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PHENYTOIN INDUCED ACUTE GENERALISED ERYTHEMATOUS PUSTULOSIS: A CASE REPORT

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ABSTRACT
Drug induced hypersensitivity reactions can be potentially life threatening. Some antiepileptics like phenytoin, carbamazepine, phenobarbitone cause these reactions. Here, we report a case of a 53 year old woman taking Tab. Phenytoin post stroke developed a severe cutaneous hypersensitivity reaction, which was diagnosed as acute generalised erythematous pustulosis. Phenytoin is the most commonly prescribed antiepileptic drug, it has a narrow therapeutic index, so physicians should be aware of its adverse reactions.

KEYWORDS: Phenytoin, generalised erythematous pustulosis, hypersensitive reactions.

INTRODUCTION
Phenytoin was synthesized in 1908 in search of sedative-hypnotic but lacked sedation. Later introduced in 1938, as an anticonvulsant for the treatment of epilepsy, generalised tonic-clonic seizures and complex partial seizures. It is the most effective and widely prescribed drug due to its low cost and easy availability.[1] Phenytoin is a hydantoin derivative that acts by limiting the repetitive firing of excitatory neurons and slowing the rate of recovery of voltage dependent membrane sodium channels, hence preventing the spread of seizure focal point.[2] Adverse reactions in patients receiving anti-epileptics is very common, most of which are acute and related to pharmacological properties, but in 3-10% patients, reactions are unpredictable ranging from mild maculopapular eruptions to severe life threatening cutaneous reactions like Steven johnson syndrome (SJS), Toxic epidermal necrolysis (TEN).[3] Acute generalised erythematous pustulosis (AEGP) is one such severe cutaneous adverse reaction characterised by acute onset of non follicular, sterile pustules on an erythematous skin occurring all over the body.[4] It is a rare condition with estimated occurrence of 1 to 5 patients per million per year.[5] Here, we report a case of Phenytoin induced acute generalised erythematous pustulosis to sensitise and caution the prescribers of this serious adverse effect.

CASE REPORT
A 53 year old woman, known case of Cerebro-vascular disorder (CVD) for 4 yrs, was brought to the hospital, diagnosed and treated for stroke. On discharge she was put on Tab. Phenytoin 100 mg BD which she took for a period of 1 month. After a month of medication she developed painful red flat lesions in the oral cavity, an insidious onset initially started on the left side and later involved the right side and the roof of the oral cavity. The pain aggravated on consuming food with no relieving factors. The patient also presented with red raised lesions over face, neck, trunk and excessive watering of eyes. Later erythematous maculopapular rash were noted on neck, trunk and both the hands. There was no history of insect bite or viral exanthema. The patient had no past or family history of allergy, drug allergy or dermatological disease. Patient has a past medical history of diabetes for 8 yrs, hypertension and CVD for 4 yrs and was on medications.

A detailed history was taken, and on clinical examination the patient was highly anxious. The vital parameters were as follows: Blood pressure 120/70 mm of Hg, pulse rate: 80/ min, respiratory rate: 14/ min. Face showed erythematous and edematous plaque over both molar areas with infralabial edema. Oral cavity shows erythematous hard palate and buccal mucosa with whitish membrane on few areas and erosion over dorsal aspect of tongue “Fig. 1”. Blanchable erythematous maculopapular rash were noted on neck, anterior chest wall and posterior aspect of trunk. The rashes were also seen on both upper limbs involving mainly extensor region, palmar and dorsal aspect of hands and on the

lower limbs "Fig. 2". Patient consulted a dermatologist, all the routine and complete blood investigations like CBC, LFT, RFT, serum electrolytes, random blood sugar were done. Phenytoin was immediately stopped and the patient was treated with Inj. Dexamethasone 6 mg (1.5 cc) IV and Inj. Pantoprazole 40 mg IV after and before meals respectively, Tab. Cetrizine 10 mg, and topical calamine lotion was applied all over the affected areas for 3 days. Serum electrolytes, liver and renal function tests showed values within normal limits, but blood sugar level was elevated and peripheral smear examination showed microcytic hypochromic anaemia.

The treatment showed improvement as the maculopapular rashes disappeared gradually and the patient recovered in 8 days with no further complications. Phenytoin was replaced with Tab. Levetiracetam 500 mg BD and was discharged with Cap. Vit D3 60,000 IU/ weekly for 2 months.

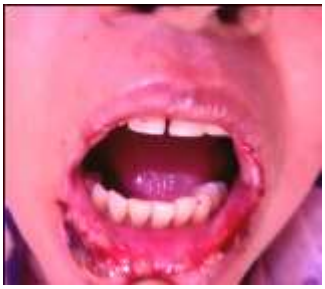

Fig. 1: Showing Erythematous Reaction In Oral Cavity.

