# Urticaria and edema in a 2-year-old boy

## The absence of blisters, the presence of mild systemic symptoms, and the patient's age guided the diagnosis.

**Jeffrey S. Cook, MD, FAAFP; Amber Angles, MD; Erin Morley, MD**
North Colorado Family Medicine Residency Program, Greeley (Dr. Cook); Delta Health Family Medicine, CO (Dr. Angles); Family Physicians of Greeley, CO (Dr. Morley)

jeffrey.cook@bannerhealth.com

DEPARTMENT EDITOR
**Richard P. Usatine, MD**
University of Texas Health, San Antonio

*The authors reported no potential conflict of interest relevant to this article.*

doi: 10.12788/jfp.0264

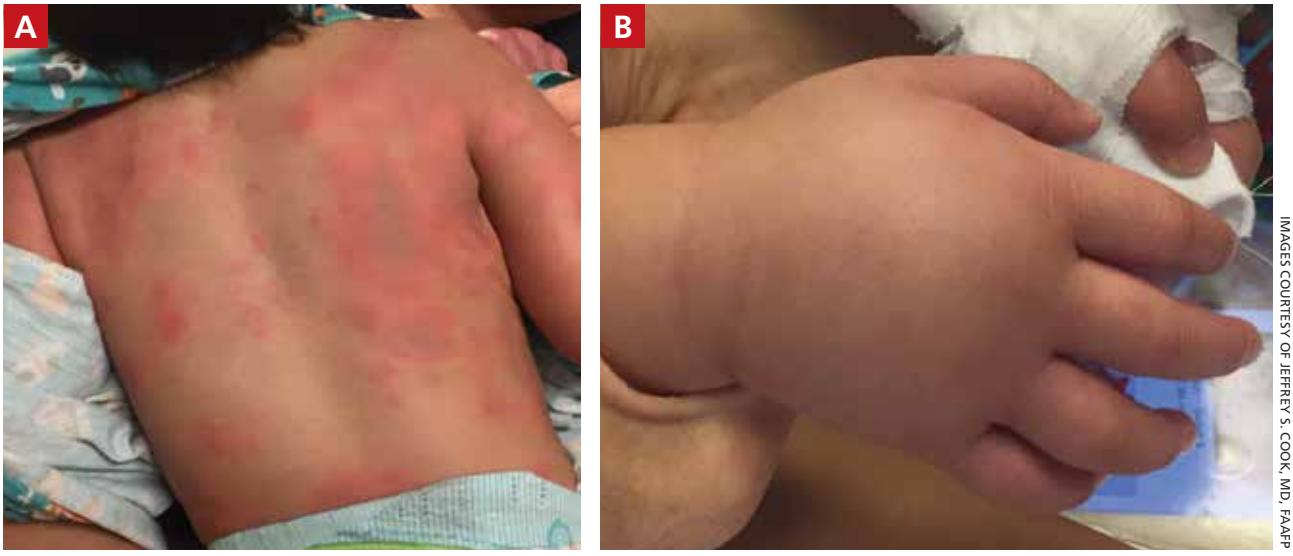
**A 2-YEAR-OLD BOY** presented to the emergency room with a 1-day history of a diffuse, mildly pruritic rash and swelling of his knees, ankles, and feet following treatment of acute otitis media with amoxicillin for the previous 8 days. He was mildly febrile and consolable, but he was refusing to walk. His medical history was unremarkable.

Physical examination revealed erythematous annular wheals on his chest, face, back, and extremities. Lymphadenopathy and mucous membrane involvement were not present. A complete blood count (CBC) with differential, inflammatory marker tests, and a comprehensive metabolic panel were ordered. Given the joint swelling and rash, the patient was admitted for observation.

During his second day in the hospital, his skin lesions enlarged and several formed dusky blue centers (**FIGURE 1A**). He also developed swelling of his hands (**FIGURE 1B**).

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

**FIGURE**
### Toddler with back lesions and hand swelling




IMAGES COURTESY OF JEFFREY S. COOK, MD, FAAFP

**Children with urticaria multiforme may have significant edema of the feet and may find walking difficult; this should not be confused with arthritis or arthralgias.**

## Diagnosis: Urticaria multiforme

The patient's lab work came back within normal range, except for an elevated white blood cell count (19,700/mm$^3$; reference range, 4500-13,500/mm$^3$). His mild systemic symptoms, skin lesions without blistering or necrosis, acral edema, and the absence of lymphadenopathy pointed to a diagnosis of urticaria multiforme.

Urticaria multiforme, also called *acute annular urticaria* or *acute urticarial hypersensitivity syndrome*, is a histamine-mediated hypersensitivity reaction characterized by transient annular, polycyclic, urticarial lesions with central ecchymosis. The incidence and prevalence are not known. Urticaria multiforme is considered common, but it is frequently misdiagnosed.[1] It typically manifests in children ages 4 months to 4 years and begins with small erythematous macules, papules, and plaques that progress to large blanchable wheals with dusky blue centers.[1-3] Lesions are usually located on the face, trunk, and extremities and are often pruritic (60%-94%).[1-3] Individual lesions last less than 24 hours, but new ones may appear. The rash generally lasts 2 to 12 days.[1,3]

Patients often report a preceding viral illness, otitis media, recent use of antibiotics, or recent immunizations. Dermatographism due to mast cell–mediated cutaneous hypersensitivity at sites of minor skin trauma is common (44%).[1] Patients often have associated facial or acral edema (72%).[1] Children with significant edema of the feet may find walking difficult, which should not be confused with arthritis or arthralgias. Generally, patients are nontoxic in appearance, and systemic symptoms are limited to a low-grade fever.[1-3]

The diagnosis is made clinically and should not require a skin biopsy or extensive laboratory testing. When performed, laboratory studies, including CBC, erythrocyte sedimentation rate, C-reactive protein, and urinalysis are routinely normal.

