Case Report

Levetiracetam-induced pancytopenia

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Abstract

Pancytopenia is a rare side effect of levetiracetam (LEV) that is associated with severe morbidity that requires hospitalization. Here, we report a patient with a right temporoparietal tumor who underwent a temporal craniotomy with resection of the mass and was started on LEV for seizure prophylaxis per the neurosurgery local protocol. The patient developed LEV-induced pancytopenia, which was successfully managed by discontinuation of this medication. Our report aims to increase awareness of this rare cause of pancytopenia among clinicians.

1. Introduction

Levetiracetam is a pyrrolidine derivative that is thought to exert its antiepileptic effects via adherence to the synaptic vesicle protein SV2A and modulation of neurotransmitter release. Levetiracetam is a watersoluble drug that is excreted by the kidneys with a half-life of 6–8 h. Thus, patients with renal impairment achieve serum levels that are typical for treating epilepsy with lower doses based on their creatinine clearance. Levetiracetam was found to be effective as adjunctive therapy in patients with refractory focal epilepsy, lowering seizure frequency by at least 50% in 40% of that population. In addition, it is used as adjunctive therapy for myoclonic epilepsy and primary generalized tonic–clonic seizures. There are no significant drug interactions between LEV and other medications, such as warfarin, digoxin, oral contraceptives, probenecid, and other antiseizure medications. However, it should be used with caution in alcoholic patients because it may increase the risks of sedation and seizures [1,6].

Levetiracetam causes several adverse neurological effects that include headache, somnolence, asthenia, dizziness, irritability, and behavioral changes. In addition, it can cause hematological side effects such as mild thrombocytopenia, leukopenia, and anemia that may not necessitate its discontinuation [1]. Pancytopenia is a very rare adverse effect of LEV. There are three case reports in the medical literature discussing the association between LEV and pancytopenia. The pathogenesis behind this relationship is unclear. Our report aims at increasing the awareness of this rare cause of pancytopenia that necessitates discontinuation of this drug.

2. Case report

A brain MRI of a 79-year-old woman with a medical history of hypertension, type II diabetes, and stroke revealed a right temporoparietal mass. She was started on dexamethasone prior to surgery because of extensive vasogenic edema. She underwent a temporal craniotomy with resection of the mass and was started on LEV for seizure prophylaxis per the neurosurgery local protocol. The patient developed LEV-induced pancytopenia, which was successfully managed by discontinuation of this medication. Our report aims to increase awareness of this rare cause of pancytopenia among clinicians.
platelet counts improved and continued to trend upward. A noticeable increase in white blood cells and hemoglobin was seen within five days as shown in Figs. 2, 3, and 4.

3. Discussion

Hematological side effects of LEV are extremely rare and have been limited to isolated cases of mild thrombocytopenia, leukopenia, or anemia [5–7]. The present case demonstrates development of pancytopenia induced by LEV with resolution after discontinuation of this medication. On literature review, three other cases of pancytopenia with the use of LEV have been reported. The first case is that of a 76-year-old woman who had a seizure in the setting of an ischemic stroke and developed pancytopenia two days after initiation of LEV [3]. The second case is a 65-year-old woman who received LEV after undergoing surgical removal of a meningioma and developed pancytopenia 9 days after initiation of treatment, with bone marrow aspiration showing medullary hypoplasia [4]. The third case is a 16-year-old young woman with history of Lafora disease who experienced pancytopenia 4 days after initiation of LEV treatment and recovered with discontinuation of the medication [2]. The fact that these patients presented with different diagnoses suggests that LEV, rather than a complication of the underlying disease, was the cause of pancytopenia. In addition, no one concomitant medication was common to all reported cases, and none of these reports studied HLA typing as a potential predisposing factor.

In the present case, all other causes of hematologic disturbance such as thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, and heparin-induced thrombocytopenia were ruled out. Other medications such as enoxaparin and pantoprazole with potential hematologic side effects were discontinued without improvement in blood counts. The patient’s hemolysis profile and blood smear did not reveal any signs of hemolysis. Therefore, we hypothesized that LEV induced pancytopenia in our patients through bone marrow suppression.

4. Conclusion

Clinicians should be aware that LEV can cause severe pancytopenia, and consider discontinuation of LEV in patients who develop pancytopenia with negative hemolysis profile. Further studies should evaluate the mechanisms by which LEV induces bone marrow suppression and possibly find a blood test for proper diagnosis.

Author contributions

Talal Alzahrani, Dana Kay, Saeed A. Alqahtani, Yamane Makke, Linda Lesky, and Mohamad Z. Koubeissi had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to the study concept and design. Talal Alzahrani acquired the data and Saeed A. Alqahtani drafted the manuscript. All authors contributed to the analysis and interpretation of data and to the critical revision of the manuscript for important intellectual content.
Conflict of interest

None of the authors contributing to this paper report any financial disclosures or conflicts of interest.

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