Chapter

Introductory Chapter: Urticaria - Meeting the Diagnostic and Therapeutic Challenge

Eleni Papakonstantinou

1. Introduction

Urticaria is one of the most common pruritic skin diseases which is characterized by the occurence of recurrent erythematous and edematous wheals with or without angioedema. These wheals appear at different body areas and dissapear within 24 hours while new lesions may occur. The disease may be characterized as idiopathic or inducible depending on the potential trigger factors and acute or chronic depending on the duration of the symptoms for less or more than 6 weeks [1].

The lifetime prevalence of chronic urticaria is about 10–20%. Urticaria can occur at any age but the chronic form is more common in adults, especially during the third and fourth decade of life. The disease can affect both women and men but there is evidence of a female predominance [2].

The pathomechanismus of urticaria is based in the release of various mediators due to degranulation of activated subepidermal mast cells. Released histamine causes local vasodilation and increased capillary permeability, resulting in intracutaneous (wheal) or subcutaneous (angioedema) edema. Furthermore, activation of sensory nerves leads to pruritus and reflex erythema. The mast cell degranulation may be caused by different mechanisms such as direct activation or IgE-mediated allergic activation and results to the release of mediators such as histamin, which is responsible for the pruritus which ist he main symptom in urticaria. Beside pruritus, these vasoactive mediators are responsible for vasodilation and subsequent erythema and edema [3].

Chronic urticaria can be characterized as spontaneous when no trigger factors are known or as inducible when the appearance of wheals is caused by specific trigger factors. There are many triggering factors for chronic urticaria but determining a specific cause is not always possible.

The most common ones include viral, bacterial or parasitic infections, specific drugs (e.g. nonsteroidal anti-inflammatory drugs and antibiotics), foods, physical factors (such as pressure, exposure to light, heat or cold, vibration, exercise and increased body temperature) and emotional stress [4]. Furthermore, autoimmune and systemic diseases and also malignancies can be the underlying factor of urticaria and should be taken into consideration in the diagnosis of the disease. Some of the most common systemic disorders involved in urticaria are lupus erythematosus, cutaneous vasculitis, Sjögren's syndrome, autoimmune thyroid disease, rheumatoid arthritis and diabetes mellitus [5]. All these factors and conditions will be thoroughly disscussed in this book giving the reader a complete guideline to diagnose and define different types of urticaria.

Diagnosis of urticaria is mainly based on anamnesis and clinical examination of the patient. However, due to the transient character of the skin manifestations this may be difficult at the time of examination. Sometimes, photos or re-examination of he patient when the lesions are present are necessary and helpful for the clinician in order to make the diagnosis. Thorough clinical history and a potential association with angioedema and/or anaphylaxis should always be asked.

Clinical manifestation of urticaria is characteristic with circumscribed wheals in any region of the body which commonly persist no longer than 24 hours and reappear at different body areas. Pruritus is the major symptom patients claim for which affects their daily activities and quality of life. If the lesions persist longer than 24 hours, appear in combination with skin manifestations such as petechia or hyperpigmentation, or are accombanied by systemic symptoms such as fever and arthralgia, more severe conditions such as urticaria vasculitis have to be excluded with a skin biopsy.

Skin biopsy can be helpful if systemic diseases such are vasculitis or mastocytosis are suspected. Histopathological findings of urticaria include interstitial edema and perivascular mixed cellular infiltrate. T-lymphocytes are predominant in this infiltrate but also eosinophils, neutrophils, and basophils may also be present.

Once the diagnosis is confirmed, it is important to find out potential trigger factors, if possible. Detailed anamnesis is important to determine any triggering infection, drugs or physical factor. Challenge tests may be then individually performed to confirm the different types of inducible urticaria.

Skin tests such as an autologous serum test may be useful in order to exclude the autoimmune type of urticaria. During this test patient's own serum is intradermally injected on the forearm oft he patient and is positiv if an urticarial reaction appears within 30 min.

Laboratory tests are in general not indicated for patients with acute urticaria unless they have signs and symptoms suggesting an underlying systemic disease. In cases of chronic urticaria besides a standard laboratory examination additional tests such as antinuclear antibody, autoantibodies, rheumatoid factor, complement C_3 and C_4 levels, thyroid parameters, Helicobacter pylori antigen, hepatitis and parasite examination are essential in ordert to exclude an infection or an underlying autoimmune disease [1, 6].

The severity of the disease can be individual evaluated using some scoring systems used for this purpose, one of which is the urticaria activity score (UAS). This is a widely used scoring system questioning the intensity of pruritus and the number of wheals in a day and can be further used to also evaluate the effectivity of the therapy in later stages [7].

If an association with trigger factors has been established, the prevention of trigger is the first step of treatment. The next step includes drugs in order to control the symptoms with minimal side effects. Second-generation H_1 antihistamines, such as cetirizine and loratadine, are used as first-line treatment options. These newer, antihistamines ahave a non-sedative character compared to the first-generation ones such as hydroxyzine and diphenhydramine and thus are mopstly preffered. In severe cases, a dose increasement up to fourfold of standard therapeutic doses is recommended by the latest guidelines. In certain cases, H_2 antihistamines may be used in combination with H_1 antihistamines.

Glucocortikosteroids may be used for a short period of time and at the lowest dose in addition to antihistamines for acute urticarial attacks, particularly when accompanied by angioedema. Long-term use of systemic glucocorticoids is not recommended because of potential adverse effects.

In chronic cases where the symptoms persist despite high-dose antihistamines. Antileukotrienes, such as montelukast, zafirlukast as well as the

5-lipoxygenase-inhibitor zileuton are added to antihistamines as second-line treatment options. Furthermore, immunosuppressive agents, such as cyclosporine, are effective in the treatment of chronic urticaria but the clinicians and the patients should be aware of the potential side effects. Other less used drugs such as dapsone, hydroxychloroquine, sulfasalazine, azathioprin and mycophenolate have also been used in the treatment of urticaria [1].

Biologic agents such as omalizumab has recently been added in the treatment of chronic urticaria in adults and adolescents that continue to be symptomatic despite the use H1 antihistamines. It is an anti-IgE monoclonal antibody which has a good efficacy and safety profile in most oft he patients and can be easily applied with monthly subcutaneous injections [8]. Further research is being made and current data indicate ligelizumab, a next-generation anti-IgE antibody as a potential valid alternative for patients with chronic urticaria unresponsive to omalizumab. Other IgE-antibodies and diverse anti-IL factors are also being studied and may show a potential role in the treatment of urticaria [9].

2. Conclusion

In view of the pathomechanism and the different forms of urticaria, the treatment of the disease is a real concern over the opportunities and therapeutic options already available and over all other strategies under development and trials. In this context, it is believed that we will be able personalize the management plan of urticaria in the future and we are close the identification of specific biomarkers for different types of the disease which could also be used as monitoring markers.

This book presents the most current knowledge in the diagnosis and management of urticaria. It also examines the scientific aspect of currently available treatments as well as potential new options for managing severe forms of the disease. The different chapters, written by expert authors all over the world, address some of the most important aspects in the diagnosis and management of urticaria.

Author details

Eleni Papakonstantinou
Private Dermatological Practice, Hautärzte am Markt, Dortmund, Germany

*Address all correspondence to: elenipap2000@hotmail.com

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