Dermatology Case Reports

Sheth et al., Dermatol Case Rep 2018, 3:2

Case Report Open Access

Ciprofloxacin-induced Acute Generalized Exanthematous Pustulosis

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Received date: Sep 18, 2018; **Accepted date:** Dec 10, 2018; **Published date:** Dec 14, 2018

Abstract

Acute Generalized Exanthematous Pustulosis (AGEP) is a cutaneous eruption characterized by sterile non-follicular pustules located on erythematous skin. This case report describes a rare instance of ciprofloxacin-induced AGEP in a patient initially admitted to the hospital for treatment of acute diverticulitis.

Keywords: Exanthematous pustulosis; AGEP; SJS; Rash

Introduction

Severe Cutaneous Adverse Reactions (SCARs) are common side effects of antibiotics [1]. Acute Generalized Exanthematous Pustulosis (AGEP) is a cutaneous eruption characterized by sterile non-follicular pustules located on erythematous skin [2]. It is often associated with fever, malaise, and leukocytosis. Unlike Stevens-Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN), it is rarely life-threatening with an average mortality rate of 2% [2]. We report a case of suspected ciprofloxacin-induced AGEP in a 59-year-old female.

Case Report

A 59-year-old female with a remote past medical history of nephrolithiasis, left-frontal hemorrhagic stroke, and necrotizing vasculitis was admitted on 8/2018 to our hospital with acute diverticulitis with micro perforation. She was managed conservatively with intravenous (IV) fluids, NPO status, and IV antibiotics ciprofloxacin 400 mg every 12 hours and metronidazole 500 mg every 8 hours.

On day 3 of the hospital admission, a diffuse rash was noted on the patient's back and IV diphenhydramine therapy was initiated to provide symptom relief. At this time, the patient's family reported a remote history of rash from ciprofloxacin. The rash worsened over the next 2 days and due to increasing leukocytosis (16.1 × 109 L) and reported allergy, antibiotics were changed to piperacillin-tazobactam 3.375 grams IV every 6 hours.

On day 6, with continued worsening of rash and leukocytosis (24.4 × 109 L) coupled with a lactate level of 2.8 mmol/L, antibiotics were broadened further to aztreonam, vancomycin, and metronidazole (Table 1). Infectious disease consultant recommended continuing the current regimen empirically. Infectious workup included enterohemorrhagic assays and skin pustule smears, which remained negative. A dermatology consult was also obtained and a skin biopsy was performed. On day 9, the rash was now diffuse, edematous and erythematous with oral and vaginal mucosal involvement (Figures 1 and 2). A C-reactive protein level of 234.76 mg/L (reference range: <7.48 mg/L), lactate of 4.3 mmol/L (reference range: 0.4-2.0 mmol/L), and intermittent episodes hypotension prompted a transfer to the intensive care unit for closer monitoring. Of note, no bullous lesions were noted and Nikolsky sign was negative. Differential diagnosis included Stevens-Johnson Syndrome, toxic epidermal necrolysis, pustular psoriasis, and staphylococcal scaled skin.

Pathology report of punch biopsy indicated several subcorneal pustules associated with moderate spongiosis and superficial dermal infiltrate without epidermal necrosis. The biopsy report combined with the patient's clinical picture led to a firm diagnosis of AGEP (Figures 3 and 4). All antibiotics were discontinued and triamcinolone cream 0.1% application and chlorhexidine bath were initiated. Rash and leukocytosis slowly improved with complete resolution of rash on day 13 of hospitalization. The patient was discharged on hospital day 17 with the recommendation of the topical application of white petrolatum as needed daily. Liver and renal function tests remained normal throughout hospitalization. Of note, patch testing was not performed.

Age	59
Sex	Female
Drug allergy	Ciprofloxacin
Previous drug reaction	Rash
Interval between drug intake and rash	3 days
Interval between drug intake and pustules	9 days
Duration of rash	13 days
Fever>38.75°C	Yes
Leukocytes	34500
Neutrophils	94%
C-reactive protein	234.76 mg/L
Lactate	4.3 mmol/L
Skin biopsy results	subcorneal pustules associated with moderate spongiosis and superficial dermal infiltrate

Resolution of rash after drug withdrawal	10 days

Table 1: Relevant patient characteristics and laboratory results.

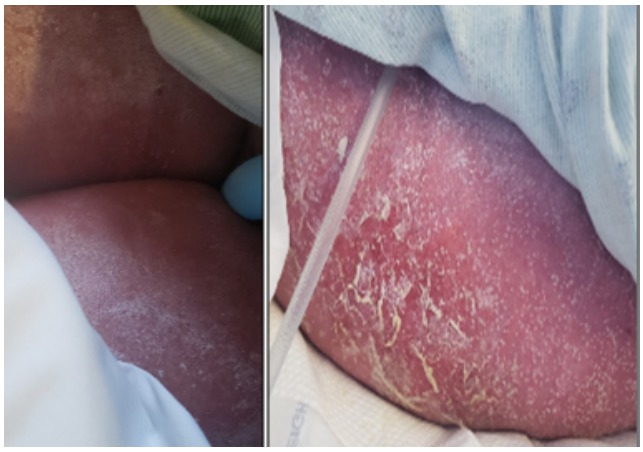

Figure 1: Diffuse rash seen on inner thighs (left) and left hip (right) on Day 5 of hospitalization.

