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ИММУНОГИСТОХИМИЧЕСКАЯ ОЦЕНКА ЭКСПРЕССИИ БЕЛКА S-100 И МОРФОЛОГИЧЕСКИХ ИЗМЕНЕНИЙ КОЖИ ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ГИПЕРТИРЕОЗЕ.

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РЕЗЮМЕ: *В статье представлены результаты морфологического и иммуногистохимического исследования кожи белых крыс при экспериментально индуцированном гипертиреозе. Установлены структурные изменения эпидермиса, дермы и её придатков, а также усиление экспрессии белка S-100 в клетках базального слоя, нервных волокнах и элементах дермальных структур. Повышение экспрессии S-100 рассматривается как проявление активации нейрогенных и метаболических механизмов адаптации тканей к тиреоидной гиперфункции. Результаты исследования подчёркивают значение тиреоидных гормонов в регуляции морфофункционального состояния кожи и позволяют рассматривать белок S-100 как перспективный морфологический маркер гипертиреоидных изменений.*

КЛЮЧЕВЫЕ СЛОВА: *гипертиреоз, кожа, морфология, белок S-100, иммуногистохимия, адаптация, крысы.*

IMMUNOHISTOCHEMICAL EVALUATION OF S-100 PROTEIN EXPRESSION AND MORPHOLOGICAL CHANGES OF THE SKIN IN EXPERIMENTAL HYPERTHYROIDISM

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RESUME. *The article presents the results of morphological and immunohistochemical studies of the skin in white rats under experimentally induced hyperthyroidism. Structural changes of the epidermis, dermis, and skin appendages were identified, along with increased expression of S-100 protein in basal layer cells, nerve fibers, and dermal components. The enhanced S-100 expression reflects the activation of neurogenic and*

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metabolic mechanisms of tissue adaptation to thyroid hyperfunction. These findings emphasize the regulatory role of thyroid hormones in maintaining the morphofunctional state of the skin and suggest S-100 protein as a potential morphological marker of hyperthyroid-induced changes.

KEYWORDS:*hyperthyroidism, skin, morphology, S-100 protein, immunohistochemistry, adaptation, rats.*

EKSPERIMENTAL GIPERTIREOZ SHAROITIDA S-100 OQSILINING IFODALANISHINI VA TERINING MORFOLOGIK O‘ZGARISHLARINI IMMUNOGISTOKIMYOVIY BAHOLASH.

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RESUME. *Maqolada eksperimental gipertireoz sharoitida oq kalamushlar terisining morfologik va immunogistokimyoviy o‘zgarishlari tahlil qilindi. Epidermis, dermis va ularning qo‘shimcha tuzilmalari darajasida sezilarli morfologik o‘zgarishlar, shuningdek, S-100 oqsilining bazal qatlam hujayralari, nerv tolalari va dermal tuzilmalar elementlarida ifodalanishining kuchayishi aniqlangan. Ushbu o‘zgarishlar to‘qimalarning tireoid giperfunksiyasiga moslashish jarayonlaridagi neyrogen va metabolik mexanizmlar faollashuvi bilan bog‘liq. Tadqiqot natijalari tireoid gormonlarining teri morfologik holatini boshqarishdagi ahamiyatini ko‘rsatadi hamda S-100 oqsilini gipertireozda yuz beruvchi o‘zgarishlarning muhim morfologik belgisi sifatida tavsiflaydi.*

KALIT SO‘ZLAR: *gipertireoz, teri, morfologiya, S-100 oqsili, immunogistokimyo, moslashuv, kalamushlar.*

INTRODUCTION

The functional activity of the thyroid gland exerts a significant influence on metabolism, growth, and tissue differentiation throughout the body. One of the most sensitive target organs for thyroid hormones is the skin, which responds to endocrine fluctuations through alterations in metabolic activity, vascular permeability, and structural organisation. In hyperthyroidism, characterised by excessive secretion of thyroxine, both intensified metabolic processes and dystrophic changes are observed in the skin structures, reflecting the exhaustion of adaptive and compensatory mechanisms.

