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The influence of Matrix Metalloproteinase-9 upon the course of psoriasis in patients suffering from liver affections

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The aim of our research has been the study of changes in the MMP-9 content in the blood of the patients suffering from psoriasis taking into account liver affection.

Materials and Methods: It has been examined 128 patients suffering from uncomplicated plaque-like psoriasis of moderate degree of severity. Liver functional state has been evaluated according to the results of ultrasound and biochemical investigations. MMP-9 content in blood serum of the patients has been assessed by means of immunofluorescence analysis.

Results: The increase of MMP-9 in the blood of patients was detected. The effect of MMP-9 for psoriasis in the direct correlation between these indices and index PASI was showed. ($r = +0.43$; $p < 0.05$)

Conclusion: The relation between MMP-9 in the blood of patients with psoriasis of moderate severity with disorder of the functional liver state was ascertained, that indicating for their combined participation in the immunopathogenesis of comorbid disorders.

Keyword: Psoriasis, Matrix Metalloproteinase-9, Liver, PASI index.

1. Introduction

Psoriasis (psora, alphas) is a chronic, inflammatory, immune-mediated genodermatosis of polyetiological origin in which the activity of keratinocytes is intensified, the process of cornification is violated and the pathologic changes in a number of organs and systems are observed [1].

Nevertheless, the molecular mechanisms of the development of skin immunoinflammatory process in patients suffering from psoriasis are studied insufficiently. Especially discussable is the question of the place of matrix metalloproteinases (MMP) in the pathogenesis of comorbid pathology that is psoriasis and liver affections of non-viral etiology.

It is known that MMP system includes a set of zinc-dependent endopeptidases with proteolytic properties – collagenases, gelatinases, stromelysins, matrilysins taking part in the processes of extracellular matrix decomposition [2]. Proteolytic activity of MMP depends on the interaction of both the factors contributing to the activation of their latent forms, namely anti-inflammatory cytokines, and the factors inhibiting these processes such as tissue inhibitors of matrix metalloproteinases (TIMP) [3, 4]. It has been proved the MMP's playing role in the development of a number of diseases – atherosclerosis, rheumatoid arthritis, psoriatic arthritis, osteoarthritis, pancreatitis, hepatitis, etc [2, 5, 6, 7, 8].

The results of immunohistochemical investigations have led to the discovery of the increase of MMP-9 expression in the skin of the patients suffering from psoriasis. It is assumed that the immunogenic fragments of normal proteins formed as a result of MMP-9 proteolytic activity initiate local autoimmune cellular reactions [9, 10]. It has experimentally been discovered the increase of TNF-alpha-induced MMP-9 expression upon keratinocytes in case of skin inflammatory processes accompanied by oxidative stress [11].

The aim of our research has been the study of changes in the MMP-9 content in the blood of the patients suffering from psoriasis taking into account liver affection.

2. Materials and Methods of Investigation

It has been examined 128 patients suffering from uncomplicated plaque-like psoriasis of moderate degree of severity (PASI > 12), 83 (64.8%) of them being men and 45 (35.2%) women aged (44.2±6.4). The continuance of the disease has made (8.54±6.55) years. Psoriatic affection was of widespread character in all of the patients. Progressive stage has been diagnosed in 72 of the patients, stationary stage – in 56. Depending on the presence of functional changes in the liver, the patients suffering from psoriasis were divided into two groups: Group 1 included 33 patients without any changes in the functional state of the liver, and Group 2 included 95 patients with the revealed changes in the functional state of the liver. Control group comprised 20 apparently healthy persons.

The severity of the disease has been assessed using PASI index (Psoriatic Area and Severity Index). Liver functional state has been evaluated according to the results of ultrasound and biochemical investigations. It has been measured blood enzyme activity: alkaline phosphatase (ALP) with the use of a set of reagents of LLC research-and-production enterprise “Filicit-Diagnostica”, aspartate aminotransferase (AST), alanine aminotransferase (ALT), cholinesterase, gamma-glutamyl transpeptidase (GGTP) with the use of a set of reagents of “PRIVA-Lachema” company (Czech Republic), arginase according to

Snipacho method modified by V. A. Khramov and H. H. Lystopad.

