Green Staining of Clothing: A Signal for Pseudomonal Infection

Eylem Yılmaz, MD; Ekin Şavk, MD; Serkan Öncü, MD; Güliz Uyar Güleç, MD; Bülent Ertuğrul, MD; Serhan Sakarya, MD; Meltem Uslu, MD; Göksun Karaman, MD; Neslihan Şendur, MD

Anticonvulsant hypersensitivity syndrome (AHS) is a nondose-related idiosyncratic reaction to aromatic antiepileptic drugs and is a cause of drug discontinuation. Pseudomonas aeruginosa *is a gram-negative bacillus that can produce infections in many different organs, including the skin and soft tissue. We report a patient with erythroderma and AHS who developed a pseudomonal infection. Green staining of the underwear served as a diagnostic clue for severe* P aeruginosa *infection that had developed because of a local flexural skin infection that spread due to a damaged skin barrier. Inspection of the patient's clothes may give information about any exudate from the skin and should be done routinely as part of the physical examination.*

Cutis. 2010;86:305-308.

Anticonvulsant hypersensitivity syndrome (AHS) is a cutaneous drug eruption to aromatic antiepileptic drugs and consists of cutaneous eruption; fever; facial edema; lymphadenopathy; leukocytosis; and internal organ involvement such as nephritis, hepatitis, or pneumonia.[1,2] Usually 2 to 8 weeks after initiation of antiepileptic therapy, a cutaneous eruption ranging from mild morbilliform lesions to severe toxic epidermal necrolysis can be seen.[3,4] Among the antiepileptics, carbamazepine, phenytoin, and phenobarbital are the common causes of AHS.[5,6]

All from Adnan Menderes University Faculty of Medicine, Aydın, Turkey. Drs. Yılmaz, Şavk, Uslu, Karaman, and Şendur are from the Department of Dermatology and Drs. Öncü, Güleç, Ertuğrul, and Sakarya are from the Department of Infectious Disease and Clinical Microbiology.

The authors report no conflict of interest.

Correspondence: Eylem Yılmaz, MD, Department of Dermatology, Adnan Menderes University Faculty of Medicine, Atatürk St, Aydın, Turkey 09100 (dreylemyilmaz@mynet.com).

Erythroderma is one of several cutaneous manifestations of AHS. Erythroderma is defined as extensive erythema and/or scaling of the skin, and the clinical diagnosis is based on involvement of 90% body surface area. Because of disruption of skin integrity, erythroderma places the patient at high risk for secondary infections.[7] Early published case series of erythroderma reported a notable mortality rate from complications including sepsis.[8] *Pseudomonas aeruginosa* is a gram-negative bacillus and can produce infections in many different organs, including the skin and soft tissue. As an opportunistic pathogen, *P aeruginosa* seldom causes disease in healthy patients. For an infection to occur, some disruption of the physical barriers (skin or mucous membranes) and/or an underlying dysfunction of the immune system generally is necessary.[9] *Pseudomonas aeruginosa* may cause severe infections that can be difficult to treat if not diagnosed early. *Pseudomonas* wound infections often are indistinguishable from similar infections caused by other etiologic agents. *Pseudomonas aeruginosa* is capable of producing multiple hydrosoluble pigments, most commonly pyocyanin (blue) and pyoverdin (nonfluorescent greenish color). On occasion, by producing these pigments, patients with *Pseudomonas* infection may present with a green exudate with a characteristic grapefruit odor. These signs are important clues for prompt diagnosis and treatment of potentially fatal severe *Pseudomonas* infections.[10-12]

We present the case of a 31-year-old woman with erythroderma and green discoloration of clothing to emphasize that these findings can be important indicators for the diagnosis of *Pseudomonas* infection.

Case Report

A 31-year-old woman was admitted to the emergency department and reported a high fever, redness of skin, and facial puffiness of 5 days' duration. She had developed generalized erythema with edema and pruritus 7 weeks after initiation of carbamazepine therapy for

epilepsy. She had been previously hospitalized with an unknown diagnosis, treated with broad-spectrum antibiotics (ie, vancomycin, cefazolin), and discharged within a couple of days. With the deterioration of her symptoms, the patient presented to our emergency department.

