# A CASE REPORT OF DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) WITH SYSTEMIC INVOLVEMENT

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## Abstract:

### Background:

Drug Reaction with Eosinophilia and Systemic Symptom (DRESS) syndrome is an uncommon but severe idiosyncratic drug-induced hypersensitivity reaction, which is accompanied by fever, extensive cutaneous eruption, hematological abnormalities, such as eosinophilia and internal organ involvement, especially the liver. The syndrome develops normally 2-8 weeks following exposure to the offending drug and has high chances of morbidity and mortality unless early identified. Typical causative agents are: antiepileptic drugs, sulfonamides, antibiotics and allopurinol.

### Case Presentation:

We submit a case of a 19-year-old female that presented with a history of fever, chills, cough with post-tussive vomiting, abdominal pain, and facial rash. This patient has a history of seizure disorder that has been treated with levetiracetam during 6 years and recently started taking sulfasalazine to treat polyarthralgia. Lab-tests showed a significant eosinophilia (35 percent) and a rise in hepatic enzymes and AST (119 U/L) and ALT (190 U/L) and bilirubin levels, making it a hepatic-involvement. The patient was rated as a probable case of DRESS syndrome according to the clinical findings and laboratory parameters to be used in the RegiSCAR scoring system.

### Management and Outcome:

The potentially causing drug was immediately discontinued, and systemic corticosteroid therapy and supportive management were conducted. The patient experienced slow clinical recovery, fever resolving, stabilization of laboratory parameters, as well as gradual improvement of the skin lesions**.**

### Conclusion:

Early detection of the DRESS syndrome and early removal of the causative drug to avoid serious systemic complications are highlighted in this case. Clinicians are advised to have a high index of suspicion of DRESS syndrome in patients who present with the manifestation of rash, eosinophilia, and hepatic involvement following recent exposure to high-risk drugs like sulfasalazine and antiepileptic medications.

**Keywords:** Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, Sulfasalazine-induced hypersensitivity, Eosinophilia, Adverse drug reaction, Hepatic involvement, RegiSCAR scoring system

## Introduction

Drug reaction with eosinophilia and systemic symptoms, known by its acronym in English as DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms), is a serious adverse reaction induced by drugs with a late clinical presentation,[1] which usually begins with prodromal symptoms consisting of general malaise, pruritus, and fever (between 38 and 40 °C). Subsequently, it progresses to skin and systemic involvement with a morbilliform rash, diffuse scaling, facial edema, and erythroderma as well as lymphadenopathy, hematological abnormalities, and end organ damage (liver, kidney, heart, lungs, endocrine system, etc. [1]

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. A higher incidence of DRESS has been observed in the black population and in women.[7,10,11] Despite the treatment instituted, the mortality rate in DRESS can range from 3.8% to 10%. In one prospective multinational study, the mortality rate was 1.7%

## Causative agents

| Group | Drugs |
|---|---|
| **Antiepileptics** | Aromatic antiepileptic drugs (Carbamazepine, lamotrigine phenobarbital, phenytoine, oxcarbazepine) |
| **Antibiotics** | Amoxicillin, ampicillin, azithromycin, levofloxacin, minocycline, sulfamethoxazole- trimethoprim, vancomycin |
| **Antituberculosis agents** | Ethambutol, isoniazid, pyrazinamide, rifampin |
| **NSAIDS** | Aspirin, celecoxib, diclofenac, ibuprofen, piroxicam |
| **Others** | Allopurinol, amitriptyline, dapsone, hydroxychloroquine, imatinib, nevirapine, omeprazole, sulfasalazine |

[2]

## Case Report

The patient is a 19-year-old female who presented to the hospital with several complaints. The admission chief complaints were:

- Temperature of 3 days, chills and rigors.
- Cough 3 days, with post-tussive vomiting.
- Facial rash for 5 days
- Vomiting 3 days, about 10 bouts a day, coming right after eating or drinking, with food particles.
- Pain in the abdomen of 3 days, gradually increasing.

## Past Medical History

The patient was already diagnosed with having seizure disorder and had been taking medication within the last 6 years. She also had polyarthralgia (seronegative arthritis), which she was treated within the last one month.

