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Case Report

Phenytoin-Induced Erythroderma

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ABSTRACT

Phenytoin is a frequently prescribed anticonvulsant/antiseizure drug due to its high efficacy. Erythroderma is an intense and widespread reddening of the skin due to inflammation which may often be associated with peeling of skin termed as exfoliative dermatitis. Erythroderma is a rare but severe Adverse Drug Reaction (ADR) of phenytoin. Here, we report a case of a patient who developed erythrodema during the treatment regimen including phenytoin prescribed for the treatment of alcoholic withdrawal seizures. ADR was confirmed by using the World Health Organization (WHO) and Naranjo's causality assessment scale. The erythroderma condition was managed clinically by withdrawing the causal medication and administration of anti-histamines and corticosteroids with other supportive therapy. This case explains the adverse drug reaction occurring drugs used for cure. Hence there is a strong need for a pharmacovigilance programme and its awareness all over the nation.

Key words: Phenytoin, Erythroderma, Anticonvulsant, Adverse drug reaction, Alcohol withdrawl seizure.

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INTRODUCTION

Phenytoin is the oldest non-sedative antiseizure/anticonvulsant drug with the chemical name 5,5 Diphenylhydantion belonging to hydantoin derivative.[1] It exerts a blocking effect on Na+ conductance arising from preferential binding to and prolongation of the inactivated state of Na+ channels.[2] Thus, reduces post-tenanic potentiation at synapses and prevents repetitive detonation of cortical seizure foci and hence, is widely indicated for the treatment of partial and generalized tonic clonic seizures.[1] In-addition to anti-convulsant activity phenytoin is used for neuro-psychological disorders as its off-label use.[3] Majority of dermatological ADRS are self limiting, Some of the severe dermatological adverse drug reactions like Stevens-Johnson syndrome, toxic epidermal necrolysis, eosinophilia and systemic symptoms are associated with hospitalization and mortality.[4,5] The phenytoin toxicity usually occurs 1-3 weeks after starting the therapy and consists of a characteristic skin eruption, facial oedema, fever, tender and generalized lymphadenopathy, diffuse erythema of oral mucosa, atypical lymphocytes and eosinophilia.[6] Liver function abnormalities are commonly reported either as jaundice or changes in liver chemistry.[7]

CASE REPORT

An 34 year old male visited the hospital with chief complaints of chills, itching, difficulty in swallowing since 3 days and history of desquamation present, complaining of pain/ burning sensation, complaining of painful lesions in oral cavity and history of loss of vision right eye since childhood following trauma to right eye and history of hyperpigmentation. His past medical history includes k/c/o alcoholic withdrawal seizures since two months back and previously admitted for the same condition and discharged. His recent medication history consists of the use of Inj phenytoin 100mg-0-100mg and tablet fluoxetine.

On examination patient Blood Pressure (BP) was 90/70 mm of hg and pulse rate was 82 BPM and patient general condition was fair, moderately built and nourished and well oriented to time, place and person. Systemic examinations were found to be normal. Examination of skin and appendages report showed the erythematous plaques involving more than 90% of body surface area desquamations positive. On laboratory examination, the Ultrasonograpgy (USG) abdomen showed the grade 1 fatty liver. His blood examinations showed an elevated aspartate aminotransferase (185 IU/L), alanine transaminase (131 IU/L), alkaline phosphate (401 IU/L) and total bilirubin (2.2mg/dl) indicating hepatotoxicity.

The patient administered with inj. dexamethasone 2cc 1-0-0 IM, inj. avil 2cc 0-0-1 IM, tab amoxicillin 625mg per oral (p.o.) b.i.d, tab vitamin B. complex o.d., tab. paracetamol 500 mg t.i.d., tab. cetirizine 10mg o.d., liquid paraffin b.i.d., clenorosh mouth gel, tab ursodeoxycholic acid150mg b.i.d., syrup mucaine gel 5ml t.i.d., peduor powder 2 tsp with a glass of water. After ten days he was discharged with tab. prednisolone 20mg o.d., tab. ursodeoxycholic acid 150mg b.i.d., tab. B.complex o.d., liquid paraffin t.i.d., tab. cetirizine 10mg o.d. and tab levetiracitam 500mg 1-0-1.

Causality assessment of this case was of probable (ADR established by the WHO causality assessment scale). The same result was obtained by Naranjo's causality assesment scale with a score of 9. Thus, assessed as probable ADR. Additionally, the temporal association was strongly suggestive of Phenytoin induced erythroderma. Re-challenge of medication was not necessary.

DISCUSSION

Phenytoin is one of among the oldest antiseizure drugs that are prescribed widely and used as first line drug instead of its relatively high incidence of side effects because of high efficacy.[8] Phenytoin is a highly