Of particular importance in studying the morphofunctional rearrangements of the skin under thyroid hyperfunction is the analysis of S-100 protein expression

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— a calcium-binding protein involved in the regulation of cellular metabolism, proliferation, differentiation, and stress response. Variations in the expression level of this protein may serve as an indicator of neurogenic, metabolic, and trophic processes occurring in the skin under hormonal imbalance.

The use of experimental models of hyperthyroidism in laboratory animals, particularly in white rats, allows for an objective assessment of the structural and functional responses of the skin and a more precise determination of the role of the S-100 protein in the formation of compensatory reactions. Morphological and immunohistochemical analyses of such models contribute to a broader understanding of the pathogenesis of skin alterations associated with thyroid dysfunction and help define the diagnostic significance of the S-100 protein as a marker of cellular adaptation under conditions of endocrine imbalance.

Aim

To investigate the morphological changes of the skin and the pattern of S-100 protein expression in outbred white rats with experimentally induced hyperthyroidism caused by the administration of L-thyroxine, in order to identify the regularities of adaptive and compensatory reactions of skin structures under conditions of thyroid hyperfunction.

Materials and Methods

A total of 18 outbred white rats of both sexes were used in this study. The experimental model of hyperthyroidism was created by administering L-thyroxine at doses that induced a persistent increase in thyroid hormone levels and the development of characteristic signs of thyroid hyperfunction.

Upon completion of the experimental period, skin tissue samples were collected for morphological and immunohistochemical analysis. In total, 18 histological micropreparations were obtained. The sections underwent standard processing procedures, including deparaffinisation, dehydration, and antigen retrieval.

Immunohistochemical examination was performed using an automated Ventana Benchmark XT system (Roche, Switzerland). To visualise protein expression, antibodies specific to the S-100 antigen were employed. This calcium-binding protein participates in the regulation of cellular metabolism and stress response.

The obtained images were analysed, and the quantitative assessment of S-100 expression was carried out using the computer software QuPath 4.4.0, which enables the calculation of the proportion of immunopositive cells in various regions of skin structures. The results were expressed as a percentage of the total number of examined cells, providing an objective basis for data comparison between experimental samples.

Results and Discussion

Immunohistochemical examination of skin micropreparations from outbred white rats with experimentally induced hyperthyroidism revealed significant

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morphological and functional alterations involving the epidermis, dermis, and hypodermis, as well as variability in S-100 protein expression, reflecting the degree of adaptive and compensatory tissue activity.

Morphological changes in the skin under experimental hyperthyroidism, when compared with control samples, were characterised by a number of typical features of thyroid hyperfunction. In the epidermis, areas of thickened stratum corneum and foci of hyperkeratosis were identified, along with irregular stratification of the cellular layers, indicating enhanced keratinisation processes and disturbed keratinocyte proliferation. In the basal layer, occasional cells exhibited signs of dystrophy and cytoplasmic vacuolisation.

In the papillary and reticular layers of the dermis, oedema, vascular dilation, and marked perivascular lymphocytic infiltration were observed, indicating microcirculatory disturbances and activation of inflammatory–dystrophic processes (Fig. 1). The subcutaneous adipose tissue demonstrated signs of fatty degeneration and focal haemorrhages, reflecting metabolic overload of the cellular structures.

