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Case Report

PHENYTOIN INDUCED FATAL ERYTHRODERMA: CASE REPORT

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ABSTRACT
Phenytoin is an antiseizure drug which is shown to be effective with frequent side effects that are rarely fatal. It is frequently prescribed antiseizure drug due to its high efficacy. Here, we report the case of a patient who developed erythroderma during the course of treatment with phenytoin that resulted in death of the patient.

Keywords: *Phenytoin, Erythroderma, Hypersensitivity, Adverse Drug Reaction*

INTRODUCTION
Phenytoin, earlier known as diphenylhydantoin is the oldest nonsedative antiseizure drug (Sharma and Sharma, 2011) and is indicated for treatment of Partial seizures and generalized tonic clonic seizures. Phenytoin has stabilizing effect on neuronal membrane by preventing repetitive detonation of normal brain cells during "depolarization shift" that occurs in epileptic patients and consists of a synchronous and usually large depolarization over which action potentials are superimposed. It exerts a use dependent blocking effect on Na^+ conductance arising from preferential binding to and prolongation of the inactivated state of Na^+ channels (McNamara, 2011). Here, we report a case of 14 years old male who developed erythroderma to Phenytoin that resulted in death of the patient.

CASES
A 14 year old male was admitted after first episode of status epilepticus and received eptoin (phenytoin) during his hospital stay and was advised phenytoin 100mg OD by oral route on discharge from hospital. Patient did not have any past or family history of allergy or dermatological disease. After 10 days of treatment patient developed generalized body pain, abdominal pain, mild fever and itching over right hand that progressed to left arm and involved entire body over 2-3 days. Patient consulted to a private practitioner and received some injectables, detail of which was not available. Patient had initial improvement followed by worsening of symptoms.
Swelling of face started after 15 days which gradually spread to involve the entire body over 3-4 days. Scaly lesions started to appear 2-3 days after edema and spread all over the body along with lesions in mouth and difficulty in swallowing. After 2-3 days this was followed by Conjunctival congestion with purulent discharge and ear ache with discharge. Patient was able to take liquid diet only. Patient was brought back to the hospital after 25 days of treatment with phenytoin. On examination there was scaling of genitals without discharge.
Laboratory investigations included deranged liver function tests, normal total leukocyte count and normal differential leukocyte count. Based on signs and symptoms a differential diagnosis of Toxic epidermal necrolysis and Erythroderma was made. TEN was ruled out by negative Nikolsky sign. Phenytoin was stopped immediately on hospitalization and treatment was started with injection dexamethasone, ciprofloxacin eye drops and ointment, liquid paraffin and injection midazolam. The condition of patient deteriorated during hospital stay and patient died after 3 days of admission into hospital.

DISCUSSION
Phenytoin is among the oldest antiseizure drug that is still being widely used instead of its relatively high incidence of side effects because of high efficacy. The kinetics of metabolism is capacity limited; changes from first order to zero order over the therapeutic range. As a result, small increment in dose produces disproportionately high plasma concentration (Hung *et al.*, 2004). Adverse effects seen at the therapeutic

levels include gum hypertrophy, hirsuitism, megaloblastic anemia, osteomalacia, fetal hydantoin syndrome and hypersensitivity reactions. Idiosyncratic reactions to phenytoin are relatively rare (Porter and Meldrum, 2011). A skin rash may indicate hypersensitivity of patient to drug. In rare cases, the lesion may be severe and exfoliative. Rarely death may occur (Yang *et al.*, 2011). Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but severe cutaneous adverse reactions and fatality is more than other hypersensitivity reactions (Alquliti *et al.*, 2014).

