A CASE REPORT OF ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS INDUCED BY DILTIAZEM

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Introduction

Acute generalized exanthematous pustulosis (AGEP) is a severe cutaneous adverse drug reaction characterized by the sudden appearance of numerous sterile, nonfollicular pinpoint pustules arising on an erythematous background. Medications—most commonly systemic antibiotics—are the predominant trigger. While the precise pathophysiology is not fully understood, AGEP is generally considered a type IV hypersensitivity reaction mediated by drug-specific T cells, leading to neutrophil recruitment and cytokine release. Clinically, AGEP presents with a rapid, diffuse pustular eruption often accompanied by fever, leukocytosis, and mild systemic symptoms. Following discontinuation of the offending agent, the eruption typically resolves with desquamation within 1 to 2 weeks. Diagnosis is primarily clinical and may be supported by histopathologic findings of spongiform subcorneal pustules with neutrophilic infiltration.

The overall prognosis is excellent; however, rare complications include secondary infection, hepatic or renal involvement, and progression to severe systemic reactions.

Case Summary

A 55-year-old woman with a past medical history of morbid obesity and hypertension presented with a diffuse, pruritic rash following a recent hospitalization for methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia and bacteremia. During her prior admission, she was treated with intravenous vancomycin and subsequently transitioned to and completed a course of oral linezolid. Her diltiazem dose had also been increased for management of paroxysmal supraventricular tachycardia. Upon the current admission, her home medications were continued.

Photographs depicting acute generalized exanthematous pustulosis throughout the torso and extremities.

Case Summary Cont.

Dermatology was consulted and recommended a punch skin biopsy, which revealed subcorneal pustules with marked papillary dermal edema, neutrophilic infiltrates, scattered eosinophils and lymphocytes, and extravasated erythrocytes within the superficial dermis. These findings supported a diagnosis of acute generalized exanthematous pustulosis (AGEP). Given the strong association between AGEP and diltiazem, along with completion of antibiotic therapy prior to admission and continued progression of the rash, diltiazem was considered the most likely offending agent.

The patient was managed with supportive wound care, systemic corticosteroids, and discontinuation of diltiazem, with plans for outpatient follow-up for ongoing surveillance and long-term management.

Discussion

In a large US cohort of 151 AGEP cases with a single suspected medication, calcium channel blockers (including diltiazem) accounted for 3.3% of cases (1). This case highlights the importance of considering non-antibiotic medications, including calcium channel blockers such as diltiazem, as potential triggers of AGEP. Clinicians should maintain a high index of suspicion for drug-induced pustular eruptions and carefully review recent medication changes, particularly dose escalations, to facilitate timely diagnosis and prevent unnecessary morbidity.

References

Creadore A, Desai S, Alloo A, et al. Clinical Characteristics, Disease Course, and Outcomes of Patients With Acute Generalized Exanthematous Pustulosis in the US. *JAMA Dermatol.* 2022;158(2):176–183. doi:10.1001/jamadermatol.2021.5390