



Drug reaction with Eosinophilia and Systemic Symptoms (DRESS Syndrome) manifesting with pseudolymphoma multisystemic organ involvement

Title	Drug reaction with Eosinophilia and Systemic Symptoms (DRESS Syndrome) manifesting with pseudolymphoma multisystemic organ involvement
Author(s)	Regan, Hilary;Sullivan, Gerard O.;Marren, Pauline
Publication Date	2026-01-15
Publisher	Wiley
Repository DOI	https://doi.org/10.1002/ccr3.71887

CASE REPORT OPEN ACCESS

Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS Syndrome) Manifesting With Pseudolymphoma Multisystemic Organ Involvement

Hilary Regan¹ | Gerard O. Sullivan² | Pauline Marren¹ ¹Department of Dermatology, Galway University Hospitals, Galway, Ireland | ²Department of Radiology, Galway University Hospitals, Galway, Ireland**Correspondence:** Pauline Marren (pamarren1@gmail.com)**Received:** 17 September 2025 | **Revised:** 12 December 2025 | **Accepted:** 26 December 2025**Keywords:** adverse drug reaction | DRESS | eosinophilia | pseudolymphoma

ABSTRACT

Drug reaction with Eosinophilia and Systemic Symptoms is a rare significant cutaneous adverse reaction with associated mortality. Extensive pseudolymphomatous multiorgan manifestations with prolonged latency from nonsteroidal anti-inflammatory exposure highlight the clinical spectrum and severity. Early recognition, timely intervention, prolonged treatment, and follow-up are essential.

1 | Introduction

Severe cutaneous adverse reactions (SCARs) are delayed heterogeneous hypersensitivity reactions triggered by drugs in the majority of cases. They present as emergencies on acute services. Manifestations of SCARs can include blistering, exfoliation, pustulation and mucosal involvement which usually alert the physician to scrutinize the drug history. The rash of DRESS is highly variable and can be non-specific in morphology raising a wider differential diagnostically. The prodromal phase of DRESS with fever, lymphadenopathy, malaise and arthralgia may also raise alternative diagnoses including lymphoma [1]. In a retrospective review of 26 cases of DRESS [2] all defined as probable or definite DRESS based on RegiSCAR validated criteria (Table 1), the initial diagnosis was presumed to be infective in 13/26 cases resulting in treatment with antibiotic therapy and delayed diagnosis. 7 patients were initially considered as possible lymphoma and only 6 were considered to be drug hypersensitivity. The drug latency period for DRESS from drug exposure to disease onset has a median (range latency) of 24.5 (1–160 days) and can frequently be overlooked as most drug induced rashes emerge within 1–3 weeks of initiation and drug history recordings tend to focus on new or recent drug initiation [3].

2 | Case History and Examination

A forty-seven-year-old Caucasian female presented with skin rash, fever, and flu-like symptoms. She had a fever of 38.9 and felt generally lethargic. She had generalized myalgia and arthralgia. Although non-specific in morphology, her rash was very extensive and maculopapular, with background confluent erythema affecting the entire trunk, upper limbs, and thighs (75% body surface area). There was no blistering or mucosal involvement. She had facial swelling with palpable bilateral parotid swelling and extensive palpable cervical lymphadenopathy (1 cm) and inguinal lymphadenopathy (1.5 cm).

3 | Differential Diagnosis Investigation and Treatment

Hematological profile showed a normal hemoglobin and a lymphopaenia 0.5 (1–3) and atypical lymphocytes were identified. She had prominent eosinophilia 1.67 (0–0.5). CRP was elevated at 94 (0–5) and ESR was elevated at 116 (0–12). LDH was elevated at 252 (135–214). Hepatic profile showed significant abnormalities with baseline ALP 155 (35–104), ALT

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2026 The Author(s). *Clinical Case Reports* published by John Wiley & Sons Ltd.

TABLE 1 | RegiSCAR DRESS validation score.

