International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 804-806 www.ijprajournal.com ISSN: 2456-4494

# Phenytoin Induced Exfoliative Dermatitis: Adverse Drug Reaction (Adr): Case Report

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Date of Submission: 01-12-2024 Date of Acceptance: 10-12-2024

**ABSTRACT**
Phenytoin-induced exfoliative dermatitis, a severe adverse reaction to the antiepileptic medication phenytoin, poses significant clinical challenges. This rare but serious condition, encompassing Stevens - Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) in its severe forms, is characterized by widespread skin inflammation, blistering, and epidermal detachment. The exact mechanisms triggering phenytoin-induced exfoliative dermatitis involve a complex interplay of immune-mediated responses and genetic predispositions. Phenytoin can induce a hypersensitivity reaction, leading to the release of inflammatory mediators and subsequent activation of immune cells in the skin. This cascade of events results in erythema, blistering, and exfoliation of the epidermis. Early recognition and prompt discontinuation of phenytoin therapy are essential to prevent disease progression and reduce the risk of complications. Management strategies often require a multidisciplinary approach, focusing on supportive care, symptomatic relief, and close monitoring. Topical and systemic therapies, such as corticosteroids and immunosuppressant, may be employed in severe cases to alleviate symptoms and attenuate inflammation.

**KEYWORDS:** SJS, TEN, CVA, Lymphoma.

## I. INTRODUCTION

Phenytoin-induced exfoliative dermatitis, also known as Stevens-Johnson syndrome (SJS) or Toxic Epidermal Necrolysis (TEN) when severe is a rare but severe adverse reaction to the antiepileptic medication phenytoin. The exact mechanism involves a complex interplay of immune-mediated and genetic factors.

Phenytoin is known to induce a hypersensitivity reaction in susceptible individuals. This hypersensitivity reaction can lead to a cascade of inflammatory responses in the body, including the skin. The process likely involves activation of the immune system and the release of inflammatory mediators, such as cytokines and chemokines. These inflammatory molecules can attract immune cells to the skin and promote inflammation, leading to the characteristic erythema (redness), blistering, and peeling seen in exfoliative dermatitis.

Furthermore, phenytoin may directly affect keratinocytes, which are the predominant cell type in the epidermis (the outer layer of the skin). Phenytoin can alter the function of keratinocytes, potentially leading to cell death and detachment from the skin surface. This disruption of the epidermal barrier can contribute to the development of blistering and skin detachments seen in exfoliate dermatitis.

Genetic factors may also play a role in the development of phenytoin-induced exfoliate dermatitis. Certain genetic variations can predispose individuals to hypersensitivity reactions to specific medications, including phenytoin. These genetic predispositions may affect the way the immune system responds to phenytoin or how keratinocytes interact with the medication, increasing the risk of developing exfoliate dermatitis.

## PHENYTOIN

Phenytoin, a widely used antiepileptic medication, belongs to a class of drugs known as hydantoins. It has been a mainstay in the treatment of various seizure disorders for over seven decades. Its efficacy in controlling seizures, particularly partial and tonic-clonic seizures, has made it one of the most prescribed antiepileptic drugs worldwide. Additionally, phenytoin has been utilized in the management of certain cardiac arrhythmias and neuropathic pain syndromes.

The primary mechanism of action of phenytoin involves the modulation of voltage-gated sodium channels in neurons. By selectively blocking these channels, phenytoin reduces the influx of sodium ions into neurons during

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Volume 9, Issue 6 Nov - Dec 2024, pp: 804-806 www.ijprajournal.com ISSN: 2456-4494

depolarization, thereby stabilizing the neuronal membrane and inhibiting the generation and spread of epileptic discharges. This mechanism is thought to underlie its anticonvulsant properties.

