occur maximally by day three and decline by day five. The CPK elevation in this patient was both delayed and persisted beyond the typical time frame of a case of seizure-induced rhabdomyolysis [4], suggesting ongoing issues of muscle breakdown despite cessation of seizure activities.

Creatine phosphokinase release occurs with insults to the sarcolemma, most notably failure of ATP production or use. Levetiracetam is not known to alter ATP functions. However, LEV was the only new drug
given, and its use – even at a low maintenance dose – and discontinuation closely mirror the trends in CPK levels in this patient. Although we suspect that LEV may have contributed to CPK elevations in this heavily muscled patient, those suspicions remain unproven. We are unaware of any muscle enzyme or other neuromuscular problems in this patient. A retrial of LEV with CPK and renal function checks, a muscle biopsy, and a repeat renal ultrasound are not planned, given that the patient's clinical issues have resolved.

4. Conclusions

This case revealed a marked and dangerous increase in CPK levels corresponding with modest LEV use. Although this scenario could indicate a delayed rhabdomyolysis, the rapid decline in CPK with LEV discontinuation suggests that, in this patient, LEV may have had effects on kidney filtration and/or muscle breakdown. Discontinuation of LEV in patients with persisting CPK elevations postconvulsive seizure should be considered.

Conflict of interest

There are no conflicts of interest from the authors in this case report.

References

[1] Hurwitz KA, Ingulli EC, Krous HF. Levetiracetam induced interstitial nephritis and renal failure. Pediatr Neurol 2009;41:57–8.
[2] Mahia A, Kim KY, Kesari S. Levetiracetam-induced interstitial nephritis in a patient with glioma. J Clin Neurosci 2012;19:177–8.
[3] Huerta-Alardín AL, Varon J, Marik PE. Bench-to-bedside review: rhabdomyolysis — an overview for clinicians. Crit Care 2005;9:158–69.
[4] Spengler DC, Montouris GD, Hohler AD. Levetiracetam as a possible contributor to acute kidney injury. Clin Ther 2014;2:1303–6.