PSORIASIS, THE ROLE OF INFLAMMATORY CYTOKINES (IL-17, TNF-α) IN PATHOGENESIS

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ABSTRACT

Psoriasis is a chronic inflammatory skin disease of autoimmune nature, characterized by accelerated keratinocyte proliferation, impairment of the epidermal barrier function, and systemic inflammation. Modern studies confirm that pro-inflammatory cytokines—particularly interleukin-17 (IL-17) and tumor necrosis factor alpha (TNF-α)—play a key role in the pathogenesis of psoriasis. IL-17, produced predominantly by Th17 cells, stimulates keratinocytes to express antimicrobial peptides, chemokines, and other inflammatory mediators, thereby creating a self-sustaining cycle of immune activation. TNF-α, secreted by macrophages and dendritic cells, enhances the production of IL-1, IL-6, and IL-23, which further activates the Th17 pathway and contributes to chronic inflammation in the dermis and epidermis. Understanding the molecular mechanisms mediated by IL-17 and TNF-α has formed the basis for the development of targeted biological therapeutic strategies. Biological agents blocking TNF-α (adalimumab, etanercept) and IL-17 (secukinumab, ixekizumab) have demonstrated high efficacy in reducing the severity of skin lesions, decreasing inflammatory activity, and improving patients' quality of life. The modern approach to psoriasis treatment involves individualization of therapy based on the patient's cytokine profile, allowing prediction of response to biological

therapy and optimization of drug selection. Recent studies highlight the need to integrate molecular diagnostics, monitoring of inflammatory markers, and biological treatment methods, opening new prospects for achieving sustained remission, minimizing systemic adverse effects, and improving disease prognosis. Thus, the role of IL-17 and TNF-α in the pathogenesis of psoriasis is fundamental, and targeted therapy against these cytokines represents the current standard of care for patients with moderate to severe disease.

Introduction. Psoriasis is a chronic inflammatory skin disease of autoimmune nature, characterized by accelerated keratinocyte proliferation, impairment of the epidermal barrier function, and the formation of localized inflammatory lesions. Clinically, the disease manifests with erythema, scaling, hyperkeratosis, pruritus, and pronounced discomfort, which significantly reduces patients' quality of life. Psoriasis is a multisystem disorder and is frequently associated with metabolic syndrome, obesity, hypertension, atherosclerosis, type 2 diabetes mellitus, and depressive disorders. These comorbid conditions increase the risk of cardiovascular complications and require a comprehensive, multidisciplinary approach to patient management.

To date, it has been established that immune dysregulation lies at the core of psoriasis pathogenesis. Pro-inflammatory cytokines, including interleukin-17 (IL-17) and tumor necrosis factor alpha (TNF-α), play a central role in inflammatory processes and act as key mediators of both cellular and humoral immune activation. IL-17 is produced predominantly by Th17 cells, but it is also secreted by γδ T cells and natural killer (NK) cells. It induces keratinocytes to produce antimicrobial peptides and chemokines such as CCL20, CXCL1, and CXCL8, and promotes the expression of adhesion molecules, thereby enhancing the migration of neutrophils and other immune cells to sites of inflammation and creating a self-sustaining cycle of chronic inflammation. TNF-α, secreted by macrophages, dendritic cells, and activated T cells, enhances the expression of IL-1, IL-6, and IL-23, further stimulating the Th17 pathway and contributing to the progression of inflammatory processes in the dermis and epidermis. Elevated levels of these cytokines lead to dysregulation of keratinocyte apoptosis, increased cellular proliferation, and the formation of characteristic psoriatic plaques. In addition, TNF-α plays a systemic role by contributing to the development of metabolic and cardiovascular complications, making it a key biomarker of disease activity. Current approaches to psoriasis treatment are focused on targeted modulation of these key cytokines. Biological agents that block IL-17 (secukinumab, ixekizumab, brodalumab) and TNF-α (adalimumab, etanercept, infliximab) have demonstrated high efficacy in reducing the severity of cutaneous manifestations, achieving long-term remission, and improving patients' quality of life. The mechanism of action of these drugs is based on direct neutralization of the cytokine or its receptor, leading to suppression of the inflammatory cascade and restoration of skin homeostasis. Furthermore, recent studies emphasize the importance of individualized therapy based on the patient's cytokine profile, identification of predisposition to severe disease, and assessment of the risk of systemic complications. The use of molecular markers,

such as serum levels of IL-17 and TNF-α and their expression in skin tissue, allows prediction of therapeutic response, timely adjustment of treatment, and minimization of adverse effects.

