Case Report

iMedPub Journals
www.imedpub.com

Medical Case Reports
ISSN 2471-8041

2019
Vol.5 No.1:88

Pediatric Acute Generalized Exanthematous Pustulosis Involving Staphylococcal Scarlet Fever

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Rec date: November 28, 2018; **Acc date:** January 18, 2019; **Pub date:** January 21, 2019

Citation: Henry SM, Stanfield MM, Dorey HF (2019) Pediatric Acute Generalized Exanthematous Pustulosis Involving Staphylococcal Scarlet Fever. Med Case Rep Vol. 5 No.1:88.

Abstract

Acute Generalized Exanthematous Pustulosis (AGEP) is a rare skin disorder that affects all ages. It is typically noted by an extensive rash, swelling, and erythema, with numerous white pustules. We present a case of a six-year-old who suffered from staphylococcal scarlet fever for several days, which progressed to AGEP, and illustrate the course of her in-patient and primary care.

Keywords: Acute Generalized Exanthematous Pustulosis (AGEP); Pustules; Cutaneous reactions; Bacterial exanthema; Rash; Staphylococcal Scarlet Fever; Dermatology

Abbreviations: AGEP: Acute Generalized Exanthematous Pustulosis, ANC: Absolute Neutrophil Count, ED: Emergency Department, LAD: Lymphadenopathy, MRSA: Methicillin-Resistant Staphylococcus Aureus, SJS/TEN: Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis, SSF: Streptococcal Scarlet Fever, SSSS: Staphylococcal Scalded Skin Syndrome, TSS: Toxic Shock Syndrome, VGE: Viral Gastroenteritis.

Introduction

Acute generalized exanthematous pustulosis (AGEP) is a cutaneous adverse reaction of very short onset characterized by an eruption of diffuse, non-follicular, sterile pustules covering an erythematous base. It is very rare, with approximately one to five cases per million per year across all ages, and is usually accompanied by fever, leukocytosis, and occasional mucous membrane involvement [1,2]. 90% of cases are caused by drug reactions, but there are reports of infectious etiology for AGEP [3-8]. Most pediatric exanthems arise from viruses; however a few stem from bacteria [9].

This report is based on one such uncommon pediatric pathology, having presented atypically from staphylococcal scarlet fever. There are examples of bacterial infection worsening to AGEP and specifically staphylococcal scalded skin syndrome (SSSS) developing into AGEP; similar to the progression we now report [10-12]. A milder form of SSSS, staphylococcal scarlet fever, is characterized by scarlatiniform rash and desquamation, yet lacks the strawberry tongue and pharyngeal infection of its streptococcal counterpart [13]. Many AGEP cases are iatrogenic in nature, but the novelty of the infectious nature in this case presents valuable insight to primary care/general practice, dermatology, and other specialties. We propose a mechanism by which acute generalized exanthematous pustulosis may be facilitated by staphylococcal scarlet fever.

Case Presentation and Assessment

A previously healthy six-year-old female presented with a confluent, macular, erythematous rash and a fever of 101°F/38°C for two days. The rashes started on her scalp and face one evening, and spread to the neck, chest, and axilla overnight. There was swelling in her face the next morning. With no obvious dietary or environmental triggers, toxic shock syndrome (TSS) was not suspected, though the patient was quite uncomfortable with pruritis. Past medical history, family/social history, and review of systems was otherwise negative.

She began a course of trimethoprim/sulfamethoxazole, following suspicion of MRSA, and was given acetaminophen and diphenhydramine in the emergency department (ED) with follow-up scheduled in primary care. She was seen two days later in a pediatric clinic, at which time the pustules had spread to the abdomen, arms, and lower extremities, consistent with normal progression of AGEP [3,14-16]. She was admitted for further evaluation of her severe rash, with concerns for significantly worsening discomfort from pruritus. Dermatology was consulted, her pustules and nares were cultured, trimethoprim/sulfamethoxazole was discontinued, and she was given triamcinolone 1% topical steroid. Ophthalmology was consulted to rule out ocular pathology; however nothing of note was found **(Figures 1 and 2)**.

