Research and Reviews: Journal of Pharmacy and Pharmaceutical Sciences

e-ISSN:2320-1215
p-ISSN:2322-0112

Case Report on Valproic Acid Derivatives Indused Papular Rash and Thrombocytopenia.

Mohana Chintha*

Department of Pharmacy practice, Krishna Teja Pharmacy College, Tirupati, Andhra Pradesh, India

Case Report

Received: 05/08/2021
Accepted: 19/08/2021
Published: 26/08/2021

***For correspondence:**
Mohana Chintha, Department of Pharmacy practice, Krishna Teja Pharmacy College, Tirupati, Andhra Pradesh, India
E-mail:
chakrabortyarindam446@gmail.com

Keywords: Valproate acid; Seizures; Drug induced hypersensitivity Syndrome; Thrombocytopenia

ABSTRACT

Valproate is a broad spectrum antiseizures drug used for a variety of clinical conditions, such as epilepsy and mood disorders. The risk of acute hypersensitivity syndrome caused by valproic acid is less known. Drug induced hypersensitivity syndrome (DRESS), accompanied by moderate anemia, thrombocytopenia, lymphocytopenia, neutrophilia and dyslipidemia has been rarely reported as Papular Rash an adverse effect of valproate monotherapy. We present a case of 33 years old male patient who suffered from hypersensitivity reactions along with other complications after two weeks of taking VPA medication for treatment of seizures. Understanding the risk factors caused by VPA and prescribing alternate medication and taking effective measures to avoid the side effects are necessary, Papular Rash.

INTRODUCTION

Valproate acid, one of the first line Antiseizure Drug, controls many types of seizures. VPA Drug induced hypersensitivity syndrome is rare in patients with seizure. DRESS is a type of severe cutaneous adverse drug reaction, characterized by popular rash. VPA-may be complicated by the development of thrombocytopenia. Age, female gender, and high doses were found to be risk factor for development of thrombocytopenia during treatment with valproate [1].

CASE REPORT

A 33-years-old male patient from urban area who is having past history of Generalized Tonic Clonic Seizures since 2 years and he used some traditional medication. Present he came with the chief complaints of seizures more than 5

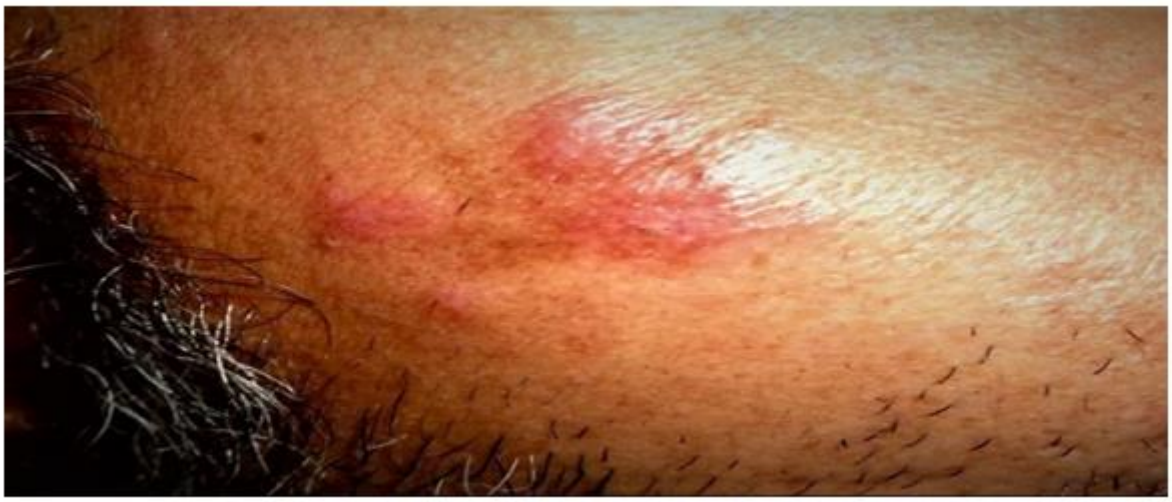
episodes with vomiting 6 episodes per day and the physician treated with Tab. VALPROL-CR 500 (Sodium Valproate + Valproic acid), BD. One week after VPA exposure, he suffered from erythematous maculopapular rash on forehead (fig.1). He didn't have feelings of pain, itch (or) burning. He also developed thrombocytopenia [2].

This patients' vital signs were stable. This patient past history includes craniectomy done and tracheostomy done on MV support. He is a chronic alcoholic. He had no history of drug allergies previously.

