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CASE REPORT

Acute Generalized Exanthematous Pustulosis (AGEP) Triggered by a Spider Bite

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ABSTRACT

Background: Acute generalized exanthematous pustulosis (AGEP) is a rare and severe cutaneous reaction usually triggered by drugs. Other causative factors such as viral infections are rarely involved. In this study, we report a case of AGEP caused by a spider bite.

Case Summary: A 56-year-old woman was referred to the allergy unit after a spider bite at the left popliteal fossa, while gardening, 5 days earlier. The offending spider was captured and identified by an entomologist as belonging to the *Loxosceles rufescens* species. No acute reaction was observed; however, after 24 hours, due to the occurrence of typical dermonecrotic skin lesions associated with erythema and edema, Cefuroxime and Clindamycin were administered intramuscularly after medical advice was given. Almost 72 hours after the spider bite, an erythematous and partly edematous eruption appeared locally in the gluteus area bilaterally, which progressively expanded to the trunk, arms and femors. Within 24 hours dozens of small, pinhead sized, non-follicular pustules were present, mainly in the folds. The patient complained of a burning sensation of the skin in addition to pruritus; and simultaneously had a fever of 38–39℃ as the eruption expanded.

Discussion: A spider bite may represent a possible causative factor of AGEP. A spider's venom contains sphingomyelinase that stimulates the release of IL8 and GM-CSF, which are involved in AGEP pathogenesis. Whether or not the con-current use of antibiotics has an effect in AGEP appearance when combined with a spider's venom, cannot be excluded.

KEY WORDS

acute generalized exanthematus pustulosis, brown spider, insect venom, loxosceles rufescens, spider bite

INTRODUCTION

Acute generalized exanthematous pustulosis (AGEP) is a rare and severe cutaneous reaction pattern characterized by a sudden onset of small sterile pustules over an erythematous skin, accompanied with fever and leukocytosis.

Apart from a slight reduction of the creatinine clearance and a mild elevation of aminotransferases, usually no involvement of any other internal organs needs to be expected. The eruption progresses and resolves relatively rapidly without treatment. Histologically, the lesions show subcorneal and/or intraepidermal pustules, edema of the papillary dermis and perivascular infiltrates with neutrophils and exocytosis of some eosinophils.[1]

A large proportion (>90%) of cases are triggered by drugs, especially macrolides and aminopenicillins.[2] In a minority of cases additional triggers, such as acute viral infections have been implicated. We present a well-documented case of AGEP triggered by a Loxosceles rufescens spider bite.

CLINICAL SUMMARY

A 56-year-old woman was referred to the allergy unit after a spider bite at the left popliteal fossa, while gardening 5 days earlier. The offending spider was captured and identified by an entomologist as belonging

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Fig. 1 Erythematous and partly edematous eruption almost 72 hs after the spider bite.

to the *Loxosceles rufescens* species. No acute reaction was observed, however, after 24 hours, due to the occurrence of typical dermonecrotic skin lesions associated with erythema and edema, Cefuroxime (Zinacef®, 750 mg × 3/d) and Clindamycin (Dalacin-C®, 600 mg × 2/d) were administered intramuscularly following medical advice. Almost 72 hours after the spider bite, an erythematous and partly edematous eruption appeared locally in the gluteus area bilaterally, which progressively expanded to the trunk, arms and femurs (Fig. 1) . Within 24 hours dozens of small, pinhead sized, nonfolicular pustules were present, mainly in the folds. The patient complained of a burning sensation of the skin in addition to pruritus; and also had a fever of 38–39℃ simultaneously, as the eruption expanded.

PATHOLOGICAL FINDINGS

Laboratory evaluation revealed leukocytosis to be present (18300/mm^3) due to an increased neutrophil count (11970/mm^3) and an elevated CRP concentration (17.1 mg/μl) . Mild eosinophilia (650/mm^3) was also observed. Results of blood and pustules cultures were negative for bacterial infection while serologic evaluation for viruses (CMV, EBV, chlamydia, adenovirus, measles, HBV, HCV) were also negative. Antihistamines and topical emollients, as symptomatic treatment, were administered. Approximately 6 days after the spider bite, a widespread cutaneous desquamation occurred although all other symptoms had disappeared. The cutaneous lesions completely resolved in 15 days after the bite occurred.