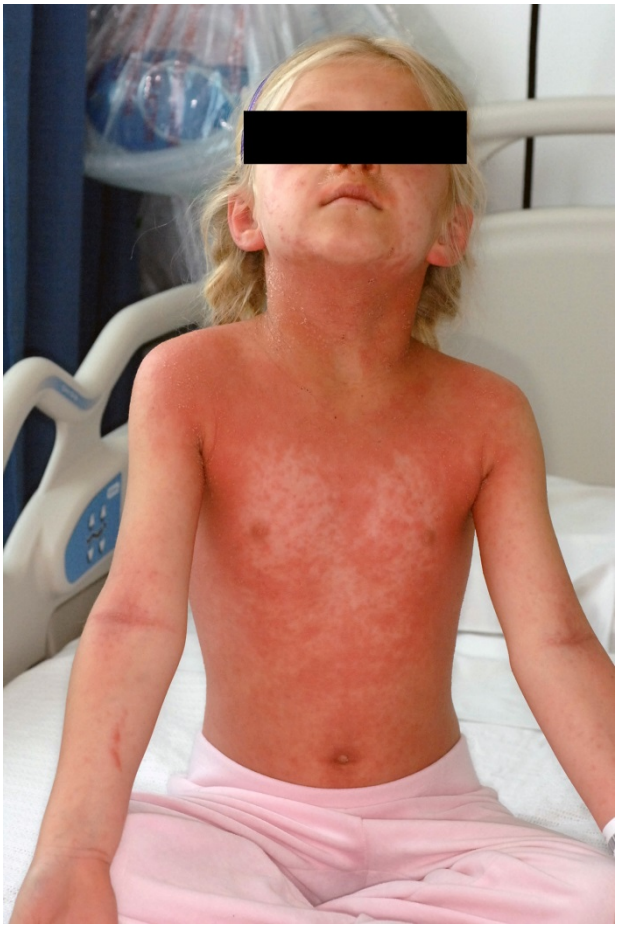

Figure 1 Lesions over the neck and chest.

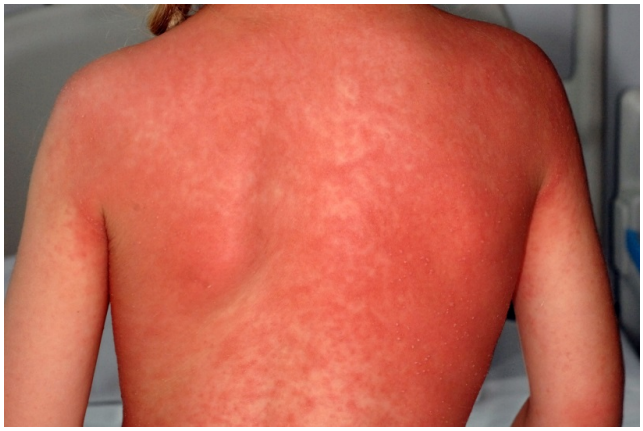

Figure 2 Lesions over axilla.

Lab cultures from a nasal swab showed a heavy growth of coagulase-positive *Staphylococcus aureus* which was pan-sensitive to antibiotics. She was discharged the next day, sent home with triamcinolone acetonide cream to be applied over her entire body, and mupirocin for the nares. Itching was controlled with diphenhydramine. The day after discharge, the patient showed much improvement and desquamation of the rash. A combination of clinical and pathological findings confirmed the definitive diagnosis of AGEP secondary to staphylococcal scarlet fever. Ongoing home care included mupirocin TID to the nares, Triamcinolone acetonide topical ointment TID to the body, and pimecrolimus ointment BID to the face **(Figures 3-6)**.

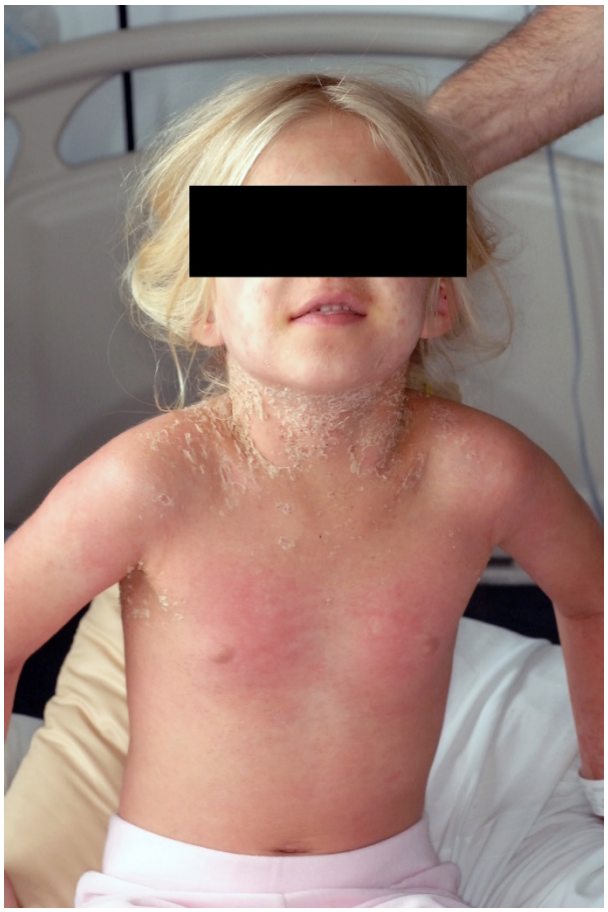

Figure 3 After treatment with triamcinolone acetonide cream.