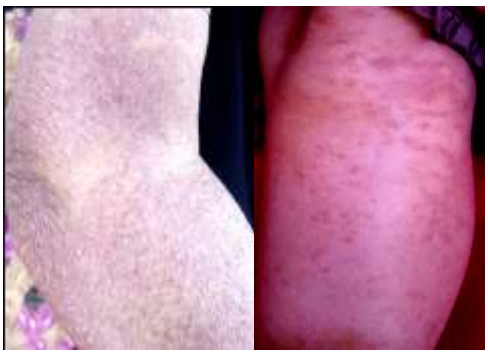

Fig. 2: showing rash on upper and lower limb.

DISCUSSION

Phenytoin, a first generation antiepileptic, used to treat seizures but has a very narrow therapeutic range of 10-20 mcg/mL. Below plasma concentration of 10 mcg/ml it follows first order kinetics. But above 10 mcg/ml, its metabolic pathway saturates and elimination shifts to zero order kinetics.[1] There is a constant phenytoin metabolism and even small increase in dose causes disproportionate increase in concentration and toxicity may be precipitated. Owing to its narrow therapeutic index, drug interactions are also common it is metabolised by hepatic enzyme cytochrome p450 by isoenzymes CYP2C9 and CYP2C19.[6] Drugs that induce or inhibit these enzymes affect phenytoin metabolism and may cause toxicity. The toxicity of phenytoin is primarily on nervous system followed by cardiotoxicity.[2] The dermatological manifestation in this patient may be attributed to hypersensitivity to Phenytoin or due to toxicity.[7]

In the present case report, a systematic approach was used to know whether the suspected adverse drug reaction was due to phenytoin or a result of any other factors. To determine the causal relationship between acute generalised erythematous pustulosis and treatment with phenytoin, Naranjo adverse drug reaction probability scale was used. Adverse drug reaction developed within a month of starting treatment and improved within 3 days of discontinuation of drug. The patient was treated with IV Dexamethasone, she recovered completely in a period of 8 days. Other differential diagnosis was ruled out. Rechallenge of the drug was not done due to ethical issues but phenytoin was replaced by Tab. Levetiracetam. Using the Naranjo scale, the score was 5, hence it is considered that the rash was probably caused by phenytoin.[8] Modified Hartwig and Siegel scale scored a severity of level 5, since the patient suffered severe reaction and was the reason for hospitalisation for 8 days including intensive medical care. The world health organisation-Uppsala monitoring centre causality assessment criteria also indicated a probable relation.

This case highlights the severity of the hypersensitivity reaction due to narrow therapeutic index of phenytoin and cutaneous manifestations can be most severe type of drug induced reactions. Regular follow up and monitoring serum phenytoin levels are to be done and the physicians should be aware about these serious reactions. The consumers should be educated to report immediately if any adverse effects, so that early diagnosis and prompt treatment of such life threatening conditions can be done.

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REFERENCE

1. Vineetha Bharathan Menon, Justin Kurian, Krishna Undela, Madhan Ramesh, Hathur Basavana Gowdappa. Phenytoin toxicity: A case report. Journal of Young Pharmacists, 2015; 7(3): 272.
2. Yaari Y, Selzer ME, Pincus JH. Phenytoin: mechanisms of its anticonvulsant action. Ann Neurol, 1986 Aug; 20(2): 171-84.
3. Park CS, Kang DY, Kang MG, Kim S, Ye YM, Kim SH et al. Korean Registry of Severe Cutaneous Adverse Reactions Consortium. Severe cutaneous adverse reactions to antiepileptic drugs: A

Nationwide Registry-Based Study in Korea. Allergy Asthma Immunol Res, 2019 Sep; 11(5): 709-722.
4. Feldmeyer L, Heidemeyer K, Yawalkar N. Acute Generalized Exanthematous Pustulosis: Pathogenesis, genetic background, clinical variants and therapy. Int J Mol Sci, 2016 Jul 27; 17(8): 1214.
5. De A, Das S, Sarda A, Pal D, Biswas P. Acute Generalised Exanthematous Pustulosis: An Update. Indian J Dermatol, 2018 Jan-Feb; 63(1): 22-29. doi: 10.4103/ijd.IJD_581_17. PMID: 29527022; PMCID: PMC5838751.
6. Watters M, Wilson H, Everitt P. Phenytoin-induced hypothermia. BMJ Case Rep, 2019 Jan 22; 12(1): e227443.
7. Indu TH, Basutkar RS. Hypersensitivity reaction associated with Phenytoin. J Basic Clin Pharm, 2015 Sept; 6(4): 119-21.
8. Naranjo CA, Busto U, Seller EM, Sandor P, Ruiz 1, Roberts EA et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther, 1981; 30: 239-45.