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BIOENERGY ASPECTS OF PSORIASIS

L. V. Kuts, PhD, MD, DSc, Associate Professor

Medical Institute Sumy State University, Ukraine, Sumy

The subject of the study is the establishment of the role of bioenergetic (purinergic) in the pathogenesis of psoriasis disorders. For this purpose were examined 120 patients with psoriasis vulgaris in progressive stage by ELISA (enzyme-linked immunosorbent assay) levels of cyclic nucleotide The imbalance of cAMP / cGMP levels were revealed may indicate not only functions violation of the second cellular mediators, but also signs of bioenergetics dysfunction with the development of changes neurotrophic functional in psoriasis skin.

Keywords: psoriasis, cyclic nucleotides, bioenergetics neurotrophic dysfunctions in the skin.

Доктор медицинских наук, доцент, Куц Л. В. Биоэнергетические аспекты псориаза / Медицинский институт Сумского государственного университета, Украина, Сумы

Предмет исследования – установление роли биоэнергетических (пуринергических) нарушений в патогенезе псориаза. С этой целью клинически и при помощи иммуноферментного анализа уровней циклических нуклеотидов в крови обследовано 120 больных в прогрессирующей стадии вульгарного псориаза. Выявленный дисбаланс уровней цАМФ/цГМФ может свидетельствовать не только о нарушении функций вторых клеточных посредников, но и о признаках биоэнергетической дисфункции с развитием нейротрофических функциональных изменений в коже при псориазе.

Ключевые слова: псориаз, циклические нуклеотиды, биоэнергетические нейротрофические дисфункции в коже.

Introduction. Psoriasis is a common chronic disease, and this inflammatory dermatosis is registered approximately up to 5 million people of the world, and in total it is sick - about 200 million people on Earth [1, p. 72-75; 2, p. 787-794; 3, p. 1198-1199; 4, p. 364-366]. A seronegative arthropathy is present up to 30% of all patients. But despite numerous studies of the etiology and pathogenesis of psoriasis, treatment of such patients doesn't enough effective and complications from disease as arthropathy and erythroderma often occur often lead to disability of patients [5, p. 195-202].

One of the reasons for the existing problems of psoriasis may be insufficient consideration of the role of bioenergetic disorders of this disease. Essential in both the pathogenesis and clinical manifestations may be the fact of functional influences that usually stimulate the organs activity (tissues). This underlies the stereotyped form of neurogenic trophic disorders (neurodystrophy), one of the clinical manifestations of which in psoriasis are trophic skin lesions in the form of altered keratinization and epidermis regeneration[6].

The aim of the study was to elucidate the significance of cyclic nucleotide content disorders in patients with psoriasis as a pathogenetic factor associated with dysfunction of bioenergetic metabolism in this dermatosis.

Materials and methods. Generally observed of 120 patients during of progressive stage of psoriasis, of which 64 (53.3%) men, 56 (46.7%) women 18 to 40 years old, who subjected immunoassay analysis to find out in the blood cellular mediators - cyclic adenosine-5 "monophosphate (cAMP) and cyclic guanosine-5" monophosphate (cGMP). The sets of test

systems "Cyclic AMP, 96" and "Cyclic GMP, 96" (pmol / ml), respectively were using.

The control group consisted of 35 practically healthy people (20 men and 15 women 20 to 35 years old who did not have any acute inflammatory diseases and who did not take immunotropic and / or restorative drugs during the last 2 months.

Statistical processing of the results was carried out on a personal computer using the licensed program "STATISTICA® for Windows 6.0".

Results of the study and their discussion. Figure 1 shows the data that indicate a significant ($p < 0.05$) decrease in the level of cAMP in patients with psoriasis (7.15 ± 0.82 pmol / ml) compared with the control group (10.64 ± 0, 62 pmol / ml).

