



A Case of Thrombocytopenia Associated with Valproic Acid Treatment in a Patient with Generalized Myoclonic Seizures

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Valproic acid also known as valproate (VPA), divalproex sodium or sodium valproate, is a medication used for treatment of epilepsy and bipolar disorders and to prevent migraine headaches. It is useful for the treatment of seizures in those with generalized seizures, absence seizures, and partial seizures. Valproic acid is commonly used and first line antiepileptic drug, especially in generalized form of seizures.

Commonly reported side effects of this drug include drowsiness, weakness, dizziness, diarrhea, nausea, vomiting, abdominal pain, infection, flu-like symptoms, congenital anomalies, tremor, alopecia, thrombocytopenia, and anorexia. Other different side effects may be nystagmus, tinnitus, pharyngitis, dyspnea, ataxia, amnesia, constipation, depression, weight gain, peripheral edema bronchitis, abnormality in thinking, and fever. In our case we will discuss the patient with severe thrombocytopenia after a month of Valproic acid treatment.

Keywords: Valproic acid, thrombocytopenia, seizures.

Introduction

Valproic acid also known as valproate (VPA), divalproex sodium or sodium valproate, is a medication used for treatment of epilepsy and bipolar disorders and to prevent migraine headaches. It is useful for the treatment of seizures in those with generalized seizures, absence seizures, and partial seizures. Valproic acid is commonly used and first line antiepileptic drug, especially in generalized form of seizures.

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One of the most prominent side effects of Valproic acid is thrombocytopenia. In thrombocytopenia, the blood has a low-

er than the normal platelet count. Normal platelet count may be among 150,000 and 450,000/ ml of blood. [1] It is problem when a platelet count is less than 150.000/ ml of blood. But the risk of serious bleeding occurs when the level is below 20,000/ml in blood. [1] Thrombocytopenia can occur in conditions such as certain cancers that affect stem cells, exposure to toxic chemicals, viruses and excessive consumption of alcohol, aplastic anemia etc., when the bone marrow fails to produce platelets [1, 2] Thrombocytopenia can also occur in different conditions when the body destroys its own platelets after the bone marrow makes enough platelets (e.g., in conditions such as idiopathic thrombocytopenic purpura, drug-induced thrombocytopenia and thrombotic thrombocytopenic purpura).Drug-induced thrombocytopenia can be caused by certain drugs such as Valproic acid, vancomycin, phenitoin, quinine, rifampin, and sulfa-containing antibiotics [1, 2, 3].

Case Presentation

Our patient, 12 years old girl presented to our neurological department with the complaints of an intensive and frequent myoclonic jerks without impairment of consciousness about 20-30 attacks per day, especially in the mornings. Myoclonic jerks appeared for the first time at the age of 9 years and started to occur frequently nearly every day in the morning hours since that time and especially symmetrically involved the arms without disturbance of consciousness. Generalised tonic-clonic seizures did not occur. Neurological examination of the patient was normal, only mild tremor was noticed at upper extremities. The girl also had severe psychiatric disturbances. The patient was confused and agitated. She suffered from auditory hallucinations and sleep difficulties. MRI of the brain was normal. Awake EEG recording showed bilateral synchronous fronto-central polyspike-wave discharges with photosensitivity which is similar to EEG features in Juvenile Myoclonic Epilepsy (Fig. 1).

Based on the clinical and EEG findings, the diagnosis was of generalized myoclonic epilepsy. She was started on Valproic acid 20mg/kg per day. After a month of prescription of the drug the patient was absolutely seizure free. We repeated EEG examination and there were no any abnormalities. Blood tests (CBC, ALT, GGT, Valproic acid blood level) were within normal limits, only platelet level was low (77,000/ml). There were no other risk factors for thrombocytopenia or any previous history. The drug was immediately stopped and another CBC was repeated after a week. Her platelet count increased to 274,000 /ml. Valproic acid was changed to levetiracetam for treatment of myoclonic jerks.