<i>Scoring criteria</i>	
1. Fever $\geq 38.5^{\circ}\text{C}$: Score 1	
Yes: 1 point	
No/Unknown: 0 points	
2. Enlarged Lymph Nodes: Score 1	
Yes: 1 point	
No/Unknown: 0 points	
3. Eosinophilia: (0–0.5) Score 2	
0.7–1.49 1 point	
≥ 1.5 : 2 points	
4. Atypical Lymphocytes: Score 1	
Present: 1 point	
No/Unknown: 0 points	
5. Skin Involvement: Score 1	
Suggestive rash: 1 point	
Rash covering $\geq 50\%$ BSA: 1 point	
Biopsy compatible with DRESS: 0 points	
6. Organ Involvement: Score 2	
1 organ: 1 point	
≥ 2 organs: 2 points	
7. Resolution Duration: Score 1	
≤ 15 days: Deduct 1 point	
> 15 days: 1 point	
8. Exclusion of Other Causes: Score 1	
Thorough investigation with no alternative cause found: 1 point	
<i>Final Score Interpretation: Total Score 10</i>	
< 2 points: No case	
2–3 points: Possible case	
4–5 points: Probable case	
> 5 points: Definite case	

81 (0–40), GGT 138 (6–42). Albumin levels were reduced 31 (39–51). Renal function showed elevated creatinine levels 122 (49–90) with normal urea, reduced sodium 126 (136–145), and reduced eGFR 45 (60–160). Hepatic virology screening was negative, as were PCR screening tests for EBV, CMV, Herpes, Mumps, Rubella, and HIV. Full autoimmune screening was negative.

Abdominal ultrasound confirmed prominent hepatosplenomegaly (14 cm spleen) (Figure 1) with prominent para-aortic and porta hepatic lymph nodes. Features were suggestive of lymphoma and she was scheduled for bone marrow and lymph node biopsy. CXR showed a lower lobe consolidation with pleural

effusion and atelectasis of the right horizontal fissure. Cardiac echo identified a pericardial effusion with normal ejection fraction (Figure 2).

The differential diagnosis initially considered was lymphoma or a severe viral exanthem.

4 | Outcome and Follow-Up

On dermatologist advice, an extended review of her drug history over the previous 4 months was undertaken which revealed exposure to diclofenac 100 mg twice weekly, and ibuprofen 600 mg 5 days a week intermittently over the previous 10 weeks for back pain. This drug history was considered highly relevant and when the validated RegiSCAR diagnostic criteria were scored (Table 1) [4] this patient scored 10 indicating a definitive DRESS diagnosis with evidence of extensive multi organ involvement. She was commenced on systemic steroids 0.5 mg/kg orally and an intensive topical therapy regime which included super potent topical steroids and emollients.

Within 72 h her fever resolved fully and her cervical and inguinal lymphadenopathy dramatically reduced to the extent that lymph node and bone marrow biopsy were deferred. Her skin rash improved and settled in 10 days. Her systemic symptoms gradually improved over the following weeks and months. Given the severity and extent of multiorgan involvement and given that DRESS has been reported to relapse and remit, she remained on a reducing steroid regime for 3 months. Regular monitoring during this time revealed that all abnormal blood parameters had gradually returned to normal values. Repeat CXR, cardiac echo and abdominal ultrasound were normal at 3 months and her steroids were stopped without relapse.

5 | Discussion

A clear drug trigger can be identified in approx. 80% of DRESS cases. Approximately 75% of cases are due to a small few high risk drugs including anticonvulsants (carbamazepine, phenytoin, and lamotrigine), allopurinol, and sulphonamide containing antibiotics, minocycline and Vancomycin and Dapsone [5] There are much fewer reports implicating drugs such as NSAID's, the likely trigger in this case and there are recent reports of DRESS associated with tyrosine kinase inhibitors, BRAF inhibitors, MEK inhibitors and Immunotherapy. With ever-expanding novel drug regimes and exposures, it is predictable that clinical presentations of DRESS will continue to present in multiple diverse clinical settings.

