RESEARCH PROGRESS IN THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

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ABSTRACT

Objective*: To study the pathogenesis and pathological mechanism of rheumatoid arthritis.*

Methods: *One or more common causes constituted the initial factors of RA, which caused the change of synovial tissue structure of RA joint and made it antigenic. The immune system responds to these autoantigens, leading to an abnormal immune response.*

Results: *Rheumatoid arthritis is a heterogeneous, systemic, chronic autoimmune disease characterized by synovitis and symmetric polyarthritis. The global prevalence rate is about 1%, and the disability rate is as high as 20% within one year of onset, which seriously affects human health and quality of life.*

Conclusion: *Heterogeneity means that patients have different genetic backgrounds, whose etiology is unknown and may not be single, so the pathogenesis may be different. At present, it is thought that the occurrence of the disease may be related to genetic variation, infection and sex hormones.*

Keywords: *Rheumatoid arthritis, autoimmunity, pathogenesis, immune system.*

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Introduction

Rheumatoid arthritis may occur after the stimulation of an immune response by some antigens or microbes in the unknown environment to people with sensitive genetic backgrounds.

The results were as follows:

• Rhematoid factor (RF), $CD4^+$(Th) and $CD8^+$(Ts) subpopulation ratio changes were detected in the peripheral blood of RA patients[1-3].

• The synovial tissue was thickened with a large number of lymphocytes and monocytes/macrophages[4-5].

• RF and various cytokines can be detected in synovial fluid, such as interleukin 1 (IL-1), IL-6, IL-8, and tumor necrosis factor (TNF)[6].

These changes are the result of the change of synovial cell function. For autoimmune diseases, it is generally believed that environmental stimulus antigens play a role at the onset of the disease and may not persist, while the subsequent sustainable development is the function of molecular simulation. Molecular simulation can be understood as the cross-reaction between antigens and autoantigens in the environment[7]. After the disappearance of antigens in the environment, autoantigens make the immune response continue. In rheumatoid arthritis, a large number of macrophages, branch cells, B cells, endothelial cells and possibly activated T cells can perform antigen presentation functions.

There are two hypotheses for the possible immune process after the entry of environmental antigens into the articular cavity. Some scholars emphasize the dominant role of T cells, while others emphasize the more important role of synovial cells. In fact, the two hypotheses are mutually exclusive and interact, hence the so-called T-cell/macrophage/fibroblast axis unification hypothesis[8].

Materials and methods

Basic information

Genetic factors are considered to be one of the main factors in the pathogenesis of RA. Domestic and foreign studies have found that among many alleles of DRBl, DR4 and DR I and DR10 in some RACES are related to the incidence of RA. Not only is it related to the onset of RA, but also dr4-positive patients have severe joint lesions, early joint destruction, multiple extra-joint manifestations, and poor prognosis [9]. Therefore, DR4 can be used as one of the clinical indicators to measure RA lesions.

Methods and observation indicators

In recent years, it has been found that in addition to RF, there are many autoantibodies in the serum of RA patients, such as anti-RA33/36 antibody, anti-SA antibody related to the early lesions of RA, AKA and APF, etc., forming the autoantibody spectrum of RA patients. These autoantibodies are a symptom of immune dysfunction in RA patients. The RF positive rate of DR4-positive patients was higher than that of DR4-negative patients, while there was no significant difference between AKA, AFF, anti-RA33 and 36 antibodies in DR4(+) and DR4(-) patients, indicating that DR4 gene is only related to RF and has nothing to do with other body antibodies[7]. The pathogenesis of RA is complex, and other factors besides DR4 are involved in the formation of autoantibodies. Recent studies have also found that the role of HLA-DR in the pathogenesis of RA is no more than 37%. In addition to DRBl, DP, DQ and HLA-i antigens also participate in the pathogenesis of RA[10].

Results

Cellular immune response

Synovium tissue in rheumatoid arthritis was digested by enzymes and dispersed into single cells, in which T cells accounted for 30-50% and most of them were CD4 cells, which was 4-14 times higher than CD8 cells (higher than the proportion in surrounding blood). Most T cells have markers of mature memory cells such as CD45RO on their surfaces, indicating past contact with the antigen.

The infiltration of T cells into the synovial tissue can be diffuse, but in some patients as many as hundreds of them cluster together (especially around blood vessels). T cell surface expression II hang the original host such as DR, has been activated. Upon activation, T cells spontaneously produce γ-interferon and interleukin-2, 3, and 4, which further stimulate macrophages (paracrine) and T cells (autocrine). T cells also produce interleukin-6 to stimulate B cells to produce antibodies. Macrophage are stimulated and activated to produce interleukin-1 and tumor necrosis factor (TNF), and then stimulate synovium fibroblasts and chondrocytes to cause cartilage necrosis and pannus formation (both fibroblasts and chondrocytes can produce collagenase, neutral egg autolase, prostaglandin and other inflammatory transmitters). Cyclosporin A mainly ACTS on CD4 cells, and cytosolic drainage mainly removes T cells, all of which can achieve certain therapeutic effects, and all of which support the hypothesis that T cell immune response is mainly used. The antigens that initially cause rheumatoid arthritis (non-environmental factors) may be present throughout the course of the disease, but are likely to be present only at the beginning, with different antigens or primary antigens targeted in the course of the disease. In rheumatoid arthritis (AMLR), cytokines produced by T cells such as interleukin-2 and Y-interferon are usually present in small amounts. Both synovial a cells and branching cells in the articular cavity may be the stimulating cells in AMRL. Autoreactive T cells can also be stimulated by molecular simulation.

Synovial cells

The study of RA synovial fluid and synovial membrane is still one of the most common means of RA research. It is generally believed that after the innate cells of the synovial membrane are activated by non-specific antigens, the secreted cytokines, chemokines and expression of adhesion factors make the lymphocytes in the synovial membrane activated and immune response occurs. Activation of synovial innate cells is involved in tissue chronic processes and bone and cartilage destruction[7]. TNF is central in the inflammatory local cytokine interaction network of RA. Most B cells and monocytes expressed CD40L in synovial fluid, and T cells from synovial fluid also expressed CD40L, which was stronger and lasted longer than peripheral blood T and B cells. The interferon (IFN/IL-6 ratio was 5 in RA synovial fluid, suggesting Th1 cytokine dominated RA.

Discussion

Rheumatoid arthritis is a chronic inflammatory polyarthritis as the main performance of systemic disease, characterized by a large number of T lymphocytes infiltrating primarily the chronic

synovitis of T cells, especially helper T cells (Th 1/T h2) on the pathogenesis of RA, the role of more and more be taken seriously, inflammation, local Thl/ Th2 cytokines patterns can affect the progress of the disease[11-12]. In conclusion, it is confirmed that there is a Thl /Th2 imbalance in RA joints. Therefore, restoring the intra-articular Thl /Th2 balance is very important for controlling chronic inflammation of RA. Animal experiments have also shown that combined treatment with IL-4/ IL-10 (Th2 cytokines) can significantly improve the condition of collagen-induced arthritis, and treatment aimed at correcting the intra-articular Th1/Th2 imbalance will be of great significance for the condition improvement and prognosis of RA[13-14].

Rheumatoid arthritis is a disease closely related to environment, bacteria, virus, genetics, sex hormones and neuromental state. The pathogenesis of rheumatoid arthritis is not fully understood. Cold, dampness, fatigue, malnutrition, trauma, mental factors and other factors can also lead to the occurrence of rheumatoid arthritis symptoms to a certain extent. Immune disorders are the main pathogenesis[15].

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