SKIN

BRIEF ARTICLE

# Acute Generalized Exanthematous Pustulosis after Oral Antihistamine

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## ABSTRACT

Acute generalized exanthematous pustulosis (AGEP) is a cutaneous adverse reaction that may be severe. It is often caused by drug exposure, most commonly antibiotics; however, many others have been implicated. We present a case of hydroxyzine associated AGEP in a 34-year-old man taking the antihistamine for anxiety. The patient presented with a pruritic, erythematous rash on the extremities, trunk and neck. He was initially diagnosed with folliculitis, although Gram stain and culture were negative. With worsening rash, a punch biopsy was performed and showed subcorneal pustules filled with neutrophils, consistent with AGEP. Additional history led to the identification of the causative agent. Hydroxyzine was discontinued, and the patient's symptoms improved. Although AGEP is usually self-limited, persisting for one to two weeks followed by desquamation, 17 percent of patients will have organ dysfunction and may require hospitalization. Clinicians should be prepared to recognize this potentially severe reaction, particularly when prescribing a new medication, including a common antihistamine, as in this rare case.

## INTRODUCTION

Acute generalized exanthematous pustulosis (AGEP) is a pustular dermatosis with acute onset that is usually widespread. It is classified as a severe cutaneous adverse reaction and is often caused by drug exposure. Antibiotics are the most commonly associated drugs. Others include calcium channel blockers, antiepileptics, and analgesics. Only three cases have been reported in the literature associated with hydroxyzine, a commonly prescribed antihistamine.

EuroSCAR AGEP validation score criteria have been developed to utilize in the diagnosis of AGEP.[1] EuroSCAR takes into consideration the morphology of skin lesions, clinical course, presence of fever, and laboratory and histopathological findings. The score ranges from -10 to +12 and classifies a patient's likelihood of having AGEP as no (-10 to 0), possible (1 to 4), probable (5 to 7), or definite (8 to 12).

## CASE REPORT

A 34-year-old Hispanic man presented with a widespread, erythematous, pruritic exanthem, which started at his right inguinal

fold then spread to his trunk and extremities. Medical history included anxiety disorder and recurrent oral herpes labialis. He noted that the exanthem seemed to occur with periods of severe anxiety. Recently, he had undergone laser hair removal. Serology tests were negative for Monkeypox and positive for herpes simplex virus (HSV). He had been prescribed oral fluconazole by primary care without improvement. Other medications included topical corticosteroids and clotrimazole for the rash, oral acyclovir for cold sore prevention, and oral hydroxyzine as needed for anxiety. He denied drug allergies. Skin examination showed widespread erythema with generalized inflammatory papules and pustules. He was empirically treated for folliculitis with doxycycline. Gram stain and cultures were negative. He returned to clinic four days later with worsening rash (**Figure 1**). On further questioning, he recalled that the rash initially appeared after he started taking hydroxyzine for anxiety and improved after stopping hydroxyzine. Upon restarting hydroxyzine, the rash recurred with a worse presentation including muscle aches and general malaise. Biopsy revealed subcorneal neutrophilic pustules, spongiotic epidermis, and abundant papillary dermal edema; eosinophils were not prominent (**Figure 2**). Histopathologic findings were consistent with acute generalized exanthematous pustulosis (AGEP). EuroSCAR AGEP validation score criteria revealed a score of 10, supporting a definite diagnosis of AGEP. The exanthem cleared quickly with superficial dry desquamation upon final discontinuation of hydroxyzine.

## DISCUSSION

AGEP is a severe cutaneous adverse reaction (SCAR) most often associated with medication use (>90% of cases).[2] Drugs associated with AGEP include most commonly oral anti-infectives at 36.5% of cases.[3] The apparent waxing and waning of his exanthem in response to initiation, discontinuation, and re-initiation of hydroxyzine is strong evidence that oral hydroxyzine was the triggering agent of his AGEP. Three cases associating hydroxyzine with AGEP have been previously reported.[4] Our case represents the second reported case of recurrent AGEP with hydroxyzine.[5]

Other differential diagnoses we considered included generalized acute pustular psoriasis. The absence of preceding clinical features of psoriasis or characteristic histology makes this diagnosis unlikely. Disseminated herpes simplex infection was also considered because of his history of recurrent cold sores and recent laser trauma to those areas where his exanthem initially presented. The absence of characteristic grouped vesicles and “punched-out” ulcers argued against HSV. Histopathology did not demonstrate cytopathic changes of HSV, and immunohistochemistry testing was negative for HSV I/II. Stevens-Johnson Syndrome (SJS) was also considered. Lack of involvement of mucosal membranes argued against this diagnosis. The histopathologic findings of SJS to include full thickness epidermal necrosis and sparse inflammatory infiltrate were not present. Monkeypox was briefly considered in the differential diagnosis, and monkeypox testing was negative.

