*Ethiopian Medical Journal 2025, 63(11)*
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*ISSN 0014-1755 eISSN 2415-2420*
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## Case report

# Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome Following Phenytoin Use: A Case Report and Review

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Abstract

***Introduction:*** *Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a rare but life-threatening hypersensitivity reaction, often triggered by anticonvulsants such as phenytoin. This case report highlights the clinical presentation, diagnostic challenges, and management of a 37-year-old male who developed DRESS syndrome following phenytoin therapy for a seizure disorder.*

***Case Presentation:*** *A 37-year-old male with a recent history of phenytoin use presented at Lancet General Hospital with diffuse exfoliative dermatitis, systemic symptoms, and laboratory findings of eosinophilia (36%), elevated liver enzymes (ALT = 336, AST = 175), and mild renal impairment (Cr = 1.5). The patient was managed with intravenous dexamethasone and supportive care after withdrawing phenytoin which results in significant clinical improvement. However, complications such as pleural effusion and pneumonia arose while the patient was managed, necessitating additional interventions.*

***Discussion:*** *DRESS syndrome is a severe drug-induced reaction characterized by multisystem involvement, including skin, liver, and hematologic abnormalities. Early recognition and prompt withdrawal of the offending drug are critical to minimize morbidity and mortality. Corticosteroids remain the cornerstone of therapy, though secondary complications may delay recovery. This case underscores the importance of vigilance in patients on phenytoin and the need for multidisciplinary management.*

***Conclusion:*** *DRESS syndrome is a potentially fatal condition requiring immediate intervention. This report emphasizes the need for heightened awareness among clinicians, particularly in patients receiving high-risk medications like phenytoin. Early diagnosis, discontinuation of the causative drug, and corticosteroid therapy are pivotal for favorable outcomes.*

***Key Words:*** *DRESS syndrome, Phenytoin, Eosinophilia, Drug-induced hypersensitivity, Systemic symptoms*
***Citation :*** *Birhanu Y, Seife H, Demssis Y, et al. Drug Reaction with Eosinophilia and Systemic Symptoms ( DRESS) Syndrome Following Phenytoin Use: A Case Report and Review..Ethiop Med J 63 11*
***Submission date :*** *19 March 2025 Accepted: 28 May2025 Published: 30 June 2025*

## Background

DRESS syndrome is a severe and potentially fatal condition that is triggered by certain medications. The pathophysiology of DRESS is thought to involve an immune-mediated hypersensitivity reaction, often in genetically predisposed individuals(1). A hallmark feature of DRESS syndrome is the combination of skin involvement, eosinophilia, and systemic organ involvement (hepatic, renal, and pulmonary)(2).

The diagnosis of DRESS syndrome requires the presence of three essential components: a drug-induced skin eruption, eosinophilia (≥1500/mm³), and evidence of systemic organ involvement, which may include hepatitis (transaminases >2 times upper limit of normal), lymphadenopathy, interstitial nephropathy, interstitial lung disease, or myocardial involvement. Supportive laboratory findings typically demonstrate eosinophilia with atypical lymphocytosis, elevated liver enzymes, and possibly renal dysfunction(3). Additionally, thyroid function tests should be performed initially and repeated after 2-3

months, as hypothyroidism may develop as a late complication of the syndrome. These diagnostic criteria help distinguish DRESS from other severe cutaneous adverse drug reactions and guide appropriate clinical management(4).

Phenytoin, an anticonvulsant commonly used in the management of epilepsy, has been implicated in numerous cases of DRESS syndrome. The incidence of DRESS in patients using phenytoin is estimated to be rare but significant enough to warrant caution(5). The management of DRESS syndrome involves prompt identification and withdrawal of the causative drug, as well as the use of corticosteroids to control the systemic inflammation and prevent further organ damage(6).

In this case, our patient experienced a rapid improvement following discontinuation of phenytoin therapy and initiation of corticosteroids, which aligns with other reports in the literature where early intervention led to favorable outcomes. It is crucial to distinguish DRESS from other dermatologic and systemic conditions, such as Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), as these require different management approaches(7). This work has been prepared in line with the SCARE guideline(8)

**Case Presentation**

A 37-year-old male, known epileptic patient for the past 3 month who lived in Debrebirhan, Ethiopia presented at Lancet General Hospital with diffuse exfoliation, redness, and swelling of the skin involving his body, including the soles, genitalia, and mouth, following one month history of taking phenytoin therapy for abnormal body movements. Otherwise the patient had no other associated symptoms. No family history of allergies or drug reactions. He reported not having an alcohol and smoking history. He has no known chronic medical illness.