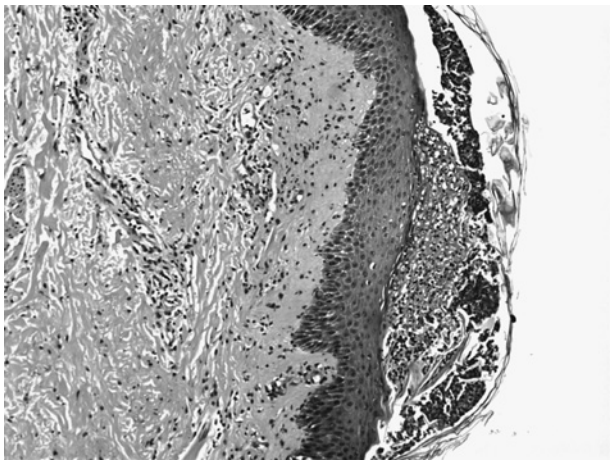

Fig. 2 Histological features with subcorneal and intraepithelial pustules, edema of papillary dermis and diffuse perivascular cellular infiltration.

Skin punch biopsy revealed subcorneal and intraepidermal pustules, edema of the papillary dermis and diffuse perivascular infiltration of neutrophils and a few eosinophils (Fig. 2) .

Cutaneous morphology, its course and histological findings were consistent with a definite diagnosis by the EuroSCAR study group[2] with a validation of 10 points in our case while the range for definite AGEP was 8 to 12.

Approximately 1 month after the eruption resolved the patient underwent an allergological evaluation using Skin Prick Tests (SPTs) to tenfold dilutions and full strength concentrations of cefuroxime and clindamycin (100 mg/ml and 150 mg/ml respectively) followed by intradermal testing (IDs) to standard non-irritating dilutions[3] (10^{-3} to 10^{-1} from full strength concentration) of both specimens. Patch testing was performed with tenfold dilutions and full strength concentrations of both agents. IDs and patch tests were evaluated after 15 minutes, at 48 and 72-hour intervals. All performed tests were negative. Accordingly, the patient underwent an open oral graded challenge with cefuroxime (Zinadol® from 1 mg to 500 mg) and continued with 500 mg × 2/day for 3 days, without any adverse effects. However, a challenge to clindamycin was not performed due to the patient's reluctance. During a 12 month period after the reaction, no re-occurrence or other possibly related disorders were reported.

DISCUSSION

Spider bites are common, however, most domestic spiders are not substantially toxic for humans. The well known exceptions are brown spiders (*Loxosceles spp*) and widow spiders (*Lactodectus spp.*). *Loxosceles rufescens*'s occurrence in Greece is well-documented.[4] Similar to its counterpart *L. recluse* (the best known

cause of necrotic arachnidism) the venom of *L. rufescens* is equally toxic. Although *Loxosceles* bites are usually mild, they may ulcerate or cause more severe, systemic reactions attributed to the multicomponent *Loxosceles* venom.

Loxosceles spiders are active at night. They are drawn to dark, dry areas such as basements and closets. Bites to human beings usually occur when the spider is pressed against the body.[5]

Induction of AGEP after a spider bite is extremely rare[6] and the mechanism responsible is unknown. In our case, the clinical history combined with laboratory findings confirms the diagnosis of AGEP. However, the possible implication of the administered antibiotics cannot be excluded and such involvement is documented in literature[7]; they may have functioned as additional triggers although the allergological evaluation does not support evidence for that. In AGEP pathogenesis, IL-8 and CM-CSF are implicated for the recruitment of polumononuclear cells into the epidermis; thus they contribute to neutrophilic infiltration and ensure neutrophil survival. IL-8 is produced by keratinocytes and T cells.[8] Since the *Loxosceles* venom contains sphingomyelinase that can stimulate the release of cytokines and chemokines, including large amounts of interleukin 8 and GM-CSF,[5] it may have acted as the underlying offender in the immunological triggering for AGEP.

In conclusion, our study implies that in rare cases pertaining to spider bites, AGEP occurrence may be triggered by the bite itself or even in combination with drug intake.

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