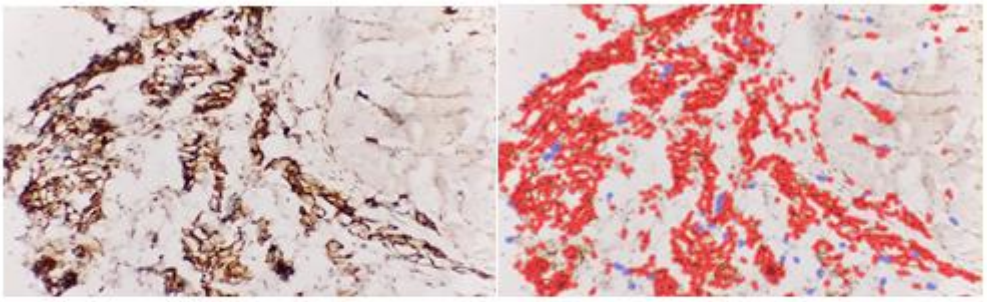

Figure 1. Expression of the immunohistochemical marker S-100 in the skin under experimentally induced hyperthyroidism.

Immunohistochemical Characteristics of S-100 Protein Expression

Immunohistochemical staining demonstrated positive expression of the S-100 protein in all examined samples; however, the intensity of the reaction varied widely, ranging from 47.6% to 94.8%.

High staining intensity (90–95%) was predominantly observed in the cells of the dermis and hypodermis, including fibroblasts and Schwann cells (Fig. 2). In these regions, a uniform distribution of immunopositive structures was noted, reflecting the activation of neurotrophic and calcium-binding mechanisms.

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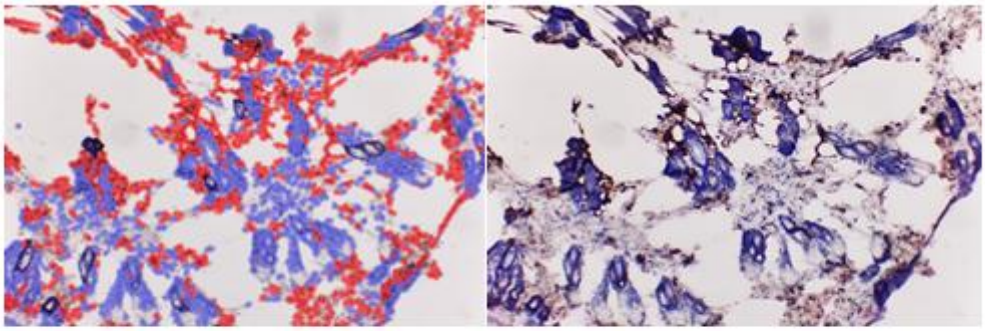

Figure 2. Expression of the immunohistochemical marker S-100 in the skin under experimentally induced hyperkeratosis.

Moderate expression (70–80%) was detected in certain areas of the epidermis and within hair follicles (Fig. 3). In these regions, the staining exhibited a focal pattern, being predominantly localised in the basal and spinous cells, which may be associated with the activation of regenerative processes and the maintenance of cellular metabolism.

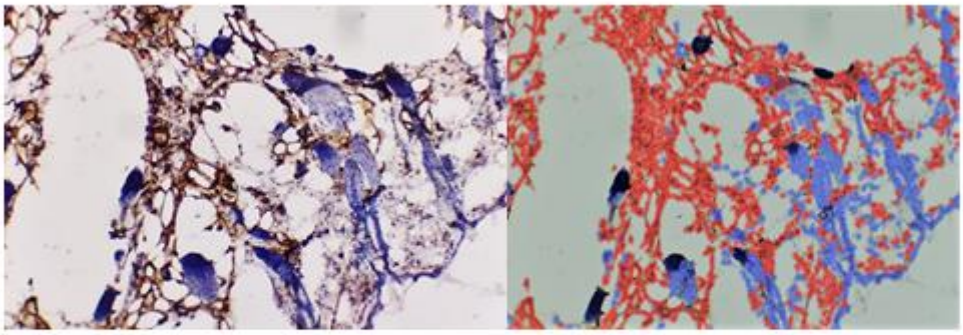

Figure 3. Expression of the immunohistochemical marker S-100 in the skin under experimentally induced hyperkeratosis.