Upon admission, the patient's temperature was 39°C. Her heart rate was normal but tachycardic. Skin examination revealed diffuse erythema, induration, and desquamation including the face, trunk, and limbs (Figure 1). More than 90% body surface area was involved. Axillary and inguinal skin was macerated and had fissures. Thick hyperkeratosis of the palmoplantar regions was observed. Facial edema was present with hyperemic conjunctivae. A painless, mobile, 0.5×0.5-cm left postauricular lymph node was detected. The remaining systemic examination did not reveal any abnormalities. During physical examination, green staining of the patient's underpants and axillary part of her undershirt also were noted (Figure 2). She had neither a history of preexisting dermatoses prior to admission nor a history of malignancy.

Laboratory examination revealed the following values: hemoglobin, 11.1 g/dL (reference range, 14.0−17.5 g/dL); hematocrit, 34.9% (reference range, 41%−50%); white blood cell count, 27,600/μL (reference range, 4500−11,000/μL); platelet count, 659,000/μL (reference range, 150,000−350,000/μL); erythrocyte sedimentation rate, 20 mm/h (reference range, 0−20 mm/h); and C-reactive protein, 36.41 mg/L (reference range, 0.08−3.1 mg/L). In a peripheral blood smear, 40% eosinophils, 30% neutrophils, 16% lymphocytes, and 10% monocytes were detected. Except for low blood protein and albumin levels, other biochemical parameters were within reference range. *Pseudomonas aeruginosa* was isolated from the hemocultures taken from the patient during the febrile period.

Based on the patient's history as well as clinical and laboratory findings, carbamazepine-dependent AHS was diagnosed. The patient was hospitalized and carbamazepine treatment was immediately stopped. Emollients constituted the topical treatment of the erythroderma. Systemic antihistamines were administered to relieve pruritus. To manage pseudomonal infection, intravenous cefepime hydrochloride 2 g twice daily was started. Fever subsided within 72 hours of antibiotic therapy. By the end of the second week of treatment, all dermatologic findings had subsided with the exception of palmoplantar hyperkeratosis. Eosinophil and white blood cell leukocyte counts returned to normal and antibiotic therapy was stopped by the 14th day of hospitalization.

Comment

Anticonvulsant hypersensitivity syndrome is a nondose-related idiosyncratic reaction to aromatic antiepileptic drugs and is a cause of drug discontinuation. This syndrome also can be seen with the use of sulfonamides, allopurinol, gold salts, and dapsone. The most common features are cutaneous eruption, prominent eosinophilia, fever, and multisystemic involvement. Cutaneous manifestations associated with this syndrome range from a mild morbilliform eruption to severe toxic epidermal necrolysis or erythroderma.[13,14] The variability in the clinical presentation of AHS is likely to reflect host-specific metabolic and immunologic reactions associated

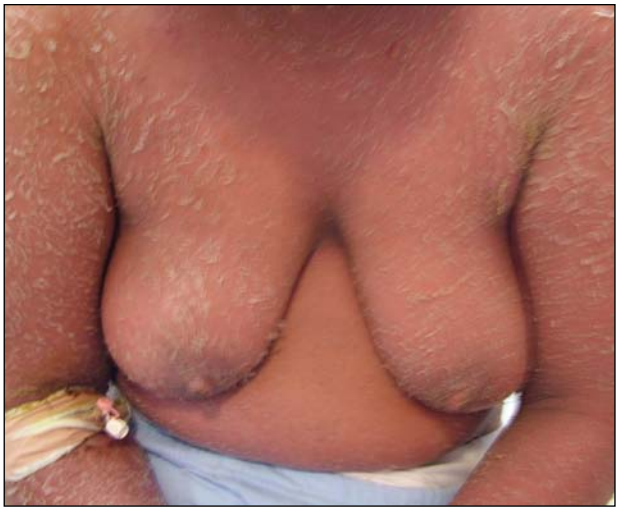

Figure 1. Diffuse erythema, induration, and desquamation involving the trunk and limbs.

