

Case Report:

Acute generalized exanthematous pustulosis

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ABSTRACT

Acute generalized exanthematous pustulosis (AGEP) is a rare reaction pattern with a typical morphology and a short clinical course that in majority of cases is related to medication administration. It is an acute pustular eruption with unique clinical features, a rapid clinical course and a typical histopathology. Herein, we report the case of a patient with acute generalized exanthematous pustulosis for its classical presentation.

Key Words: *Acute generalized exanthematous pustulosis, Chicken pox*

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INTRODUCTION

Pustular reactions have been reported in association with a number of drugs.¹ It is known by various name like toxic pustuloderma, and acute generalized exanthematous pustulosis (AGEP). It is important to differentiate AGEP from pustular psoriasis.² Two histological patterns may be seen in AGEP: (i) a toxic pustuloderma with spongiform intraepidermal pustules, papillary oedema and a mixed upper dermal perivascular inflammatory infiltrate; or (ii) a leukocytoclastic vasculitis with neutrophil collections both below and within the epidermis, suggesting passive neutrophil elimination via the overlying epidermis.^{3,4} The presence of eosinophils in the inflammatory infiltrate is a helpful pointer to consider drug as a cause.² AGEP often starts on the face or in flexural areas, rapidly become disseminated; associated fever may be present. The condition regresses spontaneously with desquamation. Facial oedema, purpura, vesicles, blisters and erythema multiforme-like lesions are also seen; transient renal failure can be noted in 32% of cases; occasionally, it can mimic toxic epidermal necrolysis.⁵ AGEP has been reported following administration of penicillins, macrolides, ampicillin/amoxycillin (with or without clavulanic acid), pristinamycin, quinolones,

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(hydroxy)chloroquine, anti-infective sulphonamides, terbinafine, diltiazem, carbamazepine and spiramycin (with or without metronidazole).⁶⁻¹⁰ There may be positive patch test reactions to the suspected drug when these patients are patch tested with offending drug.^{9,11} AGEP can result in death.⁸

CASE REPORT

A 25-year-old lady with suspected septic abortion, reported to Gynaecology out-patient service with complaints of amenorrhoea, high grade fever and generalized weakness. On clinical evaluation, she was suspected to have septic abortion and was treated with intravenous sulbactam and ampicillin along with other symptomatic measures. After 3 days of intravenous antibiotic treatment, though there was mild improvement in her general condition, she developed low grade fever, generalized pruritus and blisters all over the body and was referred to the dermatologist. On examination she had multiple, oedematous papulo-vesicular lesions over an erythematous base confined to the trunk (centripetal distribution) (Figures 1A, 1B and 1C). Few lesions had central umbilication whereas extremities and mucous membranes were spared. She did not have any past, or family history of varicella. There was no history of arthralgias, psoriasis, in the past.

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Figure 1: Clinical photograph showing lesions over abdomen (A) and extremities (B and C)

Based on the above clinical findings patient was diagnosed to have chicken pox and was started on oral acyclovir (800 mg five times a day). The differential diagnosis considered included bullous pemphigoid, dermatitis herpetiformis, impetigo, pustular psoriasis and erythema multiforme. However, the rash progressed to the extremities within 24 hours of its first appearance on the trunk and involved the whole body. The patient was comfortable, except for low grade fever, had no constitutional features that are evident in chicken pox.

By 24 hours, patient had numerous, scattered, superficial, non-follicular pustules of 3 to 4 mm size on an erythematous and oedematous background distributed bilaterally all over the body sparing face, intertriginous folds, palms, and mucosa (Figures 1B and 1C). There was no evidence of significant peripheral lymphadenopathy. Systemic examination revealed no abnormality. In our patient, EuroSCAR score¹² was 9. (a score of 8-12 is required for definitive diagnosis of AGED).

