

# Letters

## SKIN-DEEP CLUES TO A COMPLEX DISEASE

A 2-month-old boy presented to the emergency department with a recurring vesicular rash that first appeared at 3 weeks of age. On physical examination he was afebrile but lethargic. A vesiculopustular rash was distributed over his scalp, face, and shoulders (Fig 1). He was treated with acyclovir and vancomycin for suspected superinfection of eczema and sepsis. Treatment was discontinued when his infectious workup was negative for herpes simplex virus and bacterial infections. Owing to the distribution, appearance, and recurrence of the rash and lack of infectious etiology, eosinophilic pustular folliculitis was suspected. However, a scalp lesion punch skin biopsy sample showed mild epidermal spongiosis and acanthosis with perivascular infiltration of lymphocytes, polymorphonuclear cells, histiocytes, and scattered eosinophils, consistent with superficial perivascular dermatitis. He was discharged with topical corticosteroid therapy for superinfected eczema.

At 6 months of age, he returned to the hospital with severe respiratory distress and required mechanical ventilation. At that time, his rash had resolved except for a few scattered erythematous papules on his face. Chest computed tomography revealed bilateral diffuse interstitial disease, and lung biopsy demonstrated *Pneumocystis jiroveci* organisms. The diagnosis of *P jiroveci* pneumonia (PJP) prompted an extensive evaluation for T-cell immunodeficiencies, including human immunodeficiency virus 1 infection, severe combined immunodeficiency, X-linked hyper-IgM syndrome, and DiGeorge syndrome; all were ruled out. The clinical features of his previous rash—onset, distribution, and appearance—were reviewed because they have been associated with the newborn rash of hyper-IgE syndrome (HIES). Although his serum total IgE level was elevated at 153 IU/mL (reference range, 1–30 IU/mL), it was not in the range frequently seen in HIES (>2,000 IU/mL).<sup>1</sup> In our experience, infants with severe atopic dermatitis also may have serum total IgE levels greater than 50,000 IU/mL during their first year of life. Genetic testing was performed for *STAT3* mutations, which had just been demonstrated to cause the autosomal dominant form of HIES.<sup>2</sup> The patient was found to have a heterozygous G→A transition at

complementary DNA 1909 in the SH2 domain of *STAT3*, which is consistent with the diagnosis of HIES, particularly because he had PJP.

HIES is characterized by eczema, recurrent skin abscesses, lung infections, and markedly elevated serum total IgE levels.<sup>1,3</sup> It is also associated with coarse facial features and musculoskeletal, dental, and vascular abnormalities, which may not be apparent during infancy. Most HIES infections are caused by *Staphylococcus aureus* or fungal pathogens. Rare cases of PJP in HIES have been documented.<sup>1</sup> In addition to eczema and recurrent skin infections, the newborn rash of HIES has been described as a separate entity regarding its cutaneous manifestations.<sup>4</sup> Onset of this rash tends to occur during the first month of life, and recurrence is common. It has a predilection for the scalp, face, and shoulders. The rash has been described as vesicular, pustular, or papulopustular.<sup>4,5</sup> Its typical histopathologic profile is similar to that of eosinophilic pustular folliculitis or eosinophilic spongiotic dermatitis.<sup>4,5</sup> Other differential diagnoses of the newborn rash of HIES range from neonatal herpes simplex virus, eczema herpeticum, varicella, and staphylococcal scalded syndrome to the more benign erythema toxicum neonatorum and neonatal acne.<sup>6</sup> Erythema toxicum neonatorum is a common benign rash consisting of a central papule or pustule with surrounding erythema characterized by an accumulation of eosinophils in the dermis.<sup>7</sup> The rash can be found anywhere except the palms and soles. It erupts in the first 3 days of life and has a waxing and waning course but usually resolves within a week. Neonatal acne is also a common pustular rash in newborns. Onset is in the first weeks of life, and it usually resolves spontaneously in the first 2 months of life.<sup>8</sup> Unlike HIES lesions, neonatal acne lesions do not weep and are not pruritic.

