LETTERS TO THE EDITOR

Acute Generalized Exanthematous Pustulosis due to Pseudoephedrine with Positive Patch Test

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Sir,
Acute generalized exanthematous pustulosis (AGEP) is a cutaneous reaction characterized by an acute non-follicular pustular eruption overlying a scarlatiniform background, usually associated with high fever and neutrophilia. This rare disease is generally drug-induced, particularly by antibacterial drugs. Only two other cases provoked by pseudoephedrine ingestion have been reported. Patch testing has been advocated recently as a potentially useful test in patients with AGEP.

We report here a case of pseudoephedrine-induced AGEP where subsequent patch testing results were positive.

CASE REPORT
A 41-year-old man was admitted for evaluation of an acute, tender, erythematous and pustular eruption accompanied by fever and malaise. Cutaneous lesions had begun in the antecubital, inguinal and popliteal folds, quickly spreading to involve the entire body. Twenty-four hours previously the patient had ingested one tablet of Rinoebastel® (ebastine 10 mg, pseudoephedrine 120 mg) to treat nasal discharge. The patient was otherwise healthy, and had no personal or family history of psoriasis or other skin disease.

Clinical examination revealed fever (38.2°C), bilateral tender cervical, axillar and inguinal adenopathies, and generalized scarlatiniform erythema scattered with multiple non-follicular pustules and intense facial oedema. Palmar and plantar areas were spared. The inferior lip semi-mucose was erythematous and eroded. There was no evidence of other mucous membrane involvement (Fig. 1).

Laboratory studies including blood cell count, liver and renal function test and electrolytes were all within normal limits except from leukocytosis 21.3×10⁹/l (4.5–11×10⁹/l) with neutrophilia 87% (40–75%). Chest radiogram and abdominal ultrasonography were normal. Bacterial cultures from the throat and pustules produced negative results. Serological tests for HIV, cytomegalovirus, Epstein-Barr virus, hepatitis B and C, Coxsackie and Treponema pallidum were all negative.

A cutaneous biopsy showed subcorneal non-follicular pustules, epidermal spongiosis, focal keratinocytic necrosis and basal vacuolar degeneration. Papillary dermal oedema and diffuse perivascular infiltrates of neutrophils, eosinophils and lymphocytes were present in the superficial dermis. No bacterial or fungal organisms were identified.

Patch tests showed an intense positive result (++++) at 48 and 96 h with the commercial preparation Rinoebastel® 2,5% and 5% in petrolatum, as well as with pseudoephedrine 1% in petrolatum. Epicutaneous tests with ebastine 1% and 2% in petrolatum were negative (Fig. 2). The results of patch testing were reported according to the International Contact Dermatitis Research Group criteria for patch test reading.

Total resolution was observed within 7 days without specific treatment, followed by intense desquamation. The patient was instructed not to ingest drugs containing pseudoephedrine.

DISCUSSION
AGEP was first coined as an entity by Beylot et al. in 1980 (1). Today the disease is an uncommon, although
is a good alternative to prove the causative role of a
gerenalized eruption, even at a low dose. Patch testing
especially since oral rechallenge may provoke a ge
in the search for the causative agent of AGEP (6, 7),
local production of IL-8 in the skin (6).

Chromium picolinate, lacquer infections (enterovirus or parvovirus B19), cystic echi
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reported as being responsible of causing AGEP (3, 4).
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The main differential diagnosis of a generalized
pustular eruption with fever include acute pustular
psoriasis von Zumbusch type, pustulosis acuta ge
onstrations of the drug and onset of the eruption support
III hypersensitivity reaction, today most authors defend
unknown. Although initially it was considered a type
exposure to ultraviolet radiation (5).

Other aetiological factors reported so far include viral
infections (enterovirus or parvovirus B19), cystic echi
nococcosis, ingestion of chromium picolinate, lacquer
chicken, contact hypersensitivity to mercury (2) and
exposure to ultraviolet radiation (5).

The exact pathomechanism of AGEP is currently
unknown. Although initially it was considered a type
III hypersensitivity reaction, today most authors defend
a type IV delayed hypersensitivity reaction. Positive
skin patch test results and short time between introduc-
tion of the drug and onset of the eruption support
this hypothesis (2). Padial et al. confirmed the presence of a
perivascular T-cell infiltrate composed mainly of
proliferating activated memory lymphocytes in addition to
the polymorphonuclear cells and the increase in the
local production of IL-8 in the skin (6).

Patch testing is nowadays a generally accepted tool
in the search for the causative agent of AGEP (6, 7),
especially since oral rechallenge may provoke a ge-
generalized eruption, even at a low dose. Patch testing
is a good alternative to prove the causative role of a
suspected drug and it is particularly useful when there
are several potential causative drugs. Beylot et al. (8)
Wolkestein et al. (9) and Watsky (10) have reported
positive patch test results in approximately 50% of
AGEP cases (2, 8). Despite their lack of sensitivity, a
negative test result cannot definitely exclude a sensi-
tization to the substance tested (9). Recently, Mashiah
& Brenner (7) reported a case of AGEP provoked by a
patch test with acetaminophen. Interestingly, patch test
results obtained with the offending drug were negative.
The authors reported possible explanations to this nega-
tive results: low concentration of the drug being tested,
inappropriate vehicle, degradation of the substance and UV radiation
of the patch test site (7).

Pseudoephedrine is a decongestant prescribed to
relieve nasal discomfort caused by colds, allergies and
hay fever. Side-effects from pseudoephedrine are un-
common. To our knowledge, only two previous similar
cases of AGEP due to pseudoephedrine have been
reported until now (6, 11).

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