International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Leflunomide-Induced DRESS Syndrome: A Case Report Highlighting the Diagnostic Role of Medication Labelling on Hospital Attire

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Received: 15-01-2026
Accepted: 30-01-2026
Available online: 19-02-2026

ABSTRACT

Introduction: Leflunomide, a cornerstone in rheumatoid arthritis management, carries a risk of severe cutaneous adverse reactions (SCARs) like Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). Diagnosis is often delayed by incomplete medication histories, directly impacting outcomes.
Case Presentation: A 60-year-old woman with recent leflunomide initiation presented with fever, a diffuse maculopapular rash, and profound eosinophilia (64.61%) consistent with DRESS. The causative agent was promptly identified from a label on her hospital gown, leading to immediate drug cessation. Management with systemic corticosteroids resulted in rapid clinical improvement and full recovery.
Conclusion: This case underscores the life-threatening potential of leflunomide-induced DRESS and demonstrates how a simple, low-cost safety practice, visible medication labelling on patient attire, can be a critical diagnostic tool, preventing therapeutic delay and advocating for its standardized use in inpatient care.

Keywords: *Leflunomide; Adverse Drug Reaction; DRESS Syndrome; Drug Safety; Medication Labelling; Patient Identification; Rheumatoid Arthritis.*

INTRODUCTION

The accurate and timely identification of a culprit drug in a severe adverse reaction is a critical, time-sensitive challenge in clinical medicine. For immunosuppressive agents like leflunomide, a mainstay in the treatment of rheumatoid arthritis and psoriatic arthritis, this challenge is compounded by the drug's distinctive pharmacokinetics. Leflunomide's active metabolite, teriflunomide, undergoes extensive enterohepatic recirculation, resulting in a prolonged half-life that can extend for weeks. This property not only underpins its once-daily dosing convenience but also creates a significant clinical vulnerability: a latent and persistent risk of toxicity even after the drug is stopped.

While leflunomide is valued for its efficacy, it carries a well-documented, albeit rare, potential for inducing severe cutaneous adverse reactions (SCARs). [1] [4] These life-threatening syndromes, including Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Stevens-Johnson Syndrome (SJS), and Toxic Epidermal Necrolysis (TEN), are characterized by widespread mucocutaneous detachment and multi-organ involvement. Mortality rates, particularly for TEN, remain distressingly high. [8] Survival hinges on the immediate cessation of the offending agent and the swift initiation of supportive and, where possible, disease-specific therapies. In this high-stakes scenario, any delay in pinpointing the causative drug directly worsens prognosis.

Diagnostic delay often stems from a simple, yet common, gap: an incomplete or inaccessible medication history. [3] [5] This is especially true for patients who present critically ill, confused, or without family or prior records immediately available.

The resulting diagnostic uncertainty can lead to dangerous therapeutic paralysis. This case report describes a patient presenting with a fulminant systemic and cutaneous reaction of unknown origin. The pivotal clue that unravelled the mystery was not found in an electronic database or a transferred chart, but on a simple, handwritten label affixed to the patient's hospital gown. We present this case to highlight the severe toxicity of leflunomide and, more importantly, to advocate for the undervalued yet potentially lifesaving practice of visible medication labelling as a fundamental safeguard in inpatient care.

CASE PRESENTATION

Patient Profile

A 60-year-old woman (initials K.K.) with a body weight of 60 kg presented to our institution in late December 2025. She had no significant past medical history, including no known drug allergies, and no pre-existing hepatic, renal, or cardiac conditions. The patient had been diagnosed with rheumatoid arthritis and was initiated on leflunomide 10 mg orally once daily on 27 November 2025. She developed initial symptoms of malaise and rash on 30 November 2025. Before admission to our centre, she had sought evaluation at another facility for progressive abdominal discomfort and rash; however, her symptoms persisted with inadequate therapeutic response, prompting her transfer to our hospital for further management.

Clinical Findings & Diagnostic Assessment

Upon admission, the patient was febrile (38.7°C) and exhibited a diffuse, maculopapular rash involving over 60% of her body surface area. Laboratory investigations revealed a striking eosinophilia of 64.6% (absolute eosinophil count 16.48 x10^9/L.), which, in conjunction with the acute onset of fever and rash following drug initiation, was highly suggestive of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome. Renal function and other haematological parameters were within normal limits. The reaction was classified as serious due to the requirement of hospitalization and the presence of significant systemic involvement.

