

Urticaria: “You’re Probably Just Allergic to Something”

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ABSTRACT

Urticaria is a common symptom seen in pediatric patients, and it has multiple allergic and nonallergic causes. Unfortunately, it is far too common that when children present acutely for urticaria, they are told that it is an “allergy.” This statement often leads to increased anxiety while the patient waits to be evaluated by an allergist/immunologist. This article discusses the frequency that allergic reactions are involved in urticaria and provides examples of potential nonallergic causes. Additionally, the article discusses approaches to treatment that may be appropriate to initiate in the pediatrician’s office or acute setting. This article is intended to provide a broader understanding of urticaria and its management in the outpatient or emergency setting so that we are able to tell our patients more than “you’re probably just allergic to something.” [*Pediatr Ann.* 2016;45(11):e399-e402.]

A common complaint of patients presenting to pediatricians or allergists is urticaria. The descriptions regarding the appearance of the rash often differ from patient to patient—some report redness, others report “whelps,” and others report raised lesions. The rash is pruritic for some patients and for others it is not. Some patients can trace the onset of the rash back to a particular food they ate, varied environmental stimuli, or recent symptoms of an infection, whereas others are unable to ascertain any specific trigger for their rash. What most of the patients have in common is that they sought treatment from their pediatrician, an urgent care clinic, or an emergency department and they were all told a variation of the following: “You’re probably just allergic to something.”

I consider “You’re probably just allergic to something” to be one of the worst “non-phrases” in the practice of medicine. Although it may be enough to temporarily assuage a parent’s fears for their child, it offers no new information and, more often than not, creates undue anxiety for the family and the patient. The wait to see an allergist may be several weeks. During those weeks, the family often scrutinizes every exposure their child has and every single bite of food that they eat, nervous that the next meal might cause a return of their child’s hives or progression of symptoms to something more threatening, such as anaphylaxis. By the time the child’s appointment with the allergist arrives, the parents often present with the anxious demand “We want to know everything

that our child is allergic to. Test them for everything so we will know.”

When one considers the vast number of things to which we could have allergic sensitization, it quickly becomes apparent that it is physically impossible to test someone for everything. If the child continues to have hives at the time of testing, this only furthers confusion when reading the skin test. Additionally, if a physician decides to test only for the most common allergic triggers, there is no guarantee that a positive result on testing has uncovered the true origin of the urticaria. In the 2008 update to the American Academy of Allergy, Asthma, and Immunology Practice Parameter on allergy diagnostic testing, allergy skin testing was noted to have a specificity of 79% to 86% and a sensitivity of 85% to 87%.¹

Specific immunoglobulin E (IgE) testing presents another potential method to assess for allergic sensitivity, but it has a specificity of 80% to 90% and a sensitivity of 80% to 85%.¹ Although those statistics are not necessarily bad, they demonstrate that testing is not perfect. False-positive results can and do happen and often create unnecessary dietary restrictions, reduced exposure to beloved pets or past-times, and undue anxiety for the patient and their family. In a large cohort study of patients with chronic urticaria, prick tests revealed that 39.1% of patients had sensitization to one or more allergens.² When applied to the clinical history, it was found that those allergens were related to other allergic comorbidities such as allergic rhi-

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nitis or food-pollen syndrome, but were not proven to be the cause of chronic urticaria in any of the patients. Therefore, I encourage pediatricians to use testing when there is a perceived trigger that needs to be ruled in or ruled out and advise against broad testing in hopes of finding something to blame.

CATEGORIES OF URTICARIA

Urticaria is most easily separated into acute and chronic subtypes. Acute urticaria defines symptoms that have been occurring for less than 6 weeks.³ Chronic urticaria encompasses all symptoms lasting longer than 6 weeks.

Acute Urticaria

Acute urticaria will affect almost 20% of the population at some point in their life.^{4,6} In a retrospective study performed by Liu et al.,⁷ infections were the cause of acute urticaria in infants in more than 50% of cases. This prevalence decreased as patient age increased, with infection representing 42.1% and 17.1% of cases in school-aged children and adolescents, respectively.⁷ The infectious symptoms do not have to be concomitant with the appearance of the rash. In my clinic, patients have developed hives up to a few weeks after the appearance of infectious symptoms, most commonly an upper respiratory infection. The remaining 50% of cases of acute urticaria are deemed idiopathic.

