ORIGINAL ARTICLE

STUDY OF IMMUNO-PATHOGENETIC FEATURES OF PSORIASIS AND ACNE'S COURSE

DOI: 10.36740/WLek202202117

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ABSTRACT

The aim: The objective of our work was to improve the diagnostics of common chronic dermatoses (acne, psoriasis, AP) taking into account some indicators of the immune system and features of the disease course to specify their role in pathogenesis of these disease.

Materials and methods: A total of 114 patients with acne and 128 patients with psoriasis were observed.

Results: Regardless of the disease duration period, we have detected in blood serum of psoriasis patients probable changes in concentrations of stress-response mediators (decreased parameters of cellular immunity (CD3+, CD3+CD4+, CD3+CD8+ of T-lymphocytes, CD22+ fraction of B-lymphocytes and compensatory increased CD16+ of T-cells, cytokines – IL-1β, IL-8, IL- 17, IL-22, immunoglobulins IgM, IgG, and CIC), which indicate tension of their stress-induced mechanisms even despite occasional clinical stabilization of skin and articular process. Consequently, most of the patients with acne had varying degrees of changes in rates of systemic immunity. The most significant changes in rates of systemic immunity with the depletion of T-cell immunity were found in patients with papular-pustular and pustular acne, and still more significant – in patients with acne conglobate.

Conclusions: In patients with acne and psoriasis, changes in systemic immunity indexes that indicate the formation of secondary immunodeficiency state T-cell link, amid an adequate humoral immunity have been found. Relationship between the causes of changes of systemic immunity has been established.

KEY WORDS: acne, psoriasis, clinical course, immunity, diagnostic

Wiad Lek. 2022;75(2):422-426

INTRODUCTION

The most common in dermatological practice are psoriasis and acne (acne occurs in at least 90% of adolescens, and psoriasis affects about 2% of the population) the pathogenesis of which today is considered from the standpoint of immunopathological diseases[1,2].

Acne is chronic recurrent dermatosis, one of the essential skin inflammation in the structure of dermatological pathology, especially in young people of working age, often caused by persistent cicatricial changes in the skin, and affecting negatively the psychoemotional state of patients, their quality of life and working capacity [1,3]. It has been established by today that the pathogenesis acne is complex and multifactorial, and the changes of immune reactivity of the organism play an important role in its clinical course development [4] The high level of acne incidence, the tendency to a chronic course of formation of resistance to treatment, frequent cases of development of deep forms determine the important medical and social significance of the problem. [3,5] However, the information about the immune system in these patients is often ambiguous and contradictory – it is often recorded as manifestation of increased immune activity and the formation of secondary immunodeficiency state, which may contribute to chronic dermatoses and their resistance to standard therapy tools [4,6,7]. In this regard, the urgent task of modern dermatology is to establish the nature of changes of systemic immunity in patients with acne with different clinical course in order to clarify the pathogenetic factors and develop differentiated methods of treatment.

At the present stage, psoriasis is considered to be a systemic disease that affects not only skin but also joints of patients and is accompanied by possible development of typical comorbid states (cardiovascular pathology, chronic inflammatory intestinal canal diseases, and metabolic syndrome). Psoriasis affects about 2% of population. In 30-40% of occurrences arthropathic psoriasis (AP) is diagnosed and leads to 11-19% of disability cases development [1,8].

The chronic-relapsing course of psoriasis and steady progression of the disease associated with disability cases result in a significant deterioration in the quality of life of patients, which determines its medical and social significance [1,9]. Taking into account the importance of components of stress-induced immune-endocrine system at the psoriasis development it is important to clarify the role of main indicators of the immune system and cortisol stress hormone in the disease pathogenesis [10-12]. Substantial immunological changes (of humoral and cell sections of immunity), hormone and biochemical disorders, disorder of calcium-phosphorus balance naturally influence bone metabolism and cause systemic disorders in structural and functional state of bone and cartilage system in patients with AP [1,13-15]. No less actual is the relation of detected clinical-instrumental disorders, changes of some indices of hormone, immune and cytokine state.