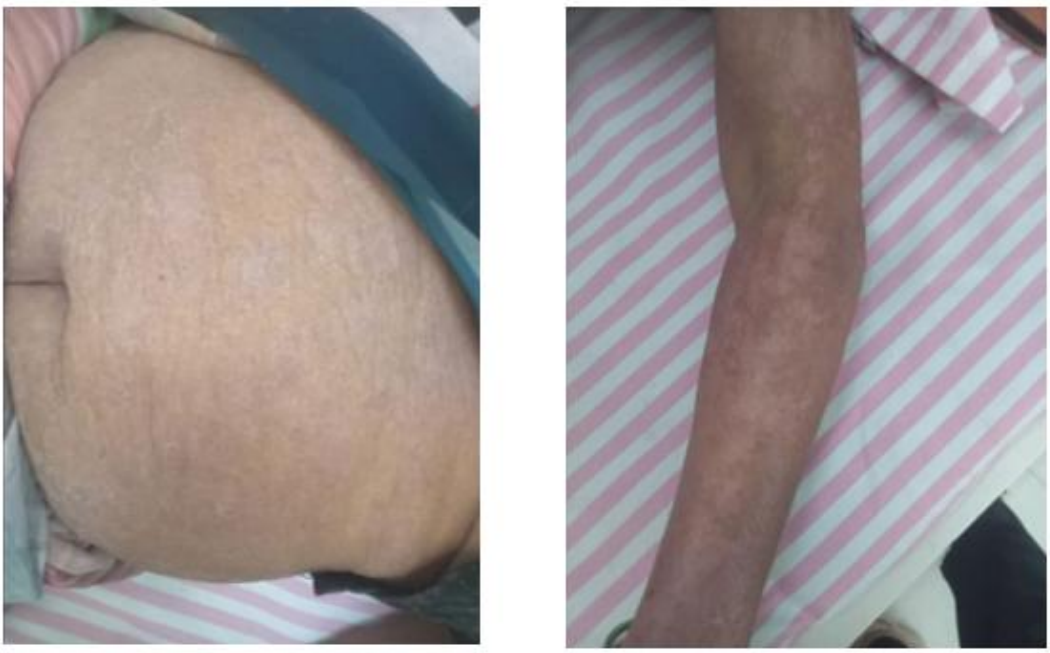

Figure 1. Cutaneous manifestations of DRESS syndrome at presentation.

CBC

Test Description	Value(s)	Unit	Reference Range
WBC	**25520**	/cmm	4000 - 11000
Neu%	**21.0**	%	50.0 - 70.0
Lym%	**11.0**	%	20.0 - 40.0
Mon%	3.3	%	3.0 - 12.0
Eos%	**64.6**	%	0.5 - 6.0
Bas%	0.1	%	0.0 - 1.0
Neu#	5.36	x10^9/L	2.00 - 7.00
Lym#	2.81	x10^9/L	0.80 - 4.00
Mon#	0.84	x10^9/L	0.12 - 1.20
Eos#	**16.48**	x10^9/L	0.02 - 0.55
Bas#	0.03	x10^9/L	0.00 - 0.10
RBC	4.64	x10^12/L	3.50 - 5.50
HGB	12.3	g/dL	11.0 - 16.0
HCT	**36.7**	%	37.0 - 54.0
MCV	**79.0**	fL	80.0 - 100.0
MCH	**26.5**	pg	27.0 - 34.0
MCHC	33.5	g/dL	32.0 - 36.0
RDW-CV	15.7	%	11.0 - 16.0
RDW-SD	**43**	fL	53.0 - 56.0
PLT	203000	/cmm	150000 - 450000
MPV	**12.1**	fL	6.5 - 12.0
PCT	0.240	%	0.108 - 0.282
NRBC#	0.000	10^3/uL	-
NRBC%	0.00	/100WBC	-

COMPLETE BLOOD COUNT

Test Description	Value(s)	Unit	Reference Range
Haemoglobin	12.3	gm/dl	11 - 16
MCV	**79.0**	fL	-
RBC	4.64	x10^12/L	-
Mentzer index	17.03	Index	
Total WBC Count	**25520**	/ cmm	4000 - 11000
DIFFERENTIAL COUNT			
Neutrophils	**21.0**	%	40 - 70
Lymphocytes	**11.0**	%	20 - 45
Eosinophil	**64.6**	%	0 - 6
Monocytes	3.3	%	0 - 8
Basophils	0.10	%	0 - 1
PERHIPHRAL SMEAR EXAMINATION			
Plateletes	203000	/cmm	150000 - 450000
Erythrocytes :	Normocytic Normochromic		
WBC	**Leucocytosis, Eosinophilia**		

Figure 2. Admission laboratory report confirming eosinophilia.

