

# Divulge the Dual Challenge: A Case Report of Phenytoin Induced Dress Syndrome and Steroid-Induced Hyperglycaemia

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## ABSTRACT

Medication-induced skin and organ damage is an uncommon systemic reaction known as DRESS. This condition is caused by medication hypersensitivity and is linked to anticonvulsants, sulfur compounds, antidepressants, NSAIDs, and antibiotics it is tough to diagnose and cure, and reports of it are rare. The patient, a 35-year-old man, arrived at the hospital complaining of fever, lymphadenopathy, rashes, and itching. With history, the patient had neurosurgery done for a road accident in the parietal epidural Hematoma and started tablet phenytoin 100 mg 2 weeks before. The patient's clinical state was identified as phenytoin-induced DRESS syndrome based on the RegiSCAR scale, and the medicine responsible was withdrawn. Corticosteroids, antibiotics, and vitamin supplements were administered to the patient. On day 6, He developed hyperglycemia brought on by steroids; nevertheless, he was able to recover by taking a pill and a tapering dosage of injection methylprednisolone. Metformin 500 mg was provided, and the patient was discharged after symptoms gradually resolved. Early discovery and withdrawal of suspected medications are crucial for managing DRESS syndrome, which can be lethal.

**Keywords:** Phenytoin, DRESS syndrome, Methyl prednisolone, Hyperglycaemia.

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## INTRODUCTION

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is a rare adverse medication reaction that causes systemic consequences. This syndrome is characterized by drug-induced cutaneous issues and organ involvement. Bouquet gave the initial description of it in 1996.<sup>1</sup> Given that DRESS syndrome has a 10% death rate, its emergence is extremely concerning. With an incidence rate of one in 5,000 to 10,000 exposures, anti-epileptic drugs like phenytoin and phenobarbital are the main culprits

Drug-Induced Hypersensitivity Syndrome (DIHS) is another term for DRESS. There are two categories of drug hypersensitivity reactions: non-immediate and immediate.<sup>2</sup>

After taking the medication, immediate reactions show symptoms within six hours, but non-immediate reactions can take several days. The DRESS condition demonstrates a non-immediate reaction.<sup>3</sup> Early warning indications of DRESS include a high fever

of 38-40°C lasting a week or more and an increase in eosinophils to above 1,500 cells/mm<sup>3</sup>. These symptoms can last long after the suspected medicine has been discontinued. Misdiagnosis may occur due to myalgia, coughing, and swollen lymph nodes. It is worth mentioning that skin eruptions and fever occur in around 90% of DRESS cases.<sup>4</sup> Drug hypersensitivity can be produced by various circumstances, including insufficient detoxifying enzymes, viral reactivation, and genetic links to human leukocyte antigens. These reactions can lead to serious consequences, including cell death, inflammation, and subsequent immune responses.<sup>5</sup> Medications linked to DRESS include anticonvulsants, sulfa derivatives, antidepressants, non-steroidal anti-inflammatory medications, and antimicrobials. Corticosteroids are used to treat DRESS syndrome but can lead to hyperglycemia due to anti-inflammatory and immunosuppressive mechanisms.<sup>6</sup>

Glucocorticoids (GCs) can boost metabolism and glucose synthesis, resulting in insulin resistance akin to type 2 diabetes. The enzyme 11 $\beta$ -hydroxysteroid dehydrogenase can alter the effects of steroids, with type 1 amplifying and type 2 decreasing local action.<sup>7</sup> This case report discusses the diagnosis and management of phenytoin-induced DRESS in a patient who experienced hyperglycemia after corticosteroid treatment.



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## CASE DESCRIPTION

A 35-year-old male patient presented to the hospital with rashes and itching all over the body for the past week, aggravated by red rashes since yesterday, palpitation in the last hour before admission, and a history of lymphadenopathy (+) with cervical and abdominal pain. Previously, the patient had undergone neurosurgery due to a traffic accident in the area of apical epidural hematoma and began following Tab. Phenytoin 100 mg 2 weeks ago. The patient has been an alcoholic for 7 years and has been sober for 2 months. When examining the whole body, the patient was alert, extremely febrile, had a rash all over the body, and was oriented, and when examining the whole body, the vital signs were normal, but when examined locally, the rash was all over the body (Figure 1).

Laboratory investigation revealed an abnormal white blood cell count in the body at  $28.9 \times 10^3/\text{mm}^3$  (normal from 4.0 to 10.0 thousand/ $\text{mm}^3$ ), with 67.1% neutrophils, 8.0% lymphocytes, and 4.0% eosinophils.

The patient was also urged to seek a dermatological opinion. A generalized maculopapular rash was observed on the face, neck, belly, and back. Using RegiSCAR (the scale), the patient received a score of 4. The patient was diagnosed with phenytoin-induced DRESS syndrome.