active and widely prescribed antiseizure agent used in the treatment of focal and tonic clonic generalized seizures. The side effects of phenytoin can occasionally engender significant morbidity. Phenytoin can induce widespread eruptions that include: A maculopapular exanthema, steven-johnson syndrome, generalized exfoliate dermatitis, toxic epidermal necrolysis, vasculitis and fixed drug eruptions. Phenytoin is linked to a hypersensitivity syndrome that manifests with fever, rash and lymphadenopathy. Parentral exposure to phenytoin may result in a spectrum of structural, developmental and behavioural changes, known as fetal hydantion syndrome.[9] Erythroderma is a state of severe skin disease. The clinical manifestations are erythematic with inflammatory skin disease, scaling on the cutaneous surface of the skin, thickened skin, itching, swollen lymph nodes, fever and finally it may lead to dehydration (loss of fluids and proteins). Phenytoin adverse reactions may start in 1-3 weeks of administration of the drug.[10] The metabolism of phenytoin is capacity limited; changes from order to zero order over the therapeutic range. As a result, a small increment in dose produces disproportionately high plasma concentration.[8] A skin rash may suggest hypersensitivity of the patient to the medication. In very few cases, the lesion may be severe and exfoliate and death may occur.[11] Steven-johnson syndrome and toxic epidermal necrolysis are rare, but severe cutaneous adverse reactions and fatality is more than other hypersensitivity reactions.[12] Erythroderma is a rare phenomenon due to phenytoin characterized by erythema and scaling involving > 90% of body surface area. Erythroderma is not a specific disease or diagnosis but the clinical manifestation of a variety of underlying causes. The estimated incidence is 1 to 2 patients per 100,000 population in a year.[13] It is more common in males and usually seen in elderly patients however the age and time of onset are primarily related to underlying etiology. Atopic dermatitis is the most common reason for erythroderma in the younger population. It may be related to drug intake, idiopathic or due to underlying malignancies. It usually evolves months to years except for drug reactions and atopy which tend to develop more acutely. It is essential to establish the correct diagnosis because specific therapy other than corticosteroids or anti-inflammatory treatment may be necessary to improve the patient's condition. Erythroderma carries a significant risk of mortality and morbidity and accounts for up to 1% of all dermatological hospital admissions.[14] Drug withdrawal resulted in improvement which is the first line step for management of drug induced erythroderma. However, the rechallange of medication was not done. Early diagnosis, appropriate treatment and awareness of this possible life threatening complication of phenytoin is essential, because as it is the commonly used in the treatment of seizures.

CONCLUSION

The case was confirmed as the ADR of phenytoin by WHO and Naranjo's causality assessment scale. Hence, the Tab. Phenytoin has changed alternatively to Tab. levetiracitam 500mg 1-0-1. Erythroderma is a rare adverse drug reaction due to phenytoin. Although it is a rare condition, the occurrence of similar events with exfoliation may have higher severity and can be life threatening. The continuous monitoring of the patient on phenytoin therapy may facilitate the early detection and documentation of events which may help to prevent the occurrence and relapse of phenytoin induced disorders. To avoid the incidence and re-occurrence of similar cases, there is a need for proper pharmacovigilance programmes and its appropriate dissemination throughout the nation.

Ethical Declaration

Patient informed consent was obtained before data collection assuring patient confidentiality.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ABBREVIATIONS

ADR: Adverse drug reaction; **WHO:** World Health Organization; **USG:** Ultrasonography; **IM:** Intramuscular; **K/C/O:** Known case of; **BP:** Blood Pressure; **IU/L:** International unit/Lire.

REFERENCES

1. Sumit T, Basavarary CK, Aruna B. Phenytoin induced fatal erythroderma: A Case report. Ind J Med Case Reports. 2017;6:27-9.
2. McNamara JO, Brunton LL, Lazo JS, Parker KL. Goodman and Gillman's The Pharmacological Basis of Therapeutics, 11th edition. 2011;407-9.
3. Rahajeng B, Ikawati Z, Andayani T, Dwiprahasto I. A retrospective study: the off-label use of anticonvulsants at a private hospital in Indonesia. Int J Pharm Pharm Sci. 2018;10(5):119-22.
4. Scheinfeld N. Phenytoin in cutaneous medicines: its uses, mechanisms and side effects. Dermatology online J. 2003;9(3):6.
5. Raut A, Pawar A, Pankaj M, Srivastava P, Mishra A. Clinical pattern and severity of cutaneous adverse drug reactions. Int J Pharm Pharm Sci. 2013;5(2):612-6.
6. Stanley J, Fallon-Pellicci V. Phenytoin hypersensitivity reaction. Arch Dermatol. 1978;114(9):1350-3.
7. Chariesworth EN. Phenytoin induced pseudo lymphoma. Arch Dermatol. 1977;113(4):477-80.
8. Hung CC, Lin CJ, Chen CC, Change CJ, Liou HH. Dosage recommendation of phenytoin for patients with epilepsy with different CYP2C9/CYP2C19 polymorphism. Ther Drug Monit. 2004;26(5):534-40.
9. Scheinfeld N. Impact of phenytoin therapy on the skin and skin disease. Expert Opin Drug Saf. 2004;3(6):655-65.
10. Botella-Estradas R, Sanmartin O, Oeiver V, *et al*. Erythroderma–a clinical, pathological study of 56 cases. Arch Dermatol. 1994;130(12):1503-7.
11. Yang CY, Dao RL, Lee TJ, Lu CW, Yang CH, *et al*. Severe cutaneous adverse reactions to antiepileptic drugs in Asians. Neurology. 2011;77(23):2025-33.
12. Alquliti K, Ratrout B, Alzaki A. Antiepileptics drug toxicity: A Case of toxic epidermal necrolysis in patients with prophylaxis post-cranial radiation for brain metastases. Saudi Pharm J. 2014;22(4):381-4.
13. Sigurdsson V, Steegmans PH, Volten WAV. The incidence of erythroderma: A survey of all dermatologists in the Nertherlands. J Am Axad Dermatol. 2001;45(5):675-8.
14. Shirazi N, Jindal R, Jain A, Yadav K, Ahmad S. Erythroderma: A clinico-etiological study of 58 cases in a tertiary hospital of North India. Asian J Med Sci. 2015;6(6):20-4.

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