### Erythema multiforme and urticarial vasculitis are part of the differential

The differential diagnosis in this case includes erythema multiforme, Henoch-Schönlein purpura, serum sickness-like reaction, and urticarial vasculitis (**TABLE**[1,2,4]).

**Erythema multiforme** is a common misdiagnosis in patients with urticaria multiforme.[1,2] The erythema multiforme rash has a "target" lesion with outer erythema and central ecchymosis, which may develop blisters or necrosis. Lesions are fixed and last 2 to 3 weeks. Unlike urticaria multiforme, patients with erythema multiforme commonly have mucous membrane erosions and occasionally ulcerations. Facial and acral edema is rare. Treatment is largely symptomatic and can include glucocorticoids. Antiviral medications may be used to treat recurrences.[1,2]

**Henoch-Schönlein purpura** is an immunoglobulin A–mediated vasculitis that affects the skin, gastrointestinal tract, and joints.[4,5] Patients often present with arthralgias, gastrointestinal symptoms such as abdominal pain and bleeding, and a nonpruritic, erythematous rash that progresses to palpable purpura in dependent areas of the body. Treatment is generally symptomatic, but steroids may be used in severe cases.[4,5]

**Serum sickness-like reaction** can manifest with angioedema and a similar urticarial rash (with central clearing) that lasts 1 to 6 weeks.[1,2,6,7] However, patients tend to have a high-grade fever, arthralgias, myalgias, and lymphadenopathy while dermatographism is absent. Treatment includes discontinuing the offending agent and the use of H1 and H2 antihistamines and steroids, in severe cases.

**Urticarial vasculitis** manifests as plaques or wheals lasting 1 to 7 days that may cause burning and pain but not pruritis.[2,5] Purpura or hypopigmentation may develop as the hives resolve. Angioedema and arthralgias are common, but dermatographism is not present. Triggers include infections, autoimmune disease, malignancy, and the use of certain medications. H1 and H2 blockers and nonsteroidal anti-inflammatory agents are first-line therapy.[2]

## Step 1: Discontinue offending agents; Step 2: Recommend antihistamines

Treatment consists of discontinuing any offending agent (if suspected) and using systemic H1 or H2 antihistamines for symptom

**TABLE**

## Selected differential diagnosis of urticaria multiforme[1,2,4]

| Condition | Characteristics |
|---|---|
| Erythema multiforme | Fixed "target" lesion with dusky, purpuric center and surrounding erythema or blisters located mostly on extremities; mucous membrane involvement is often present; occurs in all ages in response to viral illness |
| Henoch-Schönlein purpura | Triad of nonblanching, palpable purpura located in dependent areas; abdominal pain; and arthritis/joint pain. It often follows an upper respiratory illness |
| Serum sickness-like reaction | Urticarial, polycyclic wheals with central clearing associated with lymphadenopathy, arthralgias, and high-grade fever in response to antibiotics |
| Urticaria multiforme | Annular and polycyclic wheals with dusky, purpuric centers located on the trunk, face, and extremities in infants and small children. Patients present with low-grade fever, edema, dermatographism, and pruritus; there is an absence of arthralgias and lymphadenopathy |
| Urticarial vasculitis | Painful, purpuric wheals (with associated edema) and arthralgias in adults in response to infections, autoimmune disease, neoplasia, or drugs |

relief. Systemic steroids should only be given in refractory cases.

**Our patient's amoxicillin** was discontinued, and he was started on a 14-day course of cetirizine 5 mg bid and hydroxyzine 10 mg at bedtime. He was also started on triamcinolone 0.1% cream to be applied twice daily for 1 week. During his 3-day hospital stay, his fever resolved and his rash and edema improved.

During an outpatient follow-up visit with a pediatric dermatologist 2 weeks after discharge, the patient's rash was still present and dermatographism was noted. In light of this, his parents were instructed to continue giving the cetirizine and hydroxyzine once daily for an additional 2 weeks and to return as needed. JFP


References

1. Shah KN, Honig PJ, Yan AC. "Urticaria multiforme": a case series and review of acute annular urticarial hypersensitivity syndromes in children. *Pediatrics.* 2007;119:e1177-e1183. doi: 10.1542/peds.2006-1553
2. Emer JJ, Bernardo SG, Kovalerchik O, et al. Urticaria multiforme. *J Clin Aesthet Dermatol.* 2013;6:34-39.
3. Starnes L, Patel T, Skinner RB. Urticaria multiforme – a case report. *Pediatr Dermatol.* 2011; 28:436-438. doi: 10.1111/j.1525-1470.2011.01311.x
4. Reamy BV, Williams PM, Lindsay TJ. Henoch-Schönlein purpura. *Am Fam Physician.* 2009;80:697-704.
5. Habif TP. *Clinical Dermatology: A Color Guide to Diagnosis and Therapy*. 6th ed. Mosby, Elsevier Inc; 2016.
6. King BA, Geelhoed GC. Adverse skin and joint reactions associated with oral antibiotics in children: the role of cefaclor in serum sickness-like reactions. *J Paediatr Child Health.* 2003;39:677-681. doi: 10.1046/j.1440-1754.2003.00267.x
7. Misirlioglu ED, Duman H, Ozmen S, et al. Serum sickness-like reaction in children due to cefditoren. *Pediatr Dermatol.* 2011;29:327-328. doi: 10.1111/j.1525-1470.2011.01539.x