THE AIM

The objective of our work was to improve the diagnostics of common chronic dermatoses (acne, psoriasis, AP) taking into account some indicators of the immune-endocrine system and features of the disease course to specify their role in pathogenesis of these disease.

MATERIALS AND METHODS

114 patients with acne aged from 18 to 35, among which 66 women (57,89 %) and 48 men (42,11 %) and 128 patients with psoriasis aged from 18 to 55, among which 46 women (35,94 %) and 82 men (64,06 %) were observed and examined systematically. They had been selected for the study according to the following criteria: clinical signs of acne, age 18+, absence of chronic somatic diseases or their exacerbations at the moment of the study.

A comprehensive survey of patients has been performed in a randomized manner concurrently with BD pre-stratification upon obtaining written consent in accordance with the principles of Helsinki Declaration of Human Rights, Convention of Council of Europe on Human Rights and Biomedicine, and relevant laws of Ukraine.

To assess the state of systemic immunity in patients with acne we determined: the number of total lymphocytes and their subpopulations in terms of CD3 +, CD3 + CD4 +, CD3 + CD8 +, CD19 + by indirect immunofluorescence with monoclonal antibodies to differentiated antigens of the cell surface, as well as the content of serum immunoglobulins (Ig) of classes M, G, A.

We have examined AP patients with varying severity of process development, generalization and the severity of skin and osseous-articular apparatus damage, the presence of associated pathology. The diagnosis of AP was verified under the diagnostic criteria of the Institute of Rheumatology of RAMS. All patients with suspected or proved AP had their damaged joints examined radiologically (ultrasonography if necessary). Additional level of T- and B-lymphocytes subpopulations in patients with AP was determined under the guidelines on the application of erythrocyte diagnostic preparations to detect human T- and B-lymphocytes subpopulations "Anti-CD 3", "Anti-CD 4", "Anti-CD 8", "Anti-CD 16", "Anti-CD 22" produced by RDPF Granum LLC (Kharkiv). The concentration of general immuniblibulines of M (IgM) and G (IgG) classes in blood serum was determined by immune-enzyme analysis using "IgM (IgG) general - IFA – BEST" set produced by CJSC "Vector-Best –BEST", Novosibirsk. The content of IL-1β, IL-8, IL-17, IL-22 in blood serum was studied in accordance with the techniques and guidelines using appropriate test systems (CJSC "Vector-Best –BEST", Novosibirsk) which are based on the sandwich-method of solid phase immune-enzyme analysis.

Statistical analysis of the results of research was carried out by methods of statistical analysis using the computer program Statistica 7.0, the probable average difference was considered at $p<0,05$.

RESULTS

According to the clinical criteria, 22 patients (19.3%) were diagnosed with comedonal form of acne, 34 patients (29.83%) had papules, 8 people (7.02%) –papular-pustular acne, 25 of the observed (21.93%) had pustules, 9 patients (7.03%) suffered from acne conglobata, and 14 patients (10.94%) were diagnosed with post-acne. The control group consisted of 34 practically healthy people (donors) of the same age.

In determining the indices of systemic immunity in patients with acne, there were established their probable changes which indicate the development of secondary immune deficiency in these patients, byT-cell population mainly, as well as a disturbance of absolute number of total lymphocytes, T-helper ones (with CD3 +CD4 +) and T suppressor (with CD3 + CD8 +) lymphocytes, while the most significant changes in these parameters were established in patients with moderate and severe acne with chronic and deep forms [6,9].

