ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 15, Issue 12, 2022

Online - 2455-3891
Print - 0974-2441

Case Report

A CASE REPORT ON WELL KNOWN BUT HAS TO BE REPORTED ADVERSE EFFECT OF PHENYTOIN-INDUCED RASH AND ASSESSMENT OF ITS SEVERITY BASED ON ADVERSE DRUG REACTION REPORTING SCALES

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Received: 28 July 2022, Revised and Accepted: 14 September 2022

ABSTRACT

Phenytoin is an aromatic antiepileptic drug, commonly used for the purpose of treating generalized tonic clonic and partial seizures. The drug has been known to cause hypersensitivity reaction, which can be life-threatening by involving internal organs, and is referred as anticonvulsant hypersensitivity syndrome. The treatment in such cases is the immediate discontinuation of the agent causing the reaction and replacing the treatment with other non-aromatic anticonvulsant agent. This case report presents an adverse drug reaction and occurs within 1 week of starting the treatment, a well-known but has to report this adverse effect.

Keywords: Phenytoin, Hypersensitivity reaction, Antiepileptic agent.

 DOI: http://dx.doi.org/10.22159/ajpcr.2022v15i12.46006. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

The syndrome, which is known as anticonvulsant hypersensitivity syndrome (AHS), is more commonly known to affect women than men in the ratio of 1.3:1 [1]. The syndrome is associated to cause alterations in hemoglobin and all cell counts of leukocytes and platelets [2]. Phenytoin has been strongly associated to cause liver impairment and less frequently affects kidneys, heart, nervous system, and pancreas [2]. AHS, which was previously known as DRESS (Drug ruption with Eosinophilia and systemic syndrome), usually occurs with antiepileptic drugs (Aromatic agents) such as phenytoin, phenobarbital, and carbamazepine [3]. A triad of fever (usually accompanied by pharyngitis and weakness), rash, and internal organ involvement occurs in AHS [4]. The syndrome is usually seen within 2 weeks–2 months of starting the treatment [5]. The incidence is unknown as most of the cases go unnoticed and are not reported [6]. Genetic factors might contribute to the occurrence of such reactions as Human Leukocyte Antigen (HLA-A*301 has been linked to cause carbamazepine-induced cutaneous reaction in European population [7]. Reactivation of human herpes virus 6 and 7 has been linked to cause AHS [8]. The process of detoxification by Cytochrome P450 and elimination has been identified to be defective in patients presenting with AHS [9].

In this article, we report an interesting case of hypersensitivity reaction, occurred after 1 week of starting the phenytoin therapy and the reaction subsided on stopping the phenytoin. The reaction has been assessed using WHO-UMC scale and Naranjo Scale. It is a well-known adverse effect of this antiepileptic drug, which occurred in our patient also. This article will help in understanding the presentation of hypersensitivity reaction.

CASE DETAILS

A 29-year-old male patient presented to the medicine department, with complaints of abnormal body movements, that was going unnoticed (one episode in each month) since 6 months. The patient was conscious through all the episodes, but gives history of agitation, tiredness, and weakness. In the last episode, which occurred in march 2022, has been noticed by family members and was generalized (as per the history given), patient was conscious but unable to control the abnormal movements. The patient has no history of any drug abuse or alcohol intake. The electroencephalography has reported Generalized Poly Spike Wave discharges and is 0.4–1.2 s duration. Photic stimulation has been contributory (Fig. 1). Magnetic resonance imaging of brain has confirmed; no intracranial abnormality, diagnosis of sphenoid sinusitis, and right maxillary sinus polyp has been made. These findings have confirmed the diagnosis of Generalized Tonic Clonic Seizures.

Other investigations such as complete blood count, liver function, and kidney function test were normal (before starting the treatment). The patient was diagnosed to be a case of generalized tonic clonic seizures. The patient was started on Phenytoin (100 mg in the morning and 200 mg at bed time) since March 2022. Following the 7 days of treatment, patient has developed fever (100–101°F), sore throat, headache, and non-itching rash starting from upper back and thigh and has spread to abdomen, lower limbs, and face (Fig. 2). On examination, he was conscious, oriented, and cervical lymphadenopathy (painful and mild tenderness) that was present but systemic examination was normal (No Organomegaly) The WHO-UMC causality category of the reported adverse event was possible and the score on Naranjo Scale was 4. On physical examination, he was alert, conscious, and oriented. The patient was advised to stop the phenytoin and has been advised to start Loratidine, Paracetamol, and Steroid therapy by the dermatologist. The patient did not underwent complete blood count, liver function test, and kidney function test following the reaction.