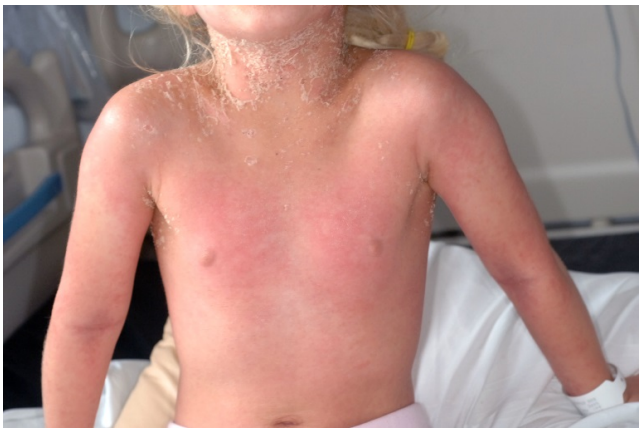

Figure 4 Improvement and desquamation of the rash.

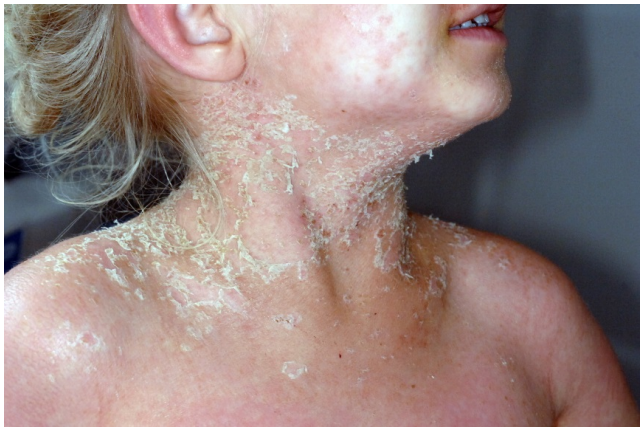

Figure 5 Skin peeling after treatment.

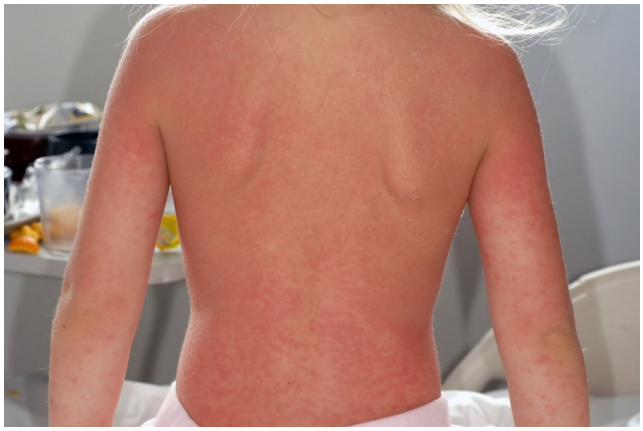

Figure 6 Patient after treatment.

Of note, five weeks later, she became ill again with a fever of unknown origin and lymphadenopathy (LAD) in setting of positive sick contact with a family member suffering from viral gastroenteritis (VGE). CBC at the time showed neutropenia with absolute neutrophil count (ANC) of 900 and right submandibular LAD, consistent with a reactive LAD. Neutropenia is clinically relevant, given that AGEP is a neutrophilic event, and elimination of granulocytes after an infection, combined with antibiotic use, can result in neutropenia [15-17]. This patient improved without any further intervention over the next month.

Histopathology

Laboratory analysis usually yields spongiform pustules rich in neutrophils and other infiltrate such as eosinophils and necrotic keratinocytes [18,19]. Despite these values however, children are often treated clinically and without invasive sampling, as punch biopsies are avoided in children when possible. If blood testing is sought, neutrophil count indicative of AGEP typically exceeds 7.0 x 10^9/L [3].

Physical characteristics

AGEP occurs rapidly (≤ 1 day), with many nonfollicular, sterile, pinhead-sized pustules on a background of edematous erythema with flexural accentuation [3]. It generally starts on the face and spreads cephalocaudally [20]. Severe cases of AGEP may have coalescent pustules that result in erosions and may present similar to Stevens - Johnson syndrome/ toxic epidermal necrolysis (SJS/TEN) [21].

