



Phenytoin induced Steven Johnson syndrome

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ABSTRACT

Phenytoin is an anticonvulsant and Hydantoin, it is mainly used in the management of Seizures, and it stabilizes the neuronal membranes and decreases seizure activity by increasing efflux or reducing the influx of sodium ions across cell membranes in the motor cortex during the generation of nerve impulses. It is available in the market in the form of oral and intravenous forms, a loading dose of Phenytoin for the management of seizures is 10-20 mg, divided into 2-3 doses. Stevens-Johnson syndrome is a rare and serious adverse effect of the skin along with the membranes of the mucous. It is caused by specific Drugs or Viral Infections. We have performed causality assessment by using the WHO and NARANJO'S ADR rating scale. It will seem, it is a Probable ADR, and severity assessed it confers a Type-A ADR, and it should be in Probably Preventable. So being a Reliable Clinical Pharmacist, we recommend to all health care professionals be aware of adverse drug reactions, and Desirable vigilance is necessitated toward safe and effective management for specific patients, strictly observe the patients in sequence anticipate Dangerous Adverse events.



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INTRODUCTION

Antiepileptic drugs are associated with severe dermatological reactions such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) (Harr and French, 2010). Phenytoin is one of the most commonly prescribed anti-epileptic. And is known to cause a plethora of adverse drug reaction (Rzany et al., 1999). Stevens-Johnson syndrome

(SJS) and toxic epidermal necrolysis (TEN) are rare and severe Clinical manifestations of idiosyncratic reaction to certain drugs. They may also be caused by infections like herpes but are more commonly associated with drugs. SJS and TEN are two entities of the same clinical condition differing only in their percentage involved in their body surface. Usually, body surface area (<10%) involvement is seen in SJS, 10-30% BSA in SJS-TEN overlap, and >30% BSA detachment is seen in TEN. Among the drugs - antiepileptic, antibiotics like sulphonamides, and isoniazid and NSAIDS are the common culprits (Karimzadeh and Bakrani, 2013). The full-blown form of the syndrome is preceded by a prodromal phase of flu-like symptoms which evolve over 1-3 weeks to cutaneous manifestations in the form of macular eruptions over the trunk, face and upper limb.4 Involvement of mucous membrane is seen in 90% of cases. Diagnosis is made on clinical suspicion and confirmed by biopsy. Prognosis depends upon the age of the patient, presence of

comorbidities, and area of detachment (Lissia *et al.*, 2010). Septicaemia is the most common complication of SJS and the major contributor towards mortality (Alquliti *et al.*, 2014). Here we report a case of SJS in an 18-year male after he was put on a prophylactic dose of phenytoin.

CASE REPORT

A 36 years female patient having weight 50 kgs admitted in the hospital with generalized darkening of skin over 6 days. She is taking Tab.Eptoin (Phenytoin) 10 mg for Epilepsy after taking the medication, she is developed darkening skin all over the body. She is a not known case of Fever, HIV/AIDS/, Systemic Connective tissue disorders. She is observed this adverse reaction with in the 6 days. She don't have any Past medical and medication history along with Family history; her general examination includes BP was 110/80 mm. Hg, PR is 82 bpm, Respiratory rate-16 min, Temperature-98.6°C. Coming to the systemic examination Per abdomen includes Enlarged Palpation of liver and Palpation of the spleen, Auscultation of lungs shows Non-vascular breath sounds. Her Clinical investigation Blood Urea Nitrogen- 69%, Random Blood Sugar -76mg/dl remains all parameters are normal. The patient was referred to the Dermatological department to confirm the ADR, in the dermatological examination shows she is having Multiple hyperpigmented and few vesicles of size 0.2 over present the body, Multiple erythema Present in the Chest and abdomen, Oral cavity examinations shows Haemorrhage crusts over both lips. We are comparing the all drugs Phenytoin Pharmacology and literature strongly support it can cause Steven Johnson Syndrome. To affirm the connection in the effect and drug, we have also dechallenge test i.e.; the drug was switched from the therapy regimen after the switched of drug manifestations was waned.

ASSESSMENT OF CASUALITY

To find of the connection of between the drug reactions, we have conducted Causality assessment by using the scales like WHO Causality assessment scale, Naranjo's Scale, by evaluating by utilizing the above scales we are examined adverse drug reaction, it will be displayed in Table 1 & Table 2.

Table 1: casuality assessment of suspected ADR

ADR scale	WHO – UMC	Naranjo's
Assessment	probable	probable

Table 2: Analysis of observed ADR

Severity Assessment	Moderate Level – 4(a)
Preventability	probably preventable
Predictability	type - a

RESULTS AND DISCUSSION

According to the World Health Organization, adverse drug reaction can be defined as "any response to the drug which is toxic or unintended and happens at a dose normally used in man for prophylaxis, diagnosis or treatment of diseases or modification of physiological function." In many types of adverse drug, reactions reported it confers the most obvious one is cutaneous drug reactions. SJS though limited, is considered as a rigid form of erythema multiform spectrum. Clinically, SJS and TEN are characterized with polymorphic lesions like erythematous macules, papules, plaques, vesicles, and bullae with a predilection for the distal extremities and is Nikolsky's sign positive. "Target" lesion with bull's eye display is characteristic of SJS and TEN. Oral, genital, and conjunctival mucosa is often involved in the form of erosion or ulceration (Pendurthi, 2018). Various literature Shows Severe cutaneous adverse reactions to antiepileptic drugs in Asians peoples showed that among antiepileptic's, Carbamazepine (CBZ) and phenytoin (PHT) were the most common cause for influencing SJS/TEN. Phenytoin-related severe cutaneous adverse reactions constantly reduce the internal organs, managing to the highest mortality amid the different antiepileptic drug-related cutaneous reactions. Most utmost of the medication has a higher incidence and Morbidity rate of SJS as well as TEN. These drugs are - Nevirapine, Lamotrigine, Carbamazepine, Phenytoin, Pheno-barbital, Cotrimoxazole, and other anti-infective sulfonamides, Sulfasalazine, Allopurinol, Oxycam-NSAIDs. Currently, no therapy modality has been established as a standard during certain patients. Due to the lack of these disorders, there are no randomized controlled trials of pharmacological agents in the management of TEN. Nevertheless, there are case reports of successful treatment with I.V immunoglobulins, systemic corticosteroids, plasmapheresis, cyclosporine, cyclophosphamide, anti-tumour Necrosis Factor- α (TNF- α) and hemodialysis but with limited data to be recommended as the first-line treatment (Mukasa and Craven, 2008).

CONCLUSION

During the Treatment as a Clinical Pharmacist, we recognize these adverse drug reactions as results. The patient was under the medication Tab. Eptoin (Phenytoin) based on the literature reviews and based on local examination and other investigations, we have confirmed this condition due to the drug Phenytoin and conducted Causality assessment, Severity, Preventability, and Predictability. After the identification of ADR, we are immediately withdrawn from the drug Tab. Phenytoin, after withdrawn of the drug symptoms, was subsided. Finally, we conclude desirable vigilance is wanted for safe and effective management for individual patients, closely monitor the patients to stop Harmful Adverse Effects. As per part of clinical Pharmacy Services, we (Clinical Pharmacists) instruct the health care Experts and Conduct knowledge to the patients to probably limit Adverse Drug Reactions.

Abbreviations

SJS-Stevens-Johnson syndrome, TEN- Toxic Epidermal Necrolysis, BSA -Body Surface Area, WHO-World Health Organization, ADR-Adverse Drug Reaction.

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