

Learning Objectives

- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is a rare drug-induced hypersensitivity syndrome with a heterogeneous presentation that can mimic many other conditions
- Diagnosis requires attention to detail given latency period from incident drug exposure and reminds us to prescribe even common-place medications thoughtfully.

Case

A 76-year-old female presented with four days of pruritic rash and two days of fever, generalized aches, nausea, vomiting, and diarrhea. She developed a dry cough around the time of presentation. She denied any recent travel or ill contacts. Medical history was significant for hypertension, and cystitis treated with trimethoprim/sulfamethoxazole (TMP/SMX) three weeks prior in the outpatient setting.

Physical examination:

- Febrile to 38.4°C, saturating 93% on room air with desaturation to 87% on ambulation
- Erythematous papular rash across bilateral lower extremities and lower abdomen, sparing palms, soles and oral mucosa (See Figure 1)
- No lymphadenopathy

Differential diagnosis:

Multi-focal pneumonia e.g. 2/2 legionella, Aspiration pneumonia, Viral syndrome/gastroenteritis, DRESS syndrome, Hypersensitivity reaction/SJS/TENS, Vasculitis

Work-up:

- **Lab tests:** WBC 12.3 with serum eosinophilia (absolute count peaked at 3) and variant lymphocytes, generally unremarkable LFTs, HIV negative. Developed AKI on hospital D3 with peak Cr 1.41 (from baseline 0.7). COVID-19, extended respiratory viral testing, mycoplasma, chlamydia and urine legionella resulted negative. Blood cultures negative
- **CXR:** Multi-lobar patchy opacities
- **Urine:** Pyuria and eosinophiluria, no nitrites or RBCs, normal protein excretion, FeNa 0.1%,
- **Skin biopsies:** Severe hypersensitivity reaction with segmental epidermal necrosis, and no immunofluorescence pattern detected

Case Continued

Management:

- Initially received moxifloxacin for multi-focal pneumonia
- As course progressed, given lack of other new exposures and results of workup, it was determined presentation was likely secondary to her recent TMP/SMX use
- Started on high dose steroids due to high suspicion for DRESS syndrome and discharged in stable condition



Figure 1. Representative section of rash

RegiSCAR Score for Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)			
Diagnoses drug reaction with eosinophilia and systemic symptoms (DRESS).			
When to Use			
Fever (≥38.5 °C)	No -1	Yes 0	Unknown -1
Enlarged lymph nodes ≥2 sites, >1 cm	No 0	Yes +1	Unknown 0
Atypical lymphocytes	No 0	Yes +1	Unknown 0
Eosinophilia	0-699 cells or <10% (no eosinophilia) 0	700-1,499 cells or 10-19.9% +1	≥1,500 cells or ≥20% +2
Skin rash extent >50%	No 0	Yes +1	Unknown 0
At least two of: edema, infiltration, purpura, scaling	No -1	Yes +1	Unknown 0
Biopsy suggesting DRESS	No -1	Yes 0	Unknown 0
Internal organ involved	1 +1	≥2 +2	
Resolution in >15 days	No -1	Yes 0	
Alternative diagnoses excluded (by ≥3 biological investigations)	No 0	Yes +1	Unknown 0
6 points	Definite case		
RegiSCAR for DRESS	Likelihood of DRESS diagnosis		
	Copy Results		
	Next Steps		

Figure 2. Example of RegiSCAR scoring system result

Discussion

- Diagnosis of DRESS is a dynamic process based on a constellation of symptoms which may differ depending on the patient, and often may not occur concurrently. Latent exposure (two to eight weeks) to a high-risk drug (such as allopurinol, sulfonamides, vancomycin and aromatic anti-epileptics) is an important anchor to the diagnosis. This latency period can lead to delay in suspecting the diagnosis, particularly if the culprit medication is no longer actively being used. The Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) scoring system helps to establish the diagnosis with varying degrees of certainty,¹ see Figure 2.
- Given an appropriate drug exposure coupled with fever preceding the onset of a typical skin eruption, eosinophilia, probable interstitial pneumonia, GI symptoms (historically present in only 10-30% of cases), and probable acute interstitial nephritis, our patient met criteria for a definite diagnosis of DRESS.
- The syndrome lies on a spectrum of cutaneous adverse drug reactions which includes exanthematous reactions (morbilliform rash without visceral involvement), and can be closely related to SJS/TEN (which may otherwise be differentiated by severe mucosal involvement).
- The case reminds us that even common-place curative drugs can have unpredictable adverse effects and empowers us to prescribe judiciously.

References

1. Kardaun SH, Sekula P, Valeyrie-Allanore L, Liss Y, Chu CY, Creamer D, Sidoroff A, Naldi L, Mockenhaupt M, Roujeau JC; RegiSCAR study group. Drug reaction with eosinophilia and systemic symptoms (DRESS): an original multisystem adverse drug reaction. Results from the prospective RegiSCAR study. Br J Dermatol. 2013 Nov;169(5):1071-80. doi: 10.1111/bjd.12501. PMID: 23855313.