No other clinical investigation was done to confirm that the reaction was phenytoin induced. Once the maculopapular rash has started resolving after withdrawing phenytoin, the patient has been started on Valproic Acid (with slowing increasing the dose), the patient has been maintained on 500 mg twice a day. The patient did not get any episode of seizure activity in the past 6 months and is doing well.

DISCUSSION

Anticonvulsants are the main culprits in causing AHS, though many other drug groups have been known to cause such reactions. Fever and malaise are the most commonly presenting symptoms in AHS [7]. To diagnose a case of DRESS, Bocquet's Criteria, RegiSCAR, and JSCAR criteria have been developed [10,11]. The symptoms due to drug induced hypersensitivity usually occur within 2–6 weeks of treatment initiation [11]. In 73–100% of the patients, skin reactions usually cover >50% of body surface area and are highly suggestive of DRESS [12]. However, in our case report, the patient had developed rash, which

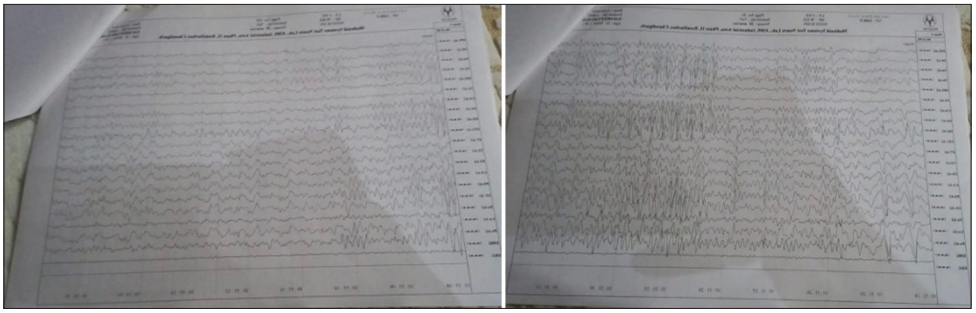

Fig. 1: Electroencephalography of the Patient

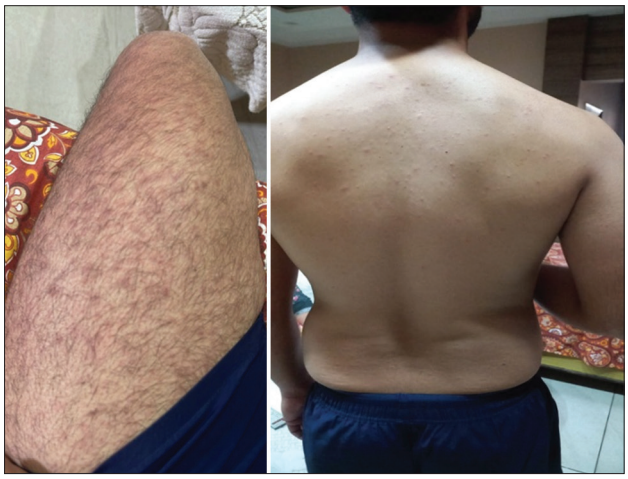

Fig. 2: Rash Eruption on affected areas

covered almost all of the body surface except sole and palm (which persisted for almost 10 days, and fever within 1 week of starting the treatment. Systemic involvement in AHS could be life-threatening [13]. The most important hematological abnormality is eosinophilia, which is seen in 58–100% [12]. Although in our case no complete blood count, liver function test has been done after the appearance of reaction.

The anticonvulsants drugs which should be avoided in such patients are conventional aromatic anticonvulsants (Phenobarbitone, carbamazepine, and phenytoin) and newer aromatic agents such as lamotrigene, oxcarbamazepine, and sonisamide, due to the existence of cross reactivity between them [13] Thus, the safe alternative treatment in such cases is Valproic acid, levetiracetam, benzodiazepines, ethosuximide, gabapentin, tiagabine, and topiramate [13].

CONCLUSION

While prescribing the drug, physicians should always be aware of the adverse effect of phenytoin and other antiepileptic drugs. It is a well-known adverse effect, but the underlying mechanism is not clearly understood. The patient should be advised to stop the drug immediately once the reaction occurs.

AUTHOR CONTRIBUTION

In reporting the Adverse Drug Reaction and helping to write the literature.

CONFLICTS OF INTEREST

Nil.

FUNDING

Nil.

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