Complete prednisone taper was accomplished after famciclovir 500 mg was given 3 times daily. The patient remains clear at 19 months on oral famciclovir 500 mg daily.

Patient 2 is a 65-year-old Caucasian woman who was seen 1 year earlier by a dermatologist for erythematosus targetoid lesions on her right lower extremity, which was treated with doxycycline 100 mg twice daily for 2 weeks without effect. Lyme titer was negative. She presented in July 2013 with an erythematos targetoid macule of her left calf with a central bulla of 5 days’ duration. Biopsy showed erythema multiforme. Five weeks of valacyclovir 1 g daily and desoximetasone 0.25% ointment twice daily failed. Confirmatory HSV 1 and 2 and M. pneumoniae titers were positive. Since switching to famciclovir 500 mg daily, the patient has been free of HAEM lesions for 7 months.

Patient 3 is a 27-year-old Latina woman with serologically proven HSV 1 and 2 who presented several years ago to a dermatologist with targetoid macules and bullae of her hands and elbows and erosions of her hard palate. After valacyclovir treatment failed, she saw a rheumatologist, who diagnosed pemphigus vulgaris, reportedly by biopsy (no anti-desmoglein titers were drawn), and initiated prednisone at varying doses as high as 80 mg, a regimen she has been on since. Her course waxed and waned, prompting a trial of IVIg and rituximab, which resulted in 5 months of improvement. Ultimately, her lesions recurred. On presentation to us in February 2014, she was Cushingoid with erythematous targetoid lesions with central bullae on her fingers and erosions on her hard palate. Biopsy and positive titers of HSV 1 and 2 confirmed HAEM. Bone densitometry predictably revealed osteopenia. Following treatment with famciclovir 500 mg orally twice daily, her palatal and cutaneous erosions resolved completely. Upon prednisone taper, some lesions recurred, prompting increase of famciclovir to 3 times daily. At 75 days since beginning treatment, she is stable on this dose and off prednisone.

Our patients failed valacyclovir, then multiple immunosuppressive medications, yet responded dramatically to famciclovir. Patients 1 and 3 suffered significant morbidity from long-term corticosteroid therapy and were exposed fruitlessly to numerous immunosuppressive medications. We have found famciclovir 500 mg orally 2 to 3 times daily to be effective initial treatment for refractory cases of HAEM with maintenance therapy at 500 mg daily. A failed trial of valacyclovir should not preclude a trial of famciclovir. All safe antiviral medications should be trialed in cases of chronic HAEM before moving to long-term immunosuppressive therapy.

Ethan Routt, BA, a and Jacob Levitt, MD b

University of Hawaii John A Burns School of Medicine, a Honolulu, Department of Dermatology, Icahn School of Medicine at Mount Sinai, b New York, New York

Funding sources: None.

Correspondence to: Jacob Levitt, MD, 5 East 98th Street–Floor 5, New York, NY 10029
E-mail: jacoblevitmd@gmail.com

REFERENCE

http://dx.doi.org/10.1016/j.jaad.2014.05.029

Acute generalized exanthematous pustulosis associated with 2 common medications: Hydroxyzine and benzocaine

To the Editor: Acute generalized exanthematous pustulosis (AGEP) is a significant adverse cutaneous reaction most often induced by drugs or acute infections. In drug-induced AGEP, determining the responsible medication is important, as is identifying cross-reactants, in that early discontinuation and future avoidance of these agents help reduce morbidity.

The clinical hallmark of AGEP is the sudden onset of multiple, disseminated, nonfollicular, sterile pustules on an erythematous background, usually with intertriginous accentuation associated with fever (temperature greater than 38°C) and neutrophilia (>7 x 10⁹/L). AGEP generally resolves 2 weeks after the causative drug is withdrawn.

In our first case, AGEP induced by benzocaine, a 67-year-old man presented with a severe, widespread, pustular eruption with associated fevers, rigors, watery diarrhea, and malaise. Twenty-four hours before the drug eruption, the patient had dental extraction and received a benzocaine spray. Examination demonstrated confluent erythema studded with nonfollicular pustules distributed on the face, trunk, and extremities. Biopsies demonstrated histologic features consistent with AGEP.

The patient was treated with oral prednisone and topical corticosteroids. After a 3-day hospitalization, he clinically improved and was discharged home.
In follow-up with the Patch Test Clinic, the patient had a 3+ pustular reaction to benzocaine at 96 hours. A biopsy of the benzocaine patch test site was consistent with allergic contact dermatitis.

In our second case, AGEP caused by hydroxyzine, a 48-year-old woman with a history of psoriasis presented to a walk-in clinic complaining of generalized pruritus. She was prescribed oral hydroxyzine. Twenty-four hours after hydroxyzine ingestion, a burning erythematous eruption developed on her trunk, extremities, and genitalia. She discontinued the hydroxyzine on day 4. Two days after discontinuing hydroxyzine, fever developed and skin eruption worsened. Skin examination revealed widespread small nonfollicular pustules on an erythematous background. Biopsies showed features of AGEP.

The patient was treated with prednisone and betamethasone valerate 0.1% ointment. She was later tested in the Patch Test Clinic and a 3+++ local reaction developed in response to 10% hydroxyzine at 48 and 120 hours. Biopsy of the test site showed a neutrophilic dermatosis favoring AGEP.

In each of the aforementioned cases, the eruption started approximately 24 hours after the drug exposure. Each patient remembered at least 1 past exposure to the responsible medication.

The sensitivity of patch testing to drugs in AGEP is up to 80%.1 Patch testing with the suspected drug can mimic AGEP clinically at the patch test site where it can be biopsied to confirm the diagnosis. The biopsy of the patch site could show classic AGEP or allergic contact dermatitis as in the cases described.