In several micropreparations, the level of expression reached 50–60% (Fig. 4). Staining was observed in the epidermal cells and connective tissue elements of the dermis. These findings indicate a partial decrease in metabolic activity associated with the depletion of energy resources under prolonged hormonal hyperstimulation.

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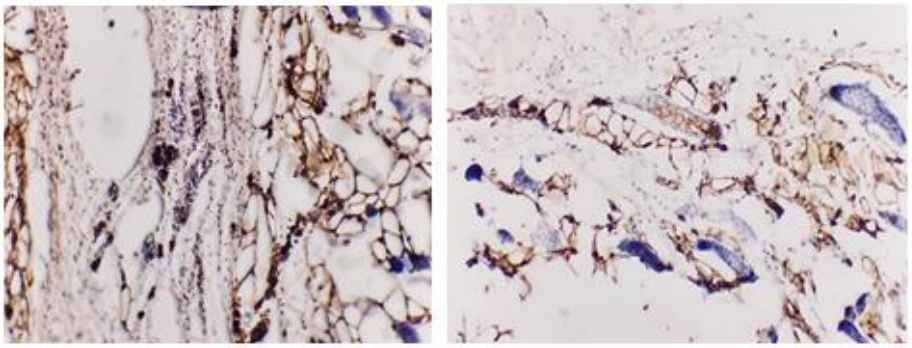
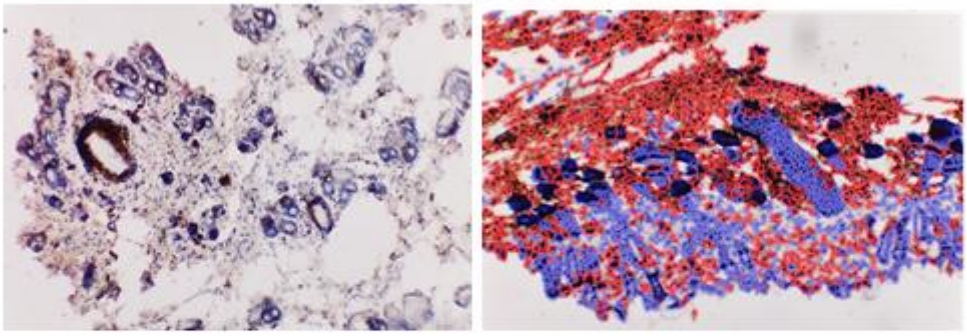


A B.

Figure 4. Expression of the immunohistochemical marker S-100 in the skin under experimentally induced hyperthyroidism:(A) Positive expression — 89.5%. (B) Positive expression — 62.5%.

Minimal expression (47.6%) was observed in samples exhibiting pronounced hyperkeratosis and epithelial cell dystrophy (Fig. 5). In these areas, a weakly positive reaction was detected in the epidermis, with no staining in the deeper layers of the dermis, indicating suppression of protein synthesis and disruption of calcium metabolism.

In some cases, moderate (55–60%) S-100 expression was predominantly observed in the cells of hair follicles (Fig. 5). This localisation likely reflects higher metabolic activity of the follicular structures compared with the surrounding epidermis.



А) Б)

Figure 5. Expression of the immunohistochemical marker S-100 in the skin under experimentally induced hyperkeratosis:
(A) Positive expression — 47.6%. (B) Positive expression — 55%.

The maximum intensity of expression — 94.8% — was recorded in samples with pronounced vascularisation and active cellular response within the dermis (Fig. 6). The diffuse distribution of stained elements indicates an

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enhancement of adaptive and compensatory mechanisms aimed at stabilising intracellular homeostasis under thyroid hyperfunction.