Chronic Urticaria

Chronic urticaria is a self-limited disorder lasting longer than 6 weeks. However, it is important when counseling patients with chronic urticaria to inform them that the average duration of symptoms can be as long as 2 to 5 years.⁶ It has been shown that if there is no identifiable trigger for the hives, spontaneous resolution of symptoms after 1 year will occur in 30% to 50%

of patients.⁶ Studies have tried to assess if there are specific symptoms or causes of urticaria that indicate who will have a longer disease course.⁸ Toubi et al.⁸ demonstrated that the presence of angioedema, disease severity, and thyroid autoimmunity may be associated with longer duration of urticaria.

Chronic urticaria is further subdivided into chronic spontaneous urticaria (80% of cases) and chronic inducible urticaria (20% of cases).³

Chronic spontaneous urticaria.

Chronic spontaneous urticaria is often caused by or seen in conjunction with autoimmunity.^{6,9} Although autoimmune thyroid disorders are the type of disorder most commonly associated with chronic spontaneous urticaria, studies have demonstrated a relationship with systemic lupus erythematosus, celiac disease, and type 1 diabetes mellitus.^{6,9,10} It is also possible to have autoimmune urticaria. Approximately 30% to 40% of patients with chronic idiopathic urticaria are found to have circulating immunoglobulin G antibodies against the Fc epsilon RI alpha (FcεR1α) receptor for IgE located on mast cells.^{6,9}

Chronic inducible urticaria.

It should be noted that cases of chronic inducible urticaria often get the attention of doctors and the general public because of their unique symptoms. These types of urticaria only appear in the presence of a specific stimulus not related to a food or drug, and they will reappear on subsequent exposures to that same stimulus.¹¹ The hives that appear in these cases do not actually represent an allergic (ie, IgE-mediated) reaction.

Dermatographism (skin writing). Stroking or scratching of the skin causes an acute appearance of wheal and flare reaction only in the area scratched. Approximately 5% of people will experi-

ence this skin condition at some point in their life.¹¹

Delayed pressure urticaria. This is the only physical urticaria that presents without a wheal. Instead, patients develop a diffuse, erythematous angioedema. This finding can occur up to 4 to 8 hours after a significant amount of exposure to some form of pressure. One of the more common presentations is children who carry heavy backpacks to and from school who later develop redness and angioedema of the arms or shoulders. Other cases can be caused by tight-fitting clothing or belts, resulting in swelling around the waistline.

Cold-induced urticaria. Exposure to cooler temperatures results in the appearance of hives, specifically at the site of exposure.^{11,12} Common presentations include patients who develop hives while in air-conditioned buildings or after swimming. Although not all urticaria create a significant risk for anaphylaxis, cold-induced urticaria does have this association, which is why patients with this diagnosis should have an epinephrine autoinjector available and should either avoid swimming altogether or swim with a partner and be mindful of their symptoms.

Vibratory urticaria. Hives appear in response to prolonged exposure to vibrations, such as occurs with operation of a jackhammer. This can be tested for in the office by placing the skin in contact with a centrifuge to provide vibratory stimulus.¹¹

Aquagenic urticaria. Small pruritic wheals appear in response to exposure to water. There have been few reported cases of this in the literature, and when a case is discovered it is often portrayed in the media as “the patient who is allergic to water!” Remember that neither aquagenic urticaria nor any other form of inducible urticaria constitutes a true allergic reaction.

Heat-induced urticaria. Exposure to warmer temperatures results in the appearance of hives. This should be contrasted with solar urticaria and cholinergic urticaria, as they could all appear in a patient playing outdoors. In the allergist's office, this can be tested by applying a test tube filled with warm water to the arm for approximately 5 minutes and then monitoring for the development of hives.

Solar urticaria. Exposure to visible and ultraviolet light results in the appearance of hives within minutes.

Cholinergic urticaria. Patients develop hives in response to an increase in their body temperature. The change in temperature does not necessarily have to be dramatic and can occur with a shift of even a few degrees. Elevation of body temperature could occur either actively (exercise) or passively (taking a hot bath). These hives can also be caused by eating spicy foods.

MANAGEMENT

Despite the variety of urticaria a patient may experience, there are only a few medications indicated for the treatment of all types of urticaria. There are some common-sense measures that can be taken first. For example, if a patient knows the stimulus for their urticaria, it is best to reduce or avoid exposure to that stimulus. Some patients note an increase in their urticaria associated with stress and should, therefore, try to control or reduce stress when able. If there is an infection, it should be treated symptomatically. I often encourage my patients to keep a diary of their urticaria including date of onset, possible triggers, and medications used to reduce symptoms. A continued review of this diary may help to elicit triggers that otherwise might have gone unrecognized. I also encourage patients to take pictures of their rash to review in the office, as patients often

refer to all rashes as "hives" or "whelps" when they may not actually be urticaria at all.