---

**General Guidelines for Patch Testing for a Suspected Drug Reaction:**

- Patch test within 6 weeks to 6 months of the drug eruption.
- Ideally no immunosuppressant for 1 month.
- Some drugs are available in commercially available patch testing kits, but others need to be prepared by the dermatologist or pharmacy for patch testing.
- Preparation of Drugs:
  - Open capsules or remove coating and crush tablets.
  - Separately test coating and powder.
  - For tablets or capsules, use 30% drug concentration in petrolatum and water. This can be typically facilitated by a hospital pharmacy and/or a compounding pharmacy. For pure drug, use 10% concentration in petrolatum and water.
  - It is recommended to use more diluted substances in severe drug eruptions including DRESS, Steven-Johnson, generalized urticaria and angioedema. It is best in these cases to start with 0.1% concentration and slowly increase to a maximum of 10%.4,5
  - Use initial low concentration (0.1%) with acyclovir, carbamazepine and pseudoephedrine to decrease the risk of severe relapses associated with patch testing.4,5
- Generally, the patch test is applied on the upper back.
  - Consider patch testing the affected site in cases of Fixed Drug Eruption or Systemic Drug-related Intertiginous and Flexural Exanthem (the so-called “baboon syndrome”).
- Readings should be done at 48 and 96 hours. If negative, then read on day 7.

---

**Fig 1.** General guidelines for patch testing for a suspected drug eruption (for the general dermatologist).4,5
Dermatologists can have medications compounded to use for patch testing (Fig 1).

To the best of our knowledge, there are no reported cases of AGEP secondary to benzocaine and only 2 previous reports of AGEP caused by hydroxyzine.2,3 It may be that these common medications have caused AGEP in the past that was either unrecognized or not reported. Regardless, it is important that dermatologists be aware of this uncommon yet important adverse event.

Ashley O’Toole, MHSc, MD, Julie Lacroix, MD, CCFP, Melanie Pratt, MD, FRCPC, and Jennifer Beecker, MD, CCFP(EM), FRCPC, FAAD

University of Ottawa, Division of Dermatology, Canada

Funding sources: None.

Conflicts of interest: None declared.

 Correspondence to: Melanie Pratt, MD, FRCPC, Division of Dermatology, Parkdale Clinic, Civic Hospital, 737 Parkdale Road, Ottawa, Ontario, Canada, K1Y4E9

E-mail: prattderm@gmail.com

REFERENCES


http://dx.doi.org/10.1016/j.jaad.2014.05.041

Erythrodermic CD8+ pseudolymphoma during infliximab treatment in a patient with psoriasis: Use of cyclosporine as a rescue therapy

To the Editor: Cutaneous CD8+ pseudolymphoma has been reported in HIV-infected patients in association with a reactive cutaneous infiltration of HIV-specific CD8+ cytotoxic T cells.1 The diagnostic features include extensive plaques or erythroderma mimicking mycosis fungoides or Sézary syndrome, eosinophilia, and a dermal CD8+ cytotoxic T-lymphocyte infiltrate without T-cell receptor rearrangement.2,3 Herein, we describe an HIV-negative patient with psoriasis in whom erythrodermic CD8+ pseudolymphoma developed after treatment with infliximab.

A 32-year-old white woman had a 3-year history of biopsy-proven severe pustular psoriasis that was unresponsive to topical corticosteroids and narrowband ultraviolet B phototherapy. After screening for infection, neoplasm, and autoimmunity, all of which were negative, the patient was given infliximab at a dose of 5 mg/kg at weeks 0, 2, and 6, and then every 2 months. Her psoriasis improved and at least a 50% reduction in body surface area compared to baseline was observed after 12 weeks. Eleven months later, severe pruritic erythroderma associated with palmoplantar hyperkeratosis and generalized lymphadenopathy developed. Serologic and/or serum DNA detection studies for Bartonella henselae, cytomegalovirus, Epstein-Barr virus, HIV, and Toxoplasma gondii were negative.

Two lesional skin biopsies showed a papillary dermal lymphocytic infiltrate composed of small and medium-sized cells with mild epidermotropism. Immunohistochemistry showed an overwhelming predominance of CD2+, CD3+, CD5+, CD7+, and CD8+ T cells in the infiltrate. Scattered eosinophils were also observed. Immunostaining of CD8 T cells showed TiA-1 and granzyme B expression, indicating their cytotoxic lineage. Clonal T-cell receptor and immunoglobulin heavy chain gene rearrangements were not detected. Direct immunofluorescence was negative. Immunophenotyping performed on lymph node and bone marrow biopsy specimens showed a polyclonal CD8 T-cell infiltrate. A blood cell count showed 1992 CD4+ T cells/mm3, 3916 CD8+ T cells/mm3, and 1160 eosinophils/mm3. The CD4/CD8 ratio was 0.51, and there were no circulating Sézary cells.

A diagnosis of erythrodermic CD8+ pseudolymphoma was made, and infliximab was discontinued. Despite infliximab withdrawal, the erythroderma persisted, and the use of topical and systemic corticosteroids followed by methotrexate was unsuccessful (Fig 1). Because of worsening skin symptoms associated with edema, chills, and overall deterioration in the patient’s condition, treatment with cyclosporine at doses up to 5 mg/kg/day was initiated. The patient’s condition dramatically improved and she was in complete clinical remission within 4 months (Fig 2). The CD4/CD8 ratio improved to 0.85.

As far as we know, in addition to our case, there have been only 2 other reported cases of cutaneous pseudolymphoma associated with anti-tumor necrosis factor (TNF) therapy. One was induced by adalimumab and subsequently the same eruption...