This case illustrates the importance of clinical evaluation for recognizing the newborn rash of HIES. Although histopathologic findings can be helpful, when clinical suspicion is strong, the diagnosis of HIES should be pursued to prevent further complications of the disease. Although testing for *STAT3* mutations can be considered, the result must be correlated with the clinical diagnosis because an autosomal recessive form of HIES without *STAT3* mutation has also been described.<sup>2</sup> Whether the newborn rash of HIES is associated with one or both forms of HIES remains to be investigated. This patient recovered from PJP and was discharged taking trimethoprim-sulfamethoxazole prophylaxis. He is now 19 months

**Disclosures:** Authors have nothing to disclose.  
© 2010 American College of Allergy, Asthma & Immunology.  
Published by Elsevier Inc. All rights reserved.  
doi:10.1016/j.anai.2009.11.015

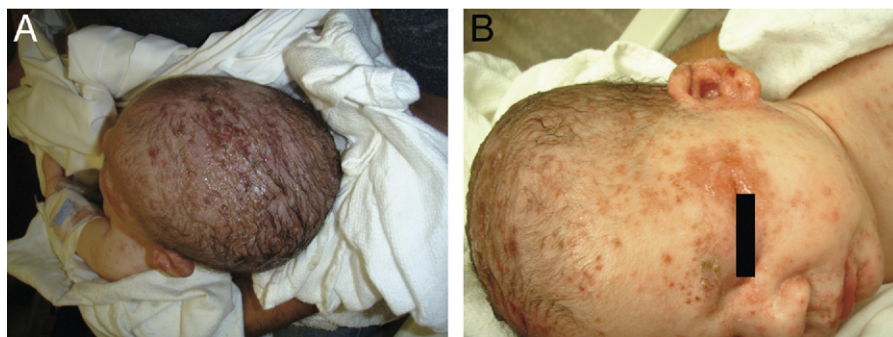


Figure 1. Distribution of a vesiculopustular rash over the scalp, face, and shoulder of an infant.

old and is doing well. His serum total IgE level remains relatively low (93 IU/mL). Because his *STAT3* mutation is a known mutational hot spot for autosomal dominant HIES, he will be closely monitored for dental, skeletal, and pulmonary complications.

## ACKNOWLEDGMENTS

We thank Dr Steven Holland and Ms Amy Hsu at the National Institutes of Health for sequencing *STAT3*.

CHRISTINE CHO, MD\*  
RONALD M. FERDMAN, MD†‡  
JOSEPH A. CHURCH, MD†‡  
PECK Y. ONG, MD†‡

\*Division of General Pediatrics  
Childrens Hospital Los Angeles  
Los Angeles, California  
†Division of Clinical Immunology and Allergy  
Childrens Hospital Los Angeles  
Los Angeles, California  
‡Department of Pediatrics  
Keck School of Medicine  
University of Southern California  
Los Angeles, California  
pyong@chla.usc.edu

1. Grimbacher B, Holland SM, Puck JM. Hyper-IgE syndromes. *Immunol Rev*. 2005; 203:244–250.
2. Holland SM, DeLeo FR, Elloumi HZ, et al. *STAT3* mutations in the hyper-IgE syndrome. *N Engl J Med*. 2007;18:1608–1619.
3. Davis SD, Schaller J, Wedgwood RJ. Job's syndrome: recurrent, "cold", staphylococcal abscesses. *Lancet*. 1966;1:1013–1015.
4. Eberting CL, Davis J, Puck JM, Holland SM, Turner ML. Dermatitis and the newborn rash of hyper-IgE syndrome. *Arch Dermatol*. 2004;140:1119–1125.
5. Chamlin SL, McCalmont TH, Cunningham BB, et al. Cutaneous manifestations of hyper-IgE syndrome in infants and children. *J Pediatr*. 2002;141:572–575.
6. Sahn EE. Vesiculopustular diseases of neonates and infants. *Curr Opin Pediatr*. 1994;6:442–446.
7. Marchini G, Ulfgren AK, Lore K, Stabi B, Berggren V, Lonne-Rahm S. Erythema toxicum neonatorum: an immunohistochemical analysis. *Pediatr Dermatol*. 2001; 18:177–187.
8. Lucky W. A review of infantile and pediatric acne. *Dermatology*. 1998;196:95–97.

## LATEX: A HIDDEN OCCUPATIONAL ALLERGEN

We present a case of occupational asthma in a 24-year-old man who worked in a butcher's shop. During the past year he developed rhinoconjunctivitis and asthma symptoms related to his work, especially when he went into the back room of the butcher's shop (an adjacent space where a coworker prepared sausages and cut veal bones). The results of physical examination and radiologic and basal spirometric studies were normal. A methacholine inhalation test revealed bronchial hyperresponsiveness (provocation dose that caused a decrease in forced expiratory volume of 20% [FEV<sub>1</sub>] of 144 cumulative breath units).