Medication History

Medication history of the patient was:

- Tablet Levetiracetam (Levipil) 500 mg by mouth twice a day in 6 years.
- Tablet Hydrocortisone 100 mg 2 days.
- Tablet Sulfasalazine 500 mg 20 days.
- Tablet Sompraz (Esomeprazole) 40 mg.
- Tablet Levocetirizine 5mg on demand when symptoms got worse.

General Physical Examination

On examination, the patient was conscious and coherent

The following systemic signs were assessed

| **Parameter** | **Observation** |
|---|---|
| **Pallor** | Negative |
| **Icterus** | Negative |
| **Cyanosis** | Negative |
| **Clubbing** | Negative |
| **Lymphadenopathy** | Negative |
| **Edema** | Negative |

## Systemic Examination

Cardiovascular System (CVS)

- Heart sounds were normal
- No murmurs detected

Respiratory System (RS)

- Normal bilateral vesicular breath sounds (NVBS) are present.
- Bilateral air entry (AE).
- No crepitations

Per Abdomen (P/A)

- Abdomen soft and non-tender
- No organomegaly detected

Central Nervous System (CNS)

- None of the neurological deficit (NFND) foci.

- Glasgow Coma Scale (GCS): 15/15
- Pupils: bilaterally intact and responding to light (NARL).

### Laboratory Investigations

| Parameter | Result | Reference Range |
|---|---|---|
| Hemoglobin | 11.2 g/dL | 11.9 – 15 g/dL |
| Total WBC | 7.0 ×10³/µL | 4.0 – 11.0 |
| Neutrophils | 55% | 42 – 72% |
| Eosinophils | 35% | 25 – 45% |
| Monocytes | 2% | 1 – 4% |
| ESR | 15 mm/hr | 0 – 20 mm/hr |
| Total Bilirubin | 2.3 mg/dL | 0 – 2 mg/dL |
| Direct Bilirubin | 2.1 mg/dL | 0.05 – 0.20 mg/dL |
| AST (SGOT) | 119 U/L | <31 U/L |
| ALT (SGPT) | 190 U/L | <34 U/L |
| TSH | 0.06 µIU/mL | Normal range varies |

The high levels of liver enzymes and bilirubin indicated involvement of the liver, which is usually observed in Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome.

**RegiSCAR scoring for DRESS syndrome**

| Symptom | Status | Score |
|---|---|---|
| Fever (>38.5°C) | Present | 0 |
| Enlarged lymph nodes (>2 sites, >1 cm) | Present | +1 |
| Atypical lymphocytes | No/Unknown | 0 |
| Eosinophilia | Present | +1 |
| Skin rash (>50% body surface) | Present | +1 |
| Edema/Infiltration/Purpura/Scaling | Present | +1 |
| Skin biopsy suggesting DRESS | No | -1 |
| Internal organ involvement (>1 organ) | Present | +2 |
| Resolution >5 days | Present | 0 |

| Symptom | Status | Score |
|---|---|---|
| Alternative diagnosis excluded | Yes | +1 |

Total score -5

**Interpretation:**

- <2- excluded
- 2-3- possible
- 4-5- probable
- >6- Definite

Based on RegiSCAR scoring system, the patient was classified as a probable case of DRESS syndrome

## Diagnosis

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome was the diagnosis of the patient, based on the clinical presentation, laboratory results, and RegiSCAR criterion. The most likely perpetrator drugs are: Levetiracetam that was in use by the patient over the past 5 years due to seizure disorder. History Sulfasalazine initiated 20 days ago in polyarthralgia. Antiepileptic drugs as well as sulfonamide derivatives are common contributors of DRESS syndrome.

## Management

The first step taken in management was instant withdrawal of the suspected offending drugs, after which systemic corticosteroid treatment was done and supportive management.

Treatment given

- Injection Dexamethasone 200 mg IV once dailyInjection
- Pantoprazole 40 mg IV once daily
- Tablet Calcium + Vitamin D3 once daily
- Calamine lotion applied over skin lesions
- Clotrimazole cream applied over genital lesions
- Tablet Levipil 500 mg twice daily
- Syrup Cremaffin 15 mL at bedtime for constipation
- Tablet Bilastine 20 mg twice daily

Corticosteroid therapy and supportive care led to a positive outcome in the patient due to improvement in fever, normalization of vital signs, and gradual healing of skin lesions.