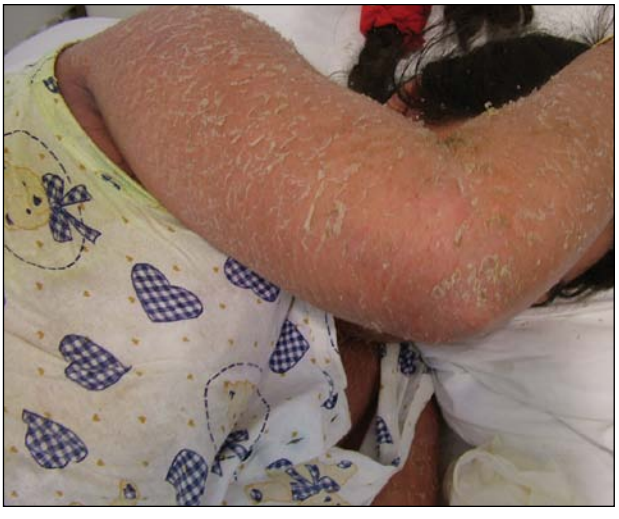

Figure 2. Green staining of the axillary part of the patient's undershirt.

with T-cell–mediated responses.[15] Onset of the syndrome usually occurs 2 to 8 weeks after initiation of antiepileptic agents. The mortality rate of AHS ranges from 10% to 20%. Prompt diagnosis of the syndrome is essential to prevent mortality. The most important therapeutic approach is discontinuation of the causal drug.[16-18]

Erythroderma is characterized by generalized erythema, induration, and scaling of the skin. Secondary infections are potential complications in erythrodermic cases.[15] *Pseudomonas aeruginosa* is an opportunistic, aerobic, gram-negative bacillus that rarely causes infection in healthy individuals but is a frequent cause of severe nosocomial infections in immunocompromised patients.[11] Occasionally it can colonize human body sites, with a preference for moist areas such as the perineum, axillae, ears, nasal mucosa, and throat. The prevalence of *P aeruginosa* colonization in healthy patients usually is low, but higher colonization rates can be encountered following hospitalization, especially among patients treated with broad-spectrum antimicrobial agents.[12] A defective skin barrier usually is caused by destruction of intact stratum corneum due to scratching, dermatitis, maceration, heat, or ulcerations. Primary skin infections may show greenish color and give fluorescence by Wood lamp examination. Our patient with erythroderma had been previously hospitalized and had used broad-spectrum antibiotics, which are both risk factors for the development of *Pseudomonas* infection. Green staining on her underwear was noticed during physical examination by chance, which was the most important clue for the diagnosis of *P aeruginosa* infection.[9,12] Kaya et al[19] reported a similar case involving blue underpants sign in the inguinal area, which was indicative of *P aeruginosa* infection. In our patient, this sign was seen on multiple areas of the underwear in contact with the inguinal and axillary regions. Green discoloration of the underwear served as a diagnostic clue for severe *P aeruginosa* infection that had developed because of a local flexural skin infection that spread due to a damaged skin barrier.

Anticonvulsant hypersensitivity syndrome may necessitate systemic glucocorticosteroid treatment.[3] However, caution is warranted when considering use of corticosteroids. Glucocorticosteroid treatment of patients with a pseudomonal infection may increase the rate of morbidity and mortality.[20] Thus, in patients with erythroderma and AHS, it is imperative to exclude the additional diagnosis of infection prior to initiation of corticosteroid treatment, as both conditions present with fever, malaise, tachycardia, hepatic dysfunction, and leukocytosis.[4] Our patient was not started on corticosteroids due to initial suspicion of systemic pseudomonal infection following inspection of her green underwear.