Pharmacogenetic studies have found an association between DRESS risk and several HLA haplotypes [6]. DRESS is a T-cell mediated immune response. The pathogenesis is not fully understood, but a drug specific immune response associated with explosive cytokine release and the possible reactivation of viruses from the Herpesviridae family e.g., HHV-6 most notably (16%–60% of cases) but also Epstein-Barr virus (EBV), and cytomegalovirus (CMV) are the suspected mechanisms.

Only 20% of DRESS patients have more than two organs involved and the condition has a reported mortality rate of up to

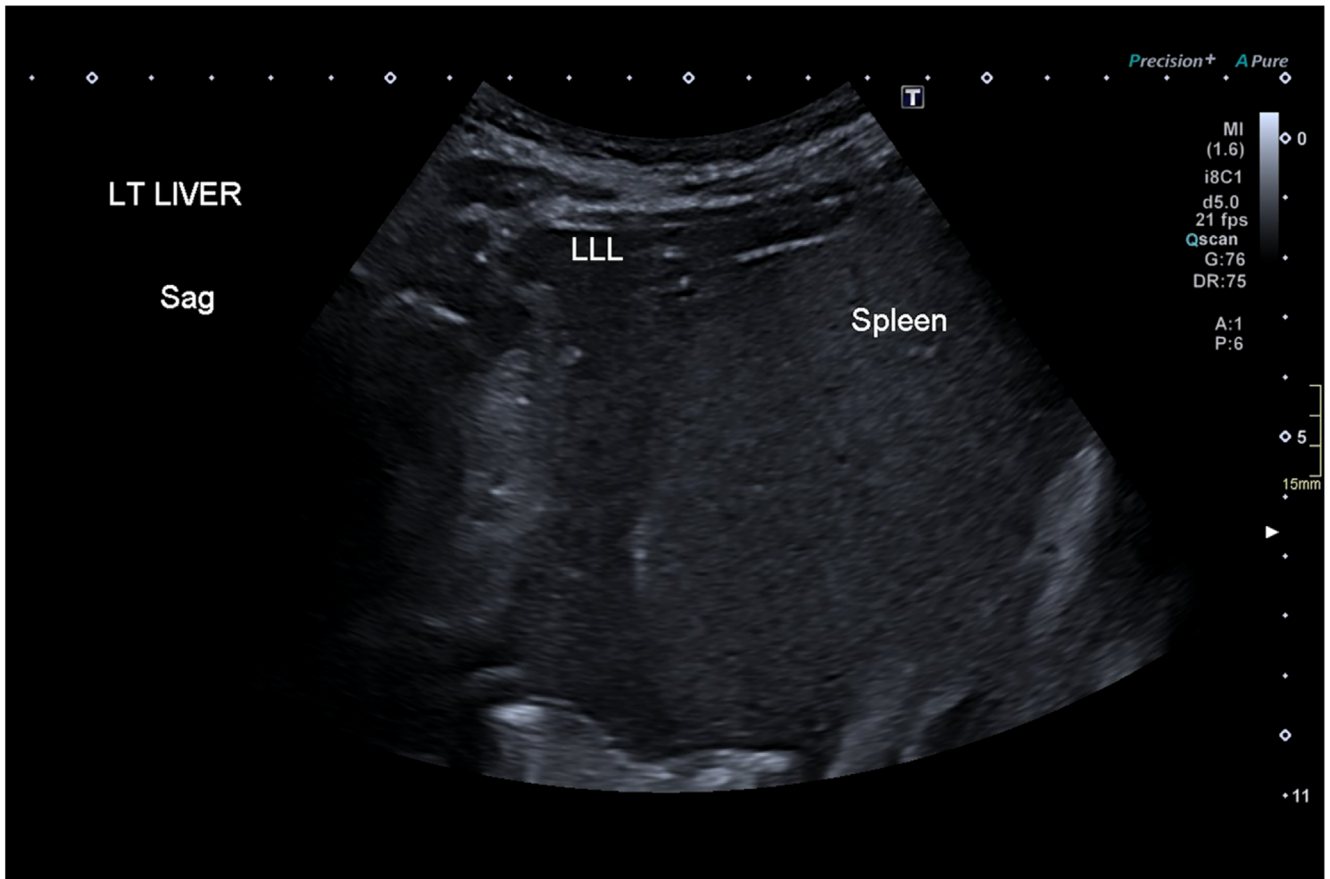


FIGURE 1 | Ultrasound abdomen illustrates splenomegaly (14cm) and prominent lymphadenopathy.