## Discussion

Drug Reaction with Eosinophilia and Systemic Symptom (DRESS) syndrome is a very uncommon but serious type of hypersensitivity of drugs that leads to fever, generalized skin eruptions, abnormal hematologic reactions that include eosinophilia, lymphadenopathy as well as organ system involvement, notably the liver. The syndrome is normally manifested 2-8 weeks after the exposure to the implicated drug, which complicates their diagnosis because of the late onset and non-homogenous clinical manifestation. Research of the RegiScAR registry characterizes DRESS as a multisystem adverse drug reaction, which commonly entails such characteristics as eosinophilia, visceral organ involvement, as well as protracted disease course. This is a serious complication that needs to be identified early as it can cause serious complications or even death when not dealt with early.[3]

Pathogenesis of DRESS syndrome is a complicated phenomenon, and includes immune dysregulation, genetic predisposition and a potential viral reactivation especially human herpesvirus-6 (HHV-6). Malfunctions in the metabolism of drugs can be followed by an increase in the levels of the active metabolites which in turn cause the activation of the strong T-cell based innate immune response which causes the systemic inflammation and eosinophilia. Moreover, the stimulation of cytokines and inflammatory factors also leads to tissue damage and dysfunction of the organs. This is due to the fact that these mechanisms give rise to the multisystem manifestations that are seen in the patients such as hepatic, renal, pulmonary and cardiac involvement.[4]

Diagnosis of DRESS syndrome is commonly determined based on the RegiScar scoring system that incorporates clinical and laboratory data including fever, lymphadenopathy, eosinophilia, the extent of rash as well as the involvement of internal organs. A score of 4-5 is probable case whereas above 6 is definite diagnosis. The most common drugs that are implicated include antiepileptic drugs, sulfonamides, allopurinol, and some antibiotics. The primary management includes early removal of the suspected drug and the administration of systemic corticosteroids in the situation with organ involvement that substantially enhances the patient outcomes and prevents the development of severe complications[5]

## Conclusion:

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a uncommon yet potentially fatal adverse drug reaction that is associated with cutaneous, hematological symptoms like eosinophilia, and multisystem organ dysfunction, specifically, liver dysfunction. In the case under discussion, a 19-year-old female presented herself with clinical manifestations such as fever, generalized rash, facial edema, and major liver enzyme increase after having been exposed to drugs of seizure disorder and polyarthralgia. The patient had been classified as a probable case of the DRESS syndrome according to the clinical manifestation, laboratory results, and the RegiSCAR scoring, with sulfasalazine as the most probable trigger drug. Timely recognition of the syndrome, immediate cessation of the offensive medication, and starting the use of systemic corticosteroids led to the achievement of a great clinical result and avoidance of further complications. The present case demonstrates the significance of screening patients put on high-risk medications with great caution and the necessity to identify the DRESS syndrome early and to treat it on time to decrease morbidity and mortality.

## ACKNOWLEDGEMENT

Not Applicable

## ABBREVIATIONS:

DRESS – Drug Reaction with Eosinophilia and Systemic Symptoms

NSAIDs – Non-Steroidal Anti-Inflammatory Drugs

CVS – Cardiovascular System

RS – Respiratory System

P/A – Per Abdomen

CNS – Central Nervous System

NFND – No Focal Neurological Deficit

GCS – Glasgow Coma Scale

NARL – Normal and Reacting to Light

WBC – White Blood Cells

AST (SGOT) – Aspartate Aminotransferase (Serum Glutamic Oxaloacetic Transaminase)

ALT (SGPT) – Alanine Aminotransferase (Serum Glutamic Pyruvic Transaminase)

TSH – Thyroid Stimulating Hormone

IV – Intravenous

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The authors declare there is no Conflict of Interest

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**CONTRIBUTIONS:**

The case report was prepared with full contributions from all authors

**ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

Not Applicable

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