Upon initial assessment, the patient appeared acutely sick looking, vital signs showed low grade fever and tachycardia of 128 beat/min. Physical examination revealed multiple fissures around the mouth. Auscultation of the chest detected bilateral basal crackles. Additionally, the patient exhibited bilateral non-pitting edema in the lower legs (Figures 1 and 2). Dermatological examination showed diffuse desquamation, erythema, and hyperkeratosis affecting 90% of the body surface area, without any skin breakdown (Figure 3). There was nothing to note on the rest of the examination

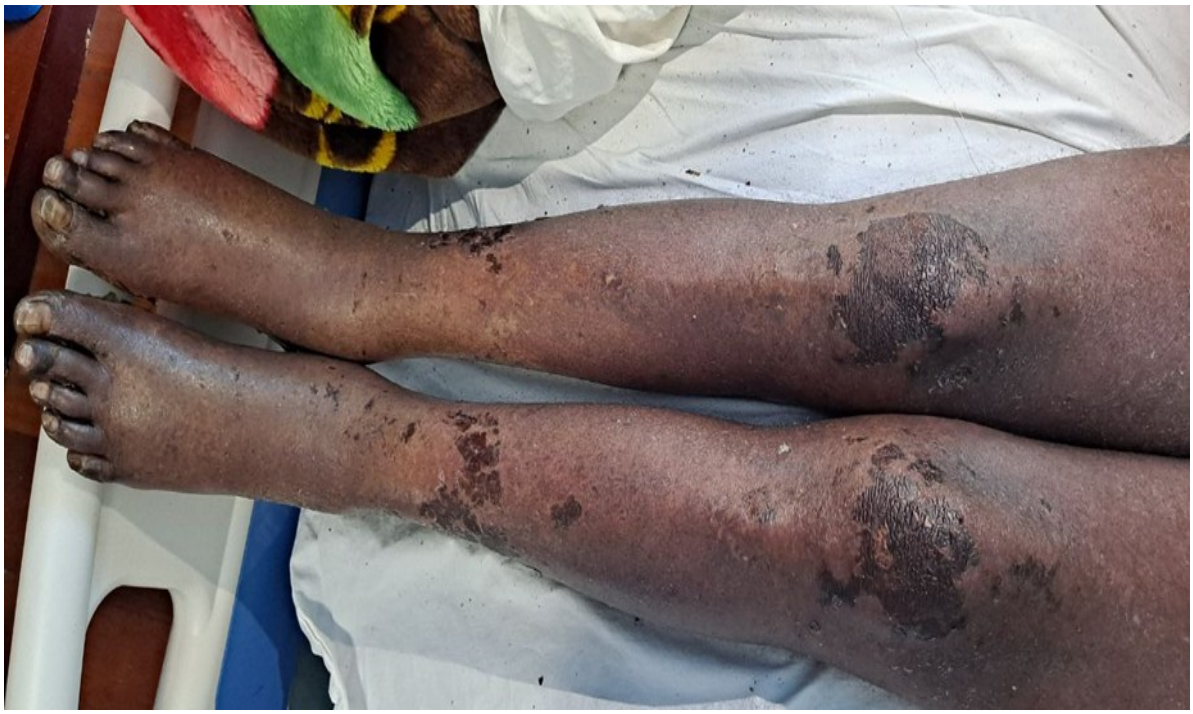


**Figure 1:** Exfoliative dermatitis and non-pitting edema over both lower limbs.

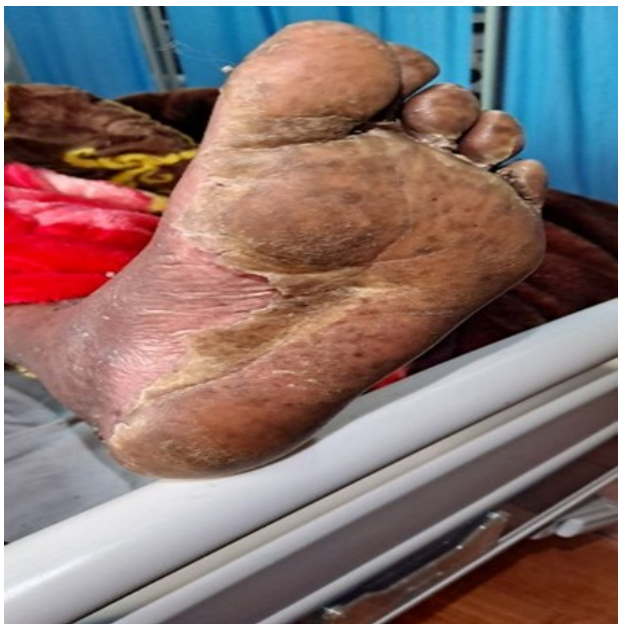
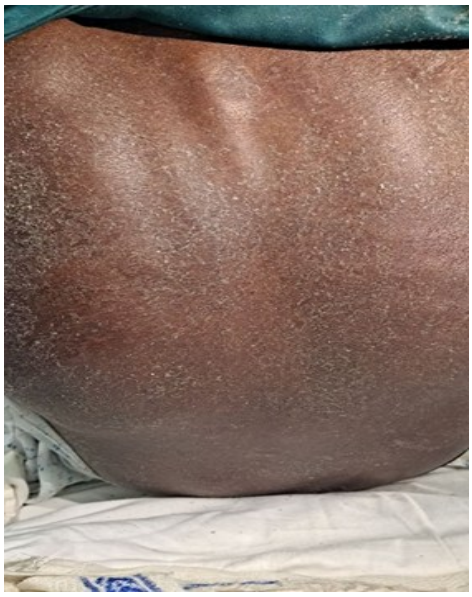


**Figure 2**: Exfoliative dermatitis over both lower limbs.



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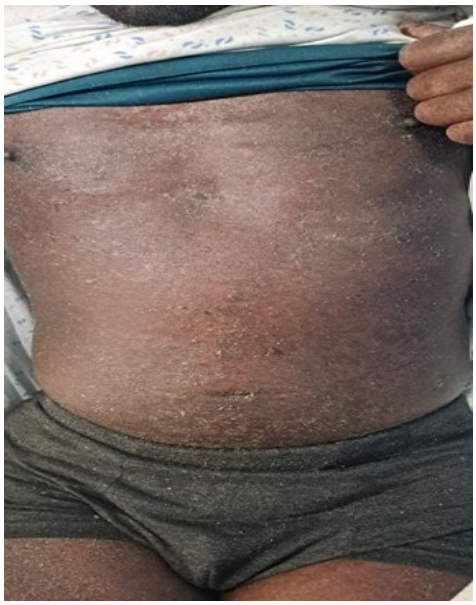

B

**Figure 3:** Multiple erythematous papule rashes over (a) back and, (b) trunk

Laboratory investigations showed a WBC count of 16 x $10^3$ and eosinophilia (36%), along with elevated liver enzymes (ALT = 336, AST = 175). Renal function was mildly impaired (Cr = 1.5), and an abdominal ultrasound revealed echogenic kidneys and a mildly thickened gallbladder, suggestive of hepatitis.

The patient was started on IV dexamethasone (12 mg daily), normal saline (1000 ml/day), and emollients (Vaseline with paraffin) applied every 2 hours. By day 2, liver enzymes improved (ALT = 278, AST = 141) with a decrease in eosinophil to 22%. By day 3, the patient showed further decre-

