

Urticaria

Urticaria is a skin disorder characterised by the presence of wheals, itchy raised areas within the superficial aspects of the skin. These 'hives' are occasionally accompanied by angioedema, swelling of the deeper layers of the skin. The urticaria can be defined as acute, lasting less than 6 weeks or chronic which often lasts considerably longer. It can be idiopathic, where no obvious cause can be found or secondary to known factors such as foods, aeroallergens, infections, physical stimuli or auto-immune disease processes. Urticaria is a common skin disorder affecting up to 20% of individuals at some point during their life and the underlying pathophysiology differs in adults and children.

Diagnosis

The diagnosis of urticaria is based on clinical history and examination of the skin. During a medical consultation, photographs of the rash, its time course of appearance and resolution, associated exposure to insects, pets and medication as well as response to anti-histamines are vital. Since infections are a common cause of urticaria in children, it is important to determine whether the child was well or unwell around the time of the rash.

Causes of acute urticaria

Food-induced urticaria is usually the easiest to diagnose and generally there is a clear history of food consumption and the appearance of the rash and/or swelling within minutes. The clinical symptoms often affect the mouth and lips first or the areas where the food has been in contact. The rash may spread to involve the entire body before it resolves, generally within 1 – 2 hours. Occasionally, food-induced urticaria is delayed up to several hours following ingestion possibly due to additional factors reducing the threshold for mast cell degranulation such as exercise, concurrent infection, non-steroidal anti-inflammatory drugs or alcohol. A characteristic feature of food-induced urticaria is that the reaction is generally short-lived and the reaction can resolve before the antihistamines have time to act. Moreover, it does not return unless the individual is again exposed to the particular food. The urticaria secondary to food allergies is often associated with marked behavioural manifestations, such as food aversion or spitting the food out and clawing at the tongue. In the vast majority of cases, the food is not enjoyed and the portion left unfinished. This is a useful differentiating factor in determining whether a localised peri-oral erythematous rash is associated with a food allergy or simply due to an irritant reaction. Irritant reactions can often be mildly pruritic, occasionally involve lip swelling but most importantly, do not involve the systemic immune system. They thus do not progress to widespread urticaria or anaphylaxis. The food (usually tomatoes, strawberries or oranges) is enjoyed and antihistamines are ineffective, even when given beforehand. These irritant reactions are commonplace in the allergy clinic and are generally associated with sensitive skin and eczematous reactions elsewhere.

Aeroallergens are another common cause of urticaria and their distribution and temporal/seasonal distribution, along with other atopic manifestations often makes the diagnosis. Pollen-induced urticaria is usually the easiest to diagnosis, being associated in the majority of cases with hay fever symptoms in the spring or summer. It is possibly however for individuals to exhibit pollen-induced urticaria in the absence of hay fever symptoms, particularly when the local concentration of pollen is high for example after sitting on grass in the summer months. Pet-induced urticaria is also usually well recognised by individuals due to the close temporal relationship between exposure to the pet and the appearance of the urticarial lesions. Unlike food-induced reactions, aeroallergen-induced

reactions can last for several days, characteristically returning when the dose of antihistamine has worn off. Usually beyond this time, further aeroallergen exposure results in depletion of cutaneous mast cell products and thus no further urticarial lesions. Instead the skin may develop an eczematous rash, responding not to antihistamines but only to topical moisturisers and steroids. Due to its nature, food and aeroallergen-induced urticaria is an acute process and not usually associated with chronic urticaria.

Other common causes of acute urticaria include infections, bee and wasp stings or drug allergies. Infection-associated urticaria is particularly evident in young children and characteristically the child is either unwell at the time or is recovering from a systemic infection. Associated symptoms can include fevers, cough, fatigue, sore throat, runny nose and abdominal pain. Most cases of infection-associated urticaria are short-lived although in some individuals the rash and swelling can persist for months or even years. Infections particularly associated with urticaria include hepatitis (A, B and C), Epstein-Barr virus, herpes simplex virus as well as streptococcal infections and chronic parasitic diseases. Drugs, particularly antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are well recognised causes of acute urticaria. The 'hive-like' rashes associated with antibiotics, especially penicillin-based medications, are usually a manifestation of a drug allergy and this drug as well as closely-related drugs in the same class should be strictly avoided. In contrast, the urticaria associated with NSAIDs and opioids are usually non-immune mediated and due to a direct action of the drug on mast cells. Thus individuals are not at risk of a severe life-threatening reaction.

Causes of chronic urticaria

Physical urticarias comprise a significant proportion of the individuals seen with chronic urticaria. These range from the relatively common dermatographism, where individuals demonstrate marked wheals in response to scratching of their skin to other rare causes such as cold urticaria, aquagenic urticaria, solar urticaria, delayed pressure urticaria and cholinergic urticaria. Interestingly these usually exist as isolated entities, suggesting the mast cells in those individuals do not have a reduced threshold for non-specific activation but that are primed in some way to respond to each of these physical stimuli.

Cold urticaria is noted particularly when individuals have been in water and are subject to high degrees of wind chill, for example when coming out of the sea on a windy beach. These reactions can occasionally be very severe resulting in anaphylaxis and thus careful consideration of an adrenaline auto-injector is warranted in cold urticaria. Aquagenic urticaria is similar however the precipitating stimulus is water, either hot or cold and individuals often notice symptoms when in the shower or when outside in the rain. Solar urticaria is rare but typical urticarial lesions occur within 10 – 15 minutes of individuals being in the sun. The rash can occur on both covered and uncovered areas of the skin and is generally triggered by ultraviolet (UV) radiation and resolves within 30 mins of UV avoidance. Cholinergic urticaria is a common cause of physical urticaria and although the stimulus might be considered to be heat, the actual precipitating cause is sweating. This may occur in response to exercise but also in response to stress or anxiety, and eating spicy foods.

Autoimmune diseases, particularly coeliac disease and auto-immune thyroid disease are occasionally associated with chronic urticaria. Moreover, antibodies directed against thyroid proteins are often seen in chronic urticaria in the absence of changes in thyroid function. The relevance of these to the disease process remains to be determined. Other autoimmune diseases which have an association with chronic urticaria include type 1 diabetes, rheumatoid arthritis, systemic lupus erythematosus, and Sjogren's syndrome.

Despite extensive investigations, a large proportion of individuals with chronic urticaria will have no obvious cause and so will be labelled as idiopathic urticaria. Some of these individuals will have auto-antibodies directed against IgE bound to mast cells, however currently there are no robust biochemical tests available on the NHS to determine the presence of these antibodies.

Treatment of urticaria

Second generation, non-sedating antihistamines are the mainstay of treatment in acute and chronic urticaria, and at appropriate doses they act to prevent the action of mast cell-derived histamine and so terminate the local oedema and itching. Generally, these drugs are started on an 'as required' basis in acute urticaria increasing to once or even twice daily dosing in chronic urticaria particularly where the lesions are present more than 3 times weekly. In resistant cases, doses of antihistamines are doubled in line with EAACI recommendations before the addition of other pharmacological agents such as montelukast. Recently, anti-IgE therapy (Omalizumab) has become available for individuals with chronic idiopathic urticaria unresponsive to alternative therapies but this is currently only available in more specialist centres.