Acute Generalized Exanthematous Pustulosis Caused by Pantoprazole

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PRACTICE **POINTS**

- Proton pump inhibitors can cause acute generalized exanthematous pustulosis (AGEP) and should be considered despite a low prevalence of adverse reactions.
- The combination of highly elevated neutrophilia and C-reactive protein may be a better marker for AGEP-precipitated extracutaneous organ involvement.

To the Editor:

A 34-year-old woman presented with a generalized pustular eruption with subjective fevers, chills, night sweats, and light-headedness. Ten days prior to admission she developed a generalized erythematous and pruritic rash; she had started pantoprazole for reflux 4 days prior to the rash. On admission, skin examination revealed facial edema and diffuse erythema covering 80% of the total body surface area with multiple 1- to 4-mm pustules coalescing into lakes of pus on the trunk as well as bilateral upper and lower arms and legs sparing the palms and soles. Desquamation and serous drainage with crust were observed on the skin of the head, upper trunk, and thighs (Figure 1). Vital signs were notable for hypotension. Laboratory tests on admission were remarkable for leukocytosis (white blood cell count: $22.5\times10^3/\mu L$ [reference range, $4.5–11\times10^3/\mu L$]) with absolute eosinophilia but no neutrophilia. C-reactive protein (CRP) was elevated (237.9 mg/L [reference range, 5.0–9.9 mg/L]). Renal and hepatic functions were normal. Blood cultures grew methicillin-sensitive *Staphylococcus aureus* (MSSA). Further infectious disease workup for viral and fungal pathogens was negative.

Skin biopsy from the left thigh revealed subcorneal, pustular, acute spongiotic dermatitis with marked intraepidermal spongiosis and papillary edema; exocytosis of eosinophils; and single cell necrosis of keratinocytes (Figure 2). These findings were consistent with acute generalized exanthematous pustulosis (AGEP). Pantoprazole was discontinued, and cardiovascular support and antibiotic therapy for MSSA bacteremia were initiated.

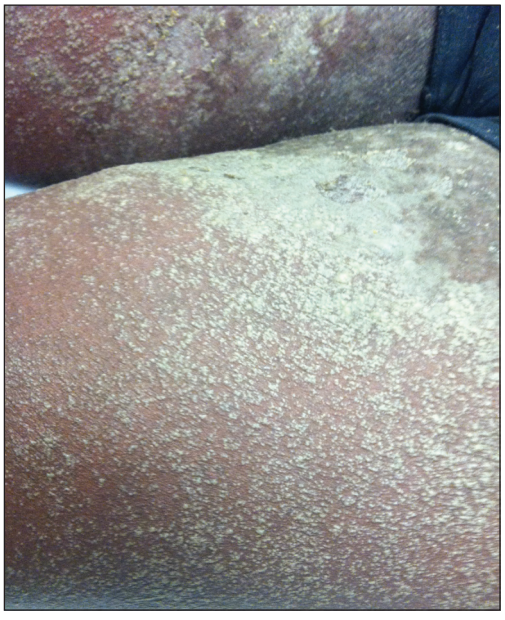

FIGURE 1. Acute generalized exanthematous pustulosis with multiple nonfollicular, 1- to 4-mm pustules coalescing into lakes of pus with areas of serous crust on the thighs.

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The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the US Government.

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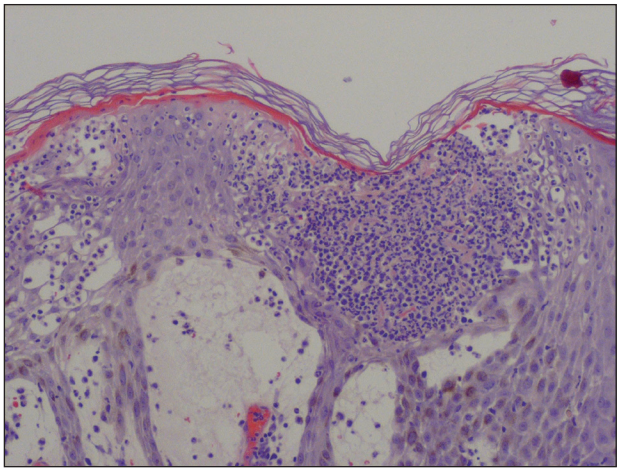

FIGURE 2. Punch biopsy from the skin of the left thigh demonstrated subcorneal, pustular, acute spongiotic dermatitis with marked intraepidermal spongiosis and papillary edema; exocytosis of eosinophils; and single cell necrosis of keratinocytes, characteristic of acute generalized exanthematous pustulosis (H&E, original magnification ×100).

Respiratory, kidney, and liver functions remained normal throughout the 11-day hospitalization, and the pustular dermatitis, MSSA bacteremia, and cardiovascular symptoms resolved within 10 days.

Acute generalized exanthematous pustulosis is an uncommon, self-limited, generalized sterile pustular eruption notable for the usual absence of systemic symptoms and extracutaneous organ involvement. Hotz et al[1] found that mean peripheral neutrophil counts (mean, $21.5\times10^3/\mu L$) and CRP levels (mean, 241.6 mg/L) were notably elevated in patients with systemic (ie, hepatic, pulmonary, renal, bone marrow) involvement. In our patient, only the CRP approached the elevated value reported by Hotz et al.[1] However, the patient exhibited only cardiovascular instability in the context of secondary bacteremia and no other systemic symptoms. The combination of highly elevated neutrophilia and CRP may be a better marker for AGEP-precipitated extracutaneous organ involvement.

Although infectious pathogens such as Epstein-Barr virus and cytomegalovirus have been implicated, the majority of AGEP cases are adverse reactions (ARs) to medications, such as β-lactam antibiotics. In our patient, the widely prescribed proton pump inhibitor (PPI) pantoprazole was the most likely cause. Acute generalized exanthematous pustulosis was reported in a patient taking another PPI, omeprazole.[2] However, PPIs are recognized to cause many cutaneous and other organ ARs, though prevalence of ARs is still low. In Thailand, Chularojanamontri et al[3] reported 13.8 per 100,000 individuals developed a cutaneous AR to PPIs, and the ARs most frequently were attributed to omeprazole. They found that drug exanthems were the most common cutaneous ARs.[3] However, more severe hypersensitivity reactions have been reported, including Stevens-Johnson syndrome, toxic epidermal necrolysis, and autoimmune eruptions such as cutaneous lupus erythematosus.[3,4] Other systemic reactions to PPIs include increased risks for urticaria, pneumonia, *Clostridium difficile* infections, and acute interstitial nephritis.[4,5]

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