Dobrzhanska Yu.

IMMUNOPATHOLOGICAL FEATURES OF PSORIASIS

Kharkiv National Medical University, Ukraine

Abstract. *Psoriasis, a common multifactor skin disease, has received attention as a target for new pathogenesis-oriented biologic therapies. Psoriasis is important to the clinician because it is common and has treatment implications beyond the care of skin lesions. It is important to the physician-scientist because it serves as a model for studies of mechanisms of chronic inflammation.*
In recent years, substantial advances have been made in elucidating the mechanisms of psoriasis. However, major issues remain unresolved, including the primary nature of the disease as an epithelial or immunologic disorder, the autoimmune cause of the inflammatory process, the relevance of cutaneous versus systemic factors, and the role of genetic versus environmental influences on disease initiation, progression
This review summarizes recent progress in understanding of the immunologic basis of psoriasis and shows how improved insight into disease mechanisms has already resulted in tangible benefits for patients, including the introduction of new targeted therapies.
Kay words*: psoriasis, cytokine, interleukin, treatments for psoriasis*

Despite the fact that psoriasis is a common multifactor skin disease, its definition by Ferdinand von Hebra as a distinct entity dates back only to the year 1841, and estimates of its prevalence – around 1-3 percent of population worldwide [1, 2]. Both Ukrainian and foreign researchers notice the following features of psoriasis: a chronic disease associated with characteristic skin rash in a form of epidermal and dermal papules considerable skin flaking. A psoriatic patch is formed on the basis of the impaired proliferation and differentiation of keratinocytes in combination with increases processes of angiogenesis and epidermal and dermal infiltration with mononuclear cells [3, 4]. Numerous family studies have provided compelling evidence of a genetic predisposition to psoriasis, although the inheritance pattern is still unclear [5]. The illness develops in as many as half of the siblings of persons with psoriasis when both parents are affected, but prevalence falls to 16

percent when only one parent has psoriasis and to 8 percent when neither parent is affected.

A key question concerns the autoimmune nature of psoriasis and the contribution of autoreactive T cells to the disease process. Currently available data do not support the notion that psoriasis is a bona fide autoimmune disease. Psoriasis is probably best placed within a spectrum of autoimmune-related diseases characterized by chronic inflammation in the absence of known infectious agents. The transport of T cells from the dermis into the epidermis is a key event in psoriasis. Psoriatic T cells predominantly secrete interferon-γ and interleukin-17 [6, 7].

The hypothesis of a cytokine network in psoriasis proposed a central role of proinflammatory cytokines, including TNF-α. In retrospect, this theory has been validated by the clinical success of anti-TNF therapy in the treatment of psoriasis. On the basis of the analysis of gene signatures in this disease, three predominant cytokines seem to be at play: type I interferon, interferon-γ, and TNF-α. Both TNF-α and interferon-γ also have anti-inflammatory properties; this might explain, in part, the counterintuitive clinical observation that anti-TNF therapy induces psoriasis in a minority of patients. In addition, dendritic cell–derived interleukin-23 and downstream products of helper T cells, including interleukin-17A and interleukin-22, are of considerable importance. Key cytokines in psoriasis act through a restricted set of signalling and transcriptional pathways [4, 8].

In spite of numerous studies performed, pathogenesis of psoriasis and mechanisms of its onset have not been clarified yet. Most accepted treatments for psoriasis have been developed empirically or were found by chance. However, recent insights into the immunopathogenesis of psoriasis have further elucidated the mode of action of some accepted compounds [9, 10] and have provided new treatment strategies [11, 12]. The severity of the disease usually determines the therapeutic approach. Approximately 70 to 80 percent of all patients with psoriasis can be treated adequately with use of topical therapy. Mainly for practical reasons, the vitamin D_3 analogues (calcipotriol and tacalcitol) and the topical retinoid tazarotene – all of which affect keratinocyte functions and the immune response – are in wider use than

is either anthralin or coal tar. Since most of the compounds that have been mentioned may irritate delicate areas of skin, topical corticosteroids are used in combination with those compounds, particularly in intertriginous areas [8, 9, 12].

In cases of moderate-to-severe psoriasis (e.g., affecting large surface areas), the use of phototherapy, systemic drugs, or both must be considered. Among the established regimens, various therapeutic methods may have distinct modes of action. For example, fumarates and cyclosporine are primarily immunosuppressive agents, whereas retinoids and methotrexate also target keratinocyte functions. Rational combination treatments target inflammation as well as epidermal alterations and may provide improved efficacy and safety. Thus, combinations of topical vitamin D_3 analogues with phototherapy or systemic retinoids plus psoralen and ultraviolet A phototherapy (RePUVA) are well-established treatment regimens for psoriasis [5, 10].

The evolution of a psoriatic lesion is based on a complex interplay between environmental and genetic factors that sets the scene for disease-initiating events. A cascade of events leads to activation of dendritic cells and, in turn, the generation of effector T cells that emigrates to and resides in skin tissue. Cross-talk between epithelial cells and immune cells shapes and maintains the inflammatory milieu. Research in the past decade has identified many of the checkpoints governing these processes and has lead to the development of new, highly effective targeted therapies. Although this progress is remarkable, there are still many unknowns, especially in the area of disease prevention and the development of drugs with appropriate long-term risk – benefit and cost profiles. Future research will need to tackle these challenges in order to establish therapeutic and preventive approaches that ultimately lead to improved outcomes for patients.

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Резюме. Псориаз распространенное заболевание кожи мультифакторной природы, находится под пристальным вниманием дерматологов и ученых исследователей всего мира в качестве мишени для изучения патогенеза и поиска новых методов лечения. Изучение псориаза очень важно как для дерматологов, так и для исследователей в качестве модели для изучения механизмов хронического воспаления.

В последние годы значительные успехи были достигнуты в выяснении механизмов псориаза. Тем не менее, основные проблемы остаются

нерешенными, в том числе этиология заболевания, патологические процессы в коже, иммунной системе, аутоиммунные причины воспалительного процесса, зависимость кожных проявлений от поражения других органов и систем, а также роль генетических факторов и воздействие окружающей среды на возникновение псориаза и его прогрессирование.

Представлены достижения в изучении иммунологического звена патогенеза псориаза и показано, как улучшение понимания механизмов болезни уже привело к повышению эффективности проводимой терапии.
Ключевые слова: псориаз, цитокины, интерлейкины, лечение псориаза.

Резюме. Псоріаз поширене захворювання шкіри мультифакторної природи, перебуває під пильною увагою дерматологів і вчених дослідників усього світу в якості мішені для вивчення патогенезу та пошуку нових методів лікування. Вивчення псоріазу дуже важливо як для дерматологів, так і для дослідників в якості моделі для вивчення механізмів хронічного запалення.

В останні роки значні успіхи були досягнуті в з'ясуванні механізмів псоріазу. Тим не менше, основні проблеми залишаються невирішеними, зокрема етіологія захворювання, патологічні процеси в шкірі, імунній системі, автоімунні причини запального процесу, залежність шкірних проявів від ураження інших органів і систем, а також роль генетичних факторів і вплив навколишнього середовища на виникнення псоріазу і його прогресування.

Представлені досягнення у вивченні імунологічного ланки патогенезу псоріазу та показано, як поліпшення розуміння механізмів хвороби вже призвело до підвищення ефективності терапії.
Ключові слова: псоріаз, цитокіни, інтерлейкіни, лікування псоріазу.

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