ment in liver enzymes (ALT = 190, AST = 59), reduced eosinophilia (2.3%), and overall improvement in the skin condition.

However, on day 5, the patient developed high-grade fever, tachypnea, and tachycardia. Chest X-ray revealed right-sided pleural effusion with consolidation. Laboratory tests showed improved liver function (ALT = 125, AST = 37) but hypoproteinemia (albumin = 1.8 g/dL), elevated gamma globulins, and mild eosinophilia (5%). Pleural fluid analysis confirmed a lymphocyte-predominant transudative fluid, consistent with reactive pleural effusion in response to pneumonia.

After receiving treatment for pneumonia, the patient showed improvement in both the pneumonia and DRESS syndrome. Consequently, he was discharged with an alternative anticonvulsant medication, ensuring that the drug responsible for the DRESS reaction was discontinued. Follow-up care was arranged to monitor for any potential recurrence of symptoms or adverse reactions, and the patient was advised to avoid the triggering drug in the future.

**Discussion**

DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) is a severe drug-induced hypersensitivity syndrome characterized by diffuse maculopapular rash, lymphadenopathy, multivisceral involvement, eosinophilia, and atypical lymphocytes with a mortality rate of 10–40%. DRESS is an uncommon severe adverse drug reaction.Although it is important to recognize the syndrome as early as possible to save the patients from unintended vulnerability, many clinicians fail to identify DRESS due to delayed onset of symptoms, involvement of one or multiple organs, and the clinical features overlapping with other severe cutaneous adverse reactions (SCARs)(9).

