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**THE ROLE OF TOLL-LIKE RECEPTORS IN THE PATHOGENESIS OF PSORIASIS**

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**Key words**: psoriasis**,** TOLL-like receptors

The skin is the main barrier organ, as well as highly organized peripheral organ of the immune system, which possesses a large number of various immunocompetent cells. Violations of the functioning of the immune system often lead to the development of severe diseases, such as immunodeficiencies of various etiologies and immune-inflammatory diseases. The number of patients with immuno-mediated diseases increases with each passing year: if in 2007 in the world there were about 90 million patients, then according to the data of 2014, the number of patients with psoriasis alone is about 120 million. [4]. Many of the immuno-mediated diseases are chronic, and existing methods of treatment can only reduce the manifestation of symptoms, but do not cure patients. Among the most common immunoregulatory skin diseases - psoriasis [5].

Psoriasis is one of the most common chronic multifactorial diseases in which the genetic component of susceptibility to the onset of the disease and violations of numerous parts of neuroendocrine, metabolic and regulatory-trophic processes prevails. The share of psoriasis in the overall structure of skin diseases ranges from 7% to 10%, and among hospitalized patients with skin diseases up to 20-25% [1, 2, 3]

According to WHO, the total number of psoriasis patients in the world is approximately 125,000,000. The distribution of patients with various forms of psoriasis and the severity of the clinical picture corresponds to the rule of "thirds": 2/3 suffer from mild and moderate severity and leakage of the disease, and 1/3 of the diseases of moderate severity and severe forms of dermatosis (psoriatic erythroderma, arthropathic psoriasis) , which lead to prolonged disability and disability of patients. [6, 2, 7].

A number of studies conducted in Europe, North America and Australia have confirmed that dermatosis is more common in white race than in other races, with the least affected by psoriasis of the local population of Asian, African and Latin American countries, from 0.3% to 0 , 9%. [6, 7, 8, 9]

The prevalence of psoriasis in India is 0.5% - 2.3%, in Malaysia it is 5.5%, in Japan it is 0.29% - 1.18%. In different regions of China (including Taiwan), it varies from 0.05% to 1.23%. In general, the representatives of the Mongoloid race, the low incidence of psoriasis is associated with low prevalence of antigen HLA-Cw6 - the main immunogenic marker of this disease [6, 7, 8].

In Central America, with an ethnic heterogeneity of populations with Indians, whites and blacks, the prevalence of psoriasis ranges from 0.7% in Guatemala, 1.2% in Honduras and 1.2% in Nicaragua to 6% in the Caribbean [6, 7].

In South American countries, prevalence of dermatoses reaches 1.3% - 4.2%, in Brazil 1.30%, in Venezuela - 2%, in Mexico - 3%, in Paraguay - 4.2%. The prevalence of psoriasis in the ethnically mixed population of Egypt is about 3%, in the population of East, Central and South Africa (0.08% -0.5%). Low prevalence is also observed in African Americans, genetically similar to East Africans. In the USA, the incidence of psoriasis is 2.4% on average, while in the northern states, the incidence rate is much higher than in the southern [6, 7, 8].

Quite interesting is the fact that the prevalence of dermatoses in white-skinned Australians is close to the West and is 2.6%, while the incidence of dermatoses in Australian aborigines that inhabit this continent for almost 30,000 years has never been found. And only the latest WHO studies found 4 cases of psoriatic arthritis [6, 7, 9,].

Recent studies indicate a significant number of patients in England (2.8%), Germany (from 3% to 6.5% depending on the region), Italy (from 0.8% to 4.5%) and France ( 3.6%) [6, 9, 10].

In Ukraine, the statistics on the incidence of psoriasis are significantly different from the average in Europe and in the world. Thus, in 2009, the prevalence of psoriasis in absolute terms was 98,544 patients, and the incidence of 13529 per 100,000 population.