One notable characteristic of phenytoin is its narrow therapeutic index, meaning that the difference between therapeutic and toxic doses is relatively small. Therefore, careful monitoring of plasma drug levels is essential to optimize therapeutic outcomes while minimizing the risk of adverse effects. Therapeutic drug monitoring allows healthcare providers to adjust the dosage to maintain plasma concentrations within the therapeutic range (10-20 mcg/mL for total phenytoin levels).

Despite its efficacy, phenytoin is associated with a range of adverse effects, some of which can be serious. Common side effects include dose-related effects such as nystagmus, ataxia, and diplopia, which are often reversible with dose reduction. Gingival hyperplasia, a non-dose-related adverse effect characterized by overgrowth of the gums, is also frequently observed with long-term phenytoin therapy. Other adverse effects include sedation, cognitive impairment, and skin rashes.

One of the most concerning adverse reactions associated with phenytoin is hypersensitivity reactions, including Stevens - Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), which can be life-threatening. These reactions are characterized by severe skin rashes, blistering, and mucosal involvement and require immediate discontinuation of phenytoin therapy.

## EXFOLIATIVE DERMATITIS

Exfoliative dermatitis, also known as erythroderma, is a rare but severe inflammatory skin condition characterized by widespread redness, scaling, and shedding of the skin's outermost layer. The condition typically presents with intense redness covering large areas of the body, resembling severe sunburn. The affected skin becomes scaly and sheds in large flakes, often leading to significant discomfort and distress for the individual. Itching is a common symptom, and the skin may also become swollen, warm to the touch, and sensitive. In severe cases, the skin may be painful, and there may be cracks or open sores present due to excessive scratching or irritation. Exfoliate dermatitis can also cause changes in skin color, thickening of the skin, hair loss in affected areas, and nail abnormalities.

There are various underlying factors that can trigger exfoliative dermatitis, including skin disorders, drug reactions, infections, and systemic diseases. Skin disorders such as psoriasis, eczema, allergic contact dermatitis, and seborrheic dermatitis can lead to exfoliative dermatitis when they become severe or widespread. Certain medications, including antibiotics, anticonvulsants, chemotherapy drugs, and NSAIDs, can cause a severe allergic reaction leading to exfoliative dermatitis. Bacterial, viral, or fungal infections can also trigger erythroderma, as well as underlying systemic diseases like lymphoma, leukemia, or autoimmune disorders.

Skin biopsies, blood tests, and allergy tests may be conducted to rule out specific triggers or underlying conditions. Treatment of exfoliative dermatitis depends on addressing the underlying cause and managing symptoms to alleviate discomfort and prevent complications. Identifying and treating the underlying cause is paramount, whether it's discontinuing offending medications, treating infections, or managing underlying skin conditions. Symptomatic relief can be achieved with topical corticosteroids, antihistamines, and emollients to alleviate itching and inflammation. In severe cases, oral corticosteroids or immunosuppressant may be prescribed, and hospitalization may be necessary for intensive monitoring and supportive care.

## CASE PRESENTATION

A 70 year old female admitted to Dermatology ward of KGH hospital with chief complaint of itching, red raised lesions all over the body. 15 days back patient had loss of consciousness and had self-fall after which she was taken to hospital and was diagnosed as Stroke. She was further developed abnormal posturing and was diagnosed as Cerebral Vascular Accident CVA (Ischemic Stroke) with acute infarct in left thalamus midbrain with focal seizure. She was then treated with tablet Phenytoin 100 mg BD, tablet Clobazam 10 mg BD. 15 days later patient was developed red raised lesions and itching all over the body associated with scaling. She was then diagnosed as Drug induced Exfoliate dermatitis a suspected drug was Phenytoin. Subsequent to identifying ADR the patient was asked to stop Phenytoin and was replaced with Levetiracetam 500 mg twice a day and treated with tablet Azithromycin 500 mg, tablet Cetirizine 10 mg, tablet CPM 40mg, and tablet B complex/Calcium/IFA, Fusidicacid cream, Liquid

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paraffin for exfoliative dermatitis and other self-administrative drugs for stroke and seizures.

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