

# Clindamycin-Induced Acute Generalized Exanthematous Pustulosis

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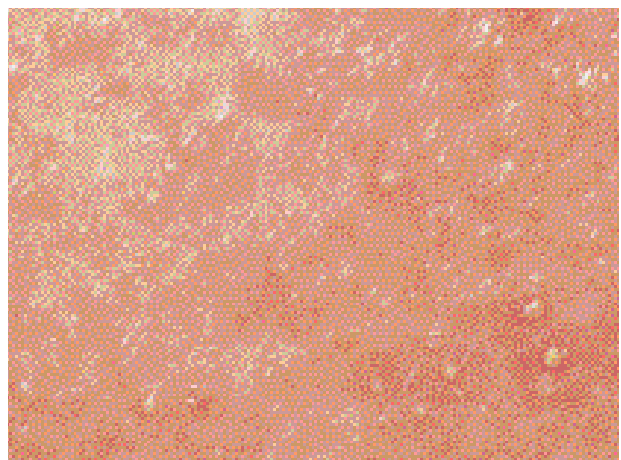
*Acute generalized exanthematous pustulosis is a rare but distinctive entity that may be associated with various etiologies. Drug exposure is the most common cause. We present the first report of acute generalized exanthematous pustulosis induced by the drug clindamycin.*

The majority of reported cases of acute generalized exanthematous pustulosis (AGEP) have been associated with beta-lactam and macrolide antibiotics. Much less common causes of AGEP include viral infections, mercury, and ultraviolet light exposure.

The diagnostic features of AGEP include an acute onset of fever ( $>38^{\circ}\text{C}$ ) and rash consisting of widespread, nonfollicular pustules ( $<5\text{ mm}$ ) arising on erythematous, edematous skin; a temporal relationship to drug exposure or other etiologic factors; histopathology revealing subcorneal or intraepidermal spongiform pustules with varying degrees of dermal edema, vasculitis, perivascular eosinophilia, and focal single-cell keratinocyte necrosis; a blood neutrophil count above  $7 \times 10^9/\text{liter}$ ; and spontaneous resolution of rash following removal of the causative agent.

## Case Report

A 72-year-old white woman presented with a pruritic generalized skin eruption. The rash began on the trunk 1 day after the patient was given oral clindamycin as prophylaxis for a rhytidectomy procedure. It quickly spread to the groin and extremities and was associated with a fever ( $38.2^{\circ}\text{C}$ ). The patient had an



**FIGURE 1.** Close-up of erythematous, edematous skin covered with numerous nonfollicular, pinhead-sized pustules.

unremarkable medical history except for a penicillin allergy. Other medications included oral estrogen, which had been taken routinely for many years. Laboratory evaluation revealed a total white blood cell count of  $29.1 \times 10^9/\text{liter}$  with 96% neutrophils, hypoalbuminemia ( $2.4\text{ g/dl}$ ), and normal serum calcium, renal, and liver function tests.

Examination of the skin revealed nontender, confluent, erythematous, edematous plaques on the chest, back, groin, arms, and legs with numerous nonfollicular pinhead-sized pustules (Figure 1). There was no involvement of the scalp, face, nails, or mucosal sites, and the Nikolsky's sign was negative.

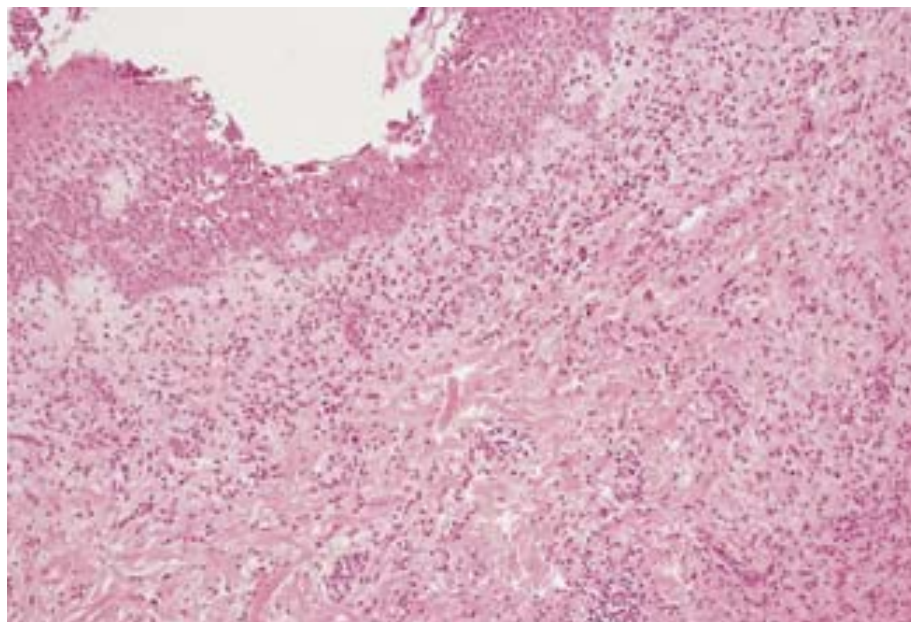
Biopsy of the skin demonstrated an orthokeratotic stratum corneum, and subcorneal and intraepidermal pustules with neutrophils, eosinophils, and focal spongiosis. The dermis contained a superficial and mid-dermal interstitial infiltrate with numerous eosinophils and neutrophils (Figure 2). Tissue for Gram's stain and periodic acid-Schiff stain was negative for bacterial and fungal elements, respectively.

