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Acute Generalized Exanthematous Pustulosis Due to Insect Bites?

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Abstract

Acute generalized exanthematous pustulosis is a rare severe cutaneous adverse reaction pattern that is mostly caused by the intake of drugs and rarely associated with viral infections, food allergens or toxins. Here we present the report of three patients who got admitted in our hospital for generalized pustulosis and fever after insect bites. The diagnosis of acute generalized exanthematous pustulosis was made by EuroSCAR scoring. The drug etiology was excluded and spider bite was implicated as the etiological agent in these cases of AGEF which are the first such reported cases in India.

Keywords: *Acute generalized exanthematous pustulosis, EuroSCAR, spider bites, sterile pustules*

What was known?

Acute generalized exanthematous pustulosis (AGEP) is a rare severe cutaneous reaction pattern caused mostly by drugs and rarely associated with viral infections, food allergens or toxins.

Introduction

Acute generalized exanthematous pustulosis (AGEP) or toxic pustuloderma is a rare severe cutaneous adverse reaction pattern that is mostly caused by the intake of drugs (in >90% cases). Rarely it can be associated with viral infections, food allergens and toxins.^[1,2] It can occur in both sexes and all age groups. The eruption in AGEF is characterized by erythematous and edematous nonfollicular papules and pustules which starts in flexures or on face and then generalizes to other parts of the body. There is usually associated history of itching and burning sensation.

Case Report

Here we present the case report of three patients (two females and one male) who presented in the summer months with acute generalized pustulosis and erythema with fever and had the history of insect bite prior to the onset of rash. The clinical features have been tabulated [Table 1]. One of these patients was admitted for spider bite and developed generalized pustular rash during hospital stay which was initially attributed to the antibiotic amoxycillin-potassium clavulanate but the pustular crops continued to appear despite the drug being stopped. The other two were admitted for the generalized pustulosis who gave the prior history of insect bite. All the routine hematological and biochemical investigations of the patients were done. Gram staining and biopsy of the pustules was carried out in all the three patients. The insect bites were presumed

to be spider bites as the patients gave history of spiders present in their houses (circumstantial evidence) and the cutaneous examination at bite site was consistent with it but due to lack of facilities the toxin identification was not possible. Symptoms of loxoscelism were not seen in these patients. The outcome was favorable in all cases with symptomatic treatment. The diagnosis of AGEF was made after validation score of the EuroSCAR study group [Table 2].

Discussion

AGEF or toxic pustuloderma is a rare severe cutaneous adverse reaction pattern that is mostly caused by the intake of drugs (in >90% cases). Rarely it can be associated with viral infections, food allergens and toxins.[1,2] Hypersensitivity to mercury has been reported as a precipitating factor. AGEF is usually due to penicillins or macrolides, especially ampicillin/amoxicillin with or without clavulanic acid, quinolones, hydroxychloroquine, sulfonamides, terbinafine, diltiazem and carbamazepine. It can occur in both sexes and all age groups. The eruption in AGEF is characterized by erythematous and edematous nonfollicular papules and pustules which start in flexures or on face and then generalize to other parts of the body. There is usually associated history of itching and burning sensation. The main differential diagnosis is pustular psoriasis.[3,4,5] Mucus membrane involvement may be seen in approximately 25% of the cases. The eruption resolves spontaneously in few days in majority of the cases. The eruption in AGEF is usually associated with fever, leukocytosis and eosinophilia.[6] Internal organ involvement is rarely seen. EuroSCAR study criteria are used for the validation of AGEF. These criteria were fulfilled by our patients.

On histopathology two patterns may be seen: (1) A toxic pustuloderma with spongiform intraepidermal pustulosis, papillary edema and a mixed upper dermal perivascular inflammatory infiltrate; or (2) a leukocytoclastic vasculitis with neutrophil collections both below and within the epidermis.[7]

In our case series three patients (2 females and 1 male) were admitted in the summer months following spider bite (which was diagnosed presumptively on the basis of clinical features and exclusions of other insect bites). One patient had taken the antibiotic amoxicillin-clavulanic acid before admission which was stopped but the eruption continued and increased in severity. There was no history suggestive of viral infection or an allergic cause. Polymorphonuclear leukocytosis (in all three) and eosinophilia (in 1 patient) was noted on routine blood testing. Histopathology was consistent with the diagnosis of AGEF in all three cases and excluded the possibility of pustular psoriasis which is the closest differential diagnosis. Spider bite was implicated as the most likely causative factor leading to AGEF as the drug etiology was excluded in all the three cases- circumstantial evidence only. The necrotic cutaneous form was seen in all the three cases and systemic symptoms were mild [Figures 1-3]. The other form known as viscerocutaneous loxoscelism was not seen. Histopathology was suggestive of AGEF in all the cases [Figure 4]. RICE therapy (Rest, application of ice compresses and elevation) was employed to reduce inflammation and pain.

The occurrence of AGEF following spider bite has been rarely reported in the literature (only six case reports to the best of our knowledge). This is probably the first such reported case from India. Davidovici *et al.* in a study from Israel reported AGEF following spider bite in three cases in 2006. The eruption (AGEF) in their case series had occurred 24 to 48 hours after a spider bite.[8] Ben Said *et al.* reported AGEF following spider bite in three cases from Tunisia in 2010. They diagnosed it on the basis of characteristic skin lesions, chronology of event and exclusion of other common causes of AGEF.[9] Ermertcan *et al.* reported AGEF with lymphangitis triggered by a spider bite in a female patient from Turkey in 2010. Because there was no history of drug use in their case, they attributed her AGEF lesions to the spider bite.[10] Makris *et al.* reported (AGEF) triggered by a spider bite in 2009;[11] Pippirs *et al.* reported AGEF following a *Loxosceles* spider bite in Great Britain in 2009;[12] and Lane *et al.* reported AGEF and Coombs-positive hemolytic anemia in a child following *Loxosceles reclusa* envenomation in 2011.[13]

The exact mechanism leading to AGEF following spider bites is not known. It is believed that the spider venom contains spingomyelinase which can stimulate the release of cytokines and chemokines especially IL-8 and GM-CSF and it is these inflammatory mediators which have been found to trigger AGEF.[14,15,16]

What is new?

