CONSTITUTIONAL MARKERS OF URTICARIA AND THEIR PROGNOSTIC SIGNIFICANCE (ANALYSIS OF SCIENTIFIC LITERATURE)

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Annotation. The purpose of the work is to analyze the scientific literature regarding the constitutional markers of urticaria and their prognostic significance. The analysis of modern scientific literature in the scientometric databases PubMed and MEDLINE is carried out. A review of the literature indicates that significant progress has been made in understanding the etiopathogenesis of urticaria in recent decades, with some clinical and anamnestic signs suggestive of adverse outcomes. However, identifying patients with the highest risk of complications remains an unresolved issue. In connection with the development and implementation in clinical practice of methods of genetic typing, much attention is paid to the search for genetic predictors of adverse course of this dermatosis. To date, phenotypic marker profiles that have been little modified over a lifetime and available for visualization in everyday clinical practice have not been properly considered in assessing the risk of urticaria. Modern anthropocentric approach to solving the problem of risk prediction in urticaria opens up the prospect of taking into account constitutional (personality-typological, somato-typological) and phenotypic marker profiles that have been little modified over a lifetime and available for visualization in everyday clinical practice and clinical manifestations, patterns severity and frequency of complications.

Keywords: urticaria, course, constitutional markers, clinical anthropology.

Introduction

Urticaria is a disease associated with mast cell degranulation, blistering, itching, and angioedema in the absence of specific triggers [31]. The medical and social significance of this disease is due to its widespread prevalence, the development of the vast majority of people of working age, high-cost treatment and a significant reduction in the quality of life of patients [28].

The aim of the work is to analyze the scientific literature on the constitutional markers of urticaria and their prognostic significance.

Materials and methods

A search in the medical literature of PubMed and MEDLINE included the terms urticaria, chronic urticaria, chronic idiopathic urticaria, severity, constitutional markers, prognosis and treatment.

Results. Discussion

Immunopathogenetic mechanisms of urticaria development vary significantly in different individuals [2]. The search for new prognostic clinical-laboratory and constitutional markers, in particular, allows to determine an individualized therapeutic approach, track changes in dermatosis activity, predict response to treatment, which is an urgent task of modern medicine [10, 16, 26].

It was found that 4% of patients with urticaria with a positive test with auto-serum had first-line relatives with a history of this dermatosis [6, 8]. Clinical and genealogical analysis suggests that the participation of atopy in the development of urticaria is quite probable. The participation of immunocomplex reactions in its development is not excluded [30]. Some hereditary defects in the complement system lead to the development of hereditary urticaria, which is accompanied by the appearance of giant blisters. The ability to synthesize cold hemolysins and cryoglobulins in the patient's body can also be hereditary, which leads to the development of cold urticaria [11, 15].

In studies by N. Dogan et al. (2020) showed the association of certain HLA antigens of classes I and II of the main histocompatibility complex with chronic urticaria [12].

Due to the fact that the main histocompatibility complex is the most polymorphic supergene known in humans, and the genes encoding HLA molecules and their frequency are different in different populations, the data of different authors differ. Thus, studies by Polish scientists have shown an increase in the frequency of antigens of the main histocompatibility complex class I - HLA-A33, HLA-B44, and MCH class II - DR B1 * 04 in patients with chronic urticaria compared with the control group. In addition, the HLA-DR B1 * 04 antigen corresponded to autoimmune urticaria. HLA-C alleles and DQ did not differ from the group of healthy people [4].

In the Turkish population, people with chronic urticaria have an increased frequency of detection of HLA-B44 antigen, but no association with HLA-A locus antigens. The main histocompatibility complex of class II DR B1 * 01 and DR B * 15 were associated with chronic idiopathic urticaria [8]. In studies of Z. Calamita (2012) no genetic association was found in the study of antigens of the main histocompatibility complex of class I [7].

Indirect evidence of genetic predisposition to urticaria is its combination with other inherited autoimmune diseases...
(autoimmune thyroiditis, celiac disease, type I diabetes mellitus) [19].

M. B. Freydin and V. P. Puzyrev (2010) using the bioinformation resource HuGE Navigator established syntropic genes of urticaria and IgE levels: TNF, IL13, IL4, IL4R, MS4A2, HLA-DRB1, HLA-DQB1, CD14, LTC4S, CTLA4, HLA-DQA1 [14]. These genes are involved in the regulation of the immune response in the process of allergic inflammation and the regulation of anti-infective immunity. Using cluster analysis and multidimensional scaling, it was shown that according to genes and gene specificity, the studied allergic phenotypes were divided into two groups: the first includes IgE levels, bronchial asthma, atopic dermatitis, allergic rhinitis and hay fever; the second - urticaria, food and drug allergies.

E. F. Hamptnerova et al. (2014) found that the rs2243250 * C allele is a marker of increased risk of developing acute urticarial [16].

As a result of research by G. F. Gimalov et al. (2017) was first associated with the development of urticaria polymorphic loci of the TLR1 gene in Tatars and TLR6 in Russians [15].

