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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.

Introduction

Levetiracetam is a pyrrolidone 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 water-soluble 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.

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 protocol, though this is not an approved use of LEV. The pathology showed glioblastoma multiforme. Postoperatively, her blood counts remained stable. Her medication regimen included LEV, dexamethasone, pantoprazole, and enoxaparin for deep venous thrombosis prophylaxis. She was noted to have an episode of melena and anemia on the fifth postoperative day, which required transfusion with two units of red blood cells with an appropriate response. No acute gastroenterological intervention was deemed necessary. The patient was also noted to have thrombocytopenia and leukopenia. Her blood smear did not show any signs of hemolysis as shown in Fig. 1. Thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, and heparin-induced thrombocytopenia were ruled out. Pantoprazole and enoxaparin were discontinued without any improvement in cell counts. The patient received a total of five units of platelets because of platelet counts of less than 100,000. Levetiracetam was replaced subsequently by lacosamide (LCM) on the tenth postoperative day, and dexamethasone was continued without change. Within 24 h of discontinuing LEV, the

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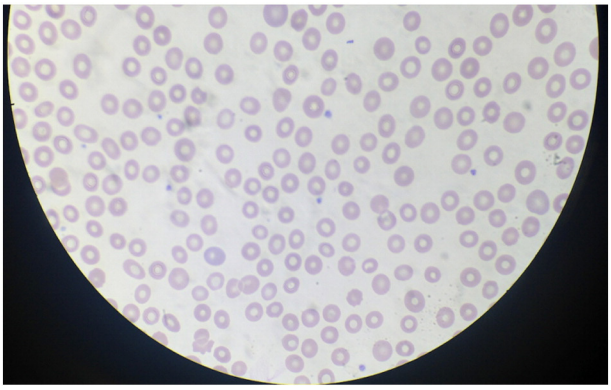

Fig. 1. Blood smear showing lack of schistocytes and immature cell lines. Findings on blood smear correlate with absence of disseminated intravascular coagulation and thrombotic thrombocytopenic purpura and are suggestive of bone marrow suppression.

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.

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.

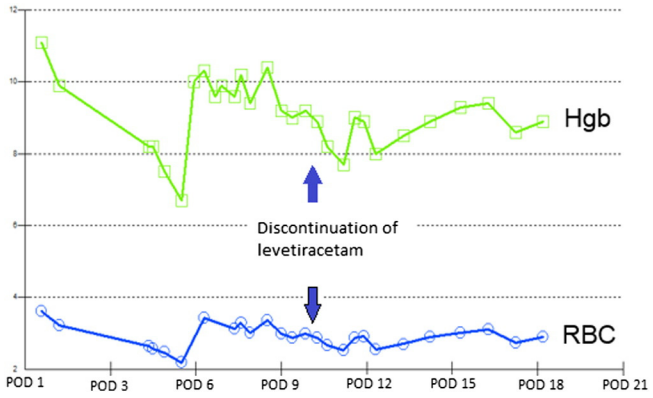

Fig. 2. Graph depicting relationship between red blood cell count and hemoglobin and number of days postoperatively (POD). LEV was started on postoperative day 0 and was discontinued on postoperative day 10. The patient experienced an acute bleed requiring transfusion of 2 units of RBC on POD 5, followed by a steady decline in Hgb and RBC. Improvement in anemia was observed with discontinuation of the medication.

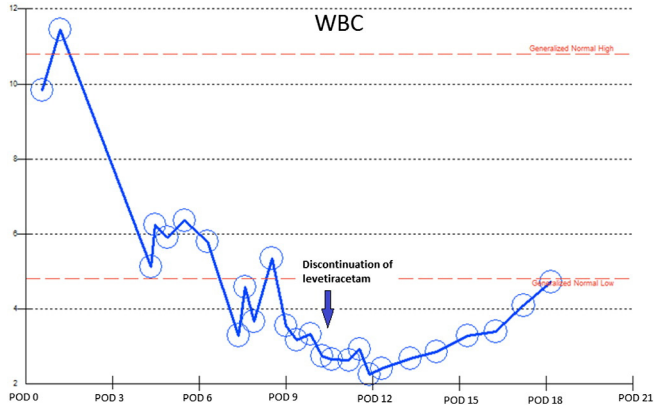

Fig. 3. Graph depicting relationship between white blood cell count and number of days postoperatively (POD). LEV was started on postoperative day 0 and was discontinued on postoperative day 10. Development of leukopenia was witnessed with start of LEV, and improvement in leukopenia was observed with discontinuation of the medication.

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.

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.

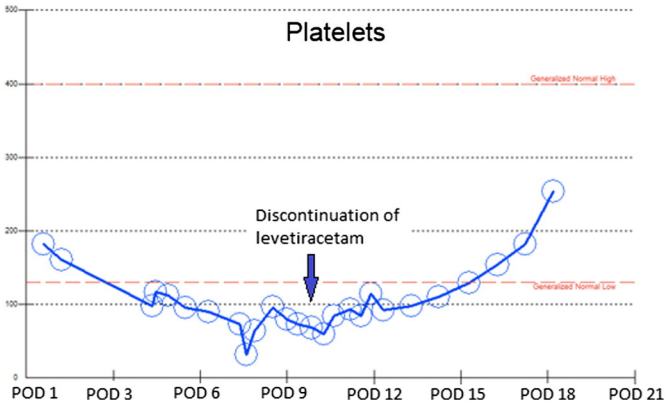

Fig. 4. Graph depicting relationship between platelet count and number of days postoperatively (POD). LEV was started on postoperative day 0 and was discontinued on postoperative day 10. Development of thrombocytopenia was witnessed with the start of LEV, and improvement in thrombocytopenia was observed with discontinuation of the medication.

Conflict of interest

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

References

[1] Two new drugs for epilepsy. Med Lett Drugs Ther 2000;42(1076):33–5.
[2] Aydogan H, Yalcn S, Karahan MA, et al. Pancytopenia associated with levetiracetam treatment in Lafora's disease. Blood Coagul Fibrinolysis 2012;23(2):175.
[3] Elouni B, Ben Salem C, Biour M. Levetiracetam-induced pancytopenia. Ann Pharmacother 2009;43(5):985.
[4] Gallerani M, Mari E, Boari B, et al. Pancytopenia associated with levetiracetam treatment. Clin Drug Investig 2009;29(11):747–51.
[5] Sirsi D, Safdieh JE. The safety of levetiracetam. Expert Opin Drug Saf 2007;6(3):241–50.
[6] De Smedt T, Raedt R, Vonck K, et al. Levetiracetam: part II, the clinical profile of a novel anticonvulsant drug. CNS Drug Rev 2007;13(1):57–78.
[7] Keppra®, product information 2009 [online]. Available from URL: http://www.keppra.com/pc/home/default.asp [Accessed 2015 April 28]