

reported food allergens.⁷ Similar to the experience of the authors of a recent publication,⁸ penicillin allergy evaluation was negative in all patients who underwent testing, which is noteworthy given the previously described morbidity associated with the use of second-line antimicrobials.⁹

Comparing patients with positive and negative test results revealed significantly higher median serum IgE levels in those with objective evidence of sensitization. We note positive test results in 3 patients with serum IgE of less than 0.35 kU/L, the lower detectable limit in our laboratory.

Our study was limited by its retrospective nature and that the analysis was contingent on documentation by treating physicians. Not all patients underwent cutaneous or in vitro testing.

We provide evidence of IgE-mediated disease in patients with CVID evaluated at our referral center. These data are illustrative of the morbidity associated with the presence of allergy in a high-risk population. In patients with CVID, testing should be considered in all patients with a history suggestive of allergic disease given the lack of identifiable features to assist in predicting those with an intact immediate hypersensitivity response.

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Acute generalized exanthematous pustulosis with multisystem manifestations

Pinpoint pustules and purulent lakes

Affecting 2% of hospitalized patients, severe cutaneous adverse reactions (SCARs) are associated with high health care cost, morbidity, and mortality.¹ SCARs are a class of life-threatening reactions that typically include Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) or drug hypersensitivity induced syndrome, and acute generalized exanthematous pustulosis (AGEP).²

AGEP is a rare adverse reaction (estimated to occur in 1 in 5 million cases annually) and is characterized by numerous, nonfollicular, sterile pustules on an erythematous and edematous base.³ Topographical distribution includes the face, limbs, and trunk, with a propensity toward intertriginous areas.³ Cutaneous manifestations are accompanied by fever and neutrophilia, with progression to a confluence of pustules (purulent lakes) and eventual resolution through desquamation of the affected areas.⁴ After this typical progression, the diagnosis of AGEP can be made clinically, but biopsy is often performed. The presence of eosinophilia on a biopsy,⁵ as well as a historical correlation with recent antibiotic use and previous or active psoriasis or arthritis, can be used to distinguish AGEP from pustular psoriasis. AGEP responds well to topical or oral corticosteroids within a few weeks, and prompt removal or abating of the causative agent is paramount (eg, anti-

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biotics, calcium channel blockers, carbamazepine, paracetamol, infections, spider bites, UV radiation).^{3,6}

Atypical presentations of AGEP have been known to cause organ dysfunction beyond the dermis. Prior reports have noted hypotension, acute renal failure, abnormal hepatic function, acute respiratory distress, and severe lactic acidosis.⁷ Because of overlapping features in their initial presentations, differentiation among different SCARs can be challenging. AGEP has been reported to occasionally display features of other SCARs.^{8,9} For example, AGEP may display facial edema or mucosal involvement suggestive of SJS or TEN. Herein, we describe a patient who experienced atypical AGEP in response to piperacillin-tazobactam.

A 66-year-old white woman presented to the emergency department from a nursing home for treatment of left leg cellulitis, manifested primarily by an area of painful and warm erythema on the medial aspect of her thigh. She had concurrent morbid obesity, paraplegia secondary to a remote spinal abscess, hypertension, diabetes, congestive heart failure, and obstructive sleep apnea, for which she was using continuous positive airway pressure. Considering her diabetic history, the patient was admitted to the hospital and prescribed a course of piperacillin-tazobactam and vancomycin. With an appropriate response to broad-spectrum treatment in 72 hours, her antibiotics were changed to amoxicillin-clavulanate on her day of discharge. On return to her nursing home and before her ingestion of amoxicillin-clavulanate, the nursing staff observed a diffuse cutaneous erythema. She returned to the emergency department within 12 hours of discharge. Initial assessment de-