Initially, the patient was recommended to discontinue phenytoin and replace it with Tablet vetiracetam 50 mg BD, an alternative anticonvulsant. The allergic reaction was treated with Injection. dexamethasone 8 mg IM BD, Injection methylprednisolone 500 mg, and Tablet. cetirizine 10 mg, as well as antibiotics such as Injection. cefotaxime 1G IV BD, Calamine Lotion L/B, and vitamins and mineral supplements.

The patient's symptoms gradually improve, but on day 6, the medicine methylprednisolone causes a rapid spike of CBG to 250 mg/dL, leading to a diagnosis of steroids-induced hyperglycemia. A dipping dose of methylprednisolone injection and Metformin 500 mg tablet were administered. On day 8, the patient's CBG levels decreased to 135 mg/dL (Figure 2). The patient was discharged on day 9 after gradually resolving all symptoms and reduction of rashes, following proper directions.

## DISCUSSION

Aromatic anticonvulsants such as phenytoin, carbamazepine, and phenobarbital are commonly associated with DRESS syndrome. The DRESS phenomenon occurs in about 1 in every 5,000 exposures to aromatic anticonvulsants.<sup>8</sup> Patrice Cacoub *et al.* analyzed PubMed-MEDLINE case reports from 1997-2009 and found 172 cases of DRESS syndrome linked to 44 medications. Anti-epileptic medications and allopurinol were found to be the

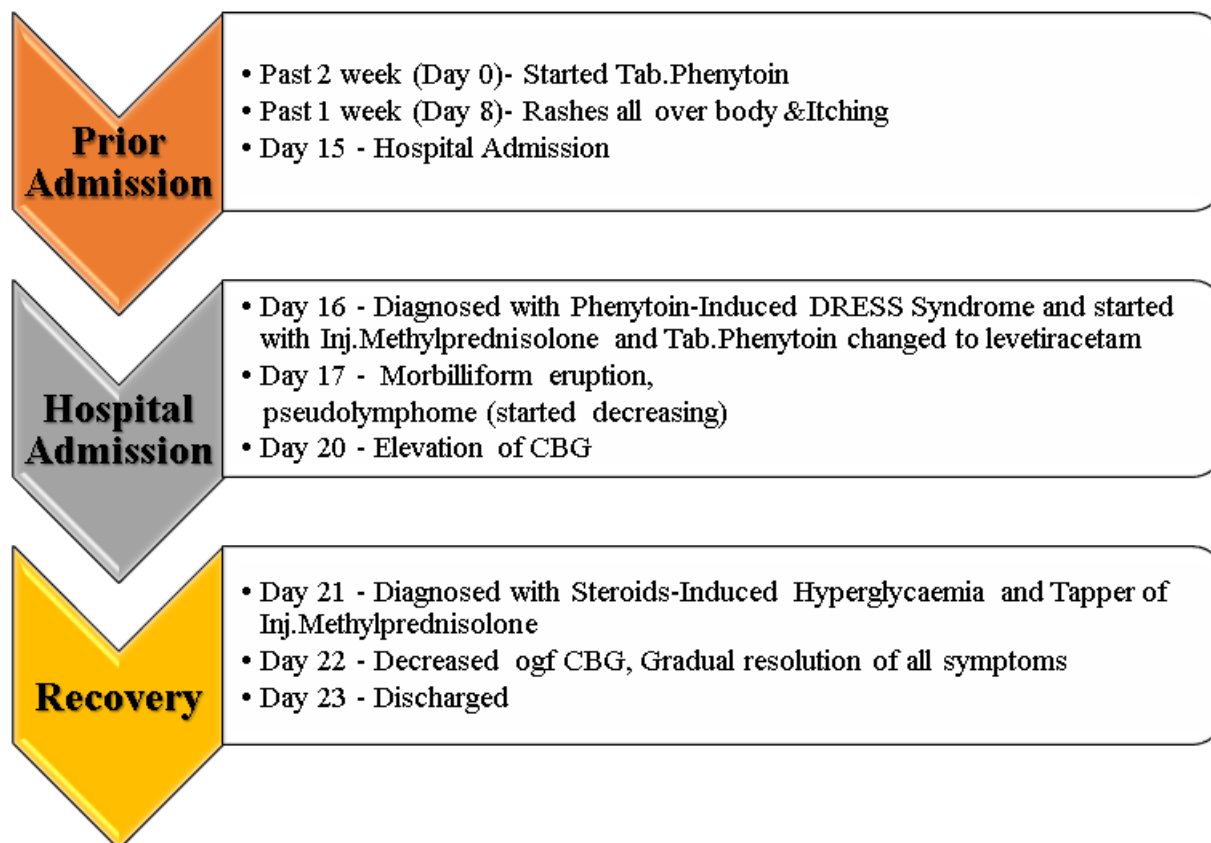
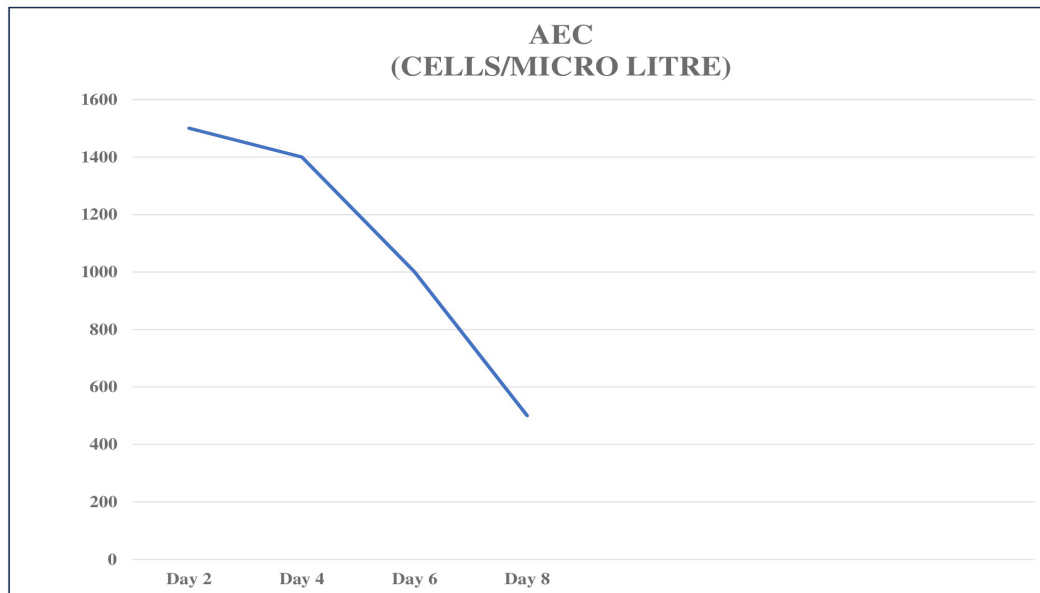