Discussion

The common hematopoietic system side effects of this highly used antiepileptic drug include abnormal bleeding time, thrombocytopenia, and partial thromboplastin time with decreased fibrinogen levels and prolonged prothrombin time leading to petechiae, hematoma, bruising and epistaxis. The drug can induce pruritic macular rashes. [3] Reported that, there are may be two possible mechanisms inducing thrombocytopenia. First on is the VPA has a direct toxic effect on bone marrow. Second mechanism is that VPA can stimulate the formation of autoantibody against platelets. It is suggested that contents of erythrocytes and thrombocytes lowered nearly 30 % and 10 %, accordingly in patients on the drug monotherapy. [4]

Our case, similar to some other cases [5], shows that treatment with valproic acid (monotherapy) can be associated with thrombocytopenia. This case shows thrombocytopenia induced by treatment with Valproic acid monotherapy in a young girl after a first the month of treatment. The risk of thrombocytopenia after using of Valproic acid is 5 %, and the risk increases with the level of Valproic acid in the blood and with the age of the patient. [6, 7]

Conclusion

The common blood test (CBC) should be checked periodically in all patients who are treated with Valproic acid. The risks caused by thrombocytopenia can be easily prevented by immediate stopping the drug and checking the patient's CBC every week until platelet count normalized.

References

1. Michelson A. Platelets. Amsterdam: Academic Press/Elsevier; 2007.
2. Murray M. Critical care medicine. Philadelphia: Lippincott, Williams & Wilkins; 2002.
3. Wheless J, Willmore J, Brumback R. Advanced therapy in epilepsy. Shelton, CT: People's Medical Pub. House; 2009.
4. Kaipainen P, Westermarck T, Atroshi F, Kaski M, Iivanainen M. Clinical and Hematological Profiles During Valproate Treatment of Epileptic Patients with Intellectual Disability—Case Study and Mini Review. In: Pharmacology and Nutritional Intervention in the Treatment of Disease 2014. InTech., DOI: 10.5772/57369
5. Nerumalla CS, Shah AA. A case of thrombocytopenia associated with valproic Acid treatment. The primary care companion for CNS disorders. 2012 Dec;15(4).
6. Acharya S, Bussel JB. Hematologic toxicity of sodium valproate. Journal of pediatric hematology/oncology. 2000 Jan 1;22(1):62-5.
7. Conley EL, Coley KC, Pollock BG, DaPos SV, Maxwell R, Branch RA. Prevalence and risk of thrombocytopenia with valproic acid: experience at a psychiatric teaching hospital. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2001 Nov 1;21(11):1325-30.

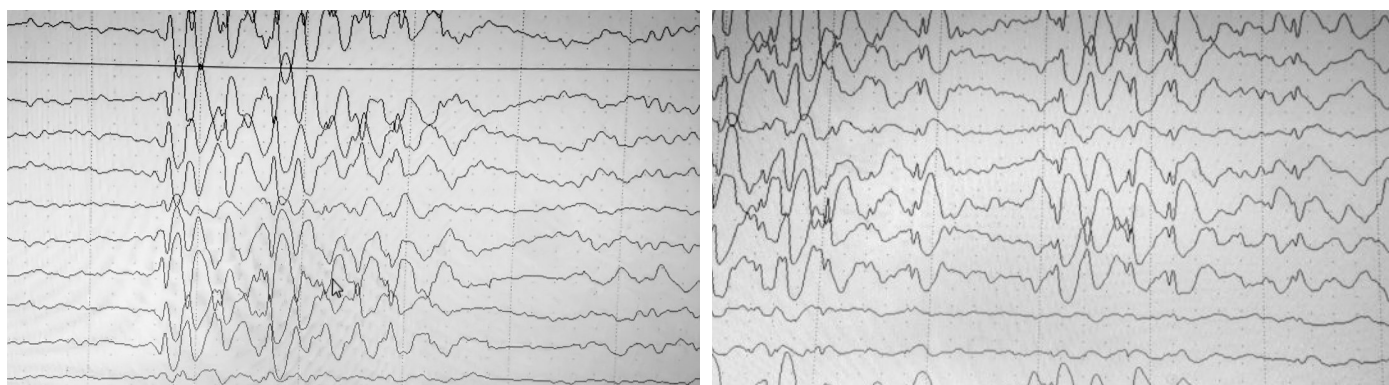


Figure 1. Bilateral synchronous fronto-central polyspike-wave discharges with photosensitivity in awake EEG which is similar to EEG features in Juvenile Myoclonic Epilepsy.