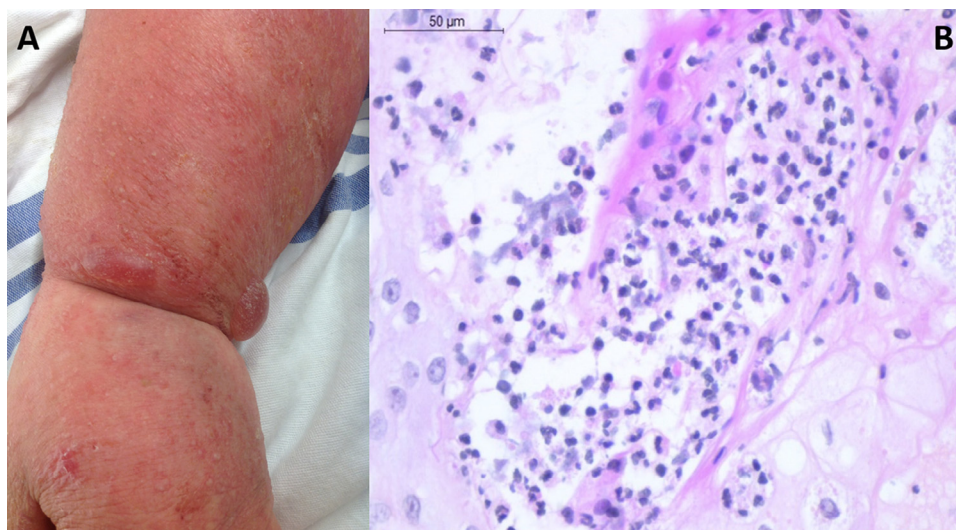


Figure 1. (A) Typical acute generalized exanthematous pustulosis rash shown on the patient's right distal extremity. Note the erythematous and edematous base and overlying confluent pustules. Blistering and desquamation are also present, which was further noted after resolution of the cutaneous reaction. (B) The superficial dermis display ectatic vessels with intraluminal neutrophils and a mild mixed perivascular inflammatory cell infiltrate, including neutrophils, few eosinophils, and rare plasma cells. No karyorrhectic debris, fibrinoid necrosis of vessel walls, or vascular thrombosis was seen. The results of special stains for fungal and bacterial organisms (not shown) were negative.

terminated she was disoriented, confused, agitated, febrile, hypotensive, and small, coalescing pustules were noted overlying the erythema (Fig 1), which were concentrated to the nape and axillary regions. On review of the patient's electronic medical record, it was discovered that she had received piperacillin-tazobactam a year prior, and records indicated that a morbilliform rash had developed days shortly thereafter, quickly resolving after cessation of the antibiotic treatment.

Given the current presentation, a clinical diagnosis of AGEF was made, with the causative agent believed to be piperacillin-tazobactam. Aspiration and culture of the pustules did not yield any culture results. Her initial blood work revealed leukocytosis (leukocyte count, $34.6 \times 10^9/L$) and eosinophilia (eosinophil count, $0.71 \times 10^9/L$). Further investigations revealed a mild elevation in liver enzymes (aspartate aminotransferase, 107 U/L; alanine aminotransferase, 73 U/L; alkaline phosphatase, 406 U/L) and an elevation in creatinine (162 $\mu\text{mol/L}$), with eosinophils on urine microscopy. Hypercarbia (venous Pco_2 71 mm Hg) was noted on blood gas. Punch biopsy revealed intracorneal neutrophils consistent with AGEF (Fig 1). Considering her clinical state, she was placed on bilevel positive airway pressure and sent to the intensive care unit. She was treated with systemic methylprednisolone at 125 mg intravenously daily and betamethasone valerate 0.1% topically, the latter for optimal control of her pain, which was thought to be contributing to a delirious state. Within 24 hours, this regimen produced a marked improvement in her skin; resolution of her systemic symptoms occurred by day 5 of treatment.

The presentation of our patient's rash is typical of AGEF; however, several systemic symptoms are uncharacteristic. In particular, liver inflammation, acute kidney injury, and respiratory distress are rarely reported with AGEF.⁷ Elevation in liver enzymes often presents in both DRESS and SJS.⁹ Liver involvement with AGEF has been previously described in the context of atypical AGEF that resembles other SCARs, with dermal features, such as acneiform and morbilliform eruptions resembling DRESS or sloughing of mucosal surfaces similar to SJS/TEN.⁸ Less frequently, respiratory disease has been reported in select cases and headed by severe cutaneous involvement; aseptic neutrophilic tissue infiltration has been proposed as a pathophysiologic mechanism of parenchymal injury.⁷ Complicating the respiratory findings is our patient's obstructive sleep apnea, which

would have predisposed her to hypercarbic respiratory failure and requirement of noninvasive mechanical ventilation. Of note, however, occurrences of acute respiratory distress have been reported in the literature,⁷ highlighting the importance of considering these less typical presentations of AGEF.

One pertinent finding is the development of AGEF after a previous reaction to piperacillin-tazobactam.¹⁰ The first regimen of the antibiotic may have primed the immune system to result in a more severe hypersensitivity reaction with second administration. Therefore, it remains crucial that physicians prescribing medications maintain a high degree of suspicion for potential adverse reactions. An increased understanding of the possibility of serious systemic complications after administration of any medications can lead to improved identification and treatment of SCARs. We believe our rare case confirms that overlap exists between AGEF and other cutaneous drug reactions in regard to disease presentation and severity and that detailed documentation of prior reactions to medications can aid in diagnosis and prevent adverse drug reactions from occurring. Increased awareness of cutaneous drug reactions will hopefully lead to a decreased incidence of SCARs, as well as create potential research avenues to identify predisposed patients and predict when SCARs will develop.