While determining the indicators of the systemic immunity in 114 patients with acne, we established their probable ($p<0.001$) changes, as compared with the indicators for patients in the control group: decrease in relative and absolute number of total lymphocytes pool – by 20.4 % (28.9±0.69 %, in the control group – 36.1±0.92 %) and by 21.2 % (1.92±0.053 G/l (this index marks giga-/ liter) in the control group – 2.41±0.10 G/l), T-lymphocytes (CD3+) – by 19.2 % (47.1±1.31 %, in the control group – 58.3±1.07 %) and 33.7 % (0.955±0.033 G/l in the control group – 1.42±0.078 G/l), T-helpers (CD3+CD4+) lymphocyte subpopulations – accordingly by 11.7 % (33.2±0.32 %, in the control group – 37.3±0.88 %) and by 22.9 % (0.613±0.022 G/l in the control group – 0.792±0.052 G/l), and the relative number of T-suppressors (CD3+CD8+) lymphocytes – by 13.9 % (18,5±0,15 %, in the control group – 21.5±0.93 %) against the backdrop of increasing relative and absolute number of B lymphocytes (CD19+) – by 14.3 % (25.6±0.30 %, in the control group – 22.4±0.81 %) and 35,2 % (0,488±0,014 G/l in the control group – 0,360±0,020 G/l) and IgM levels – by 25.7 % (1.81±0.047 G/l in the control group – 1.44±0.06 G/l) and IgG – by 40.4 % (12.9±0.25 G/l in the control group – 9.52±0.36 G/l) (Fig.1).

The analysis of systemic immune system indexes in patients with acne, taking into account its different the clinical form and depth of skin lesions presented in the table, has showed that in patients with comedonal form of acne there is a decrease in the relative amount of the total pool of lymphocytes by 10.9 %, $p<0.05$, with papular form of acne – by 13.9 %, $p<0.01$, a decrease in the relative and absolute amount of T-lymphocytes (with comedonal form – by 8.5 % and by 21.5 %, $p<0.01$, with papular form – by 7.5%, $p<0.001$ and by 20.1 %, $p<0.01$, with post-acne – by 12.2 %, $p<0.001$ and by 18.7 %, $p<0.05$), the relative amount of T-helpers (CD3+CD4+) with comedonal form of acne – by 9.9 %, $p<0.001$, with papular form – by 6.24% and with post-acne – by 8,1%, $p<0.05$ and absolute amount of B lymphocytes (with comedonal form – by 29.4 %, with papular form – by 35.7 %, and with post-acne – by 47.4 %, $p<0.001$.

At the same time, probable decrease ($p<0.001$) in the absolute and relative amount of the total pool of lymphocytes was identified in patients with papular-pustular acne, as compared with the control group: by 33.9 % and by 47.9 %, with pustular acne – by 35.4 % and by 46.8 %, with acne conglobata – by 45.3 % and by 33.9 % correspondingly. These patents were also defined with probable decrease in the relative and absolute amount of T-lymphocytes (CD3+), as compared with the control group: in

