CASE REPORT

Acute generalized exanthematous pustulosis associated with coccidiomycosis infection

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INTRODUCTION

Acute generalized exanthematous pustulosis (AGEP) is a rare cutaneous eruption of small, non-follicular, sterile pustules on an edematous and erythematous background. This cutaneous eruption is frequently accompanied by systemic findings, including fever and leukocytosis. Although the vast majority of AGEP cases are associated with medications, infectious causes have been implicated.1-3 Once the underlying cause is addressed, symptoms typically resolve spontaneously within 2 weeks. Given the potential for serious comorbidities, identifying the underlying cause is imperative for successful outcome. This case report describes AGEP associated with an acute coccidioidomycosis infection.

CASE REPORT

Inpatient dermatology was consulted to evaluate a 65-year-old man admitted to the hospital for a generalized, pruritic rash. In the 3 days prior to arrival, the patient complained of headache, dizziness, sore throat, dyspnea, decreased appetite, nausea, and fatigue. A pruritic patch developed over his right flank with associated perioral swelling. Within hours, the rash quickly disseminated from his flank to the majority of his skin, and he presented to the hospital for further evaluation.

Prior to hospitalization, the patient was healthy. He noted extensive landscaping performed on his property 3 weeks prior to his onset of symptoms. His past medical history was significant for benign prostatic hyperplasia, and he had been taking his prescribed tamsulosin for the previous 5 months. He denied taking any new medications or over-the-counter supplements. He denied any personal or family history of psoriasis.

On examination, the patient had a temperature of 39.5°C. A focused dermatologic examination revealed a generalized, non-follicular pustular eruption on an erythematous base that involved approximately 75% of body surface area (Figs 1 and 2). Mucous membrane involvement was absent. Facial edema was also present, with secondary areas of impetigo noted in a perioral distribution. Edematous urticarial lesions were distributed over the proximal thighs bilaterally. The palms and soles were notably unaffected. Two 4-mm punch biopsies were obtained from the patient’s upper back. One biopsy was from an isolated pustule, and the second was from uninvolved skin. Hematoxylin and eosin staining revealed a neutrophilic and eosinophilic inflammatory cell infiltrate present within the superficial dermis and involving the folliculosebaceous unit and the eccrine ducts (Fig 3). The findings were noted to be suggestive of a neutrophilic dermatosis, consistent with AGEP.

The laboratory results revealed mild leukocytosis (12.8 × 10³/µL) with an elevated absolute neutrophil count (11.3 × 10³/µL) but were otherwise unremarkable, including normal eosinophil count. The results of an extensive infectious workup, including COVID-19, were unrevealing. Initial coccidioidomycosis screening was negative. Chest
computed tomography revealed mediastinal and hilar lymphadenopathy as well as a nodular, patchy, ground-glass infiltration of the right lower lobe. Empiric antimicrobial therapy was started with ceftriaxone and fluconazole. Over the next several days, repeated *Coccidioides* serologic examination revealed positive IgG and IgM, suggesting an acute reaction. The patient received a diagnosis of an underlying coccidiomycosis pneumonia, and antifungal treatment was continued. Topical triamcinolone acetonide 0.1% cream was started along with topical mupirocin ointment for secondary impetigo. The patient’s condition gradually improved with continued antimicrobial therapy and topical corticosteroid use, with no new cutaneous lesions prior to discharge.

Follow-up in the dermatology clinic 11 days after hospital discharge showed near resolution of the pustular eruption. Diffuse postinflammatory hyperpigmentation was noted, with prominent desquamation. The pruritus had completely resolved, and the patient was no longer using the triamcinolone cream.

**DISCUSSION**

AGEP is an exceptionally rare entity, reported to occur in one to five patients per million per year. It commonly presents with fever, a neutrophil-predominant leukocytosis, and a cutaneous eruption with nonfollicular, sterile pustules on an erythematous base. The EuroSCAR study developed a scoring system with diagnostic criteria to help clinicians make the diagnosis of AGEP. The criteria include morphology of the cutaneous eruption, clinical course, and histopathologic findings (Table I). Based on these criteria, our patient’s presentation falls within the definitive diagnostic range for AGEP as outlined in the table.

In the majority of reported cases, AGEP is caused by medications. However, our patient denied using any new medications or over-the-counter supplements prior to the onset of the clinical presentation, making a medication etiology for the eruption unlikely. Pustular psoriasis is a similar entity to AGEP and should be excluded prior to establishing a diagnosis. Our patient denied a personal or family history of psoriasis, making a psoriatic eruption unlikely. Infections are another important, yet less common, cause of AGEP. Previous case reports described *Chlamydia*, Cytomegalovirus, and Parvovirus as infectious causes of AGEP. Given our patient’s clinical scenario, with an underlying pneumonia and positive IgM and IgG *Coccidioides* antibodies, coccidiomycosis is the most likely cause of his AGEP.

*Coccidioides* is a genus of dimorphic fungi most commonly found in warm, dry climates, such as the southwestern United States. Primary cutaneous
infections, although rare, can manifest as indurated nodules, abscesses, verrucous plaques and ulcers, or draining sinuses. More commonly, secondary cutaneous manifestations are reported, including erythema nodosum, acute exanthems, erythema multiforme, Sweet’s syndrome, and interstitial granulomatous dermatitis. This pathogenesis likely represents a reactive process whereby skin lesions do not contain visible microorganisms but occur from a systemic inflammatory eruption. Protection against coccidiomycosis has been convincingly related to induction of T helper 1 cell (Th1)-associated immune responses, with the induction of interferon and other Th1-associated cytokines. Similarly, the etiology of AGEP is thought to be a predominant Th1 cytokine profile process with elevated interferon gamma and granulocyte/macrophage colony-stimulating factor, which leads to augmented neutrophil survivability, enhancing formation of sterile pustules. This chemical profile overlap seen with both coccidiomycosis infections and AGEP may explain the development of an AGEP eruption in our patient with an acute coccidiomycosis pneumonia.

Although AGEP is most commonly associated with medications, clinicians should also consider the potential for an underlying infectious etiology, especially when subtle clinical findings are present.

### Conflicts of interest
None disclosed.

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| Variable | Description | Score |
|----------|-------------|-------|
| Morphology | Pustules | Typical | +2 |
| Erythema | Typical | +2 |
| Distribution/pattern | Compatible | +1 |
| Postpurpular desquamation | Yes | +1 |
| Course | Mucosal involvement | No | 0 |
| Acute onset | Yes | 0 |
| Resolution (<10 days) | Yes | 0 |
| Fever >38.5°C | Yes | +1 |
| Polymorphonuclear cells >7000/mm² | Yes | +1 |
| Histology | Subcorneal and/or intraepidermal | +2 |
| | nonspongiform or NOS pustule(s) with papillary edema | |

**AGEP**, Acute generalized exanthematous pustulosis; **NOS**, not otherwise specified.