Our cases and the few others published in the literature indicate that spider bites may be added to the list of the possible causes of AGEP.

Footnotes

Source of support: Nil

Conflict of Interest: Nil.

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Figures and Tables

Table 1

Sex	Site	Cutaneous lesion of spider bite	Onset of AGEF	Fever	Drug in take prior to AGEF	Gram staining of pustules	Eosinophilia
Female	Neck	Erythema, edema, necrosis and ulceration	2 days	Yes	Amoxicillin-clavulanic acid	Sterile	Nil
Female	Lower back	Erythema, edema and necrosis	2 days	Yes	Nil	Sterile	Present
Male	Right shoulder	Erythema, necrosis and ulceration	3 days	Yes	Nil	Sterile	Nil

AGEF: Acute generalized exanthematous pustulosis

Clinical data of the three patients

Table 2

Parameter	Case 1	Case 2	Case 3
Morphology			
Pustules	Typical (nonfollicular and sterile)	Typical	Typical
Erythema	Typical	Typical	Typical
Distribution	Compatible	Typical	Compatible
Postpustular desquamation	+	+	+
Score	6	7	6
Course			
Mucosal involvement	-	-	-
Acute onset (<10 days)	+	+	+
Resolution of pustules (<15 days)	+	+	+
Fever	+	+	+
PNN count (>7000/mm ³)	+	+	+
Score	2	2	2
Skin histology	Subcorneal pustule with mild edema	Subcorneal pustule with papillary dermal edema and perivascular infiltrate in upper dermis	Subcorneal pustule with papillary dermal edema and perivascular infiltrate in dermis
Score	2	2	2
Total score*	10	11	10

*Interpretation=0- No AGEP, 1-4 Possible, 5-7 Probable and 8-12 definite. AGEP: Acute generalized exanthematous pustulosis

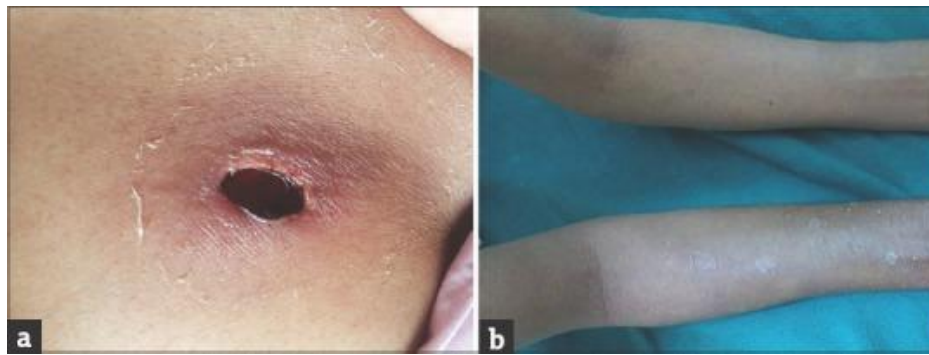
AGEP validation score of the EuroSCAR group

Figure 1

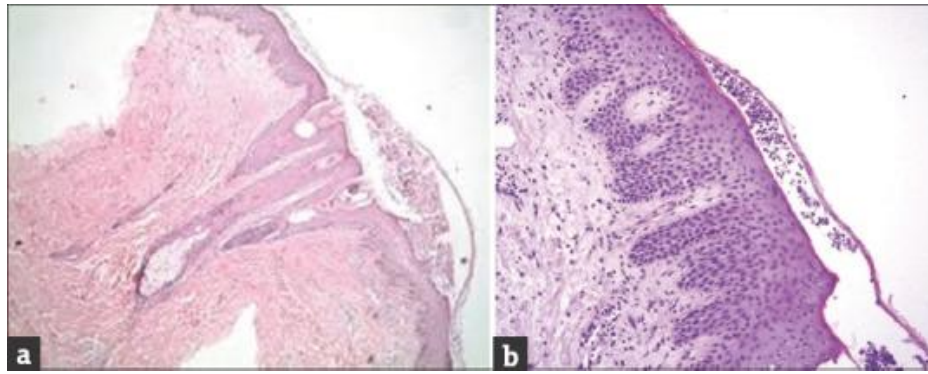
(a) Spider bite on neck presenting with necrosis, ulceration, erythema surrounded by pustules. (b) Diffuse erythema and pustules on the body

Figure 2

(a) Spider bite on lower back with erythema, edema and necrosis. (b) Diffuse erythema and pustules mainly in skin folds

Figure 3

(a) Spider bite on right shoulder with erythema, necrosis and ulceration. (b) Post pustular desquamation

Figure 4

(a) Photomicrograph showing subcorneal bulla filled by acute inflammatory cell infiltrate with edema of superficial dermis and dermal inflammation (H and E $\times 40$). (b) Photomicrograph showing subcorneal pustule formation with edema of papillary dermis and mild dermal inflammatory cell infiltrate (H and E $\times 100$)

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