Acute localized exanthematous pustulosis induced by fosfomycin

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INTRODUCTION

Acute localized exanthematous pustulosis (ALEP) is a drug reaction characterized by the abrupt onset of multiple, localized nonfollicular, pinhead-sized, and sterile pustules over an erythematous and edematous background. It is regarded as a rare form of acute generalized exanthematous pustulosis (AGEP). Ninety percent of reported ALEP and AGEP cases present within 3 to 5 days of drug ingestion and often resolve after withdrawal of the trigger.[1]

Fosfomycin is a US Food and Drug Administration–approved broad-spectrum antibiotic that is currently used in women with uncomplicated urinary tract infections caused by *Escherichia coli* and *Enterococcus faecalis*.[2] It has been found to be highly efficacious against multidrug-resistant, extensively drug-resistant, and pandrug-resistant organisms. It acts through irreversible inhibition of the early stages of bacterial cell wall synthesis by inhibiting peptidoglycan biosynthesis. Herein, we present a case of ALEP induced by fosfomycin use. The objective of this report is to highlight the importance of ALEP as one differential diagnosis for a pustular lesion especially a recent drug has been started.

Abbreviations used:

AGEP: acute generalized exanthematous pustulosis
ALEP: acute localized exanthematous pustulosis

CASE REPORT

A 67-year-old woman with diabetes mellitus, hypertension, dyslipidemia, and stage IV chronic kidney disease presented to the emergency department with 1-week history of dysuria and a 4-day history of a mildly pruritic skin rash. The rash started over the bilateral inguinal regions then progressed to the right side of the abdomen, right inner arm, and left forearm. She denied a history of fever, personal or family history of psoriasis. The patient has a history of recurrent hospital admissions due to urinary tract infections. She had started a 3-day course of fosfomycin for a urinary tract infection caused by an extended-spectrum β–lactamases-producing organism 4 days prior to the rash onset.

Her home medications included insulin, amlodipine, furosemide, candesartan, metoprolol, aspirin, atorvastatin, and darbepoetin. No other recent drugs or herbal medicines were taken in the prior month. There was no previous personal or family history of dermatological conditions such as psoriasis. Additionally, there were no previous allergic episodes due to systemic or topical treatments.

On physical examination, the patient was hemodynamically stable. Clinical skin examination showed Fitzpatrick skin type III with multiple tiny annular pustules and fine desquamation centrally over an erythematous base; the lesions were predominantly localized over the right inner arm, left forearm, and right side of the abdomen (Fig 1). Face, oral, and genital examinations were unremarkable.

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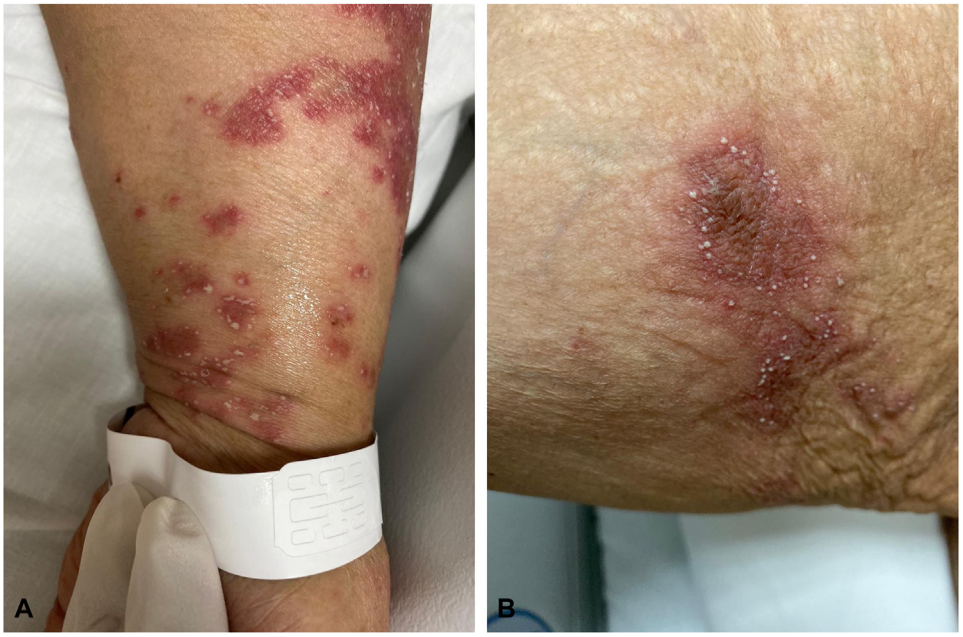

Fig 1. Physical examination of acute localized exanthematous pustulosis. **A,** Multiple annular pustules superimposed on background erythema over the forearm. **B,** Multiple annular pustules superimposed on background erythema over the arm.