Korean researchers [22] conducted a population study that showed an increased prevalence of urticaria among first-degree relatives compared to the general population. Of course, genetic factors make an important contribution to the susceptibility to the development and progression of the disease, especially subtypes such as urticaria with aspirin intolerance. The first target genes identified by candidate gene identification were genes associated with mast cell activation and histamine, including FcεRI, HNMT, HRH1, HRH2, TNF-α, TGFβ1, ADORA3, and IL-10. Genes related to the arachidonic acid pathway, including ALOX5, CysLTR1, LTC4S and PTGER4, HLA class I and II alleles, have also been identified. Other genes that may have been involved in the pathogenesis of CU were UGT1A6, CYP2C9, NAT2, ACE and PTPN22.

Genetic variants associated with the arachidonic acid pathway in patients with acute urticaria caused by non-steroidal anti-inflammatory drugs have been identified in two Spanish populations and have shown significant associations with this clinical phenotype [9].

Antigen HLA-Bw4 (Turkey) [3], HLA-B14 (Brazil) [7] and HLA-B44 (Poland and Turkey) [4, 8] may be responsible for susceptibility to this dermatosis. It is noteworthy that the prevalence of HLA-B14 was higher in patients with urticaria with high levels of IgG to thyroperoxidase [7].

Studies by Japanese and Mongolian scientists have shown that polymorphism of Taq1, Bsm1, Fok1 and Apal genes with vitamin D receptors is associated with chronic spontaneous urticaria [17, 23].

The results of a study by foreign scientists show that chronic urticaria, especially if it persists, may be associated with overweight and obesity, while weight gain may lead to later onset of urticaria symptoms. A population-based study from Italy found a positive correlation between the risk of dermatosis and obesity, as determined by body mass index [21].

However, Korean researchers have found that high waist circumference [17] rather than high body mass index [18] may be a prognostic factor in the long-term risk of chronic spontaneous urticaria. They used multivariate Cox proportional risk models to determine the risk factor for long-term illness (more than 3 years) according to waist circumference and body mass index. A total of 52,667 subjects were included in the study, with a mean age of 54.5 years. After adjusting for other mixed variables, the group with high waist circumference and high body mass index had a 1.062-fold higher risk (95 %, 1.028-1.098) than the normal group. Interestingly, the group with a large waist circumference and a normal body mass index showed a significantly higher risk (95 %, 1.008-1.101) than the control group.

Urticaria is a polyetiological dermatological disease [5, 29]. Personality traits have been shown to be associated with dermatological disorders. For example, patients with psoriasis, alopecia, or urticaria were more hostile and neurotic than people with other dermatological conditions. Some authors have reported that subjects with urticaria have significantly interpersonal, depressed, more hysterical, and suspicious personality traits compared with controls [20, 23, 25].

Turkish researchers have studied the personality factors of patients with chronic idiopathic urticaria, as well as the correlation between the duration of the disease, the severity of itching, urticaria activity and temperament type. A total of 70 patients with dermatosis and 60 healthy individuals were included in the study. The group of people with urticaria had significantly higher rates of novelty search and lower rates of cooperation, reliance on remuneration and self-focus than the control group [1].

Potential biomarkers of urticaria severity and/or duration include basophil count and susceptibility to activation, inflammatory markers, external coagulation pathway activation markers, immunoglobulin E, and vitamin D [27].

Based on the literature review, the studied clinical markers include older age of onset, female sex, long-term disease and hypersensitivity to aspirin/nonsteroidal anti-inflammatory drugs may be associated with both severe and long-term spontaneous remission [13, 24, 23].

The literature on genetic research in the field of research on genetic markers of urticaria is extensive, and it is unfortunate that there are almost no Ukrainians among the authors. However, without taking into account these factors, it is not necessary to talk about the prevention of this dermatosis in our country.

Thus, a review of constitutional markers was conducted to evaluate their importance in determining the severity or prediction of urticaria in adult patients.

**Conclusions and prospects for further development**

1. A review of the literature has shown that there are a number of papers in the scientific literature on the
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research should be representative, well-characterized, and technically and economically accessible. Population studies are needed to determine the significance of these clinical and biological markers for predicting disease severity and course. In the process of studying diseases with hereditary predisposition, it is very important to determine the phenotypic predictors of urticaria, which can be used as constitutional features of man.

References


[12] Dogan, N., Çıldag, S., Yenisey, Ç., & Şentürk, T. (2020). The relationship between anthropometric indicators and urticaria. Data on the ratio of anatomical components of the body in patients with dermatitis and their relatives can be used not only to determine body types, the impact of major body components (bone, muscle, fat) on urticaria, but also to justify approaches to its diagnosis and prevention.

Although the markers described are promising, further research should be representative, well-characterized, and technically and economically accessible. Population studies are needed to determine the significance of these clinical and biological markers for predicting disease severity and course. In the process of studying diseases with hereditary predisposition, it is very important to determine the phenotypic predictors of urticaria, which can be used as constitutional features of man.


