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Delayed diagnosis of DRESS syndrome in a patient with skin of color

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Abstract

We describe a particularly severe case of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome with hemodynamic instability, erythroderma, profound eosinophilia, and severe organ dysfunction. We attribute the severity in part to a delay in diagnosis due to patient's skin of color, as the erythroderma was not noticed until a dermatologist was consulted. This case highlights how even severe skin disease can present less conspicuously in patients with darker skin types. We outline several strategies that can help clinicians to recognize DRESS and other skin disease phenotypes in patients of color, thereby avoiding delays in diagnosis as seen in this case.

Keywords: ceftriaxone, DRESS, drug reaction, eosinophilia, erythroderma, skin of color, systemic symptoms, vancomycin

Case Synopsis

A man in his 70s with recent osteomyelitis of the right calcaneus treated with vancomycin followed by a six-week outpatient course of intermittently dosed ceftriaxone presented to the hospital with fever to 102.5°F, new-onset dyspnea, and hypotension as low as 70/50mmHg. Given concern for sepsis, he was treated with vancomycin, cefepime, and metronidazole without improvement in his fever or hemodynamic stability after six days. On admission the patient was noted to have some "dry and flaky skin" on his lower extremities (**Figure 1**), but he had not noticed the rash and denied any pruritis. No erythema was appreciated until a dermatologist was consulted six days later for a "flaky rash without erythema" in the setting of continued fever and worsening eosinophilia. On examination, the dermatologist noted erythroderma with 80-90% body surface involvement and areas of scaling and superficial desquamation (**Figure 2**). At this time the patient did note generalized pruritis but denied any facial swelling. Shotty cervical and inguinal lymphadenopathy were also present on examination.