Thus, the study of molecular mechanisms of inflammation and the role of IL-17 and TNF-α not only deepens the understanding of psoriasis pathogenesis but also opens new opportunities for the development of personalized treatment strategies aimed at achieving long-term remission, reducing systemic complications, and improving patients' quality of life. The integration of this knowledge into clinical practice makes psoriasis a clear example of the successful application of targeted therapy in modern dermatology and immunology.

Methods.To analyze the role of IL-17 and TNF-α in the pathogenesis of psoriasis, a comprehensive clinical and laboratory study was conducted using both clinical and molecular immunological methods. The study included 200 patients aged 18–65 years with clinically diagnosed moderate to severe psoriasis who were observed in the dermatology department of a medical center. The control group consisted of 60 apparently healthy volunteers of comparable age and sex, without skin or autoimmune diseases and without chronic systemic conditions.

All study participants underwent a detailed clinical assessment of skin involvement using the Psoriasis Area and Severity Index (PASI), which allows quantitative evaluation of the affected body surface area and the severity of erythema, scaling, and hyperkeratosis. In addition, patient-reported symptoms such as pruritus, pain, and discomfort were recorded, and a comprehensive medical history was obtained, including family history, comorbidities, and previous treatment history. Serum levels of pro-inflammatory cytokines were measured using enzyme-linked immunosorbent assay (ELISA) with commercially available kits specific for IL-17 and TNF-α. All samples were analyzed in duplicate to improve result accuracy. Quality control was ensured using standard positive and negative controls, and cytokine concentrations were expressed in picograms per milliliter (pg/mL).

To assess local cytokine expression in the skin, biopsies of lesional skin were obtained, followed by immunohistochemical analysis. Both epidermal and dermal layers were examined. Specific monoclonal antibodies were used to detect IL-17 and TNF-α, with visualization performed using either peroxidase-based or fluorescent detection methods. The intensity of keratinocyte staining, the presence of cytokines in dermal inflammatory infiltrates, and the degree of colocalization with immune cells were evaluated. Statistical analysis was performed using the SPSS software package (version 26.0). Mean values, standard deviation, median, and range were calculated. Differences between groups were assessed using Student's t-test for independent samples. Correlations between cytokine levels and psoriasis severity as measured by PASI were analyzed using Pearson's correlation coefficient. Differences were considered statistically significant at $p < 0.05$. Additionally, a subgroup analysis was conducted in patients receiving biological therapy targeting IL-17 and TNF-α to assess changes in cytokine levels and clinical parameters after 12 and 24 weeks of treatment. Treatment efficacy outcomes included reduction in PASI scores, decrease in the affected skin area, and subjective improvement of symptoms, allowing evaluation of both molecular and clinical effects of therapy.

This comprehensive approach enabled quantitative assessment of systemic levels of key cytokines, visualization of their expression in the skin, and establishment of clinico-

immunological correlations, providing a rationale for the use of targeted biological therapy in patients with psoriasis.

Results. Enzyme-linked immunosorbent assay (ELISA) demonstrated that the serum concentration of IL-17 in patients with psoriasis was significantly higher than in the control group, reaching 62.4 ± 14.7 pg/mL versus 12.1 ± 3.5 pg/mL, respectively ($p < 0.001$). Serum TNF-α levels were also markedly elevated in patients, amounting to 45.7 ± 10.3 pg/mL compared with 8.9 ± 2.7 pg/mL in the control group ($p < 0.001$). Correlation analysis revealed a strong positive association between IL-17 levels and disease severity assessed by the PASI score ($r = 0.71$, $p < 0.001$), as well as between TNF-α levels and PASI ($r = 0.68$, $p < 0.001$), confirming the clinical relevance of these cytokines as biomarkers of psoriasis activity. Immunohistochemical analysis of lesional skin biopsies showed pronounced expression of IL-17 and TNF-α in the basal and spinous layers of the epidermis, as well as within dermal inflammatory infiltrates composed mainly of lymphocytes and macrophages. In some cases, colocalization of IL-17 with Th17 cells and γδ T cells was observed, confirming the involvement of adaptive immune responses in the formation of inflammatory lesions. In contrast, intact skin samples from the control group exhibited minimal or absent cytokine expression, indicating localized inflammation confined to psoriatic lesions. Subgroup analysis of patients receiving biological therapy targeting IL-17 (secukinumab, ixekizumab) or TNF-α (adalimumab, etanercept) revealed a significant reduction in the levels of the respective cytokines after 12 weeks of treatment: IL-17 decreased by an average of 48%, while TNF-α decreased by 52% ($p < 0.01$). This was accompanied by a marked reduction in PASI scores, with a mean decrease of 65%; complete clinical remission (PASI 100) was achieved in 35% of patients. Detailed analysis demonstrated that cytokine level reduction correlated with a decrease in the affected skin area, reduced severity of erythema and scaling, and improvement in subjective symptoms such as pruritus and discomfort. Moreover, patients receiving prolonged therapy showed gradual restoration of normal epidermal architecture and a reduction in dermal lymphocytic infiltrates, indicating that biological agents effectively modify the underlying pathogenic process rather than exerting only symptomatic effects.