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Dexamethasone for inpatient childhood asthma exacerbations is as effective as short-acting corticosteroid treatment



Acute asthma exacerbations result in over 130,000 childhood hospitalizations in the United States annually.¹ Systemic corticosteroids (SCS) are a fundamental component of exacerbation management and reduce relapse rates after hospital discharge.² Use of prednisone or other short-acting SCS during hospitalization may require continuation of this medication after hospital discharge, yet a recent study demonstrated that only about half of these prescriptions are filled within 3–7 days of discharge.³

Dexamethasone has a half-life of 36–72 hours and a greater affinity for the glucocorticoid receptor compared with short-acting corticosteroids.⁴ Investigations comparing relapse rates after emergency department (ED) treatment of exacerbations have consistently demonstrated no difference between children treated with 1 or 2 doses of dexamethasone and those treated with a 5-day course of prednisone/prednisolone.^{5–8}

Despite those findings, there is limited knowledge of the comparative effectiveness of dexamethasone and short-acting SCS for children hospitalized with exacerbations. In a recent study by Parikh et al, children hospitalized for exacerbations had shorter length of stay (LOS) and comparable 7- and 30-day readmissions after dexamethasone treatment when compared with children given short-acting SCS.⁹ Their study did not report dexamethasone dosing regimens or whether the children in the dexamethasone group received discharge SCS prescriptions. Our objective in this study was to examine relapse and readmission rates among children hospitalized with exacerbations treated with short-acting SCS compared with those treated with exclusive inpatient dexamethasone.

We performed a retrospective analysis of data for children 2–18 years of age who presented to our academic children's hospital ED and were hospitalized for acute asthma exacerbations between January 1, 2012 and March 31, 2015. We used data from the Pediatric Health Information System database (Children's Hospital Association, Overland Park, Kansas) to identify children hospitalized with a principle diagnosis of asthma (*International Classification of Diseases, 9th Revision*, 493.xx). We merged the data with institutional pharmacy data for inpatient medication administration and prescription production. Patients' characteristics included age, gender, insurance type, and complex chronic condition.¹⁰ Exacerbation severity was defined as the mean relative cost weight for each All

Patient Refined Diagnosis-related Group and severity-of-illness level for each cohort. The project was approved through our institutional review board (protocol #151380).

We categorized patients into those who received exclusively short-acting SCS, dosed at 1 to 2 mg/kg per day for 5–7 days, and those who received exclusively dexamethasone, dosed at 0.6 mg/kg (maximum 16 mg per dose) and administered in the ED with a second dose 48 hours later or before discharge, whichever occurred first. We excluded children who received no SCS or both a short-acting SCS and dexamethasone, those who required intensive care unit (ICU) care, and those who were treated with dexamethasone and received a prescription for any SCS at discharge.

Our primary outcome was 30-day asthma readmission rate. Secondary outcomes included hospital LOS, 7-day readmission rate, and 7- and 30-day relapse rates. We defined readmission as a repeat asthma hospitalization at our institution, and relapse was defined as a return to our ED for an exacerbation.

Descriptive statistics are presented as median (interquartile range) or as proportion. The χ^2 , Wilcoxon rank sum, and Kruskal-Wallis tests were used to determine univariate associations. We used multivariable regression models to examine the adjusted associations between relevant covariates (age, gender, asthma exacerbation severity, insurance type, and SCS preparation) and 30-day relapse, readmission, and hospital LOS. Multivariable analysis was not performed for the outcomes of 7-day relapse or readmission, as there were too few patients for a stable model. $P < .05$ was considered statistically significant. Stata version 14.1 (StataCorp LLC, College Station, Texas) was used for all analyses.

There were 1,257 children hospitalized for asthma exacerbations during the study period. Of these, 346 were cared for in the ICU, 108 received both short-acting SCS and dexamethasone, 11 received no SCS during their hospitalization, and 30 received dexamethasone but also received an SCS prescription at discharge and were all excluded, leaving a total study population of 762. Among the 762 children, 263 (34.5%) received only dexamethasone and 499 (65.5%) received only short-acting SCS. The short-acting SCS group had higher median severity scores (Table 1). In univariate analyses there were no differences in 30-day readmissions ($P = .78$) or relapses ($P = .95$) or in 7-day readmissions ($P = .95$) or relapses ($P = .90$) (Table 1). In the multivariable logistic regression analysis, there were no differences between the 2 corticosteroid groups in 30-day readmission (adjusted odds ratio for short-acting SCS, 1.06; 95% confidence interval [CI], 0.36–3.14) or relapse (adjusted