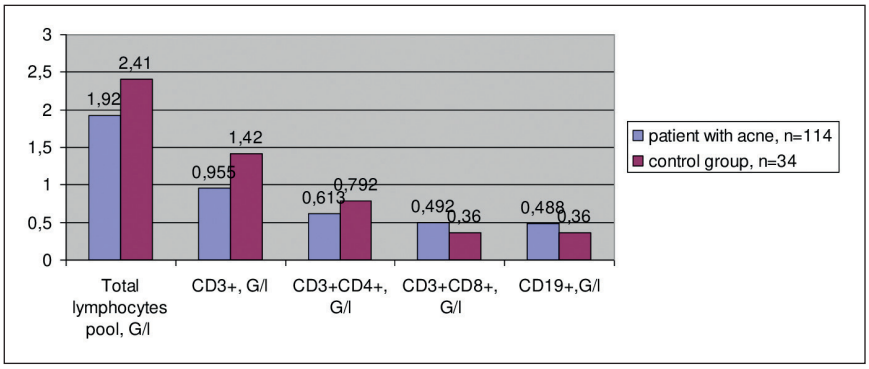

Fig. 1. Indicators of the systemic immunity in patients with acne

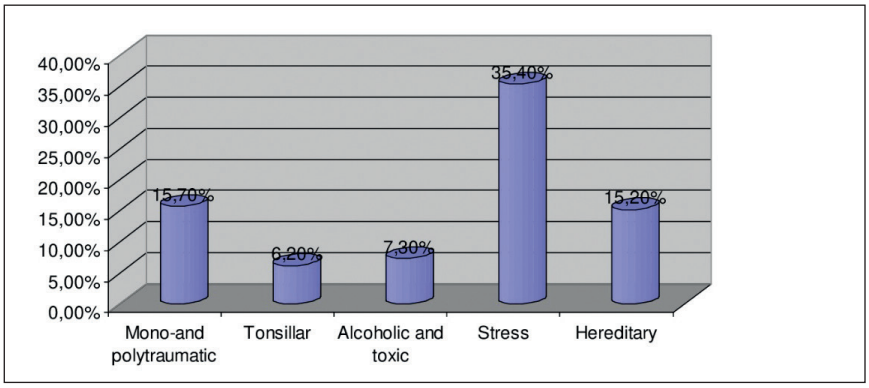

Fig. 2. Trigger factor in the development of psoriasis in examined patients

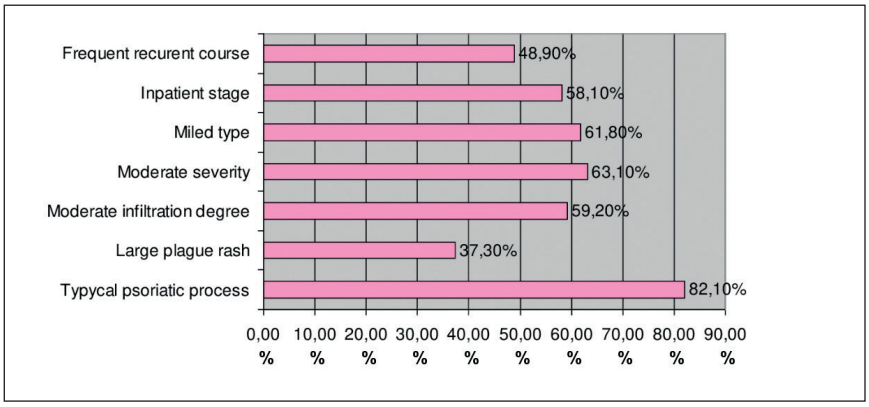

Fig. 3. Trigger factor in the development of psoriasis in examined patients

patients with papular-pustular acne – by 24.2 % and by 62.3 %, in patients with pustular acne – by 15.8 % and by 34.7 %, and in patients with acne conglobata – by 28.9 % and by 54.5 %, p<0.001) accordingly. Alongside, a decrease in the relative and absolute amount of T-helping (CD3+CD4+) lymphocytes has been identified, as compared with the control group: in patients with papular-pustular acne – by 27.5 % and by 56.3 %, p<0.001, in patients with pustular acne – by 17.5 %, p<0.001 and by 21.9 %, p<0.01; in patients with acne conglobata – by 33.5 % and by 49.8 %, p<0.001).

The analysis of indicators of systemic humoral immunity in patients with different clinical forms of acne revealed a significant increase in the relative and absolute amount of B-lymphocytes (CD19+), as compared with the control group: in patients with papular-pustular acne (correspondingly, by 15.6 %, p<0,05 and by 33.8 %, p<0,001), in patients with pustular (by 23.4 % and by 51.4 %, p<0,001), and in patients with acne conglobate (by 38.4 % та 35.1 %, p<0,001). Moreover, in patients with certain clinical forms of acne, a probable increase in levels IgM and IgG has been observed, as compared with the relative indexes of control (correspondingly, in patients with papular-pustular acne – by 45.6 % and by 63.2 %, with papular form of acne – by 53.9 % and by 67.5 %, with acne conglobate – by 98.4 % and by 90.7 % p<0.001).