Haematological investigations showed haemoglobin of 10.6 g/dL, total leucocyte count of 12,600/mm³, differential leucocyte count showed neutrophils 76%, lymphocytes 14% and eosinophils 10%. Liver function tests and other biochemical parameters were normal. Gram staining of pus smears, pus culture and blood culture were negative after 48 hours. The Tzank smear did not reveal any significant findings, such as, multinucleate giant cells, so acyclovir was stopped. Skin biopsy was not done as the patient improved spontaneously with

characteristic pin-point post-pustular desquamation in few days. A diagnosis of AGEP was made.

DISCUSSION

AGEP was first described by Baker and Ryan in 1968 as a form of acute pustular eruption in response to medication.¹³ It was again described in 1980 by Beylot et al,¹⁴ who named it as, *pustuloses exanthematique aigues generalizes* (PEAG) in French. He described pustular eruptions with certain common features such as acute onset following a bout of infection or drug ingestion.¹⁴ AGEP is a pruritic eruption characterized by the acute onset of numerous small, non-follicular, sterile, superficial pustules amidst erythematous and oedematous skin.¹⁵ Usually the eruption begins on the face and intertriginous regions, and the patient commonly manifests associated systemic involvement with an estimated mucosal involvement in 20 percent of the patients.^{4,12} The incidence of this condition is estimated to be 1-5 per million per year.¹⁵ The disease is self-limiting, fever and pustules lasting for 7 to 10 days, followed by desquamation.⁴

The aetiology of this condition is not clear. Often drugs and viral infections are implicated. Recently several reports consider that these eruptions are a new form of drug reaction.¹⁶ Antibacterials are the main class of drugs implicated in the development of AGEP.⁴ Our patient had exposure to β -lactam antibiotics 3 days prior to her skin eruption which is consistent with time frame of AGEP. A

thorough medical history, drug history, with clinico-pathologic correlation is important in a patient presenting with acute diffuse pustular lesions to make a diagnosis of this condition.

Drugs, especially penicilins are implicated as a common cause of AGEp.⁴ In a review of 63 cases,⁵ only 18% of implicated medications were found to be drugs other than antibiotics.⁴ Other aetiologies implicated have been viruses (Parvo virus B19 and enterovirus), mercury, spider bites, and other medications.^{4,17,18} Although sulfphonamides often cause other severe skin eruptions, they are not a frequent cause of AGEp.

The sensitivity of patch testing to drugs in AGEp is approximately 50%.¹⁹ Systemic reactions have been reported with patch testing with acetaminophen and diltiazem.²⁰ Different tests that have been used to elucidate the cause of AGEp are in vitro tests such as macrophage migration inhibition factor (MIF) test, the mast cell degranulation (MCD) test¹² and the lymphocyte transformation test (LTT).²¹

Criteria employed for the diagnosis of AGEp⁵ include: (i) numerous, non-follicular pustules (<5 mm) arising on widespread edematous erythema; (ii) histopathological evidence of sub corneal and/or intraepidermal pustules often with dermal oedema and perivascular infiltrates of neutrophils or eosinophils; (iii) fever temperature >38 °C; (iv) peripheral blood neutrophils greater than $7 \times 10^9/L$; and (v) acute onset with spontaneous resolution of pustules in less than 15 days.⁴ A comprehensive validation score for AGEp has been described based on a multinational epidemiological case-control study on severe cutaneous adverse reactions (EuroSCAR).¹² Score is assigned based on morphological (presence of pustules, erythema, distribution of lesions, postpustular desquamation), and histopathological criteria (presence of sub corneal, intraepidermal pustules, spongiosis, papillary oedema). A score of 8-12 points is considered diagnostic for AGEp and our patient's score was 9.

Discontinuation of the offending agent and symptomatic treatment are generally agreed in the treatment of AGEp. In our patient, only symptomatic measures were instituted and the response was satisfactory. Systemic corticosteroids have been utilized for treatment of terbinafine-induced AGEp in the majority of cases described in the literature, but the benefit remains unclear.²² AGEp has been described in a woman on chronic low doses of oral corticosteroids for bullous pemphigoid.²² Furthermore, they observed that the time for resolution with corticosteroids was longer than the time for resolution without corticosteroids. Interestingly, it is unclear whether the amount of corticosteroid given or the relative severities of corticosteroid-treated cases of AGEp were confounding factors.

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