Identification of Causative Agent & Management

The primary suspect drug was leflunomide, initiated three days before symptom onset and rated as having a 'probable' causality based on the Naranjo algorithm and clinical chronology. A concomitant course of trimethoprim-sulfamethoxazole (Septran DS) was also noted, but leflunomide was deemed the most likely precipitant given the typical latency for DRESS. Leflunomide was permanently discontinued on 31 December 2025. An enhanced elimination protocol with cholestyramine was not initiated due to the severity of the acute presentation and the immediate focus on immunosuppression. Management consisted of supportive care and systemic corticosteroids. She received intravenous dexamethasone (4 mg twice daily), along with intravenous pantoprazole for gastric protection and ondansetron (Emset) for nausea. A brief, two-day empirical

course of meropenem was discontinued when a drug-induced etiology was confirmed. Her condition showed marked improvement within 48 hours of initiating corticosteroid therapy and withdrawing the suspect drug.

Outcome and Follow-up

The patient's fever subsided, and the rash began to resolve with desquamation. Her eosinophil counts steadily declined over the subsequent week. She was discharged in stable, improving condition in early January 2026. At a two-week follow-up, she had made a full clinical recovery with no sequelae. Rechallenge with leflunomide was strictly contraindicated and was not attempted.

Table: Clinical Timeline

Date	Event
27 Nov 2025	Initiation of leflunomide 10 mg/day for rheumatoid arthritis.
30 Nov 2025	Onset of malaise and cutaneous rash.
Late Dec 2025	Hospital admission with fever (38.7°C), widespread maculopapular rash.
31 Dec 2025	Lab confirmation: Eosinophilia (64.61%). Leflunomide discontinued.
Jan 2026	Treatment with IV corticosteroids was initiated. Rapid clinical improvement.
Early Jan 2026	Discharged in stable condition.
Mid-Jan 2026	Full clinical recovery at follow-up.

DISCUSSION

This case illustrates a classic, severe presentation of leflunomide-induced DRESS syndrome, a rare but well-documented adverse effect with an estimated incidence of less than 0.1%. [5] The typical latency of 2-6 weeks between drug initiation and symptom onset, coupled with the hallmark triad of rash, fever, and hematologic abnormalities (notably eosinophilia and atypical lymphocytosis), aligns perfectly with our patient's course. [2] The rapid clinical deterioration following initiation underscores the aggressive nature of this reaction.

The causality assessment in this case favoured leflunomide over the concomitant trimethoprim-sulfamethoxazole. While sulphonamides are frequent culprits in SCARs, the very short three-day latency from leflunomide initiation to symptom onset, though at the extreme lower end, is reported in accelerated hypersensitivity reactions to this drug. [2] Furthermore, the decision to forgo a teriflunomide elimination protocol with cholestyramine, despite its proven efficacy in reducing the drug's half-life, was a clinical judgment based on acuity. In the setting of severe systemic inflammation and organ involvement, immediate immunosuppression with corticosteroids is the priority intervention to halt the immune-mediated damage, a strategy supported by management guidelines for DRESS. [5]

The most significant aspect of this report transcends the pharmacology of leflunomide. It lies in the critical juncture where diagnosis was secured: the handwritten medication label on the patient's hospital gown. In an era dominated by electronic health records (EHRs), this low-technology intervention served as a vital failsafe. EHRs can be fragmented across health systems, inaccessible during transitions of care, or lack real-time updates. [3] For a critically ill, transferred patient, this label provided an immediate, unambiguous, and continuously visible medication history to every clinician at the bedside. It prevented diagnostic delay, directly facilitating the correct and timely decision to stop leflunomide. This practice represents a profound application of human factors engineering, making critical information perceptible and accessible in a high-stakes clinical environment. [7]

We argue that such visible medication labelling should be standardized as a core component of inpatient safety protocols, especially upon admission to emergency departments and general wards. Its cost is negligible, but its potential to prevent medication errors, expedite diagnosis in complex drug reactions, and improve interdisciplinary communication is substantial. This case serves as a compelling testament to its value.