## CONCLUSION

In this case, AGEP was associated with hydroxyzine and recurred with use of the medication. This highlights that AGEP may be recurrent with repeat exposure to the etiologic agent. The diagnosis of AGEP may be difficult and is best established with careful medical history, biopsy, and

**Figure 1.** Physical exam showed widespread erythema with generalized inflammatory papules and pustules.

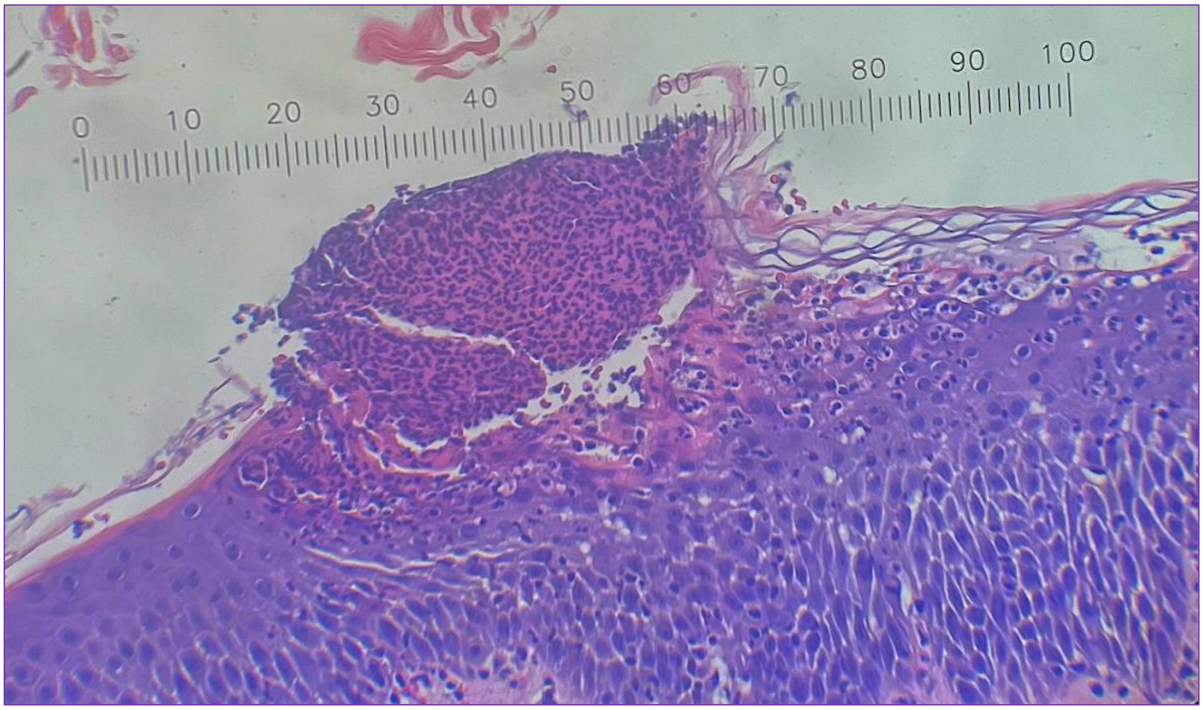


**Figure 2.** Hematoxylin and eosin stain of pathology from the biopsy revealed subcorneal neutrophilic pustules, spongiotic epidermis, and abundant papillary dermal edema; eosinophils were not prominent.

consideration of EuroSCAR criteria. Although the association with antibiotics is well established, awareness that hydroxyzine may also be the underlying culprit will help clinicians keep AGEP in the differential diagnosis of a widespread pustular rash.

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