Drug reaction with eosinophilia and systemic symptoms (DRESS) successfully treated with tumor necrosis factor-α inhibitor

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INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS), also referred to as *drug-induced hypersensitivity syndrome* is a rare, potentially life-threatening adverse drug reaction characterized by rash with fever, lymphadenopathy, hematologic abnormalities such as eosinophilia or atypical lymphocytes, and internal organ involvement. DRESS occurs within 2 to 6 weeks after the beginning of the pharmacologic treatment.[1]

Treatment of DRESS consists of stopping the offending medication and providing supportive care. The use of systemic steroids remains controversial because the etiology of the rash is unknown and the use of systemic corticosteroids has associated risks.[2]

Recently, tumor necrosis factor (TNF)-α as a pro-inflammatory mediator has attracted the clinician's attention. Over the last decade, TNF-α inhibitors, such as infliximab and etanercept, have been used to treat toxic epidermal necrolysis (TEN) and Stevens Johnson syndrome (SJS), with anecdotal success.[3,4] However, to our knowledge, there is no report yet on whether a TNF-α inhibitor is effective to treat DRESS. Here we present a case of DRESS associated with lithium carbonate successfully treated with a TNF-α inhibitor (Recombinant Human TNF Receptor-IgG Fusion Protein; Qiangke, Celgen Biopharmaceutical Co, Ltd. Shanghai, China).

Abbreviations used:

DRESS:	drug reaction with eosinophilia and systemic symptoms
SJS:	Stevens Johnson syndrome
TEN:	toxic epidermal necrolysis
TNF:	tumor necrosis factor

CASE REPORT

A 31-year-old Asian woman was admitted to the hospital because of high fever and a pruritic erythematous morbilliform eruption of 7 days' duration. She had bipolar disorder diagnosed 2 years before and had been taking mirtazapine with olanzapine tablet since then. Twenty days before the onset, her doctor changed her medication to lithium carbonate. She denied any history of hypertension, diabetes, hepatitis, tuberculosis, tumor, drug allergy, and other infectious diseases.

On physical examination, she had a fever of 38.7°C and a pruritic erythematous morbilliform rash all over her body including back, chest, legs, and arms. Other vital signs were normal. During admission, she had facial swelling, poor appetite, and swollen superficial lymph nodes.

Laboratory investigation found leukocytosis with eosinophilia and elevation of C-reactive protein, transaminases (aspartate transaminase and alanine transaminase), lactate dehydrogenase, α-hydroxybutyrate dehydrogenase, and γ-glutamyl

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Table I. Test results at admittance

Test	Value		Reference values
Red blood cell count	5.00 $\times$ 10^{12}/L	N	4.5-6 $\times$ 10^{12}/L
Hemoglobin	144 g/L	N	135-175 g/L
White blood cell count	14.4 $\times$ 10^{9}/L	↑	3.5-10.5 $\times$ 10^{9}/L
Neutrophils	4.0 $\times$ 10^{9}/L	N	2.0-7.0 $\times$ 10^{9}/L
Lymphocytes	55.90%	↑	20%-48%
Monocytes	9.80%	N	3%-11%
Eosinophils	0.7 $\times$ 10^{9}/L	↑	0.02-0.52 $\times$ 10^{9}/L
Platelets	141 $\times$ 10^{9}/L	↓	150-450 $\times$ 10^{9}/L
C-reactive protein	24 mg/L	↑	0-10.0 mg/L
Aspartate aminotransferase	426 U/L	↑	7-38 U/L
Alanine aminotransferase	678 U/L	↑	4-43 U/L
γ-glutamyl transferase	220 U/L	↑	11-50 U/L
Lactate dehydrogenase	1142 U/L	↑	109-245 U/L
Urea	2.4 mmol/L	↓	2.8-7.1 mmol/L
Creatinine	70 μmol/L	N	45-84 μmol/L
α-hydroxybutyrate dehydrogenase	780 U/L	↑	72-182 U/L
Fasting blood glucose	6.44 mmol/L	↑	3.89-6.11 mmol/L

Table II. Scoring system for classifying DRESS cases

Score	-1	0	1	2
Fever $\geq$ 38.5°C	No/U	**Yes**		
Enlarged lymph nodes		No/U	**Yes**	
Eosinophilia		No/U		
Eosinophils			**0.7-1.499 $\times$ 10^{9}/L**	$\geq$1.5 $\times$ 10^{9}/L
Eosinophils, if leukocytes <4.0 $\times$ 10^{9}/L			10%-19.9%	$\geq$20%
Atypical lymphocytes		No/U	**Yes**	
Skin involvement				
Skin rash extent (% body surface area)		No/U	**>50%**	
Skin rash suggesting DRESS	No	U	**Yes**	
Biopsy suggesting DRESS	No	Yes/**U**		
Organ involvement*				
Liver		No/U	**Yes**	
Kidney		No/**U**	Yes	
Muscle/heart		No/**U**	Yes	
Pancreas		No/**U**	Yes	
Other organ		No/**U**	Yes	
Resolution $\geq$15 d	No/U	**Yes**		
Evaluation of other potential causes				
Antinuclear antibody				
Blood culture				
Serology for HAV/HBV/HCV				
Chlamydia/mycoplasma				
If none positive and $\geq$3 of above negative			Yes	
Final score	6			

From Kardaun SH, Sidoroff A, Valeyrie-Allanore L, et al. Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: does a DRESS syndrome really exist? *Br J Dermatol*. 2007;156:609-611; reprinted with permission.
Bold indicates that the patient had this score/criteria during admission.
HAV, Hepatitis A virus; *HBV*, hepatitis B virus; *HCV*, hepatitis C virus; *U*, unknown/unclassifiable.
*After exclusion of other explanations: 1, one organ; 2, two or more organs. Final score <2, no case; final score 2-3, possible case; final score 4-5, probable case; final score >5, definite case.

transferase (Table I). These laboratory results of hypertransaminasemia and leukocytosis with eosinophilia, coupled with the clinical findings of fever, swelling, systemic erythematous rash, and the recent ingestion of lithium carbonate, supported the diagnosis of DRESS. The scoring system