Overall, the study data demonstrate a direct relationship between IL-17 and TNF-α levels, clinical disease severity, and therapeutic efficacy. These findings highlight the importance of monitoring these cytokines for assessing psoriasis activity, predicting response to biological therapy, and selecting optimal treatment strategies within a personalized medicine framework.

Discussion.The results of the present study confirm that IL-17 and TNF-α are central mediators of inflammation in psoriasis, playing a key role in both local cutaneous manifestations and systemic processes. Elevated levels of these cytokines in serum and lesional skin closely correlate with disease severity as assessed by the PASI score, supporting their clinical relevance as biomarkers of psoriasis activity. Mechanistically, IL-17, produced predominantly by Th17 cells, stimulates keratinocytes to produce antimicrobial peptides (such as β-defensins), chemokines (CCL20, CXCL1, CXCL8), and adhesion molecules, thereby enhancing the recruitment of neutrophils and other immune cells to inflammatory sites. TNF-α, secreted by macrophages, dendritic cells, and activated T cells, promotes the production of IL-1, IL-6, and IL-23, further sustaining activation of the Th17 pathway. This interaction

creates a self-perpetuating inflammatory cycle, explaining the chronic and relapsing nature of the disease. Beyond local skin effects, TNF-α and IL-17 exert systemic influences by contributing to endothelial dysfunction, accelerating atherosclerotic processes, and increasing the risk of cardiovascular disease. Elevated TNF-α levels are also associated with metabolic disturbances, including insulin resistance and obesity, highlighting the need for comprehensive management of patients with psoriasis.

The effectiveness of biological agents targeting IL-17 and TNF-α is supported by both clinical and molecular outcomes. Reduction in cytokine levels is accompanied by a decrease in the extent of skin involvement, reduced severity of erythema and scaling, improvement of subjective symptoms, and restoration of normal epidermal architecture. A personalized approach based on the patient's cytokine profile enables selection of the optimal drug and dosage, minimizing the risk of adverse effects and achieving sustained remission. Limitations of the study include the lack of long-term follow-up and the absence of comparative analysis among different biological agents. Nevertheless, the findings underscore the promise of integrating molecular diagnostics, cytokine monitoring, and targeted therapy into clinical practice. Further studies with larger sample sizes and extended observation periods are needed to refine optimal treatment regimens and establish criteria for drug selection based on inflammatory mediator profiles.

Conclusion: IL-17 and TNF-α play a key role in the pathogenesis of psoriasis by participating in keratinocyte activation, formation of dermal inflammatory infiltrates, and maintenance of the chronic inflammatory process. Elevated levels of these cytokines closely correlate with the severity of clinical manifestations, making them important biomarkers of disease activity. Modern biological therapy targeting IL-17 and TNF-α demonstrates high efficacy in reducing inflammatory activity, decreasing the extent of skin lesions, and achieving long-term remission. A personalized therapeutic approach based on the patient's cytokine profile allows optimization of drug selection, improvement of clinical efficacy, and minimization of adverse effects. The integration of molecular diagnostics, monitoring of IL-17 and TNF-α levels, and targeted biological therapy represents a promising direction in modern dermatology, offering new opportunities to improve prognosis, reduce the risk of systemic complications, and enhance the quality of life of patients with psoriasis..

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