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Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome

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A 78-year-old woman presented to the emergency department in June 2022 with progressively worsening rash for 4 days. The patient recently completed a 4-week course of vancomycin for right-hand abscess and Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia. On physical examination, the patient was afebrile with a temperature of 99.5 degrees Fahrenheit, a heart rate of 81 beats per minute, blood pressure of 79/39 mmHg, a respiratory rate of 17, and oxygen saturation of 91 % on room air. The patient was alert and oriented to person, place, and time, but she was in mild distress and ill-appearing with dry mucous membranes but without oral ulcers, facial edema, or lymphadenopathy. Her cardiac, pulmonary, and abdominal examinations were unremarkable. Examination of her extremities showed a right dorsal hand wound that was clean, dry, and intact with mild erythema, yet without purulent drainage or surrounding erythema. Examination of the integument system showed diffuse, maculopapular blanchable rash on the chest, abdomen, arms, and legs involving greater than 80 % of her body surface area (BSA) as seen on Figure 1. There were no vesicular or bullous lesions, peeling, drainage, or tenderness to palpation on examination. The initial laboratory tests showed kidney injury with serum creatinine (SCr) of 1.98 mg/dL (baseline, 0.9 mg/dL), alanine aminotransferase (ALT) of 19 U/L (normal, 0–34 U/L), aspartate aminotransferase (AST) of 18 U/L (normal, 15–46 U/L), alkaline phosphatase of 72 U/L (normal, 38–126 U/L), and elevated C-reactive protein (CRP) of 51.6 mg/L (normal, 0.0–9.9 mg/L). Repeat laboratory tests 3 days later showed new leukocytosis of $13.3 \times 10^3/\mu\text{L}$ (normal, $3.6\text{--}10.7 \times 10^3/\mu\text{L}$) and absolute eosinophilia of $2.0 \times 10^3/\mu\text{L}$ (normal, $0.0\text{--}0.5 \times 10^3/\mu\text{L}$) with

15.1 % eosinophils (normal, 1–6 %). The peripheral blood smear showed leukocytosis with absolute mature neutrophilia and absolute eosinophilia. A skin-punch biopsy showed vacuolar interface and spongiotic dermatitis with patchy extravasated erythrocytes compatible with adverse drug eruption. The patient was diagnosed with a drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome and started on intravenous methylprednisolone 1,000 mg daily for 5 days with improvement of her rash and SCr to 1.17 mg/dL. She was discharged to a skilled nursing facility on a 2 week course of prednisone 80 mg daily followed by a 4 week taper.

DRESS is a rare, potentially life-threatening severe hypersensitivity drug reaction involving the skin and multiple organs. It usually develops 2–6 weeks after exposure to causative drugs, such as aromatic anticonvulsants, antimicrobials, and allopurinol [1, 2]. Vancomycin is a relatively rare drug to cause DRESS, with only 23 cases reported at the time of a literature review completed in 2017. It is important to be aware of vancomycin as a potential causative agent of DRESS because it is a commonly administered antibiotic in the hospital setting [1]. The exposure to causative drugs induces T-cell-mediated hypersensitivity response, including type IVb rash induced by Th2 lymphocytes and internal organ damage induced by CD8+ cells [2]. Patients usually present with maculopapular rash along the trunk and extremities associated with fever, lymphadenopathy, transaminitis, kidney injury, leukocytosis, and eosinophilia [1, 3, 4]. Diagnosis is confirmed or excluded utilizing the Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) scoring system, which includes fever, lymphadenopathy, atypical lymphocytes, eosinophilia, skin rash (extent, edema, infiltration, purpura, scaling), biopsy suggestive of DRESS, internal organ involvement, and days to resolution [1, 3–5]. RegiSCAR requires the patient to have an acute rash suspected to be a drug-related reaction requiring hospitalization to diagnose DRESS. A score <2 suggests no DRESS, a score of 2–3 suggests possible DRESS, a score of 4–5 suggests probable DRESS, and score >5 suggests definite DRESS. Eosinophilia is not an absolute requirement to diagnose DRESS utilizing the RegiSCAR scoring system, but it is the greatest contributing factor for the diagnosis. Additionally, a

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Figure 1: Diffuse maculopapular and blanchable rash on (A) chest, (B) legs, and (C) arm.

skin biopsy is not required to diagnose DRESS, but it can be useful in ruling out DRESS [3, 5]. It is important to note that the duration of DRESS is longer than typical drug reactions because it can last several weeks and because one of the RegiSCAR criteria is resolution of the rash greater than 15 days [2, 4, 5]. Differential diagnosis of DRESS commonly includes Stevens-Johnson syndrome/toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythroderma. Other differential diagnosis includes adult T-cell leukemia/lymphoma, viral infections, and hyper-eosinophilic syndrome [4, 5]. The clinical features of Stevens-Johnson syndrome/toxic epidermal necrolysis include bullae, necrosis, atypical target lesions, and severe mucosal involvement without eosinophilia. Acute generalized exanthematous pustulosis typically presents with pustules after

approximately 2–3 days of exposure to the offending drug. Erythroderma presents as diffuse erythema and scaling affecting more than 90 % of the total BSA [5]. DRESS is managed with discontinuation of the offending drug followed by a topical steroid if mild with no organ involvement or only mild with liver involvement or by a systemic steroid if severe with single- or multiple-organ involvement [4]. If systemic steroids are required, it should be tapered over 6–8 weeks to prevent relapse [5].

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