The case of the magenta woman (DRESS syndrome)

Ritu Swali, MD^a, and Armen Ghazarian, BS^b

^aDepartment of Medicine, University of California, Irvine, Irvine, California; ^bSchool of Medicine, University of California, Irvine, Irvine, California

ABSTRACT

Drug reaction with eosinophilia and systemic symptoms, otherwise known as DRESS syndrome, is a rare, potentially life-threatening drug-induced hypersensitivity reaction that primarily involves a widespread skin rash, fever, hematological abnormalities, lymphadenopathy, and organ injury. Anti-epileptics, sulfonamides, and allopurinol are the most common triggers, but other offending medications have been reported in the literature. Vancomycin has been increasingly reported over the past 5 years, with 26 cases reported to date. Here we describe a case of a 44-year-old woman who presented with a cutaneous drug reaction with single-organ damage to the kidneys, likely triggered by 1 month treatment of osteomyelitis with intravenous vancomycin. The patient's clinical picture was initially consistent with recurring red-man syndrome that eventually became persistent after failing treatment with infusion rate reduction and diphenhydramine. This case highlights the need for a detailed review of medications taken within 2 months of the onset of the rash, as well as the importance of being cognizant of medications that incite multiple drug reactions.

KEYWORDS Antibiotics; dermatology; dermatopathology; drug rash; vancomycin

CASE PRESENTATION

A 44-year-old woman presented from a skilled nursing facility with high fever and a pruritic, diffuse, and erythematous rash for 2 weeks. The initial rash demonstrated prominent erythema that would suddenly develop on the face every morning and then resolve over the next hour. Over the next week, this rash slowly began to persist, despite administration of antihistamines. Additionally, it appeared on the legs and then gradually spread to the trunk and upper extremities. Of note, the patient had been on intravenous vancomycin for osteomyelitis for a month prior to onset of the rash. On physical exam, she had diffuse erythematous to violaceous patches, confluent on the face with periorbital sparing, and discrete patches on the extremities and trunk without blistering (*Figure 1*). There was also notable bilateral conjunctival injection, facial edema, fissuring of lips, lymphadenopathy, and a left heel ulcer without erythema that probed to bone. Initial labs were remarkable for leukocytosis with 13% eosinophilia, creatinine of 5.4 mg/dL, and electrolyte abnormalities. Punch biopsies from the abdomen and right anterior thigh demonstrated spongiosis with small Langerhans abscess, interface dermatitis in lichenoid pattern with cellular

infiltrates in the upper dermis, and the presence of eosinophils (*Figure 2*).

Overall, on the basis of the patient's history, physical examination, and histopathological exam findings, drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome was diagnosed. Treatment with high-dose oral prednisone and fluids resulted in significant clinical improvement of both the skin eruption and acute kidney injury. The patient was discharged on an oral prednisone taper with close outpatient follow up.

DISCUSSION

DRESS syndrome is a rare, potentially life-threatening drug-induced hypersensitivity reaction. The clinical manifestations of DRESS are not immediate and usually appear 2 to 8 weeks after introduction of the triggering drug. Common features consist of widespread skin rash, fever, hematological abnormalities, lymphadenopathy, and organ injury. Antiepileptics, sulfonamides, and allopurinol are the most common triggers; however, vancomycin has also been reported. Increased long-term requirements for vancomycin treatment for patients with osteomyelitis and endocarditis

Corresponding author: Ritu Swali, MD, Department of Medicine, University of California, Irvine, 333 City Blvd. West, Suite 400, Orange, CA 92868 (e-mail: rituswali@gmail.com)

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Figure 1. Diffuse, erythematous patches that developed into violaceous confluent patches on (a) the leg, (b) the face, and (c) posterior bilateral lower extremities.

Figure 2. Superficial perivascular and subtle interface dermatitis with eosinophils, suggestive of drug reaction (hematoxylin and eosin, 4×).

necessitate close monitoring for hypersensitivity reactions. Vancomycin-triggered DRESS has been increasingly reported over the past 5 years, with 26 cases reported to date.¹

Vancomycin is the standard of care for methicillin-resistant *Staphylococcus aureus* infections; the rising prevalence of this entity has also subsequently increased vancomycin hypersensitivity reactions.^{2–4} For this reason, along with increased reports of vancomycin-induced DRESS syndrome, as seen in this case, an increase in the incidence of red man

syndrome, Stevens-Johnson syndrome, and toxic epidermal necrolysis has also been found in the literature. Red man syndrome, a common adverse reaction to parenteral vancomycin administration, is strongly correlated with high infusion rates. It generally presents with a pruritic, erythematous rash that involves the upper body more than the lower and resolves within minutes to hours, as this patient's rash initially appeared. However, red man syndrome is thought to be triggered by mast cell activation because of its relief by antihistamines such as diphenhydramine. Organ involvement with eosinophilia is rare in red man syndrome, although cases of cardiotoxicity have been reported, thus making red man syndrome less likely in this patient. The most concerning possibility of this patient's presentation was Stevens-Johnson syndrome/toxic epidermal necrolysis, but the delayed timing, nonblistering character and distribution, and sparing of periorbital areas and oral mucosa made it less likely to be on this spectrum.⁵ Acute generalized exanthematous pustules is another drug-induced hypersensitivity reaction that manifests predominantly with neutrophilia and pustules that concurrently appear with erythematous patches. The lack of these findings makes this condition less likely.⁵

As illustrated above, the diagnosis of DRESS syndrome can be difficult due to its variation in presentation and overlap with other drug reactions. Attempts have been done to standardize the diagnosis with the regiSCAR criteria and distinguish it from other severe cutaneous adverse reactions.³ Overall, early withdrawal of the offending drug is the only proven treatment to improve mortality. However, supportive therapy in addition to high-dose corticosteroids has been part of the mainstay treatment. Additionally, patients recovering from DRESS syndrome must be monitored closely over the next year for subsequent development of autoimmune disease. This case highlights the need for a detailed review of medications taken within 2 months of the onset of the rash, as well as the importance of being cognizant of medications that incite multiple drug reactions.

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