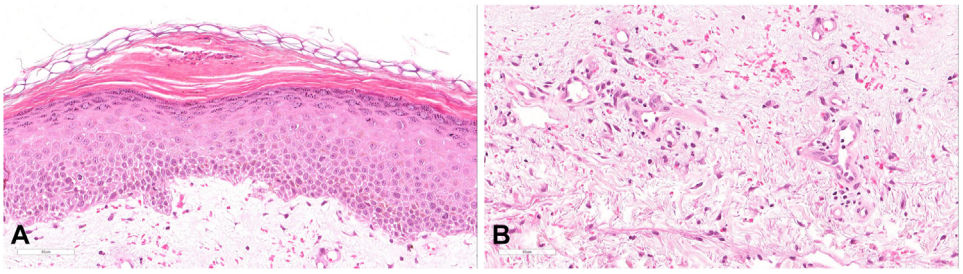

Fig 2. Histology of acute localized exanthematous pustulosis. **A,** Reactive epidermal hyperplasia and spongiosis. **B,** Neutrophilic and eosinophilic infiltration of the deep and superficial dermis. **A** and **B,** Hematoxylin-eosin stain; original magnifications: **A,** ×400; **B,** ×400.

Laboratory studies revealed normal hematologic, renal and liver function tests. Erythrocyte sedimentation rate was elevated (83 mm/h). Direct florescence antibody test and polymerase chain reaction test for herpes simplex virus types 1 and 2 as well as varicella-zoster virus were negative. Swabs for candida and dermatophytoses were also negative.

A punch biopsy of the lesions was obtained from the right inner arm and histological examination revealed reactive epidermal hyperplasia, spongiosis, and neutrophilic infiltration. The dermis showed superficial and deep perivascular and interstitial eosinophils and neutrophils (Fig 2). Additionally, an abundance of extravasated red blood cells with vasculitic reaction consistent with drug eruption was also observed. There was no evidence of herpetic viral changes or fungal organisms on periodic acid-Schiff stain and tissue culture. The surrounding skin showed absence of immunoglobulin deposition on direct immunofluorescence.

Upon the constellation of these findings, a diagnosis of ALEP was made. The patient was started on topical treatment of clobetasol propionate 0.05% ointment twice daily and hydrocortisone acetate 1% twice daily over the body and bilateral inguinal area respectively for a 2-week course. She showed a positive response to treatment with resolution of pustules and erythema within 1 week, with no hyperpigmentation or scarring.

DISCUSSION

ALEP has rarely been reported in the literature compared to AGEP. Multiple medications are known to trigger ALEP, such as antibiotics (eg, β-lactams,

clindamycin, trimethoprim-sulfamethoxazole), nonsteroidal antiinflammatory drugs (eg, diclofenac, ibuprofen), and other various drugs (eg, finasteride, lamotrigine, sorafenib, docetaxel, and allopurinol).[1,3] Skin lesions in ALEP and AGEP are predominantly localized on the face, neck, and chest.[4] The pathogenesis of ALEP and AGEP is described as a delayed type hypersensitivity reaction of types IVc and IVd involving cytotoxic T cells (CD8+) and neutrophils, respectively.[5] Laboratory findings are usually normal in ALEP compared to the generalized form which may reveal leukocytosis.[1] Clinical and histologic examination of ALEP and AGEP show nonfollicular, sterile, subcorneal pustules with spongiosis and perivascular infiltrate of neutrophils and eosinophils.[1] Management of ALEP mainly consists of discontinuation of the suspected medication and supportive treatment with topical or oral corticosteroids.[6]

The differential diagnoses of ALEP include Stevens-Johnson syndrome/toxic epidermal necrolysis, pustular psoriasis, and AGEP. The absence of mucosal membrane involvement, short duration of treatment, absence of previous or current psoriatic lesions, and the localization of lesions in ALEP distinguishes it from its differential diagnoses.

In this case, the patient's history of recent antibiotic use, absence of systemic symptoms— although fever can present in some cases of ALEP—and the resolution of lesions upon withdrawal of the culprit drug led to the diagnosis of ALEP.

Conflicts of interest

None disclosed.

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