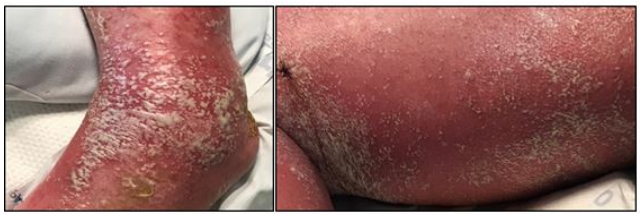

Figure 2: Significant pustular erythematous rash seen on left foot (left) and left hip (right) on day 9 of hospitalization.

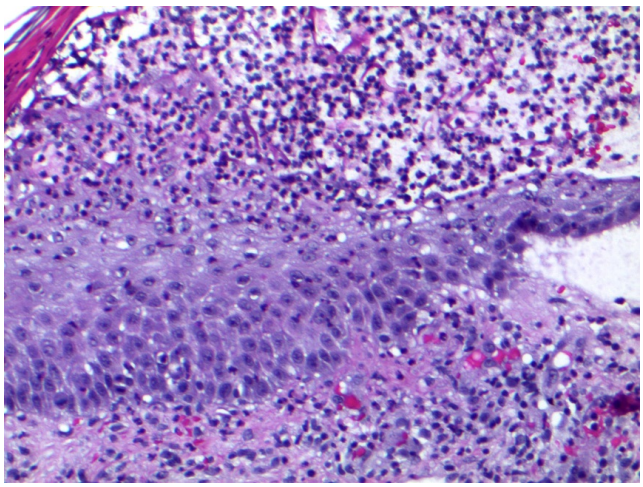

Figure 3: High power view of a subcorneal pustule showing numerous neutrophils within a pustule, mild/moderate spongiosis and a mild superficial dermal lymphocytic infiltrate.

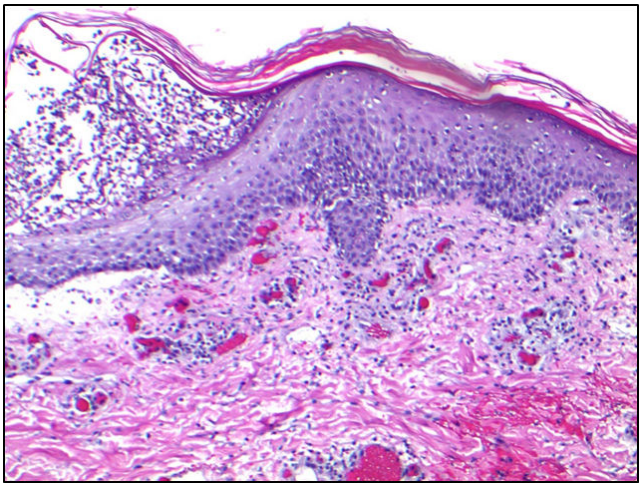

Figure 4: Low power view demonstrating prominent spongiotic subcorneal pustule. Acanthosis is not prominent. A mild perivascular lymphocytic infiltrate is present in the superficial dermis.

Discussion

This case demonstrates a rare instance of ciprofloxacin-induced AGEP. While AGEP is known to be self-limiting after drug discontinuation, severe cases have been reported in elderly and immunocompromised patients [1]. Commonly, antibiotics implicating in causing AGEP are penicillins, cephalosporins, and fluoroquinolones [1]. The average length before AGEP eruption is 1-11 days, with antibiotics causing an earlier symptom-onset [3]. Faster courses have been observed when patients are re-challenged with an offending agent, regardless of the severity of the initial reaction [1]. In this case, the patient was re-exposed to ciprofloxacin and symptom onset was approximately 1.5 days. Typical clinical features of this case included diffuse, progressive edematous and erythematous rash and a consistent histological pattern accompanied by fevers, neutrophilia, and leukocytosis [2]. Atypical symptoms included involvement of mouth and vaginal mucosa, only seen in 20% of AGEP cases [1]. AGEP validation score derived through the EuroSCAR criteria was 9, signifying "definite" AGEP based on morphology, clinical course, and histology (range for definite AGEP: 8-12) [4].

To our knowledge, this is the fourth reported case of ciprofloxacin-induced AGEP, with only one, confirmed via patch testing [5]. We cannot fully rule out metronidazole-induced AGEP.6 However, due to patient's previously reported allergy to ciprofloxacin, acuteness of symptom-onset with re-exposure and lack of metronidazole-induced AGEP case reports, it is reasonable to attribute this case to ciprofloxacin. Patch testing is a useful and noninvasive way to confirm the culprit agent but is characterized by sensitivity of only 60% [6]. After reviewing this case, antibiotic stewardship, a thorough review of allergies, and early recognition of cutaneous reactions are essential for appropriate clinical diagnosis and improved patient care.

References

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