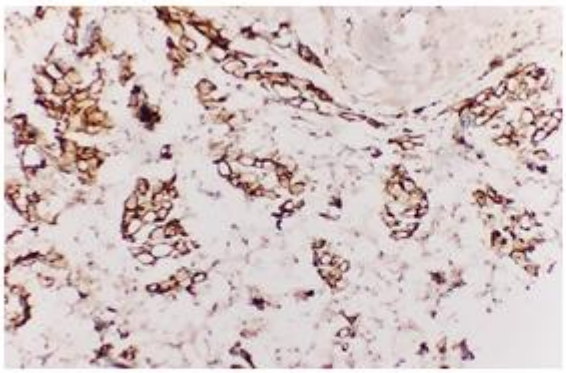

Figure 6. Expression of the immunohistochemical marker S-100 in the skin under experimentally induced hyperthyroidism. Positive expression — 94.8%.

Quantitative Characteristics

A comprehensive assessment of the intensity of the immunopositive reaction showed that:

in 10 animals (56%), S-100 expression ranged between 50–60%;

in 4 animals (22%), it was 70–80%;

and in 4 animals (22%), it reached 90–95%.

Thus, the variation in staining intensity reflects the heterogeneity of the skin's adaptive responses under hyperthyroidism, which is determined by the differing sensitivity of cellular populations to elevated levels of thyroxine.

Discussion

Analysis of the overall data demonstrated that hyperthyroidism induces a complex of morphofunctional changes within the skin structures, affecting the epidermis, vascular–connective components of the dermis, and the hypodermis. The S-100 protein, acting as a calcium-binding regulatory factor, exhibits a sensitive response to endocrine stimulation, serving as an indicator of metabolic activity and cellular adaptation.

Increased S-100 expression (up to 90–95%) may be regarded as a manifestation of compensatory activation of regenerative processes aimed at maintaining ionic homeostasis and preserving the structural integrity of tissues. Conversely, reduced staining intensity (down to 47.6%) indicates dystrophic and degenerative processes arising from the depletion of adaptive mechanisms.

The identified patterns are consistent with literature data showing that the S-100 protein participates in the regulation of the cell cycle, apoptosis, and stress response. Under thyroid hyperfunction, changes in its expression level can serve as a sensitive morphofunctional indicator reflecting the

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stages of skin adaptation — from activation to destabilisation of cellular processes.

Thus, the findings of the present study confirm that the S-100 protein is an informative immunohistochemical marker of metabolic and neurogenic alterations in the skin under hyperthyroidism. The variability in its expression level reflects the balance between compensatory and dystrophic tissue responses, defining the functional state of the skin under endocrine dysregulation.

Conclusion

The morphological and immunohistochemical examination of the skin of outbred white rats with experimentally induced hyperthyroidism revealed pronounced structural and functional alterations reflecting the response of skin tissues to thyroid hyperstimulation.

Morphological changes were characterised by thickening of the stratum corneum, the development of focal hyperkeratosis, dystrophic alterations in basal layer cells, dermal oedema, vascular dilation, and perivascular lymphocytic infiltration. These features indicate impaired microcirculation and the activation of inflammatory–dystrophic processes.

Immunohistochemical analysis demonstrated that S-100 protein expression was preserved in all examined samples; however, its intensity varied from 47.6% to 94.8%, reflecting different degrees of adaptive and compensatory tissue responses.

Maximum expression (90–95%) was observed in areas of active regeneration, predominantly in dermal and follicular cells, indicating compensatory enhancement of metabolic processes. Minimal expression (down to 47.6%) was detected in regions with marked hyperkeratosis and epithelial cell dystrophy, interpreted as a sign of energy depletion and disruption of calcium homeostasis.

The S-100 protein proved to be a sensitive morphofunctional marker reflecting metabolic activity, neurogenic regulation, and tissue stress response under endocrine disturbances.

The obtained results broaden the understanding of the pathogenesis of skin alterations in hyperthyroidism and may serve as a basis for developing morphological diagnostic criteria and assessing the effectiveness of therapeutic interventions in thyroid dysfunctions.

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