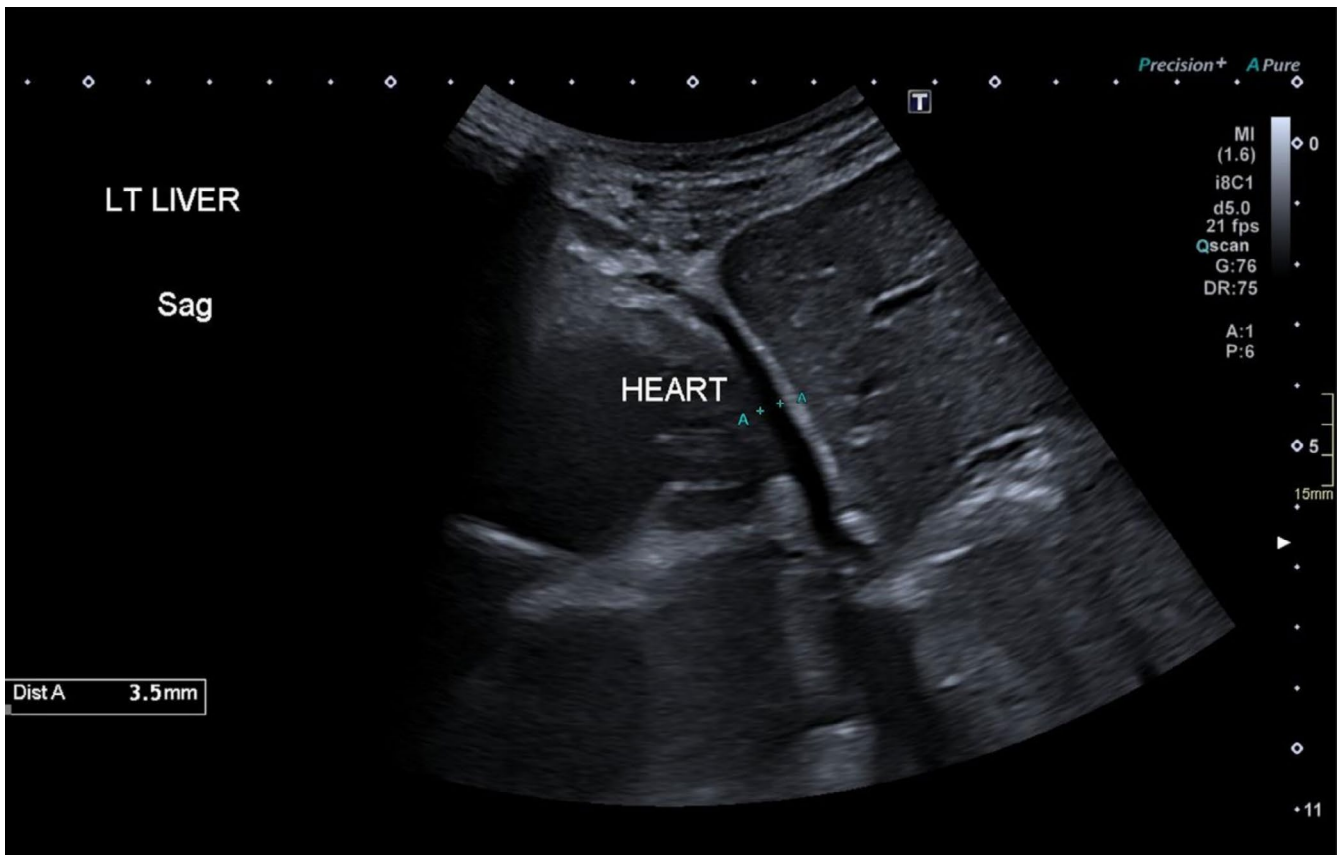


FIGURE 2 | Cardiac ultrasound illustrates pericardial effusion (3.5mm).

10% which rises when cardiac and renal involvement and advancing age are features. 11% of DRESS patients experience long term autoimmune sequelae thyroiditis, diabetes or chronic renal failure [7]. Early withdrawal of any drug trigger and prompt intervention with topical and systemic steroids is critically important. For corticosteroid refractory cases, A Delphi-based International Consensus group have published recommendations in 2024 based on the current limited published evidence [8] It agreed that Cyclosporine, anti IL-5, or anti IL-5R antibodies or Intravenous Immunoglobulin may be clinically helpful for these patients. Early Recognition and prompt intervention is vital and ultimately will help to distinguish DRESS from diseases that it can closely mimic most notably lymphoma. This will prevent diagnostic delay prior to appropriate intervention and will help avoid unnecessary investigations.

Prospective RegiScar Study,” *British Journal of Dermatology* 169 (2013): 1071–1080.

5. T. Tempark, P. Satapornpong, P. Rerknimitr, et al., “Dapsone Induced Severe Cutaneous Drug Reactions Are Strongly Linked With Allele HLA-B*13:01 in Thai Population,” *Pharmacogenetics and Genomics* 12 (2017): 429–437.

6. F. Miyagawa and H. Asada, “Current Perspective Regarding the Immunopathogenesis of Drug-Induced Hypersensitivity Syndrome / DRESS,” *International Journal of Molecular Sciences* 22 (2021): 2147.

7. “Long Term Sequelae of Drug Reaction With Eosinophilia and Systemic Symptoms –a Retrospective Cohort Study From Taiwan,” *Journal of the American Academy of Dermatology* 68 (2013): 459–465.