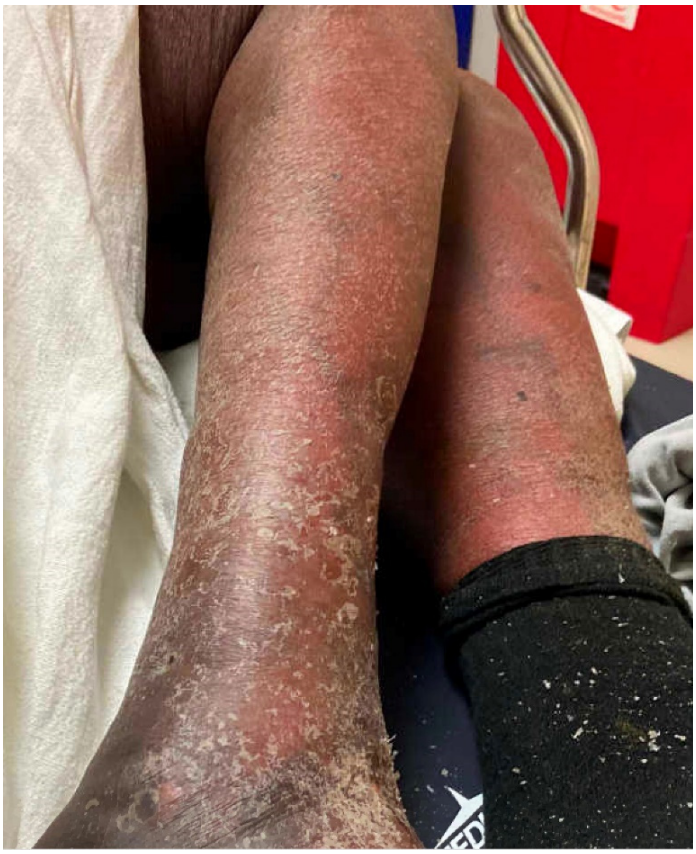

Figure 1. *Exfoliative erythroderma of the lower legs.*

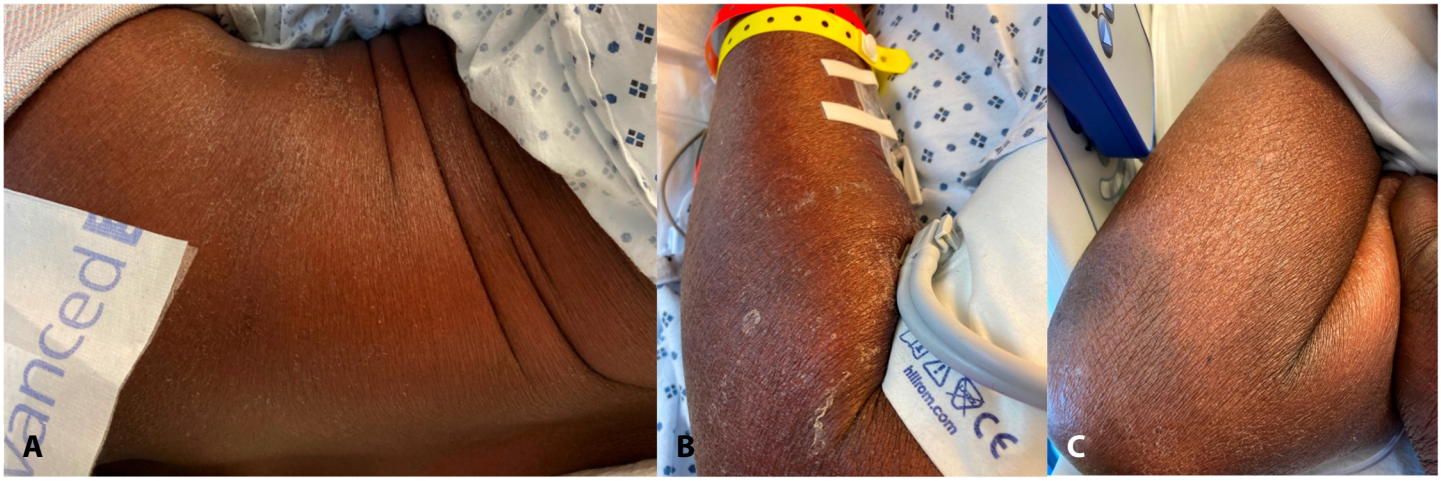

Figure 2. ***A)*** *Exfoliative erythroderma of the lumbar region.* ***B)*** *Exfoliative erythroderma of the left forearm.* ***C)*** *Exfoliative erythroderma of the right forearm.*

Laboratory values were significant for normocytic anemia (hemoglobin 11.2g/dL), leukocytosis (white blood cell count 15.4×10^9 cells/L) with 39.7% eosinophils (absolute count, 6100 cells/µL) and no atypical lymphocytes. Creatinine was markedly elevated to 3.6mg/dL (baseline ~1.0mg/dL), but liver enzymes were normal (alanine transaminase 15U/L, aspartate aminotransferase 18U/L). The patient had no prior history of heart failure, but his pro-brain natriuretic peptide was elevated to 3269pg/mL and ejection fraction measured 34% with unknown baseline.

A skin biopsy was obtained from the abdomen. Histopathological examination revealed dense interface lichenoid inflammation composed mainly of lymphocytes, neutrophils, and rare eosinophils (**Figure 3**). Immunohistochemical stains revealed a normal CD4/CD8 ratio. A diagnosis of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome was made given the clinical picture, a RegiSCAR score of 7, and compatible histopathology in the setting of extended exposure to antibiotics. All antibiotics were discontinued and the patient was started on intravenous methylprednisolone 2mg/kg daily and triamcinolone 0.1% ointment soak and smear twice daily. The patient's skin improved significantly over several days and he was discharged with complete resolution of his skin eruption and improved organ function.

