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Case Report

PHENYTOIN-INDUCED ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS

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ABSTRACT

Phenytoin is the first line antiepileptic for generalized tonic-clonic seizures. It is still the "go to" drug despite the availability of newer anti-epileptics, chiefly because of its low cost and high efficacy. Phenytoin is associated with toxicities involving multiple organ systems such as brain, blood, and skin. One of the most common adverse effects is the development of skin rashes. It can range from mild to life-threatening skin eruptions. This is a case report of a young girl who developed acute generalized exanthematous pustulosis following phenytoin therapy for post-traumatic seizures.

Keywords: Drug-induced rash, Anti-epileptic, Type-4 hypersensitivity, Hydantoin

INTRODUCTION

Phenytoin is commonly prescribed first line agent for epilepsy. Though newer drugs are available, owing to its high efficacy and low cost, phenytoin is still popular among clinicians. However, it comes at a price, as it can be toxic to multiple systems in the body (such as skin, brain, and blood). Phenytoin causing skin rash is not uncommon. The spectrum may range from mild rash to severe life-threatening conditions like Stevens–Johnson syndrome [1].

Unlike toxic epidermal necrolysis (TEN) and Stevens–Johnson syndrome (SJS) which are well-known entities, acute generalized exanthematous pustulosis (AGEN) is a less-known drug-induced skin reaction. AGEN is characterized by multiple sterile pinhead-sized pustules, which are self-limiting in nature. It is also known as pustular psoriasiform eruption, pustular drug rash, and toxic pustuloderma. It is mostly drug-induced, the usual suspects being macrolides, quinolones, and aminopenicillins. However, it may also be due to other causes like spider bites, infections, etc. [2].

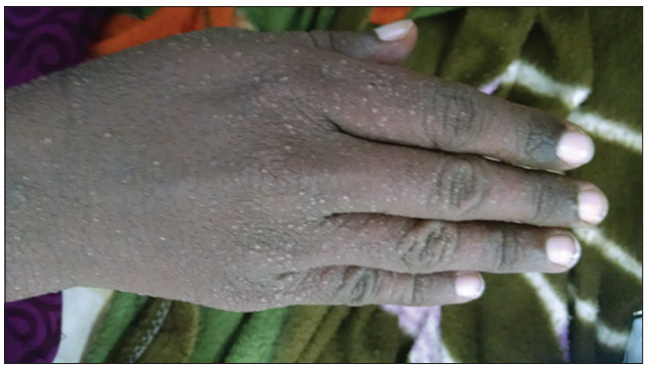
Given below is a case report of phenytoin-induced AGEN.

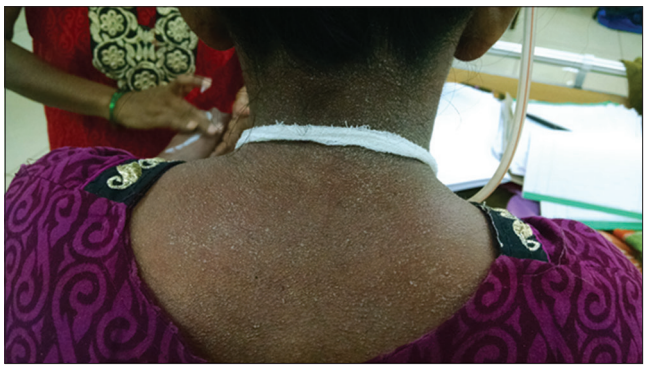
CASE REPORT

A 22-year-old girl met with a road traffic accident in March 2015. Following this, she had on/off a headache for a period of 6-month. On the 4th of September, she had an episode of seizure, for which she was taken to a local hospital, treated for the same and sent home the same day. 2 days later, she had another episode of seizure, for which she was admitted. A magnetic resonance imaging (MRI) scan of the brain was normal, but cerebrospinal fluid analysis showed an increased level of white blood cells with lymphocytic predominance. The girl was admitted in our hospital a week later. On admission, she was febrile and tachycardic. Muscle power was 3/5 in all the limbs, with hypotonia and bilateral extensor plantar reflex. A diagnosis of meningoencephalitis with post-traumatic seizures was made.

The patient was started on intravenous (IV) levetiracetam 1 g twice a day, IV phenytoin 100 mg thrice daily, IV sodium valproate 500 mg twice daily, IV ceftriaxone 2 g twice a day, IV acyclovir 500 mg thrice a day and IV metronidazole 500 mg twice daily. Her GCS dropped 2 days later, and she was intubated and started on artificial ventilation. Her seizures were under control with the triple anti-epileptic cover that was being given. A week later, metronidazole was stopped, and ceftriaxone was replaced by meropenem. All antibiotics and antivirals were stopped on the 4th of October. Her anti-epileptics were continued (phenytoin and valproate were switched from injections to tablets). The patient was shifted toward after another week.

On the 17th of October, the patient complained of generalized pruritis, which settled down on administering IV pheniramine maleate. The next day, she developed erythema over her neck, trunk, and extremities. On the subsequent day, pustules were seen over her extremities, trunk, back and neck (Figs. 1 and 2).





Both valproate and phenytoin were withheld, and a dermatologist's opinion was sought. The dermatologist diagnosed the skin lesion as AGEN. Further, he advised the treating clinician to stop phenytoin and to continue valproate. He also advised topical therapy with clobetasole cream, moisturizing lotion and ketoconazole soap.

Based on Naranjo's algorithm for causality assessment, the adverse drug reaction fell into the "possible" category.

DISCUSSION

AGEN is the most common encountered with the use of antibiotic medication, as is the case in SJS/TEN as well. While anti-epileptics are usual suspects in the etiology of the latter, they are not frequently listed as the causative agents for the former [2]. However, there are rare instances wherein there is an overlap between the features of SJS/TEN and those of AGEN, which may interfere in the diagnosis and management [3]. Most of the case reports available are secondary to the administration of antibiotics, although other drugs like anti-epileptics (as in the present case), paracetamol and diltiazem have also been cited as culprits [4].

Another important differential diagnosis is pustular psoriasis, which may present in a similar fashion. The absence of a clear drug history, more generalized rashes, a longer course of illness and the classical absence of self-limiting nature are chief features of pustular psoriasis [5].

The general consensus on the management of AGEN is immediate discontinuation of the suspected drug. A specific management may not be essential as AGEN is a self-limited condition. Corticosteroids and antihistaminics may be given if the condition is severe. Topical therapy with moisturizers is also advised for symptomatic relief [5].

CONCLUSION

To conclude, AGEN is a self-limiting condition and does not usually cause significant morbidity and mortality, as seen in the case of SJS/TEN syndromes. However, cautious history elicitation and drug patch testing may help in avoiding the development of AGEN, thus preventing unnecessary hospital stay and cost on the patient's side. Since antibiotics are the most frequently implicated drugs, extreme caution is to be exerted before and during the administration of the same.

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