Mini Review

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Innate Immune System in Chronic Endometritis

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Background

The innate immune system is one of the two main immunity strategies found in human [1,2]. Unlike adaptive immunity, the innate immune responses are not specific to a particular pathogen and recognize some general groups of proteins and phagocytic cells. The major function of the innate immune system is to maintain the human body homeostasis and genetic identity by protecting the host from the toxins, infectious agents and endogenous cell waste products [3-5]. The critical role in the regulation of the innate immunity belongs to proteins of the Toll-like superfamily that express both intra- and extracellular and induce cytokines and interferons productions [6-8]. This study set out to investigate the innate immunity factors expression in the endometrium of women diagnosed with chronic endometritis.

Materials and Methods

This investigation takes the form of a prospective case-study of 43 patients aged 34,4 ± 2,7 years old. Criteria for selecting the subjects were as follows: chronic endometritis approved by histology and immunohistochemistry; absence of sexually transmitted infections; absence of severe somatic diseases; received informed consent to participate in the study. A comparison group includes 15 healthy women with BMI from 19 to 24 kg/m2 without any history of pregnancies, sexually transmitted infections, uterine interventions, and severe gynecological or other somatic diseases. The first step in the study was to conduct the endometrial aspirational pipelle biopsy (on 20-24 days of the menstrual cycle) and the morphological and immunohistochemical examination of samples with an assessment of CD138 (B-A138, syndecan-1 Roche-Ventana), CD20, CD8, CD4, CD56 (123C3 Roche-Ventana), and HLA-DRII. After that, in order to analyze the expression TLR-4, TLR-2, HBD1-defensin и TNFa genes, the Real Time-PCR and the

reverse transcription reaction were run. To measure the HNP1-3 antimicrobial peptide levels, the enzyme-linked immunosorbent assay (ELISA) was used (Human HNP1-3, HycultBiotech).

Statistical Analysis

Data management and analysis were performed using Microsoft Excel 2016 and Statistica 6.1. Means reflecting conditions before and after the treatment were compared using the Wilcoxon signed-rank test. Results were considered to be significant when p<0,01.

Results

Compared to the healthy women group, rates of Epstein - Barr virus identification in endometrium were significantly higher in the group of women diagnosed with chronic endometritis (in 55,8%). Besides from the Epstein - Barr virus, a significant increase in activity of CD138 (detected in 82,8% in study group comparing to 5,2% in the group of the healthy women), CD20 (in 53,5% comparing to 6,9%), CD8 (in 58,8% comparing to 4,7%), CD4 (in 59,2% comparing to 9,3%), CD56 (in 51,2% comparing to 9,3%), and HLA-DRII (in 55,8% comparing to 6,9%) was found in endometrial samples with chronic endometritis. Regarding the innate immune system proteins genes, their activity was variable in the endometrium of healthy women and women with chronic endometritis. Analyzing the two groups, a significant up-regulation of TNF α and TLR-2 genes expression (2517,9±413,1 x10³ copies/ ml and 1481,5±216,2 x103 copies/ml respectively comparing to 2218,7±305,2 x103 copies/ml and 1225,6±109,2 x103 copies/ml respectively in healthy women group) and a down-regulation in TLR-4 and HBD-1 genes expression (376,5 ±103,2 x103 copies/ml and 1013,7±211x103 copies/ml respectively comparing to 610,7±94,2 x103 copies/ml and 1354,7±199,2 x103 copies/ml respectively in healthy women group) was found in the endometrium of women



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diagnosed with chronic endometritis. The HNP1-3 gene activity was absent in healthy endometrium, while its activity in tissue with chronic endometritis was up-regulated, resulting in the production of significant amounts of protein (7,3±1,1 ng/ml).

Conclusion

One of the more significant findings to emerge from this study is that the cell types prevail in the endometrium with chronic endometritis are plasmatic cells (CD138), B-lymphocytes, large granular lymphocytes (CD56) and T-helpers (CD4). Also, analysis of such samples revealed a presence of chronic viral infections, whereas the Epstein – Barr virus was the most common one (identified in 55,8%). Chronic endometritis is a pathological condition involving the breakdown of balance between immunocompetent cells and cytokines, leading to disrupt in receptiveness and proliferative activity of cells. This study has approved the immunological disbalance occurring in the endometrial tissue in the state of chronic inflammation.

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