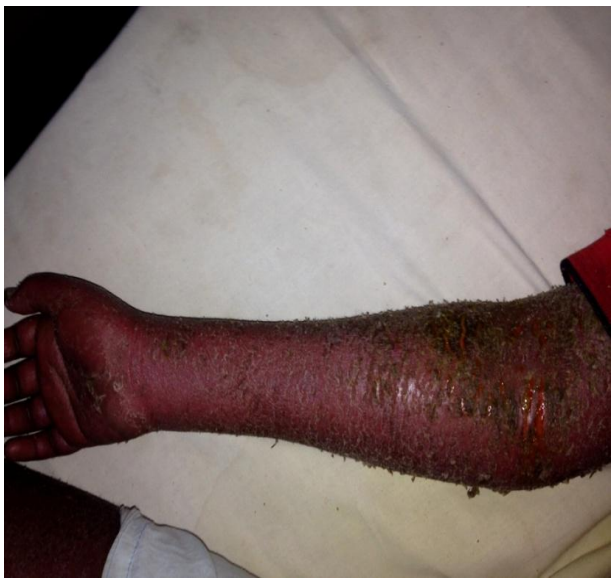

Figure 1: Erythroderma and Swelling of Arm and Forearm

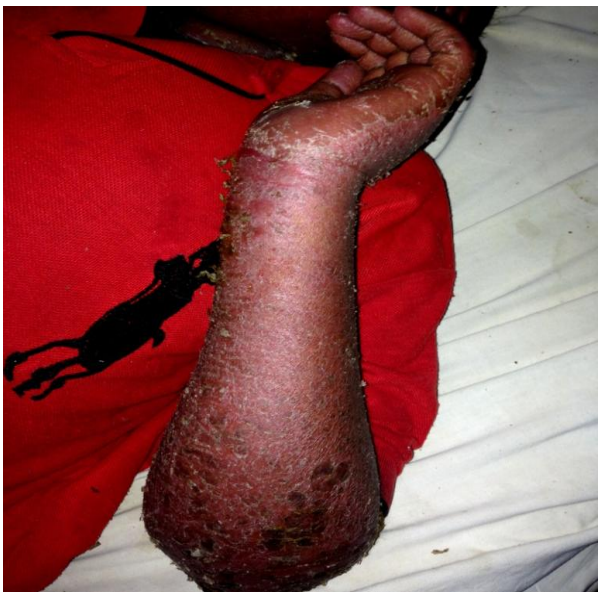

Figure 2: Erythroderma and Swelling of Forearm

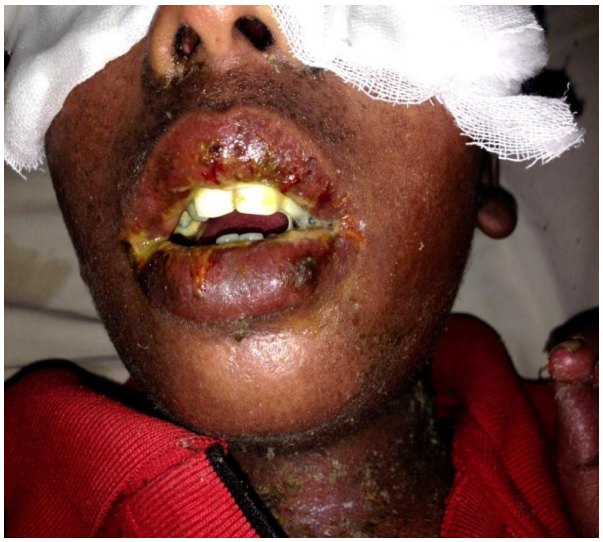

Figure 3: Involvement of Neck, Face, Oral Cavity and Lips

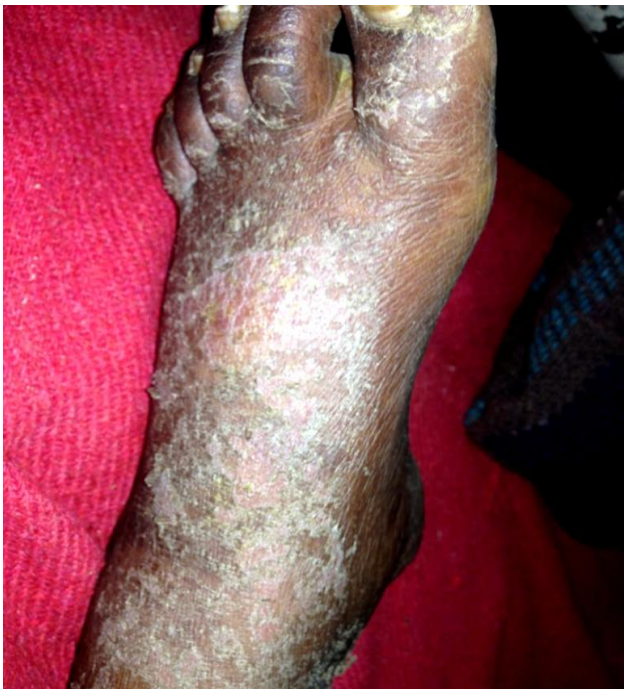

Figure 4: Swelling and Erythroderma of Lower Limb

In this case a systematic approach was followed to determine whether the suspected adverse drug reaction was due to drug or as a result of other factors. Noranjo's causality scale was used to determine a causal relationship between erythroderma and treatment with phenytoin. There are previous conclusive reports available on hypersensitivity reactions caused by phenytoin, skin hypersensitivity started after phenytoin administration, there are no alternative causes that could have caused the reaction. Hence, it was considered that the ADR is "probably" caused by phenytoin (Noranjo score +6). WHO-Uppsala monitoring centre (UMC) causality criteria also indicated a probable association. Early recognition, aggressive management and awareness of this possible life threatening complication of phenytoin is essential, as it is commonly used in treatment of epilepsy.

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