After the hospitalization, laboratory test showed moderate anaemia (Hb- 7.8g/dl) thrombocytopenia(PLT -80 ×109 L), Leukocytosis (WBC-12700 cells/cumm), Lymphocytopenia (10%), Neutrophilia (84%), serum LDL (38 mg/dl), serum HDL (32 mg/dl).

Chest radiography revealed chronic inflammatory changes in bilateral lungs without any infections (SPO2-100%), CT demonstrated T.C movements of both upper and lower limbs with fronting from mouth (Figure 1) [3].

Figure 1. Papular rash over fore head.



Coming to treatment the drug Tab.VALPROL-CR-500 started at 3-06-2019 to 17-06-2019 with the dose of 500mg-BD. The patient experienced Papular rash over fore head on 15-06-2019 and thrombocytopenia (75 * 109 /l) on 5-06-2019 and the platelet count was gradually getting decreased to (60 * 109 /l) on 6-06-2019. Later the patient was insisted to take a tapered dose 250mg- BD from 18-06-19 to 20-06-2019. Later the drug was stopped completely on 21-06-2019 and prescribed an alternate drug Tab. Chymoral forte- 1mg-TID, this drug was given to reduce the rash from 18-06-2019 and Inj. Levetiracetamine-1gm-bd started from 20-06-2019. The rash was suppressed slowly.

DISCUSSION

Cutaneous eruptions are one the most common type of drug-related adverse reaction and accounted for 2-3% in hospital-based series4. More than 10% of patients receiving anti-epileptic drugs develop skin rash.

In our case, the patient had DRESS and moderate anaemia, thrombocytopenia, leukocytosis, neutrophilia, lymphocytopenia and decreased levels serum LDL and serum HDL after 2 weeks of using of VPA for his seizures. The exact mechanism is still not known. As previous studies say, human leucocyte antigen (HLA) alleles are the genetic factors involved DRESS. Although, no, specific HLA allele is identified as a biomarker of VPA-related DRESS, a genetic predisposition and related immunologic reactions could be the potential explanation [4].

Furthermore, our patient decreased the dosage of VAP from 500mg/dl to 250mg/dl in second week. Although slower titration rate is commonly recommended to reduce the risk of severe rash, ASDs-induced SCARs are generally considered idiosyncratic, unpredicted and non-dose dependent.

There are few reports concerning Sodium valproate in combination with LFG causing acute hypersensitivity syndrome (AHS) with multiple organ dysfunction but all these patients had a concomitant use of LTG and VPA, not VPA alone. More over Arevalo-Lorido et al. described a 36years-old man with AHS caused by VPA 2weeks after initial CBZ, which was discontinued because of severe skin rash.

There are some reports of VPA combination with other drugs besides for ASDs. One case presented a 26 years-old man with DRESS and acute liver failure after an intracerebral bleed for 5month and seizures for 1.5 months, taking VPA, baclofen, clemastine and acetaminophen daily. Another case of 20 years old Brazilian female patient with DRESS after treatment and VPA and haloperidol [5].

Moreover, YANG et al concluded that most of the patients tolerated nonaromatic ASDs, especially VPA, after their SCARs episodes caused by aromatic ASDs. When using VPA as a replacement therapy there should be a close monitoring the clinical features and laboratory results are quite necessary.

CONCLUSION

In our case report of VPA monotherapy in seizures accompanied by moderate anaemia, leukocytosis, thrombocytopenia, decreased serum LDL, serum HDL, lymphocytopenia and neutrophils. Taking effective measure to avoid side effects due to VPA are necessary. When skin rash and thrombocytopenia occur in a patient taking VPA, possibility of the reaction to the drug should be considered and prescribing an alternate drug or dose and frequency monitoring may be a good option.

Finally, if VPA is considered for patients, with other co-morbidity (or) under polytherapy for other diseases, the clinical and laboratory observations of their patients should be monitored. Additional studies should be done in order to find out the potential mechanisms of VAP-induced DRESS in the future.

REFERENCES

1. Zhou P, et al. Structural modeling of HLA-B*1502/peptide/carbamazepine /T-cell receptor complex architecture: implication for the molecular mechanism of carbamazepine induced stevens-Johnson syndrome/toxic epidermal necrolysis. J Biomol struct Dyn. 2016;34:1806-1817.
2. Illing PT, et al. Immune self-reactivity triggered by drug- modified HLA-peptide repertoire. Nat. 2012;486:554-558.
3. Buoli M, et al. The risk of thrombocytopenia during valproic acid therapy: A critical summary of available clinical data. Drug RG. 2018;18:1-5.
4. Sharma VK, et al. Clinical spectrum of drug rashes due to antiepileptic. J Assoc Phys India. 1998;46:595-597.
5. Dhar S, et al. clinical pattern of cutaneous drug eruption among children and adolescents in north India. Pediatr Dermatol 1995;12:178-83.