The results of skin prick tests to common aeroallergens, milk, and veal proteins were all negative. The results of prick-prick tests with veal, pork, sausage, a mixture of preservatives and spices used in the manufacture of sausages, cochineal red, carmine red, and powdered veal bone provided by the patient were all negative. The result of a

skin prick test with latex was positive. A handling test with latex gloves was then performed with a negative result.

Blood analysis revealed eosinophilia (11%; eosinophil count of 580/mm<sup>3</sup>). The total serum IgE level was 323 kU/L. The specific IgE level (ImmunoCAP System; Phadia, Uppsala, Switzerland) for latex was 17 kU/L (reference range, <0.35 kU/L).

The result of a specific bronchial challenge test with an aqueous extract of natural latex (500 µg/mL; ALK-Abelló, Madrid, Spain) was positive with an immediate response (10 minutes after administration of the last dose, 5 inhalations of 50 µg/mL of latex extract, a 28% decrease in FEV<sub>1</sub> was observed).

Air concentrations of latex were analyzed by a volumetric air measuring device (Air Sentinel; ICx Technologies, Arlington, Virginia) at the butcher's shop itself (0.26 ng/m<sup>3</sup> of air), the back room of the shop (0.80 ng/m<sup>3</sup> of air), and the bedroom of the patient's home (0.09 ng/m<sup>3</sup> of air).

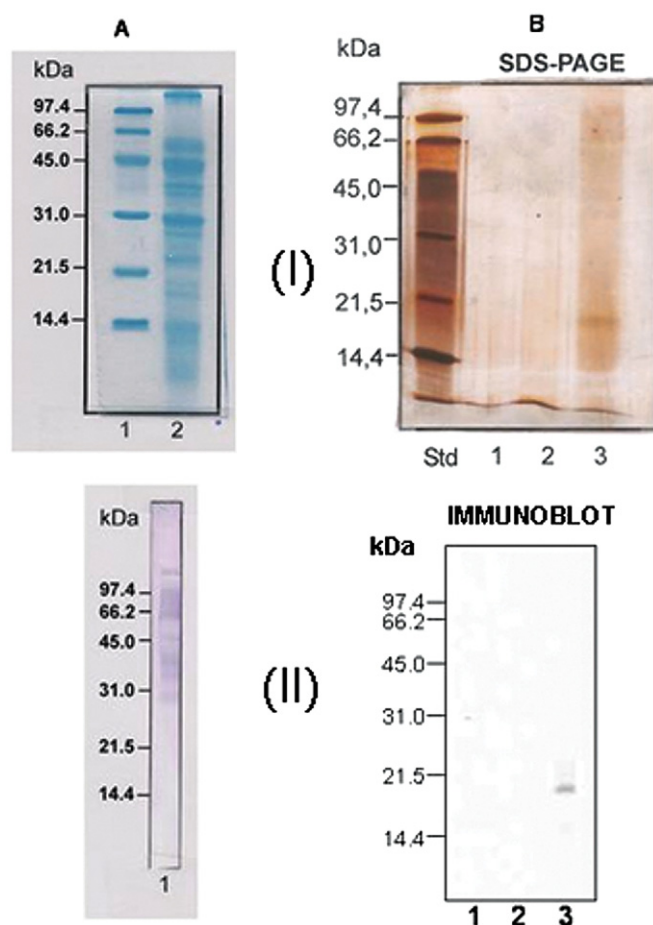


Figure 1. I. A, Sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE) analysis. A, Latex extract, 100 µg (Coomassie stain). Lane 1: standard low molecular weight; lane 2: latex extract. B, Extract from filters (silver staining). Lane Std: standard low weight; lane 1: filter butcher's shop; lane 2: filter patient's bedroom; lane 3: filter back room. II. Immunoblot experiments (chemiluminescence). A, Solid phase. Latex extract, 100 µg. B, Solid phase. Extracts from filters. Lane 1: filter butcher's shop; lane 2: filter patient's bedroom; lane 3: filter back room.

**Disclosures:** Authors have nothing to disclose.

© 2010 American College of Allergy, Asthma & Immunology.

Published by Elsevier Inc. All rights reserved.

doi:10.1016/j.anai.2009.11.016