

# Trimethoprim-Sulfamethoxazole Induced Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Complicated by Acute Liver Failure

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## Introduction

- DRESS is a serious delayed adverse drug reaction that manifests as severe cutaneous lesions and multiorgan failure with associated fever, hematologic abnormalities, and lymphadenopathy.
- The clinical presentation appears 2-6 weeks from the time of the exposure to the causative drug
- The average recovery time is within 6-9 weeks.
- It has a mortality rate of 10% with most cases usually due to hepatic involvement with resultant fulminant hepatitis.
- Multiple causative agents of DRESS are reported including Trimethoprim-Sulfamethoxazole (TMP-SMX).
- The best-used criteria for its diagnosis are based on the RegiSCAR scoring system.
- Studies showed link between DRESS risk and HLA variants.

## Case Presentation

- A 57-year-old Asian male is admitted after 2 weeks of complaints of high-grade fever, fatigue, and purpuric rash with desquamation.
- He underwent surgical resection of inverted sinus papilloma and was prescribed a 14 days course of TMP-SMX 1 month prior.
- He was afebrile on admission. Physical exam was notable for scleral icterus, jaundiced skin, and purpuric rash over all extremities with desquamation.
- He denied alcohol consumption and illegal drug use.
- He reported that his mother and brother had a history of severe reaction to TMP-SMX.
- Infectious and autoimmune workup was negative.
- Further testing was negative for hemolysis, HUS, TTP, and DIC.
- Abdominal ultrasound and CT were unremarkable. Liver Doppler ultrasound demonstrated patent hepatic vasculature.
- A liver biopsy was not performed due to severe thrombocytopenia.
- TMP-SMX was stopped, and prednisone was started. He was evaluated for a liver transplant but did not require it due to eventual improvement of clinical status and labs.

## Laboratory results

Test	On admission	Within 1 week	2 -3 weeks after admission	3-4 Months post discharge	Reference Range
Hemoglobin	11.9	8.8	10.3	13.8	12-17 g/dL
WBC	9.56	16.6	18	6.95	4.31-10 thousands/uL
Eosinophils %	29%		16%	0%	0-6%
Absolute eosinophils	2.77		3.9	0	0-0.04 thousands/ul
Atypical lymphocyte	N/A		3%		0%
Platelets	2	33	163	186	149-390 thousands/uL
ALT	376	3303	226	99	12-78U/L
AST	283	955	38	56	5-45U/L
ALP	1476	1616	598	269	46-115U/L
Total bilirubin	20.5	22.19	11.8	1.12	0.2-1 mg/dL
Direct bilirubin	15.68	17.56	9.1		0-0.2 mg/dL
Total Protein	6.6	4.4	4.8	7.9	6.4-8.2 g/dL
Albumin	2.5	1.8	1.8	4.1	3.5-5 g/dL
INR	1.2	1.96	1	0.93	0.84-1.19
PT	15.2	22.1	12.3	12.1	11.6-14.5 seconds
PTT	38	33.3			23-37 seconds
Sodium	136	135	136	139	136-145 mmol/L
Potassium	4.7	3.6	3.7	3.7	3.5-5.3 mmol/L
Creatinine	2.51 ( baseline 1 )	1.24	1.08	1.25	0.6-1.3 mg/dL
GFR	27	64	60	63	
Calcium	8.4	7.4	8	9.4	8.3-10.1 mg/dL
Viral hepatitis	Negative				
AMA	Negative				
ASMA	Negative				
ANA	Negative				
Acetaminophen level	Normal				

## RegiSCAR Scoring

Clinical item	Score			Comment
	-1	0	+1	
Fever > 101.3F	No/Unknown	Yes		
LAP		No/Unknown	Yes	>1 cm, at least 2 sites
Eosinophilia >0.7x10 <sup>9</sup>		No/Unknown	Yes	Score 2 points of ≥1.5 × 10 <sup>9</sup>
Atypical lymphocyte		No/Unknown	Yes	
Skin Rash				Suggestive features: ≥2 facial edemas, purpura, infiltration, desquamation
Rash suggestive of DRESS	No	Unknown	Yes	
Extent of >50% of BSA		No/Unknown	Yes	
Skin biopsy suggestive of DRESS	No	Yes/Unknown		
Organ involvement		No	Yes	1 point for each organ involvement, maximum score: 2
Disease duration >15days	No/Unknown	Yes		
Exclusion of other etiologies		No/Unknown	Yes	1 point if 3 of the following tests are performed and are negative: HAV, HBV, HCV, mycoplasma, chlamydia, ANA, blood culture

## Discussion

- Antibiotics attribute to 74% of DRESS cases. Sulfonamides compromised 3% of the cases.
- The sulfonamide component of TMP-SMX is the most common culprit of liver injury, which manifests as cholestatic, hepatocellular, or mixed.
- Patients with slow acetylation are more prone to delayed hypersensitivity reaction of TMP-SMX.
- Our patient has a RegiSCAR score of 6 which strongly suggests DRESS.
- Treatment includes stopping the causative drug and supportive therapy. Steroids are used for severe cases.
- We recommend avoiding TMP-SMX in patients with a strong family history of sulfa allergy