Diagnosis

Biopsies are helpful, but rapid onset, presentation, and strong clinical suspicion in conjunction with laboratory findings are keys to proper diagnosis. Though not used at the time of this patient's care, we appreciate the scoring system provided by the European Study of Severe Cutaneous Reactions (EuroSCAR) study group in evaluating AGEP [16]. **Table 1** illustrates the clinical and pathological factors relevant to this patient's history and **Table 2** lists pertinent laboratory values.

Table 1 Summary of findings.

Clinical criterion or variable	Patient attributes
Presentation in clinic	
Polymorphous, pin-sized pustules	Present
Erythema	Present
Distribution (e.g. intertriginous areas)	Fully consistent
Course	
Acute onset (≤ 1 day)	Yes
Fever of at least 38°C	Yes
Mucous membrane involvement	Slight
Rapid resolution	Yes
Histology	

Intra or subcorneal spongiform pustules	Present
Superficial, interstitial, and mid-dermal infiltrate rich in neutrophils > 7.0 × 10^9/L	Not tested at time of staph infection
Eosinophils in pustules	Yes
Necrotic keratinocytes	Yes
Gram stain	Negative for bacteria

Table 2 Lab results five weeks after original diagnosis, showing neutropenia

CBC w/ differential	Units	Ref Rng
WBC	2.5 (L) × 10^3/mcL	(5.0-15.5)
RBC	4.76 × 10^6/mcL	(4.2-5.4)
Hemoglobin	12.0 g/dL	(12.0-16.0)
Hematocrit	0.374	(37.0-47.0)
MCV	78.5 (L)fL	(81.0-99.0)
MCH	25.2 (L)pg	(27.0-31.0)
MCHC	32.2 g/dL	(31.0-36.0)
RDW CV	0.118	(11.5-14.5)
MPV	8.8 fL	(6-12.5)
Platelets	128 (L) × 10^3/mcL	(130-400)
Neutrophils	41.5 (L)%	(50-70)
Lymphocytes	46.7 (H)%	(20-40)
Monocytes (%)	10.9 (H)%	(2-8)
Eosinophils	0	(0-5)
Basophils	0.009	(0-1)
ABS Neutrophils	1.0 (L) × 10^3/mcL	(1.8-7.7)
ABS Lymphocytes	1.2 × 10^3/mcL	(1.0-4.0)
ABS Monocytes	0.3 × 10^3/mcL	(0-0.8)
ABS Eosinophils	0.01 × 10^3/mcL	(0-0.5)
ABS Basophils	0.01 × 10^3/mcL	(0-0.2)

Differential diagnosis

Alternatives to consider include: generalized acute pustular psoriasis, SJS/TEN, drug reaction with eosinophilia and systemic symptoms (DRESS), subcorneal pustular dermatosis, bullous impetigo, subcorneal IgA dermatosis, and generalized pustular psoriasis [3], pustular eruptions (caused by bacteria, funguses, herpes viridae, and the varicella zoster virus), SSSS [16], streptococcal scarlet fever, and pustulosis acuta generalisata. Timing and physical features during the course of the ailment is key to diagnosing correctly.

Treatment and Prognosis

Cases generally resolve on their own one to two weeks after discontinuation of an offending drug or resolution of an underlying illness. With the exception of extremely rare systemic involvement [17], it is limited to the skin and heals without scarring, although the desquamation can be alarming to patients, thus reassurance may be necessary, in addition to keeping the skin clean and the patient well hydrated to avoid complications [20]. During the pustular phase, consider moist dressings and antiseptics; during the desquamation phase, consider emollients. Treat pruritus as needed with topical steroids or other anti-pruritic creams (e.g. camphor/menthol topical ointment). Avoid oral steroids, as these exanthems are not long-lasting, and oral routes have not been shown to shorten the overall duration of the condition or improve outcomes [22]. If a drug reaction is suspected, consider patch testing for confirmation, which is much preferred to punch biopsy in children.

Discussion and Conclusion

This young girl had an unusual presentation of a rare condition. Although it is most commonly an adverse drug reaction in adults, it is important to consider acute generalized exanthematous pustulosis when examining cutaneous pathology in acutely-ill pediatric patients. Viral and bacterial exanthems are far less frequently encountered and may escape initial investigation.

Treating with oral antibiotics have not been shown improve the condition, and side effects from antibiotic treatment may be worse than the condition itself. Topical antibiotics are an excellent alternative in a non-toxic pediatric patient, but for deteriorating patients who may have disseminated staphylococcus or streptococcus infection, early treatment with IV antibiotics such as bactericidal clindamycin can be life-saving. While AGEP is not associated with high rates of mortality, it is important to control in young, elderly, or pregnant patients, in addition to those that may be immune-compromised, such as certain surgical and/or admitted patients, or those with existing infection.

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