

Allergic Contact Dermatitis from Methylchloroisothiazolinone, with Acute Exanthematous Pustulosis-Like Histopathologic Changes

To the Editor:

A 37-year-old woman presented with pruritic erythematous lesions on the trunk and limbs. She was in week 28 of her first uncomplicated pregnancy and denied drug intake. The patient was treated with a topical corticosteroid, and oral prednisone was started at 0.5 mg/kg and tapered over 3 weeks. At the end of therapy, the symptoms progressed, and she developed a pruriginous maculopapular rash on the trunk, arms, and hands. Physical examination showed numerous symmetrically distributed erythematous macules and plaques on which there were numerous nonfollicular pin-sized pustules (Fig 1).

Blood samples showed leukocytosis (15.9×10^9 per liter with 80.3% neutrophils) and an elevated globular sedimentation rate (56 mm). Other blood samples were unremarkable.

A skin biopsy specimen revealed psoriasiform epidermal hyperplasia and a heavy infiltrate of neutrophils in the upper epidermal layers, with the formation of subcorneal and intraepidermal spongiform pustules (Fig 2). There was also a moderate subepidermal edema and a mild superficial and perivascular mixed inflammatory cell infiltrate of neutrophils and eosinophils. Periodic acid–Schiff staining was negative for fungal organisms. Direct immunofluorescence of the skin lesion was negative.

A diagnosis of pustular psoriasis of pregnancy was made on clinicopathologic grounds, and oral prednisone (0.5 mg/kg) was commenced. The onset of numerous pustular lesions followed the decreasing of dosage. After the vaginal delivery of a healthy baby, cyclosporine was initiated, and the prednisone was tapered over the next 4 months. Lesions first improved but then progressed

with the development of new pustules when cyclosporine was decreased and discontinued after 7 months of treatment.

Another skin biopsy specimen showed similar changes with less neutrophilic infiltrate but more spongiosis in the epidermis. Patch tests with the Spanish standard, textiles, and cosmetics series were performed, and a positive reaction was seen to methylchloroisothiazolinone/methylisothiazolinone at 48 and 96 hours. 5-Chloro-2-methyl-4-isothiazolinone was found as a preservative in the bath gel used by the patient. She was told to avoid the use of cosmetic products containing isothiazolinone derivatives, and the cutaneous lesions resolved completely within 2 weeks, with no other treatment. She was asymptomatic at the 4 months' follow-up visit.

The case was finally diagnosed as allergic contact dermatitis with acute exanthematous pustulosis-like histopathologic changes, and methylchloroisothiazolinone was considered a relevant allergen.

Acute generalized exanthematous pustulosis (AGEP) is a cutaneous reaction characterized by numerous small nonfollicular sterile pustules arising on areas of edematous erythema, fever above 38°C, peripheral blood neutrophilia, and spontaneous resolution of pustules within 15 days after the cessation of causal stimuli. Histopathologic findings are spongiform pustules within the most superficial layers of the epidermis, dermal edema, and a mixed perivascular infiltrate of neutrophils and some eosinophils. These changes may be misdiagnosed as pustular psoriasis.¹

AGEP is drug induced in more than 90% of cases. Occasionally, AGEP may represent a hypersensitivity reaction to mercury or be seen in association with viral infections.¹ Exceptionally, it can be caused by the application of topical products.

AGEP or AGEP-like eruptions have rarely been reported to be caused by topical corticosteroids,² topical lindane,³ topical mephenesin (used for its analgesic and antiinflammatory properties),⁴ or the potent nonsteroidal antiinflammatory topical drug buprenorphine.⁵

The isothiazolinones are widely used in cosmetic, body care, and industrial products. They are well-known sensitizers and are an important and relatively frequent cause of dermatitis. Multiple cases of allergic contact dermatitis, airborne contact dermatitis, and sensitization following chemical burns⁶ (but no pustulation by methylchloroisothiazolinone) have previously been reported. In

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DOI 10.2310/6620.2011.10067

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Figure 1. Plaques with numerous nonfollicular pin-sized pustules.

the present case, the bath gel was responsible for the lesions. Avoiding the product, the patient became asymptomatic.

We proposed our case as the first report of allergic contact dermatitis with AGEP-like histopathologic changes from methylchloroisothiazolinone. In conclusion, AGEP or AGEP-like eruptions induced by topical agents are rarely reported, but we should keep them in mind once common causes have been excluded.

Acknowledgments

Financial disclosures of authors and reviewer(s): None reported.

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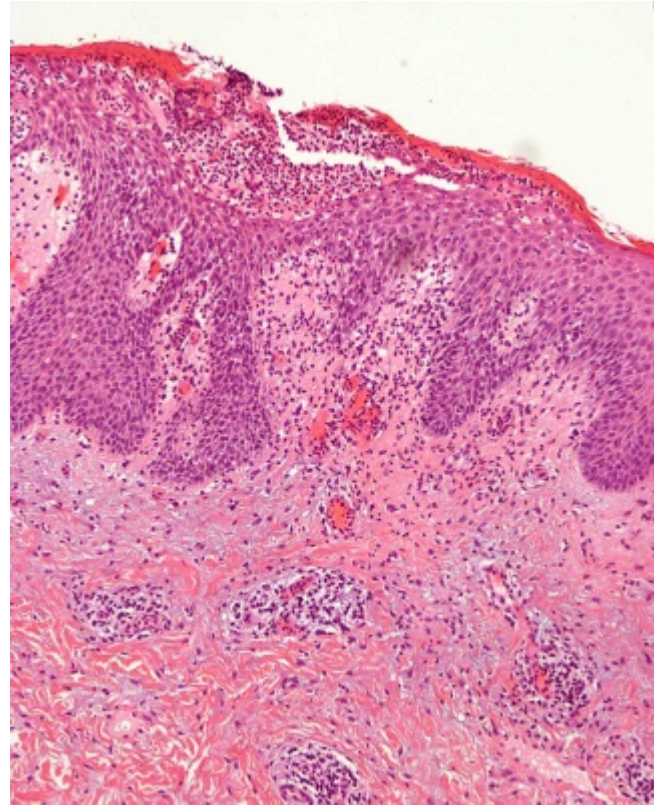


Figure 2. Subcorneal spongiform pustules, subepidermal edema, and a mild superficial and perivascular mixed inflammatory cell infiltrate (hematoxylin and eosin staining, $\times 200$ original magnification).

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