

Urticaria Multiforme—A Case Report

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Abstract: The term “urticaria multiforme” has recently been proposed to replace acute annular urticaria and refers to a benign cutaneous hypersensitivity reaction characterized by the acute onset of large, polycyclic, and annular wheals with ecchymotic centers. It is associated with acral and facial angioedema, dermatographism, favorable response to antihistamines, and a self-limited course. It is most often mistaken for erythema multiforme and occasionally for serum sickness-like reaction. We report a case of urticaria multiforme in a 4-month-old infant, followed by a review of the literature.

Urticaria is a common condition characterized by transient, pruritic, erythematous wheals. Acute urticaria is defined as lasting no more than 6 weeks, while urticaria that lasts longer than 6 weeks is considered chronic. Acute urticaria is the most common form encountered in childhood and is frequently caused by infection, drugs, and food allergies (1).

Acute annular urticaria—a clinical subtype of acute urticaria—is a benign cutaneous hypersensitivity reaction characterized by the acute onset of large, polycyclic and annular wheals with dusky centers (2). This condition is frequently misdiagnosed; it is most often mistaken for erythema multiforme and occasionally for serum sickness-like reaction. In 2007, Shah et al proposed the term “urticaria multiforme” to replace acute annular urticaria in order to highlight the distinct clinical features of this urticaria variant. Shah et al argued that “urticaria multiforme” is a more apt descriptive term than annular urticaria as a way to help avoid misdiagnosis and unnecessary diagnostic testing.

CASE REPORT

A 4-month-old Caucasian infant presented to the emergency department with a rash on her trunk and legs of 12 hours duration. Review of systems was positive for a fever of 103 degrees Fahrenheit and diarrhea on the prior day. She had received no medications but had received vaccinations for *Rotavirus*, *Haemophilus influenzae type b*, *diphtheria*, *tetanus*, and *pertussis* 5 days prior to presentation. The patient was born of an uncomplicated, spontaneous delivery at term.

Physical examination revealed polycyclic and annular erythematous wheals on the trunk and bilateral lower extremities, with dusky blue centers (Figs. 1 and 2). No true target lesions with central necrosis or blistering existed. The remainder of the physical examination was normal. Based on clinical presentation, the patient was diagnosed with urticaria multiforme, and systemic antihistamines were recommended. The parents reported the rash resolved within 24 hours of the emergency

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Figure 1. Annular and polycyclic erythematous wheals with dusky blue centers.



Figure 2. Annular and polycyclic erythematous wheals with dusky blue centers.

department visit and administration of a single dose of diphenhydramine. The patient was seen 3 days following her initial presentation in our dermatology clinic, where no evidence of the initial rash was seen (Fig. 3).

COMMENTS

In 1997, Tamayo-Sanchez et al first introduced the term “acute annular urticaria” for the clinical form of acute urticaria that is characterized by the acute onset of large, polycyclic and annular wheals with ecchymotic centers (2). In 2007, Shah et al proposed the term “urticaria multiforme” to replace acute annular urticaria in order to highlight the distinct clinical features of this urticaria variant and believed it to be a more apt descriptive term (3).

Urticaria multiforme primarily affects infants and preschool aged children. Eighty-three percent of the



Figure 3. Urticaria multiforme resolved on 3-day follow-up.

cases reported by Shah et al were between 2 months and 3 years of age, although patients as young as 10 weeks and as old as 17 years were affected (3). All 34 children reported by Tamayo-Sanchez et al were between the ages of 4 months and 4 years (2).

Numerous potential triggers for urticaria multiforme have been proposed. Tamayo-Sanchez et al found that 65% of their cases were preceded by a history of diarrhea treated with furazolidone, a drug used to treat intestinal giardiasis, and that 26% had a recent history of pharyngitis. In the case series of urticaria multiforme reported by Shah et al, 67% of patients reported a preceding upper respiratory infection, otitis media, or viral symptoms. Two of the 18 cases had received routine immunizations prior to the onset of urticaria, and 44% had ongoing or recent antibiotic exposure (3).