Figure 1: Flowchart of Patient History.



**Figure 2:** Graph of AEC levels (day by day).

most commonly related drugs in these situations.<sup>9</sup> Our case also includes phenytoin-related DRESS syndrome.

Phenytoin is frequently the first line of treatment for patients with seizure disorders. Anti-epileptic drugs can cause cutaneous eruptions such as maculopapular rashes, hypersensitivity syndrome, psoriatic dermatitis, and rare severe reactions like Steven Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme. In a 2007 survey by Chatterjee *et al.*, urticaria and fixed drug rashes were the most prevalent reaction types, with carbamazepine (16.23%), phenytoin (15.15%), and cotrimoxazole (13.53%) being the most often contributing medicines.<sup>10</sup> Haematological abnormalities like eosinophilia or atypical lymphocytes may indicate DRESS syndrome in this case.

The RegiSCAR scoring system is a revolutionary technique for evaluating DRESS syndrome that has been created and used.<sup>11</sup> Bocquet *et al.*'s 1996 diagnostic criteria for DRESS syndrome state that three symptoms must be present simultaneously. Symptoms may include drug-induced skin eruption, eosinophilia of 1500/mm<sup>3</sup>, and systemic abnormalities such as lymphadenopathy, hepatitis (transaminases >2 ULN), interstitial nephropathy, interstitial lung disease, or cardiac involvement.<sup>12</sup> The French Society of Dermatology recommends using systemic corticosteroids if serum transaminase levels are high or other organs are affected.<sup>13</sup>

Our case earned a RegiSCAR score of 4, indicating the possibility of DRESS syndrome.

To treat DRESS syndrome, we discontinued phenytoin and administered corticosteroids and antibiotics after meeting the RegiSCAR criteria. The patient's symptoms progressively

improved and they fully recovered. Despite the syndrome's recurrent relapses, none occurred. The Naranjo Adverse Drug Reaction Causality Assessment Scale gave a score of 7, indicating that phenytoin was the likely cause of DRESS syndrome in this patient.

## CONCLUSION

Consider DRESS syndrome for cutaneous eruptions and elevated eosinophil levels. There are numerous recorded cases of DRESS syndrome in both infants and adults, but the underlying mechanisms remain unclear. Patients experiencing skin eruptions, fever, eosinophilia, or liver and hematological issues should be investigated for the DRESS syndrome, a potentially lethal multi-system adverse drug event. Early detection and withdrawal of suspected medications are crucial for managing DRESS, as a delayed diagnosis can lead to death.

The use of supportive treatment and corticosteroids may avoid systemic symptoms. To maintain patient safety, follow recommendations and promptly report any adverse medication reactions.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**DRESS:** Drug Rash with Eosinophilia and Systemic Symptoms;  
**RegiSCAR:** International Registry of Severe Cutaneous Adverse Reactions; **DIHS:** Drug-Induced Hypersensitivity Syndrome.

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