Conclusion

The presence of green staining on the underclothes should be a warning sign of the presence of *Pseudomonas* infection. All physicians should be familiar with this sign, especially in patients with erythroderma because its recognition may enable early treatment, thereby improving the chances of survival. The prognosis of *Pseudomonas* infection is poor. Inspection of the patient's clothes may give information about any exudate from the skin and should be done routinely as part of the physical examination. In summary, examination of not just the patient but also the attire is a rewarding medical practice.

REFERENCES

1. Baba M, Karakaş M, Aksungur VL, et al. The anticonvulsant hypersensitivity syndrome. *J Eur Acad Dermatol Venereol.* 2003;17:399-401.
2. Syn WK, Naisbitt DJ, Holt AP, et al. Carbamazepine-induced acute liver failure as part of the DRESS syndrome. *Int J Clin Pract.* 2005;59:988-991.
3. Kaminsky A, Moreno M, Díaz M, et al. Anticonvulsant hypersensitivity syndrome. *Int J Dermatol.* 2005;44: 594-598.
4. Kaur S, Sarkar R, Thami GP, et al. Anticonvulsant hypersensitivity syndrome. *Pediatr Dermatol.* 2002;19:142-145.
5. Hautmann G, Lotti T. Psychoactive drugs and skin. *J Eur Acad Dermatol Venereol.* 2003;17:383-393.
6. Walia KS, Khan EA, Ko DH, et al. Side effects of antiepileptics—a review. *Pain Pract.* 2004;4:194-203.
7. Sehgal VN, Srivastava G, Sardana K. Erythroderma /exfoliative dermatitis: a synopsis. *Int J Dermatol.* 2004;43:39-47.
8. Rothe MJ, Bernstein ML, Grant-Kels JM. Life-threatening erythroderma: diagnosing and treating the "red man". *Clin Dermatol.* 2005;23:206-217.
9. Silvestre JF, Betlloch MI. Cutaneous manifestations due to *Pseudomonas* infection. *Int J Dermatol.* 1999;38: 419-431.
10. Vostrugina K, Gudaviciene D, Vitkauskiene A. Bacteremias in patients with severe burn trauma. *Medicina (Kaunas).* 2006;42:576-579.
11. Viola L, Langer A, Pulitanò S, et al. Serious *Pseudomonas aeruginosa* infection in healthy children: case report and review of the literature. *Pediatr Int.* 2006;48:330-333.
12. Rossolini GM, Mantengoli E. Treatment and control of severe infections caused by multiresistant *Pseudomonas aeruginosa*. *Clin Microbiol Infect.* 2005;11(suppl 4):17-32.
13. Roujeau JC. Clinical heterogeneity of drug hypersensitivity. *Toxicology.* 2005;209:123-129.

14. Chang CC, Shiah IS, Yeh CB, et al. Lamotrigine-associated anticonvulsant hypersensitivity syndrome in bipolar disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2006;30:741-744.
15. Krauss G. Current understanding of delayed anticonvulsant hypersensitivity reactions. *Epilepsy Curr*. 2006;6:33-37.
16. Schlienger RG, Shear NH. Antiepileptic drug hypersensitivity syndrome. *Epilepsia*. 1998;39(suppl 7): S3-S7.
17. Wolf R, Orion E, Marcos B, et al. Life-threatening acute adverse cutaneous drug reactions. *Clin Dermatol*. 2005;23:171-181.
18. Allam JP, Paus T, Reichel C, et al. DRESS syndrome associated with carbamazepine and phenytoin. *Eur J Dermatol*. 2004;14:339-342.
19. Kaya TI, Delialioglu N, Yazici AC, et al. Medical pearl: blue underpants sign—a diagnostic clue for *Pseudomonas aeruginosa* intertrigo of the groin. *J Am Acad Dermatol*. 2005;53:869-871.
20. Rady MY, Johnson DJ, Patel B, et al. Corticosteroids influence the mortality and morbidity of acute critical illness. *Crit Care*. 2006;10:R101.