URTICARIA

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Background and Classification

The term urticaria is widely used to describe an eruption of short-lived itchy weals "hives", angioedema or both together. Urticaria is usually classified based on clinical features to guide appropriate investigations and management. The table below summarises the clinical classification of urticaria:

1) Ordinary urticaria

- Most common pattern, usually spontaneous.
- Can be divided into:
  - Acute (usually resolves within 24 hours, but can last up to 6 weeks). Most common type presenting in A+E
  - Chronic (6 weeks or more of continuous activity).
  - Episodic (acute intermittent or recurrent activity)

2) Physical urticarias

- Reproducibly induced by one or more physical stimuli.
- These stimuli can be mechanical (e.g. delayed pressure urticaria), thermal (e.g. cold contact urticaria) or other types of stimuli (including aquagenic urticaria, solar urticaria and exercise-induced anaphylaxis).
- Weals are usually gone within an hour except for delayed pressure urticaria, which can take up to 48 hours to fade.

3) Angio-oedema without weals

- May be idiopathic, drug-induced or caused by C1 esterase inhibitor deficiency.
- Can last up to 3 days without treatment.

4) Contact urticaria

- Usually occurs on contact with allergens or chemicals, never spontaneous.
- Weals usually last up to 2 hours.
- May progress to anaphylaxis in a highly sensitized individual (e.g. latex allergy).

5) Urticarial vasculitis

- Presents with urticaria clinically but small vessel vasculitis histologically.
- Weals usually persist for days, and patients may have systemic disease including joint and renal involvement.

6) Rare autoinflammatory syndromes which can present with urticated weals, but usually also other features that define the disease phenotype

- These syndromes can either be inherited (e.g. Muckle-Wells syndrome) or acquired (e.g. Schnitzler syndrome).

Aetiology

There are 3 main aetiologies of urticaria: idiopathic, immunological and non-immunological. The term idiopathic is assigned after all allergic, infectious, physical and drug-related causes have been excluded as far as possible. About 30% of patients with chronic ordinary urticaria are thought to have an autoimmune aetiology. This is primarily an acute immunoglobulin E (IgE)-mediated hypersensitivity reaction involving degranulation of mast cells and basophils after activation of IgE receptors by histamine and other cytokine-releasing autoantibodies. Immune complexes that are formed can be lodged in blood vessels, such as in the case of urticarial vasculitis. In non-immunological urticaria, degranulation of mast cells and basophils occur independently of IgE receptor activation, usually after exposure to certain drugs (e.g. opiates, aspirin, non-steroidal anti-inflammatory drugs and angiotensin-converting enzyme inhibitors) or other agents (such as radiocontrast media).

Associations

Autoimmune thyroid disease is more prevalent in patients who have chronic ordinary urticaria compared to matched population controls (14% versus 6%). A significantly higher prevalence of coeliac disease in children and adolescents with severe chronic urticaria than in case-matched controls has also been reported. At present, there is little to no evidence to support associations between chronic urticaria and occult infections (e.g. dental abscesses and gastrointestinal candidiasis) or malignancy.

Investigations

The diagnosis of urticaria is primarily clinical. Any investigations must be guided by the history and should not be routinely performed in all patients. Below is a summary of investigations which could be relevant in a patient presenting with urticaria:

Acute or episodic ordinary urticaria

No investigations required except where suggested by history.
However if acute allergic or contact urticaria is suspected, skin prick testing and/or radioallergosorbent (RAST) blood tests may be useful to help confirm this.

Chronic ordinary urticaria

No investigations required in mild disease and those responsive to anti-histamines.

For more severe disease, patients should have following blood tests:
- full blood count and white cell differential.
- erythrocyte sedimentation rate (ESR).
- thyroid autoantibodies and thyroid function tests (especially if autoimmune aetiology likely).

Angio-oedema without weals

Serum C4 should be used as initial screening test if hereditary and acquired C1 esterase inhibitor deficiency is suspected. If this is low, then proceed to carry out quantitative and functional C1 inhibitor assays.

Urticarial vasculitis

Patients should have a lesional skin biopsy to confirm the presence of small vessel vasculitis. All patients should have a full vasculitis screen, including serum complement assays for C3 and C4.

Management

1) General measures

- Try to minimize or avoid any aggravating factors that could potentially worsen urticaria (e.g. overheating, stress, alcohol and certain foods and drugs). Consider if there is any underlying infection.
- Cooling anti-pruritic lotions such as calamine lotion or menthol in aqueous cream (in strengths of 1%, 2% or 5%) can be soothing.
- Explain to patients that the cause of the condition is unlikely to be found but in most cases of urticaria, the prognosis for eventual recovery and resolution of symptoms is excellent.
- It may be useful to give patients a clear, well-written information sheet such as the British Association of Dermatologists' publication on urticaria and angioedema. The link for this publication is: http://www.bad.org.uk/for-the-public/patient-information-leaflets.

2) Specific measures

- Anti-histamines, primarily those working on H1 receptors, are the mainstay therapy for urticaria. It is preferable for patients to be prescribed non-sedating H1 anti-histamines (e.g. fexofenadine telfast 180, cetirizine, levocetirizine, loratadine or desloratadine) rather than sedating anti-histamines (e.g. hydroxyzine or chlorphenamine); although the addition of the latter at night may help patients sleep better. European urticaria

guidelines recommend increasing the dose of anti-histamines above the manufacturer's licensed recommendations in patients who do not respond, provided the benefits outweigh the risks. All patients should be offered the choice of at least two anti-histamines because responses and tolerances vary between individuals. Note: please consult the British National Formulary (BNF) or relevant data sheets for prescribing anti-histamines in special groups; such as pregnant women, children under the age of 12 years and those with renal or hepatic impairment.

- For resistant cases, it may be worth considering an anti-leukotriene drug (e.g. montelukast). The use of these combinations is presently on an off-licence basis.

- Oral corticosteroids should be restricted to short courses (e.g. prednisolone 30mg daily for 3 days in adults) for patients with very severe urticaria or angio-oedema affecting the mouth and throat. Other more advanced therapies including immunodulating drugs (e.g. ciclosporin and Omalizumab) should not be commenced until a full consultation and discussion has been made with a specialist.

3) When to refer

- It may be appropriate to refer patients for consultation with a specialist (dermatologist, allergist, immunologist or rheumatologist) in select cases, particularly cases which are complicated, recurrent, severe or refractory to treatment; as well as cases of suspected or confirmed urticarial vasculitis.

Useful References

1) Guidelines for evaluation and management of urticaria in adults and children. Grattan CE, Humphreys F; British Association of Dermatologists Therapy Guidelines and Audit Subcommittee. *Br J Dermatol. 2007 Dec;157(6):1116-23.*
2) Dermnet Urticaria section: http://www.dermnetnz.org/reactions/urticaria.html.