CONCLUSION

Leflunomide remains a valuable DMARD but requires vigilant monitoring for early signs of severe hypersensitivity. This report of DRESS syndrome reinforces that need. More importantly, it highlights a simple, human-centric safety practice, the labelling of patient attire with current medications, that can bridge dangerous information gaps in modern healthcare. We strongly advocate for the formal adoption and study of this practice as a standard of care to enhance patient safety and diagnostic accuracy.

DECLARATION

Conflicts of interests: The authors declare no conflicts of interest.
Author contribution: All authors have contributed in the manuscript.
Author funding: Nill.

Acknowledgements: The authors thank the nursing and clinical staff involved in the patient's care. We also sincerely thank the patient for consenting to share her story to advance medical knowledge. Special thanks to Dr. Manoj Kadam, Apollo Multispecialty hospital Latur.

REFERENCES

1. Hsu, D. Y., Brieva, J., Silverberg, N. B., & Silverberg, J. I. (2016). Morbidity and Mortality of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in United States Adults. *The Journal of investigative dermatology*, *136*(7), 1387–1397. https://doi.org/10.1016/j.jid.2016.03.023
2. Chu, M. T., Chang, W. C., Pao, S. C., & Hung, S. I. (2023). Delayed Drug Hypersensitivity Reactions: Molecular Recognition, Genetic Susceptibility, and Immune Mediators. *Biomedicines*, *11*(1), 177. https://doi.org/10.3390/biomedicines11010177
3. Ratwani, R. M., Savage, E., Will, A., Arnold, R., Khairat, S., Miller, K., Fairbanks, R. J., Hodgkins, M., & Hettinger, A. Z. (2018). A usability and safety analysis of electronic health records: a multi-center study. Journal of the American Medical Informatics Association: JAMIA, 25(9), 1197–1201. https://doi.org/10.1093/jamia/ocy088
4. Gibson, A., Deshpande, P., Campbell, C. N., Krantz, M. S., Mukherjee, E., Mockenhaupt, M., Pirmohamed, M., Palubinsky, A. M., & Phillips, E. J. (2023). Updates on the immunopathology and genomics of severe cutaneous adverse drug reactions. *The Journal of allergy and clinical immunology*, *151*(2), 289–300.e4. https://doi.org/10.1016/j.jaci.2022.12.005
5. Hung, S. I., Mockenhaupt, M., Blumenthal, K. G., Abe, R., Ueta, M., Ingen-Housz-Oro, S., Phillips, E. J., & Chung, W. H. (2024). Severe cutaneous adverse reactions. *Nature reviews. Disease primers*, *10*(1), 30. https://doi.org/10.1038/s41572-024-00514-0
6. Chen, C. B., Abe, R., Pan, R. Y., Wang, C. W., Hung, S. I., Tsai, Y. G., & Chung, W. H. (2018). An Updated Review of the Molecular Mechanisms in Drug Hypersensitivity. *Journal of immunology research*, *2018*, 6431694. https://doi.org/10.1155/2018/6431694
7. Bowie, P., Baharnah, A. A., Alkutbe, R., Abid, M. M., Almelaifi, A., & Abid, M. H. (2024). Using Human Factors Science to Improve Quality and Safety of Healthcare. *Global journal on quality and safety in healthcare*, *8*(2), 93–96. https://doi.org/10.36401/JQSH-24-X8
8. Kane-Gill, S. L., Dasta, J. F., Buckley, M. S., Devabhakthuni, S., Liu, M., Cohen, H., George, E. L., Pohlman, A. S., Agarwal, S., Henneman, E. A., Bejian, S. M., Berenholtz, S. M., Pepin, J. L., Scanlon, M. C., & Smith, B. S. (2017). Clinical Practice Guideline: Safe Medication Use in the ICU. *Critical care medicine*, *45*(9), e877–e915. https://doi.org/10.1097/CCM.0000000000002533