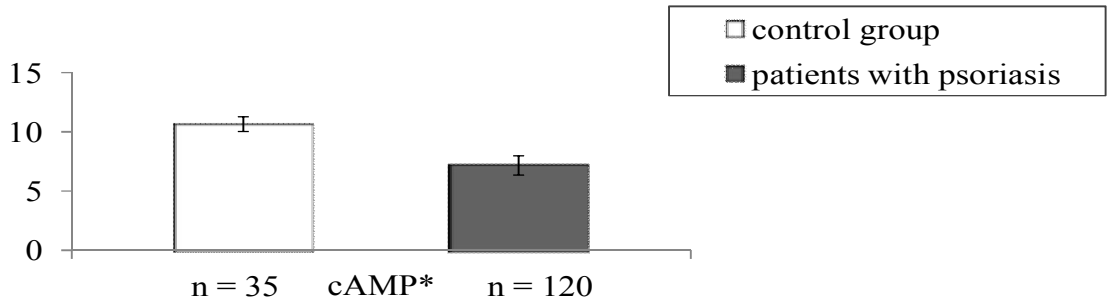

Figure 1 – The blood content of cAMP (pmol / ml) in patients with psoriasis and those in the control group (significance of the difference * - p <0.05)

According to the data shown in Fig. 2, in patients with psoriasis there is a significant ($p < 0.01$) increase in blood cGMP (15.29 ± 1.56 pmol / ml), compared with the control group (6.76 ± 0.45 pmol / ml).

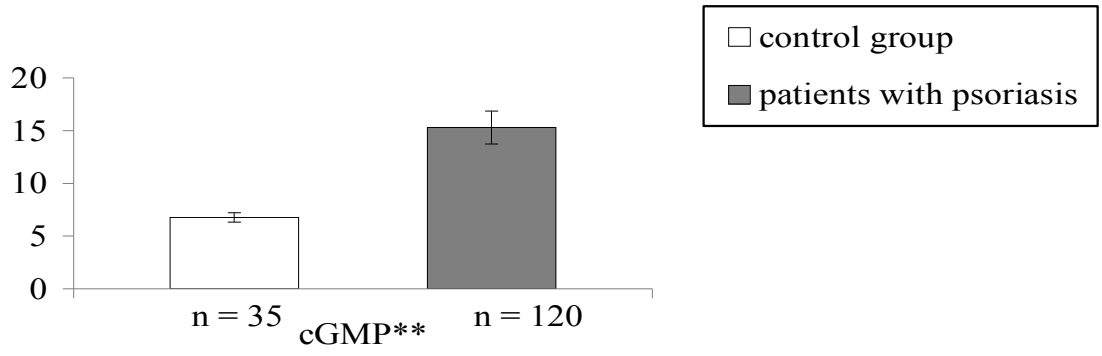

Figure 2 – Blood content of cGMP (pmol / ml) in patients with psoriasis and controls (reliability of differences ** - p <0.01)

Thus, psoriasis patients have multidirectional changes secondary cellular mediators in the blood (in comparison with the control group), namely, a 1.4-fold decrease in cAMP and an average increase in cGMP by 2.1 times. According to currently information, these disorders affect the mitotic cycle of keratinocytes and cause their uncontrolled division, since cAMP is an intracellular mitotic inhibitor (it level was significantly lowered), and cGMP on the contrary a proliferation stimulator (it level was significantly elevated) that leads to the development of structural (chemical) defects and as a consequence a functional character and manifests characteristic clinical changes known as «psoriatic skin».

However the well-known fact about one of the key roles of cAMP / cGMP imbalance in the pathogenesis of psoriasis can have a new ("bioenergetic") interpretation. Totally know that cAMP and cGMP are universal mediators of intracellular signaling and they participate in the transfer of adaptive-trophic influences of the neuroendocrine and immune system to the cells and tissues of the body psoriasis patients. According to currently biochemical studies, the human enzyme systems [7, p. 52] mainly synthesize nucleotide structures based on biomolecule precursors. In particular the sequential addition of carbon and nitrogen atoms to the

ribose-5-phosphate molecule provides the synthesis of de novo inosine-5 "monophosphate (IMP) which is converted into adenosine-5" monophosphate (AMP) and guanosine-5 "monophosphate, and this way of synthesis requires considerable expenditure of metabolic energy. Receptors that perceive the signals of ATP and adenosine are classified as "purinergic". As a result of direct or mediated damage to receptors conducting neural pathways and neurons as well as their synaptic contacts (both pre- and postsynaptic formations) a kind of "functional denervation" and "isolation" is formed damaged tissue from nervous influences. Perhaps this explains the absence of pronounced nociceptive sensations in patients with psoriasis since such a "functional denervation" prevents the flow of intense signals into the focus of inflammation.