The actual incidence of DRESS is diverse, because it may vary depending on the type of medication and the immune status of each patient; also because many cases remain undiagnosed or untreated. In the general population, the estimated incidence is more than 1 case per 10 000 exposures to medications. Other data show an incidence of 0.9/100 000 inhabitants and 10 cases per million in the general population. In hospitalized patients, the incidence ranges from 2.18 to 40/100 000 inpatients(1).

At least 44 medications have been associated with DRESS. Those most frequently implicated are aromatic anticonvulsants (phenytoin, carbamazepine, and phenobarbital); sulfonamides; sulfones (dapsone); nonsteroidal anti-inflammatory drugs (piroxicam, ibuprofen, and diclofenac); beta-lactam antibiotics, vancomycin, allopurinol; minocycline and antiretroviral(1).

Our patient presented with diffuse exfoliation of the skin, redness, and swelling involving his body, including the soles, genitalia, and mouth, following one month of phenytoin therapy (100 mg PO BID) for abnormal body movements.

DRESS syndrome diagnosis includes the simultaneous presence of three conditions: Drug-induced skin eruption, Eosinophilia ≥ 1500/mm3 and At least one of the following systemic abnormalities, Lymphadenopathy, Hepatitis (transaminases >2 ULN), Interstitial nephropathy, Interstitial lung disease, Myocardial involvement. Also a laboratory data that include complete blood cell count that usually shows eosinophilia and mononucleosis like atypical lymphocytosis, liver function parameters, serum creatinine levels and urinalysis. Thyroid stimulating hormone levels should also be measured and repeated after 2–3 months as hypothyroidism can emerge as a late complication(10).

Our patient meets three key criteria: drug-induced skin eruption, increased eosinophilia, and hepatitis. Additionally, his white blood cell count was elevated at 16 x $10^3$, renal function showed mild impairment (Cr = 1.5), and an abdominal ultrasound indicated echogenic kidneys.

The gold standard therapy for DRESS involves the withdrawal of the culprit drug, supportive therapies, and administration of corticosteroids. However, in cases of primary treatment failure or suboptimal response, there arises an urgent need for alternative interventions immunosuppressive agents, intravenous immunoglobulin, plasmapheresis, biologics, and small molecule drugs(11).

Our patient received IV dexamethasone and emollients applied every 2 hours. On day 2, liver enzymes improved (ALT = 278, AST = 141) with a decrease in eosinophils to 22%. On day 3, the patient showed further improvement with normalized liver enzymes (ALT = 190, AST = 59), reduced eosinophilia (2.3%), and overall improvement in the skin condition.

The prognosis for DRESS syndrome suggests a mortality rate of approximately 3.8%. The primary causes of death are fulminant hepatitis and liver necrosis. Several factors have been associated with a poorer prognosis, including an eosinophil count greater than 6000 × $10^3$/μL, thrombocytopenia, pancytopenia, leukocytosis, and coagulopathy. Additionally, other critical factors that can affect prognosis include organ involvement, particularly renal or cardiac dysfunction, as well as the timing of intervention. Early recognition and prompt treatment are crucial in improving outcomes for patients with DRESS syndrome(1).

**Conclusion**
This case highlights the importance of recognizing DRESS syndrome, especially after phenytoin use, and underscores the need for early diagnosis and appropriate management, including systemic corticosteroids and supportive care. Additionally, the development of secondary complications like pleural effusion should be closely monitored, as they may complicate the clinical course.

**Acronyms**
ALT- Alanine aminotransferase
Cr- Creatinine
DRESS- Drug Reaction with Eosinophilia and Systemic Symptoms
SCARs- Severe Cutaneous Adverse Reactions
SJS- Stevens-Johnson Syndrome
TEN- Toxic Epidermal Necrolysis

**Ethical consideration**
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Avalablity of data and material**
Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

**Conflict of interest**
The authors declare that there is no conflict of interest regarding the publication of this article

**Funding**
No specific grant was obtained for this case report from any funding agency.

**Author's contribution**
Author[1] - Conceptualized the case report, contributed to the diagnosis and treatment information, and assisted in manuscript writing.

Author[2] - Supervised the study, provided mentorship, and approved the final manuscript for submission.
Author[3] - Primary doctor who treated the patient, revised manuscript.
Author[4] - Collected clinical data, drafted the manuscript, and revised it critically for intellectual content.
Author[5] - performed the literature review, and contributed to the discussion section.
All authors read and approved the final manuscript.

**Acknowledgement**
We would like to acknowledge the patient for providing us consent to share his history as a case report and Lancet general hospital for evaluating the case and giving us ethical clearance.

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