In 84 (65.63%) out of 128 examined AP patients joints were damaged in 5-15 years after the onset of skin psoriatic process. In 59 (46.09%) cases the dependence of the onset of joint damage with the subsequent manifestations of psoriatic skin rash was detected. According to medical history data, the examined patients typically associated the onset of psoriatic skin and joints damage with hereditary (15.62%), stress (35.16%), alcoholic and toxic (7.03%), tonsillar (6.25%), mono- and polytraumatic (16.41%) factors (Fig.2).

In 89 (69.5%) AP patients the prevalence of generalized skin psoriatic process with typical (82.1%), large plaque rash (37.3%), moderate infiltration degree (59.2%), moderate severity (63.1%), mixed type (61.8%), inpatient stage (58.1%) and frequent recurrent course (48.9%) was observed (Fig.3).

It has been established that in 83 (64.84%) AP patients joints damage occurred in 5-15 years after the onset of skin psoriatic process. In 89 (69.5%) of examined patients the prevalence of generalized skin psoriatic process with typical 106 (82.81%), moderate infiltration degree 78 (60.93%), frequent recurrent course 56(43.75%), nails psoriatic damage and polyarthritis complicated with the damage of small joints of hands or feet was observed 107 (83.59%).

Upon conducting functional tests (in order to determine sacroilitis – Kushelevsky 1-2, Patrick, Mennel and spondylitis – Shober, Thomayer), sacroilitis has been revealed and further instrumentally confirmed in 4 (3.13%) cases and spondylitis of thoracic and lumbar sections in 8 (6.25%) cases. Using the RAIS index, in 113 (88.28%) of patients it has been verified moderate-severe and severe dermatosis course. A significant impact of AP on the quality of life of patients per the DLQI index has been recorded in 71 (55.47%), and very significant in 56 (43.75%). A pronounced correlation between the increase in joints functional deficiency, the AP course duration and the deterioration in the quality of life of patients has been established. A high degree of polyarthritis detection rate complicated with the damage of small joints of hands or feet associated with a functional insufficiency of average degree of activity 73 (57.03%) though the preservation of professional ability has been diagnosed in 56 (43.75%) of patients.

In this context we have determined pathognomonic signs of AP, which include simultaneous psoriatic damage of skin 128 (100%) and nails 89 (69,53%); asymmetric 102 (79,69%) mono- or oligoarthritis 91 (71.09%) mainly of peripheral joints and especially associated with the hand DIPJ damage 114 (89.06%); osteolysis 112 (87.5%); negative reaction for rheumatoid factor 124 (96,88%).

We have pathogenetically grounded the primary localization of pathological joint process in AP patients in the areas of increased traumatization of tendon-ligamentous apparatus and its relationship with nails psoriatic damage. Therefore, ultrasound diagnostics and MRI examination of joints for the purpose of determination of periarticular and articular damages is justified since in 14 (10.94%) of examined patients enthesopathy and osteitis in the absence of abnormal articular X-ray changes have been detected by ultrasound diagnostics and MRI. In our opinion, osteitis in psoriatic patients signals an early premonitory symptom of the AP development.

During radiological examination of patients with AP it was detected 65 (50.78 %) cases of AP and 52 (40.62 %) cases of deforming AP, at that, in 91 (71.01 %) of cases AP was the dominant disease on clinical picture in the form of poly- or periarthritis of distal interphalangeal joints, at that, in 14 (10.94 %) of cases it was associated with axial affection of spine. At early stages of AP development using radiological examination the following facts were accurately defined more frequently than the others: non-uniform narrowing of joint gap, osteoporosis in bone epimetaphys area, erosions of distal flanges of feet and hands. In the case of progressing – partial or total destruction of closing plates with prevailing osteo-destructive (osteolysis, ankylosis) and osteo-proliferated (hyperostosis, periostitis) pathological processes over osteoporosis.

