Chronic Urticaria: Soothing the Itch

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Chronic urticaria

More than six weeks of daily urticaria has been arbitrarily chosen to distinguish chronic urticaria from acute urticaria. Chronic urticaria will affect up to 3% of the population at some point in their lives. The incidence of chronic urticaria is not increased in people with atopy. Females are more affected than males by a ratio of four to one.

Physical urticarias

Physical urticarias are conditions, such as dermatographism, in which physical pressure on the skin causes urticarial rashes to occur. Urticarial lesions are often linear, following scratch marks. Cholinergic urticaria is identified by small papular urticarial lesions that tend to occur with:

• heat,
• exertion, or
• emotional stress.

Physical urticarias have lesions that usually last less than two hours.

Izzy’s Itch

Izzy, 34, presents with daily hives for two months (Figures 1 and 2)
Individual lesions last six hours to 12 hours and are quite pruritic
Lesions are exacerbated by scratching
She has had some episodes of lip and periorbital swelling
Eliminating various foods from her diet has not resulted in any improvement
She has been using diphenhydramine intermittently and finds it somewhat helpful, but quite sedating

Figure 1. Urticarial lesions.
Figure 2. Urticarial lesions.

For more on Izzy, go to page 69.

Urticaria and angioedema affects 15% to 25% of the population at some point in their lives. There are various causes for urticaria and angioedema (Figure 3). Urticarial vasculitis and urticaria pigmentosa are rare conditions (Table 1) but should be differentiated from urticaria. Diagnosis of these conditions is made by a biopsy.
Chronic autoimmune and idiopathic urticaria

Chronic urticaria, whether idiopathic or autoimmune, have lesions lasting up to 36 hours. Approximately 40% of individuals with chronic urticaria will also experience angioedema, which typically involves the:
- periorbital area,
- lips,
- tongue,
- pharynx,
- extremities.

Unlike the angioedema which occurs with C1 inhibitor deficiency or angioedema caused by angiotensin-converting enzyme inhibitors, the angioedema with chronic urticaria does not cause life-threatening upper airway obstruction.

Approximately 40% of individuals with chronic urticaria have IgG autoantibodies to the alpha subunit of the IgE receptor on mast cells.1 Five per cent to 10% of patients with chronic urticaria have IgG autoantibodies to the IgE antibody.2 These autoantibodies directly trigger mast cells to release inflammatory mediators leading to the urticaria. The autoantibodies can also activate the classical pathway of complement and generate C5a that can also activate mast cells, which augment the reaction.3 Up to 27% of patients with chronic autoimmune urticaria have been shown to also have antithyroid antibodies.4 Some of these individuals can also go on to develop autoimmune thyroid disease.

Table 1

<table>
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<tr>
<th>Urticarial vasculitis</th>
<th>Urticaria pigmentosa</th>
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<tr>
<td>Lesions lasts &gt; 48 hours and resolve with purpura</td>
<td>Cutaneous manifestation of mastocytosis</td>
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<td>Lesions are more tender than pruritic</td>
<td>Urticarial lesions appear over hyperpigmented patches, particularly when rubbed (known as Darier’s sign)</td>
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<td>Lesions can be associated with hypocomplementemia</td>
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The underlying cause of the urticaria in 40% to 60% of cases is still not known. Clinically, it is not possible to distinguish chronic autoimmune urticarial from chronic idiopathic urticaria. Biopsy of urticarial lesions, for both the autoimmune and idiopathic types, reveal similar findings of perivascular non-necrotizing infiltrate of CD4 positive lymphocytes, consisting of a mixture of TH1 and TH2 subtypes, plus monocytes, neutrophils, eosinophils and basophils.

Other associations

Case studies have suggested an association between *Helicobacter pylori* (*H. pylori*) infection and chronic urticaria. In rare cases, chronic urticaria has been associated with:

- parasitic infection,
- viral hepatitis,
- malignancies and
- connective tissue disorders.

These conditions should be considered if suspicion arises from the patient’s history or physical examination and not solely because the patient has chronic urticaria. The following is no longer believed to play a role in the development of chronic urticaria:

- psychophysiologic reactions,
- first-line nonsedating antihistamines
  - Desloratadine, 5 mg, q.d.
  - Fexofenadine, 120 mg to 480 mg, q.d.
  - Loratadine, 10 mg to 40 mg, q.d.
  - Cetirizine, 10 mg to 40 mg, q.d.

- Second-line
  - Add sedating antihistamines at night:
    - Hydroxyzine 25 mg to 50 mg
    - Doxepin 10 mg to 150 mg
  - Add on H2 antagonist:
    - Ranitidine, 150 mg, b.i.d
    - Cimetidine, 300 mg, q.i.d
  - Hydroxyzine, 50 mg, q.i.d

- Third-line
  - Leukotriene receptor antagonist (montelukast)
  - Colchicine
  - Sulfasalazine
  - Thyroid hormone
  - Androgenic steroids (danazol)
  - Corticosteroids
  - Immunosuppressant (cyclosporine)
  - Intravenous immunoglobulin

Chronic urticaria can be exacerbated by

- Acetylsalicylic acid and non-steroidal anti-inflammatory drugs
- Opiates
- Alcohol

Up to 27% of patients with chronic autoimmune urticaria have been shown to also have antithyroid antibodies. Some of these individuals can also go on to develop autoimmune thyroid disease.
Chronic Urticaria

- food allergies,
- adverse reactions to food additives and
- cutaneous fungal infections.

Investigations

Investigations to consider for patients with chronic urticaria include antithyroid antibodies and thyroid stimulating hormone (there is no commercially available test to detect anti-IgE receptor or anti-IgE autoantibodies).

Other investigations to consider include:
- complete blood count,
- H. pylori serology or urea breath test,
- viral hepatitis serology,
- stool for ova and parasite,
- complement levels,
- antinuclear antibody,
- serum protein electrophoresis and
- serum immunoglobulins.

Treatment

Treatment of chronic urticaria, whether autoimmune or idiopathic, is aimed at symptomatic control. Patients need to be made aware that there is no simple cure. First-line treatment consists of second-generation (non-sedating) antihistamines (Table 2). Higher than recommended doses are sometimes required for better control. H2 agonists can also be added. Medications in the third-line treatment have shown some success in case studies and small clinical trials.

References


Take-home message

1. Chronic urticaria is an autoimmune condition in 40% of cases
2. In most other cases, the cause is unknown
3. Chronic urticaria is not due to food allergies
4. Management of chronic urticaria is aimed at symptomatic control with high dose non-sedating antihistamines as the first-line choice

Natural history: Chronic urticaria can last over one year in more than 70% of cases and in 14% of cases, it can still exist after five years.