Case Discussion

DRESS syndrome is a severe hypersensitivity reaction characterized by morbilliform eruption, fever, and life-threatening organ dysfunction, most frequently

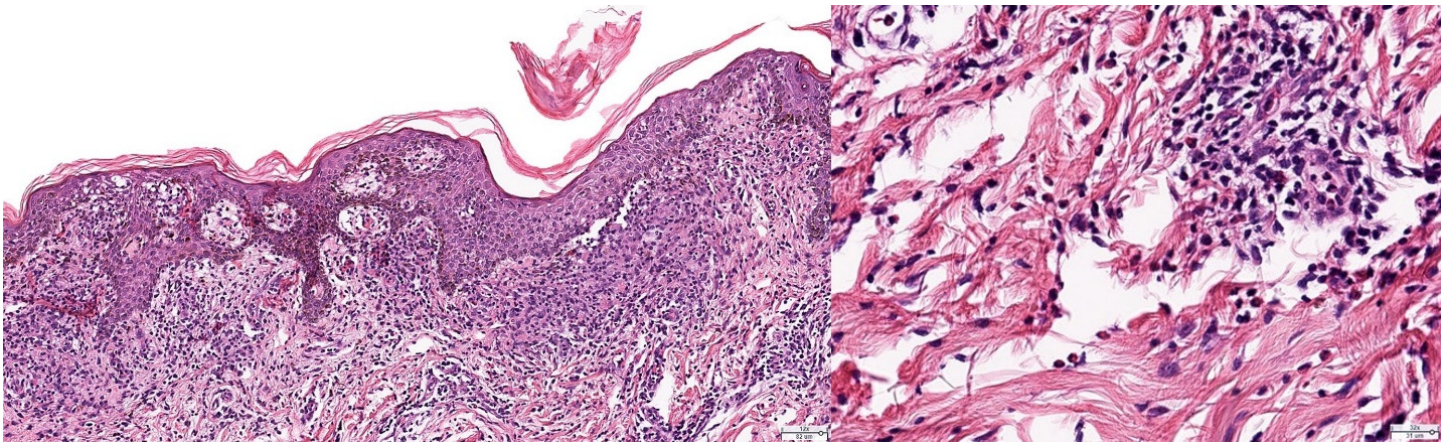

Figure 3. *Histopathology shows a dense interface lichenoid inflammation composed mainly of lymphocytes, neutrophils, and rare eosinophils. Immunohistochemistry shows a normal CD4/CD8 ratio with T cells expressing CD3, CD5, CD7; these cells are negative for CD30. H&E, 40× and 100×.*

involving the liver, kidneys, and heart. Diagnosis can be delayed because of its variable presentation, course, severity, relatively late onset, gradual evolution, and long duration of symptoms [1]. The pathophysiology of DRESS syndrome remains incompletely understood but is often associated with reactivation of human herpes viruses (HHV6 or HHV7), against which the body may mount a strong immune response [2]. Anticonvulsants, allopurinol, sulfonamides, and antibiotics are the most common offending agents. Among the antibiotics, vancomycin is most common, but ceftriaxone has also been noted to cause DRESS [3].

In this article, we present a particularly severe case of DRESS syndrome with hemodynamic instability, erythroderma, profound eosinophilia, and severe organ dysfunction, likely caused by vancomycin or ceftriaxone. We attribute the severity primarily to a delay in diagnosis due to the patient's skin of color. The exact onset of the rash remains unclear. Photographs taken on admission suggest the erythroderma was present when the patient arrived at the hospital but was not noted until six days later when a dermatologist was consulted, a diagnosis of DRESS syndrome was made shortly thereafter.

Conclusion

This case highlights how even severe skin disease can present less conspicuously in patients with darker skin types. Erythema, for example, often presents with a faint pink or purple hue rather than the bright pink or red hue seen in less pigmented skin [4]. One clue to picking up light erythema on dark skin is to press on the skin and look for return of subtle erythema as blanching subsides [5]. Some experts recommend side-lighting with a penlight at a 45° to 90° angle to identify other possible features, such as urticaria, papules, or vesicles [6]. Furthermore, tactile examination may detect induration and textural changes that otherwise would be difficult to appreciate [6]. These strategies can help clinicians to recognize DRESS and other unique skin disease phenotypes in patients of color, thereby avoiding delays in diagnosis as seen in this case.

Potential conflicts of interest

The authors declare no conflicts of interest.

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