In 79 (61.72%) AP patients the presence of inflammatory biochemical serum and cholecystobiliary syndromes has been testified, which indicates metabolic character of the disease course. The analysis of laboratory examinations indicates the decreased number of thrombocytes, expressed hypoalbuminemia, hypergammaglobulinemia. In 1/3 of patients with AP anaemia was identified as well as increasing of BSR within the limits of 15-20 mm/h, from 21 to 40 mm/h – in 26 (20.31 %) of patients, more than 40 mm/h – 14 (10.93%). The increased glucose level was identified in 31 (24.22 %) of patients, cholesterol and LDL – in 90 (70.31 %), creatinine – in 58 (45.32 %). Alkaline phosphatase (AP) and its bone izoenzyme activity were within the limits of normal values except the patients who have been suffering from the disease for more than 20 years. This means that AP activity exceeds the norm more than 2.3-2.5 times and bone izoenzyme AP decreased in 2.6-2.7 times. Creatinine content in blood serum was lower than the norm in 60 (46.88%) of patients notwithstanding the duration of the disease.

DISCUSSION

The current problem of modern dermatology are psoriasis and acne, the pathogenesis of which today is considered from the standpoint of immunopathological diseases [1,2].

According to literature [4,11] in patients with acne and psoriasis changes in systemic and humoral immunity indexes have been found. It has been established by today that the pathogenesis acne, psoriasis and arthropathic psoriasis is complex and multifactorial, and the changes of immune reactivity of the organism play an important role in its clinical course development. But the information about the immune system in these patients is often ambiguous and contradictory.

Most of the patients with acne had varying degrees of changes in rates of systemic immunity – the likely reduction in relative and absolute number of total lymphocytes, T-lymphocytes and their subpopulations against the growing number of B lymphocytes and the level of IgM and IgG, which generally indicates the formation in these patients secondary immunodeficiency state of T-link intensified by activation of humoral immunity in response to the development of skin inflammation. The most significant changes in rates of systemic immunity with the depletion of T-cell immunity were found in patients with papular-pustular and pustular acne, and still more significant – in patients with acne conglobate, which justifies differentiated treatment by immunomotropic drugs for these patients.

It has been determined that the occurrence of pathological immune process in all variants of AP course was triggered by a possible blood serum decrease ($p<0.01$) of immunocompetent cells of phenotype CD3+ by 49.43 %, CD 22+(B-lymphocytes) by 46.62 %, moderate decrease of CD3+CD4+ by 12.91%, CD3+CD8+ by 19.6 % and increased content of CD16+ by 18.42 %; increased levels of cytokines IL-1β by 5-11 times, IL-8 by 60 times, IL-17 by tenfold, IL-22 by 5 times, IgG by 5 times and immunoglobulins IgM by threefold, which testify the fact of tension of stress-induced mechanisms in patients even at the stage of clinical stabilization of skin and joint process. A statistically significant increase of the above cytokine concentration in blood serum (by more than 2-3

times) and in synovial fluid (by more than 2-5 times against the respective values in blood serum ($p < 0.05$)) during the first months starting from the PD joint syndrome onset can serve as an additional diagnostic criterion for early AP diagnostics.

It has been set that the character of correlation between changed indicators of immune-endocrine system in AP patients indicated the autoimmune nature of the disease chronicity and development. It has been justified that decreased levels of cytokines IL-1β, IL-8, IL-17, IL-22, IgM, IgG are the key mediators of the immune system since they cause inflammation and osteolysis on the one hand and regulate the processes of articular contractions formation on the other hand.

CONCLUSIONS

In patients with acne and psoriasis, changes in systemic immunity indexes that indicate the formation of secondary immunodeficiency state T-cell link, amid an adequate humoral immunity have been found. Relationship between the causes of changes of systemic immunity has been established. The improvement of patients with acne and psoriasis diagnostics taking into account some indicators of the immune-endocrine system and specifics of the disease course, will contribute to improving therapy and mended quality of life of patients.

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Conflict of interest:

The Authors declare no conflict of interest.

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Received: 31.05.2021
Accepted: 27.10.2021

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article