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REPRINTS are not available.



**FIGURE 2.** Skin biopsy demonstrates subcorneal and intraepidermal pustules with neutrophils, eosinophils, and spongiosis. In the dermis, a mixed interstitial infiltrate of neutrophils and eosinophils is present.

Clindamycin therapy was discontinued. Treatment with systemic corticosteroids and supportive care resulted in the complete resolution of the pustular eruption over a 1-week period.

### Comments

Acute generalized exanthematous pustulosis (AGEP) is a rare but distinctive entity associated with various etiologies. Drug exposure is the most common cause.<sup>1-10</sup> Antimicrobials, such as beta-lactam and macrolide antibiotics, have accounted for the majority of reported cases.<sup>1-10</sup> Other antimicrobials, such as the tetracyclines, quinolones, and sulfonamides, and oral antifungal agents, such as terbinafine and itraconazole, have been implicated in inducing AGEP. Non-antimicrobial drugs, such as the calcium channel blockers, angiotensin-converting enzyme inhibitors, anticonvulsants, tricyclic antidepressants, antimalarials, analgesics, and antipyretics have also been reported as causative agents in AGEP. Much less common causes of AGEP include viral infections, mercury, and ultraviolet light exposure.<sup>1,2,4,6-10</sup> Clindamycin is a lincosamide antibiotic that is chemically derived from the drug lincomycin.<sup>11</sup> It is structurally unrelated to previously mentioned agents.

The criteria for the diagnosis of AGEP were established by Roujeau *et al*<sup>1</sup> in 1991. The diagnostic features include an acute onset of fever ( $> 38^{\circ}\text{C}$ ) and rash consisting of widespread, nonfollicular pustules ( $< 5$  mm) arising on erythematous, edematous skin; a temporal relationship to drug exposure or other etiologic factors (usually short, between  $\leq 1$  day up to 18 days, with a mean of 5.1 days following drug exposure); histopathology revealing subcorneal or in-

traepidermal spongiform pustules with varying degrees of dermal edema, vasculitis, perivascular eosinophilia, and focal single-cell keratinocyte necrosis; a blood neutrophil count above  $7 \times 10^9/\text{liter}$ ; and spontaneous resolution of rash following removal of the causative agent (usually less than 15 days).

The differential diagnosis of AGEP includes generalized pustular psoriasis and subcorneal pustular dermatosis. Differentiation of AGEP from these entities can typically be made by the combination of clinical history and histologic features. AGEP is characterized by the acute onset of disease with rapid progression, associated fever, and a temporal relationship to a causative agent. Patients with acute generalized pustular psoriasis (von Zumbusch) may also present with the acute onset of sheets of sterile pustules on erythematous skin, fever, and polymorphonuclear leukocytosis; however, they typically have a prior history of psoriasis. Histologically, both AGEP and generalized pustular psoriasis may exhibit subcorneal or intraepidermal neutrophilic spongiform pustules or both. Histologic features that favor AGEP include dermal edema, eosinophilia, vasculitis, and single-cell keratinocyte necrosis.<sup>1,2,5,8-10</sup> In contrast to AGEP, subcorneal pustular dermatosis (Sneddon-Wilkinson disease) is characterized by recurrent, large, localized, flaccid pustules without associated fever. The classic histologic feature of subcorneal pustular dermatosis is a subcorneal neutrophilic pustule without intraepidermal spongiform neutrophils.<sup>2,5,9,10</sup>

True confirmation of establishing a drug as the cause of AGEP can only be accomplished by rechallenging the patient with the suspected drug. Since this is not a prudent choice, patch testing has been

utilized in an attempt to produce a pustular eruption at the test site that mimics AGEF both clinically and histologically.<sup>2,9</sup> However, patch testing is not always successful. Rechallenge and patch testing were not performed in our case. In our patient, the use of clindamycin resulted in a distinctive skin eruption that met all of the established criteria for the diagnosis of AGEF. This case represents the first report of AGEF induced by the drug clindamycin.

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