

A Delayed Presentation of Acute Generalized Exanthematous Pustulosis (AGEP)

Case Report

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Abstract

Acute Generalized Exanthematous Pustulosis (AGEP) is a Type IVd hypersensitivity reaction that usually occurs within 1-5 days of drug exposure. The diagnosis is clinical and confirmed by skin biopsy. A scoring algorithm has been developed which assigns points to characteristic clinical signs in order to aid in the diagnosis. AGEP is a self-limited disease with a favorable prognosis in most cases. We present an unusual delayed presentation of AGEP secondary to hydroxychloroquine.

Keywords: AGEP; Type IV Hypersensitivity; Adverse Drug Reaction; Hypersensitivity Delayed;

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Introduction

Acute Generalized Exanthematous Pustulosis (AGEP) occurs in 1-5 million cases per year, and has 2-5% mortality [1, 2]. It is most frequently characterized by an acute episode of erythematous and edematous eruptions of sterile pustules within 1-5 days of drug exposure. AGEP has a female predominance [3] as well as a genetic susceptibility related to HLA B51, DR11, and DQ3 [4].

Case Report

A 70-year-old female with polymyalgia rheumatica on corticosteroids for 2 years presented with pruritic rash. The rash began on her face and spread to her scalp, chest, upper and lower extremities. The patient self-increased her prednisone from 7mg to 40mg a day with no relief and experienced subjective fevers, chills,

malaise, increased thirst and anorexia requiring hospitalization. Medications on admission included lorazepam, hydrochlorothiazide/triamterene, fluticasone, tiotropium bromide, alendronate, ibuprofen, prednisone, and hydroxychloroquine. The patient was seen by Dermatology who noted diffuse erythematous pustular lesions (Figure I) on her scalp (Figure II), chest (Figure III), abdomen (Figure IV), and back (Figure V) and performed two skin biopsies. The differential diagnosis included Steven-Johnson's syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), pustular psoriasis, and infectious etiologies.

Laboratory workup was relevant for leukocytosis with left shift (22,630 polymorphonuclear cells) and elevated CRP. Early signs of SJS and DRESS were monitored closely. Her biopsy results described pustular and erythematous lesions, spongiform subcorneal pustules with dermal acute and chronic inflammation with the presence of neutrophils. The cultures showed no growth. The skin biopsy along with the lack of eosinophils on blood smear favored a diagnosis of AGEP. Upon further questioning, she had started hydroxychloroquine three weeks prior to her cutaneous manifestations. Immediate skin prick testing was not performed. Patch testing may be considered in selected patients presenting with delayed type IV. However, this has not been validated and is not utilized at our Institution. Clinical history and histopathology supported an AGEP diagnosis despite an uncharacteristic three-week span between inciting drug administration and reaction. Consequently, hydroxychloroquine was discontinued. Recovery occurred slowly over a three-week period and was complicated by *S.aureus* bacteremia secondary to skin integrity loss, requiring nafcillin treatment.

Discussion

AGEP is considered a Type IVd hypersensitivity reaction, characterized by drug specific T-cells secreting neutrophil attractant IL-8/CXCL8 [5, 6]. Common causes of medication induced

Figure 1. Diffuse erythematous pustular lesions.

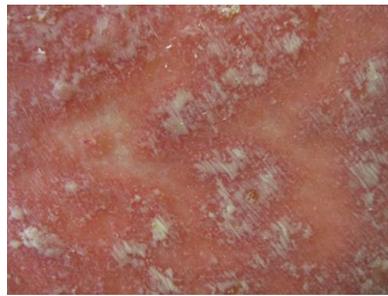


Figure 2. Scalp with erythematous pustular lesions.



Figure 3. Chest with erythematous pustular lesions.



Figure 4. Abdomen with erythematous pustular lesions.



Figure 5. Upper back with erythematous pustular lesions.



Table I. Medications that induce AGEP.

| |
|-----------------------------|
| Aminopenicillins |
| Quinolones |
| Anti-infective sulfonamides |
| Hydroxychlorquine |
| Pristinamycin |
| Terbinafine |
| Diltiazem |
| Costicosteroids |
| Macrolides |
| NSAIDs |
| Antiepileptics |

AGEP [7] are shown in Table I. With regards to hydroxychloroquine, the average time between drug initiation and the onset of reaction has been reported to be 12 days, with 78% of cases presenting in the first 15 days [3].

The diagnosis is dependent upon histopathology identifying subcorneal, intraepidermal pustules, edema of the papillary dermis, perivascular infiltrates with neutrophils and eosinophils, focal necrotic keratinocytes, and vasculitis [8]. This is frequently confused with generalized pustular psoriasis, with the key difference being the lack of acanthosis and papillomatosis in AGEP [7, 8]. A scoring algorithm has been developed which assigns points to characteristic clinical signs in order to aid in the diagnosis [1]. According to the algorithm, our patient had a highly probable diagnosis, losing points for delayed onset and slow recovery [1]. AGEP is a self-limited disease with a favorable prognosis in most cases. The recommended treatment consists of withdrawal of the suspected drug and supportive therapy [1]. Secondary skin infections are a common complication in the elderly and immune compromised patients.

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