MMP-9 content in blood serum of the patients has been assessed by means of immunofluorescent analysis with the use of a set of reagents Human MMP-9 Platinum ELISA E-Bioscience Company.

Statistical processing of the received investigation results has been performed with the help of a personal computer using the programme “Statistica 10 Enterprise x 64”. The difference has been considered credible at $p < 0.05$.

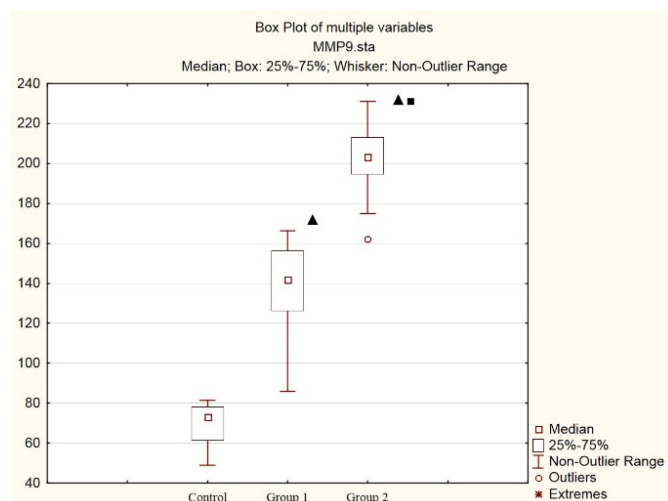
3. The Received Results and their Discussion

Clinical examination of the patients revealed symmetric location of the pathologic nidi represented by papule-plaquelike rash usually on the bending surfaces of the lower and upper extremities, lateral surfaces of the trunk and upon the lumbodorsal area; hairy part of the head was affected in 94 (73.44%) of the patients. PASI index taking into consideration the stage of hyperemia, infiltration, peeling and the area of affection made up 19.31±1.84. Comparing with the patients of Group 1 PASI index was higher by 41.15% in the patients of Group 2 and constituted 24.76±2.90 ($p < 0.05$).

The results of the investigation have led us to the discovery of the increased blood MMP-9 content in 95.31% of the patients suffering from psoriasis of moderate degree of severity, its average index was 186.16±3.05 ng/ml and it was 2.68 times as high ($p < 0.05$) as in healthy people (69.58±2.23 ng/ml). Analyzing blood MMP-9 level in the patients of both Group 1 and Group 2, it was revealed its higher content in the patients of Group 2 – (135.59±4.41 ng/ml) and (203.74±1.39 ng/ml) correspondingly ($p < 0.05$), that shows the role of MMP-9 in the pathogenesis of the combined pathology: psoriasis and liver affection (scheme 1).

The correlative relation has been noticed between the index of blood MMP-9 level and PASI index ($r = +0.43$; $p < 0.05$) that points out the influence of MMP-9 upon the severity of psoriasis course. Likewise, direct correlations have been seen between blood MMP-9 content index and the

indices of changes in the functional state of the liver – GGTP, ALT, AST activity ($r = +0.43$; $r = +0.36$; $r = +0.33$; correspondingly $p < 0.05$), that indicate MMP-9 participation in liver affection. Thus, we suppose that the received results evidence that the presence of comorbid pathology – psoriasis and liver affection – aggravates the course of psoriasis because of the inclusion of complex immune interactions and MMP-9 involvement in the pathogenesis.



Scheme 1: Blood MMP-9 level in patients suffering from psoriasis depending on liver affection, ng/ml

Note: Group 1 – patients with psoriasis having no liver affection; Group 2 – patients with psoriasis suffering from liver affection; ▲ – reliability of difference from the healthy, $p < 0.05$; ■ – reliability of difference in the indices of the patients of Group 1 and Group 2, $p < 0.05$.

4. Conclusion

There has been revealed the increase of blood MMP-9 level in patients suffering from psoriasis of moderate degree of severity particularly in the presence of liver affection; it points out MMP-9 participation in immune pathogenesis of comorbid pathology. 2. It has been shown the influence of MMP-9 upon the severity of the course of psoriasis at direct correlation between these indices and PASI index.

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