PATHOGENETICALLY SIGNIFICANT RISK FACTORS FOR DEVELOPMENT ANDROGENETIC ALOPECIA.

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ABSTRACT
The actual problem of the pathogenesis of androgenetic alopecia is the "microinflammation" of hair follicles, which is a multi-stage process of the inflammatory response. Langerhans cells and keratinocytes can present antigen to infiltrating T lymphocytes and induce T cell proliferation. Antigens are selectively destroyed by infiltrating macrophages or natural killer cells

The actual problem of the pathogenesis of androgenetic alopecia is the "microinflammation" of hair follicles, which is a multi-stage process of the inflammatory response. Langerhans cells and keratinocytes can present antigen to infiltrating T lymphocytes and induce T cell proliferation. Antigens are selectively destroyed by infiltrating macrophages or natural killer cells. With a long-term inflammatory process, along with remodeling of the connective tissue, where collagenases play an active role, perifollicular fibrosis is noted. The latter play an important role in the synthesis of chitinase-3-like protein 1 (YKL-40), which is a heparin and chitin-binding glycoprotein. Although the biological function of YKL-40 is still unknown, involvement of YKL-40 has already been proven in extracellular matrix remodeling, cell migration and proliferation, angiogenesis, macrophage-induced inflammation, and T-cell activity (Hansen J.W., Thomsen S.F., Porsbjerg C. , Rasmussen L.M. 2015). YKL-40 is stimulated by local pro-inflammatory cytokines such as TNF-α and IL-1β and correlates with the latter.

The purpose of the study: to study the state of the extracellular matrix and cytokine status in the pathogenesis of androgenetic alopecia.

Materials and methods. We observed 90 male patients with androgenic alopecia aged 18 to 45 years. According to the classification of Norvoerd-Hamilton, III degree was observed in 28 patients (31.2%) and was clinically expressed in pronounced bald patches in the forehead; III-IV degree - in 39 patients (43.3%), in which hair loss was noted not only in the forehead, but also in the parietal region; IV-V degree - in 23 patients (25.5%) men and there was a fusion of foci of hair loss in the parietal and frontal areas of the scalp, forming extensive areas of

alopecia. The study did not include patients with the following diseases: diabetes mellitus, thyroid disease or other endocrine diseases; kidney or liver failure; chronic inflammatory or autoimmune diseases; malabsorption syndromes; cardiovascular disease and other serious illnesses. The control group consisted of 20 people, representative of age and gender. Determination of parameters of remodeling of the extracellular matrix (chitinase-3-like protein (YKL-40)) and cytokine status (TNF-α, IL-1β) was carried out by an automated ELISA method using the HumareaderSingle apparatus.

Research results. The study of chitinase-3-like protein YKL-40 in male patients with androgenetic alopecia showed a highly significant increase compared to the same indicator in the control group: in grade III -54.2±1.7 ng/ml (p= 0.001), with III-IV degree - 63.5±3.1 ng/ml (p= 0.001), with IV-V degree - 77.8±4.9 ng/ml (p= 0.001) (Table 1).

Table 1

Parameters of extracellular matrix remodeling and cytokine status in male patients with androgenetic alopecia.

N	Cytokines (ng/ml)	Control group (N=20)	Patients with androgenetic alopecia (N=90)		
			III degree (N=28)	III-IV degree (N=39)	IV-V degree (N=23)
1	YKL-40	32,2±6,0	54,2±1,7***	63,5±3,1***	77,8±4,9***
2	TNF-α	2,5±0,9	15,9±2,3***	24,8±4,2***	28±3,7***
3	IL-1β	2,0±1,1	16,9±2,04***	21,5±3,9***	32,6±5,1***

Note: * - differences relative to the data of the control group are significant (*** - P<0.001).

It should be noted that with an increase in the severity of the disease, an increase in the YKL-40 index in the blood of patients with androgenetic alopecia is observed. Apparently, microinflammation, which is one of the leading pathogenetic links in the development of androgenetic alopecia, promotes remodeling of extracellular matrix tissues due to an increase in chitinase-3-like protein (YKL-40). In addition, an increase in pro-inflammatory cytokines stimulates the synthesis of the YKL-40 protein, also leading to tissue remodeling. As for pro-inflammatory cytokines (TNF-α, IL-1β), as can be seen from Table 1, the indicators of the latter significantly increase with the severity of androgenetic alopecia. So, in grade III androgenetic alopecia, the TNF-α cytokine index was 15.9±2.3 ng/ml (p= 0.001), in grade III-IV - 24.8±4.2 ng/ml (p= 0.001) , IV-V degree - 28±3.7 ng/ml (p= 0.001), while the same indicator in the control group was 2.5±0.9 ng/ml. Indicators of IL-1β in the blood of patients with androgenetic alopecia also significantly increased compared to the control group. In stage III androgenetic alopecia, the IL-1β cytokine index was 16.9±2.04 ng/ml (p= 0.001), in degree III-IV - 21.5±3.9 ng/ml (p= 0.001), IV -V degree - 32.6±5.1 ng/ml (p=0.001), while the similar indicator of the control group was 2.0±1.1 ng/ml. The obtained results of the cytokine status in patients with androgenetic alopecia prove its inhibitory and proapoptotic effect, inducing the catagen phase of the hair follicle rhythm.

Conclusions: Thus, the study of the state of the extracellular matrix and cytokine status in patients with androgenetic alopecia establishes their decisive role in the pathogenesis of the disease and inhibition of the rhythm of the hair follicle.