Toll-like receptors (TLRs) are a class of conserved receptors that recognize pathogen-associated microbial structures. The system of congenital recognition, formed during the evolution of vertebrates, is realized with the help of effector cells involved in the first line of defense against all antigenically algebras. These include the following types: epithelial cells, macrophages, dendritic cells, granulocytes, smooth cells, NK cells, and others. These effects have phagocytic and killer activity, provide a network of signals that activate and guide the antigen-specific response cells of the adaptive immune system. These cells serve as a bridge between pathogen-associated molecular structures (PAMPs) and antigen-specific cells of the adaptive immune response, transmit signals of specific hereditary coded receptors (PRRs) in soluble mediators that bind to T and B cells through specific cytokine / chemokine receptors. One of the key events in significance is the synthesis of a complex of proinflammatory cytokines, which stimulates most of the stages of inflammation and which activates various types of cells involved in the maintenance and regulation of inflammation. Of the several functionally different classes of PRRs, the most well-characterized Toll-like receptors (TLRs) are signaling PRRs and are an important component of the innate immune system. Numerous experimental studies, as well as results from clinical practice, convincingly testify to the key role of Toll-like receptors in the pathogenesis of immunopathological diseases [11,12,].

The role and function of TLRs in human skin has been the subject of study relatively recently. In foreign literature, there are a few information about the presence of various TLRs on keratinocytes of different layers of the epidermis of healthy individuals. Therefore, we conducted a study of TLRs in the skin of patients with psoriasis.

Under the supervision were 30 patients with normal psoriasis. Patients were subjected to biopsy studies from the skin, affected by psoriatic eruptions, as well as from areas of intact skin. In addition, to compare the results of the immunohistochemical study, 5 healthy people were examined for biphilic material.

The superficial layers of the epidermis, as in patients with psoriasis, and in healthy people from the control group, contained only single cells that had a weak positive color. Similarly, in the skin there were areas without signs of swelling and a negative reaction to TLR4 and TLR9. Single TLR4 and TLR9-positive cells were detected in the dermis in small clusters of inflammatory cells.

In psoriatic plaques, the skin of the patients significantly thickens the layer of the epidermis, increases the number of TLR4 and TLR9-positive cells. A pattern is observed: TLR4 and TLR9-positive cells in the epidermis are found in the areas of edema and much less in areas of compact placement of epithelial cells.

Epithelial cells have mild and moderate nuclear and cytoplasmic staining. Macrophages that migrate in the vessels of the papillomas of the dermis have a pronounced positive expression of the markers.

TLR4 and TLR9-positive monocytes and macrophages are found in the vessels and perineum of the papillary layer of the dermis. The greatest number of positive cells is determined in the vessels that are in the papillae. In follicular clusters of inflammatory cells in the papillary layer of the dermis, directly under the epidermis, the positive expression of TLR4 and TLR9 in large macrophages and a slightly positive reaction in the part of the lymphoid cells is detected.

It should be noted that part of the TLR4 and TLR9-positive cells in the epidermis are inflammatory cells that migrate from the papillary layer of the dermis. These cells include, in the first place, macrophages and activated lymphoid cells, as well as neutrophils.

In the intact skin of patients with psoriasis in the epidermis focal-shaped, the more active expression of TLR4 and TLR9 is determined. Topographically, these areas correspond to enlarged papillae or formed papillae. In the epidermis above them, the positive color of the epithelial cells is determined for the entire thickness of the epidermis.

In the control group in the skin of healthy people, the expression of TLR 4 and TLR9 in the epidermis is most pronounced in the basal parts and in the studded dermis layer.

Closer to the stratum corneum, single cells with positive staining are determined. It should be noted that the clear delineation of cells with a positive reaction and cells that have negative expression is determined. In the dermis, the positive marker expression is determined in single inflammatory cells. Expression of cells is mainly nuclear, in the cytoplasm of epithelial cells the positive color is minimal.

At present, it has been established that inflammation in the skin of patients with psoriasis begins with the activation of keratinocytes. The involvement of immune system cells in the pathological process also occurs under the influence of activated skin cells.

Thus, the study of the expression of TLRs by skin cells is important for a deep understanding of the mechanism of the development of immune inflammation in the skin of patients with psoriasis, which is an important link in the pathogenesis of the disease.

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