8. M. C. Bruggen, S. Walsh, M. M. Ameri, et al., “Management of Adult Patients With Drug Reaction With Eosinophilia and Systemic Symptoms,” *JAMA Dermatology* 160, no. 1 (2024): 37–44.

Author Contributions

Hilary Regan: data curation, writing – original draft, writing – review and editing. **Gerard O. Sullivan:** investigation, software. **Pauline Marren:** supervision, validation, writing – review and editing.

Funding

This work was supported by the College of Medicine, Nursing and Health Sciences, University of Galway.

Ethics Statement

Ethical Approval from our Hospital or University was not required for this submission.

Consent

Informed consent has been obtained from the patient according to the journal guidelines which includes consent for inclusion of clinical details and radiological images. Oral and written consent has been obtained.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

References

1. J. Mangana, E. Guenova, K. Kerl, et al., “Angioblastic T-Cell Lymphoma Mimicking Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS Syndrome),” *Case Reports in Dermatology* 9 (2017): 74–79.

2. H. Y. Lee, S. Walsh, and D. Creamer, “Initial Presentation of DRESS: Often Misdiagnosed as Infections,” *Archives of Dermatology* 148, no. 9 (2012): 1085–1087.

3. K. Kridin, M. C. Bruggen, S. Walsh, et al., “Management and Treatment Outcome of DRESS Patients in Europe: An International Multicentre Retrospective Study of 141 Cases,” *Journal of the European Academy of Dermatology and Venereology* 37 (2023): 753–762.

4. S. H. Kardaun, P. Sekula, L. Valeyrie-Allanore, et al., “Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS): An Original Multisystem Adverse Drug Reaction. Results From