Clinically, urticaria multiforme is characterized by transient, annular and polycyclic wheals with central clearing or ecchymotic centers affecting the trunk, extremities, and face. Other associated findings reported by Shah et al. include pruritus (94%), facial or acral angioedema, or both (72%), dermatographism (44%), and fever (44%) (3). Of note, no true target lesions as in erythema multiforme exist, and no skin necrosis, blistering, mucous membrane involvement, arthralgias, or arthritis are seen.

The diagnosis of urticaria multiforme is made on clinical grounds and should not necessitate elaborate laboratory testing or a skin biopsy. Tamayo-Sanchez et al found that a complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein

TABLE 1. *A comparison of the clinical features of urticaria multiforme with serum sickness-like reactions*³

Population	Urticaria multiforme	Serum sickness-like reactions
	Infants and small children	Children and adults
Implicated etiologies	Viral illness, immunizations, antibiotics	Medications especially antibiotics
Cutaneous eruption	Transient annular/polycyclic wheals with prominent dusky blue or clear centers	Fixed maculopapular, erythema multiforme-like or urticarial eruptions that occasionally evolve to have dusky centers
Fever	Occasional, low-grade	Significant, high-grade
Dermatographism	Yes	No
Myalgias, arthralgias and lymphadenopathy	No	Yes
Angioedema of the face, hands, and feet	Common	Less common

(CRP), and throat swabs were all normal or negative in their patients. Only 2 of 10 patients whose serum IgE levels were measured had elevated levels (2). Of note, a modest but not significant elevation may occur in acute phase reactants (3). Skin biopsy in urticaria multiforme is indistinct from other acute urticarias and should not be necessary to make the diagnosis.

The duration of individual lesions in urticaria multiforme is less than 24 hours, and a favorable response occurs to antihistamines within 24 to 48 hours. The condition is self-limited and typically resolves within 2 to 12 days. Treatment includes discontinuation of any triggering antibiotic medication, systemic antihistamines, and rarely systemic corticosteroids (3).

Urticaria multiforme is frequently mistaken for other annular skin disorders, most notably erythema multiforme and less often serum sickness-like reactions, conditions which have completely different pathogenesis, prognoses, and treatments. A thorough clinical history and physical examination is invaluable in the identification of important clues, which will help to differentiate urticaria multiforme from these two disorders. The distinct dusky blue centers of urticaria multiforme lesions are most often misdiagnosed as erythema multiforme. Significantly, the lesions seen with urticaria multiforme show no skin necrosis or blistering, and the mucous membranes are spared, helping to differentiate from the true target lesions of erythema multiforme (4). Of note, pruritus is a common symptom in urticaria multiforme but not erythema multiforme, where burning and pain are more frequent. In addition, acral and facial edema is rarely seen in erythema multiforme. Although serum sickness-like reactions can manifest with polycyclic wheals and angioedema similar to those seen in urticaria multiforme, this condition can be distinguished by its prominent fever, arthralgias, myalgias, and lymphadenopathy (Table 1) (5). Additionally, individual lesions in both erythema multiforme and serum sickness-like reactions are fixed and last days to weeks, while in urti-

caria multiforme individual lesions are transient and last less than 24 hours. Furthermore, dermatographism does not feature in either erythema multiforme or serum sickness-like reactions but does in urticaria multiforme.

Replacing the name of acute annular urticaria with urticaria multiforme has sparked some debate. In 2008, Katoulis et al argued that the Latin adjective “multiformis” refers to an entity having many forms or appearances, something that is true for erythema multiforme but not for acute annular urticaria, where no clinical variety of lesions is seen. Katoulis et al believed a more appropriate term would be “erythema multiforme-like urticaria” or “urticaria with targetoid lesions” (6). Although the renaming of this condition may be debatable, urticaria multiforme is an important condition to correctly identify in order to render a precise diagnosis, avoid unnecessary skin biopsies and laboratory testing, reassure parents, and develop an appropriate treatment plan.

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