Intercellular interactions of the neuro-trophic nature are carried out by the movement of the neuroplasma from the nucleus to the periphery of the neuron and in the opposite direction. The neuron and cells they contain as well as satellites (glia, Schwann cells, and connective tissue cells) form a certain regional trophic microsystem (the so-called "deterministic region") which functions as a single microsystem which is provided by intercellular interactions with the help of trophic factors - "trophogenes". Damage to this trophic contour or blockade of the axoplasmatic current that transports trophogens causes structural changes in both the skin and the corresponding neuron. Known trophogens refer to substances of protein (but possibly - and nucleic and other) nature and they have separated from the axon endings enter the synaptic cleft and from it move to the innervated cell. Regulators of this process include classical neurotransmitters which in turn change the level of the secondary intracellular mediator and such of them as cAMP and cGMP even through protein kinase mechanisms can affect the nuclear apparat and change the activity of genes that determine the formation of trophic factors. Known trophogens refer to substances of

protein (but possibly - and nucleic and other) nature, and they, having separated from the axon endings, enter the synaptic cleft, and from it move to the innervated cell. Regulators of this process include classical neurotransmitters, which Changes in nerve effects and neurotrophic function in turn affect microcirculation and formation of vascular exudative processes can increase the permeability of microvessel walls and damage endothelial cells. In one of the characteristic phenomena in psoriasis (Kebner) in extracellular space the concentration of adenine nucleotides the sources of which are not only damaged skin cells but also purinergic nerve endings or as a result of mechanical damage without disrupting the integrity of the skin (prolonged squeezing) also increases; such a source is platelets (as a result of mechanical damage with violation of the integrity of the skin - injections, injuries, etc.). However, with genetically determined cAMP deficiency in psoriasis patients, conditions are created to accumulate an excessive amount of its predecessors (including adenosine). Thus, the above-mentioned changes lead to disturbances in the provision of cells, first of all – postcapillary venules (a universal place for triggering the body's response in any form of inflammation) by high-energy compounds (ATP, ADP) and disrupt the energy exchange in the venous wall.

Primary importance in the development of the inflammatory-reparative process is given to the endotheliocytes of postcapillary venules, and it is important to note that the main source of energy in them are the processes of aerobic glycolysis, and not oxidative phosphorylation. The content of ATP in these cells is several times higher than in cells of other types, and its value is extremely high, including because the ectonucleotidase system of the venous wall (ecto-ATP-ase, ecto-ADP-ase, ecto-AMP-ase) is an enzymatic cascade providing fast hydrolytic cleavage of extracellular adenine nucleotides (ATP, ADP, AMP) to adenosine. The same three enzymes regulate vascular tone (through the formation of adenosine - the

most active natural vasodilator), vascular platelet hemostasis (through changes in the concentration of ADP), purinergic neural effects on smooth myocytes.

In smooth myocytes, which constitute the main population of cells and provide the majority of venous wall functions, bioenergetic processes also play a significant role, since there are several mechanisms of conjugation of excitation with the activity of myocytes. One such mechanism is associated with the development of the action potential and is characteristic of venous vessels that perform spontaneous contractile activity. The second mechanism is a prolonged depolarization of the membrane without development of the action potential which is typical for veins, which are not characterized by spontaneous electrical or contractile activity. Another "bioenergetic mechanism" that affects the functioning of the venous wall is to ensure its contraction without changing the membrane potential of smooth myocytes.

Central to these energy disturbances is ATP since not only a number of such important processes as mechanical work biosynthesis and active transport of substances activation of substrates phosphorylation of enzymes and non-enzyme proteins are carried out due to accumulated energy in the wall of venous vessels but also - formation of cAMP. Violations of the processes of bioenergetic metabolism also concern the mechanisms of fine regulation of autonomic nervous centers, and this primarily concerns such processes as: a) regulation of glycolysis and tissue respiration (via ADP); b) regulation of glycogenolysis (via AMP, Ca^{++} ions and activation of adenylate cyclase); c) regulation through inhibition of phosphodiesterase (an enzyme catalyzing the conversion of cAMP to 5'-AMP).

Conclusions. The decrease in the level of cAMP in psoriasis patients the increase in cGMP may indicate not only the disturbances in the system

of secondary intracellular intermediaries (cyclic nucleotides) but also the presence of bioenergetic (purinergic) imbalance which plays an important role in the development of clinical signs of this disease.

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