Antihistamines are the recommended first-line therapy for urticaria.¹³⁻¹⁸ The type of antihistamine that is used may vary according to the patient's symptoms. If a patient is only experiencing intermittent hives that improve with one dose of oral antihistamines, use of a faster-acting, first-generation antihistamine such as diphenhydramine or hydroxyzine may be recommended.⁸ If a patient requires medication more frequently or needs to avoid the potential sedative effects of first-generation antihistamines, then second-generation antihistamines may be used. One common reason for failure to respond to antihistamines is because the dose used is too low. Although some patients may respond to current weight-based guidelines for antihistamine use, these guidelines more often are recommended for treating allergic rhinitis or conjunctivitis and may be ineffective for chronic urticaria.^{13,17,18} Current literature recommends increasing the daily dose up to 2 to 4 times the recommended dose of second-generation antihistamine to adequately control symptoms.^{17,18} The decision to use increased doses should be considered on an individual basis and can vary depending on the patient's other medications and tolerance of oral antihistamines.

The use of H₂ blockers (eg, ranitidine, cimetidine, famotidine) remains a subject of debate. Although current guidelines suggest attempting a trial of these medications (because the risk of adverse effects is low), there is not significant evidence to demonstrate much efficacy of these medications as primary treatment for urticaria.¹⁴

Leukotriene receptor antagonists (eg, montelukast, zafirlukast) are another medication commonly added to therapy when oral antihistamines do not seem to be

helpful. However, these medications have failed to demonstrate consistent efficacy, even as an adjunctive medication.^{13,16}

Although corticosteroids may help reduce the severity of urticaria and angioedema in the short term, there are no guidelines that favor the chronic use of this medication in the treatment of urticaria due to its side-effect profile.¹⁴

Cyclosporine has proven useful when a patient's urticaria responds poorly to antihistamines.^{14,16} It is one of the only immune suppressants known to inhibit histamine release from basophils and skin mast cells. Clearance has been demonstrated in 60% to 80% of patients, with resolution seen in as little as 1 week.¹⁴ Because the known side effects of this medication include hypertension and reduced renal function, frequent laboratory blood draws are needed for any patient taking this medication, which may deter some patients from its use.

Omalizumab is currently approved by the US Food and Drug Administration for the use of chronic idiopathic urticaria. Injections typically occur once a month and patients have shown dramatic improvement in their symptoms with as little as one injection.¹⁴ The efficacy of this medication is dose-dependent, and the high cost of this medication must be considered prior to its initiation. However, for patients who have failed all other therapies, this provides an easy once-a-month, in-office treatment for recalcitrant urticaria.

One study has evaluated the success of a host of other medications, such as dapsone, sulfasalazine, intravenous immunoglobulin, colchicine, and methotrexate.¹⁴ Although some authors have demonstrated benefit with these medications, it has been reported that there is no double-blind, placebo-controlled challenge for any of these therapies that demonstrates success in more than 30% of patients.^{14,19}

SUMMARY

As an allergist, I encourage pediatricians to attempt initial management of urticaria in their office. This management begins with effective history taking. It cannot be overemphasized that the clinical history is one of the most important tools for obtaining an appropriate diagnosis in a patient with urticaria. Although it is true that urticaria can be allergic in origin, these cases represent only a small percentage of the causes of urticaria. Clinical history is vital in distinguishing whether urticaria is truly allergic or nonallergic, as well as determining the potential triggers for symptoms. The duration of symptoms helps classify the type of urticaria. Reviewing any possible triggers with the patient may help to uncover one specific stimulus for their hives or it may demonstrate no identifiable trigger, possibly indicating that the urticaria are idiopathic in origin. Reviewing any recent symptoms that may indicate infection or an autoimmune disease may provide the cause. It may also prevent unnecessary allergy testing in the hope that “something might be positive,” as this more often creates undue anxiety without providing a true solution. I encourage pediatricians to give the patient oral antihistamines for reduction of their symptoms. Clinicians should not be afraid to increase the dose incrementally if response is less than optimal, remembering that the literature has supported doses at more than

twice the recommended weight-based guidelines for second-generation antihistamines.^{17,18} If the physician exceeds their comfort level for care of urticaria, the patient should then be referred to an allergist-immunologist for further evaluation. I ask that, as pediatricians, we remember the importance of educating our patients and their families and providing them with reassurance that hives are not uncommon and that most cases can be easily managed with medication and often resolve on their own. Most importantly, I advise doctors to remember that not all hives are allergic in origin and should not be reported as such.

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